

9. SPECIFICATION GUIDELINES FOR MICROBIAL PESTICIDES

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9.1. INTRODUCTION

9.1.1 *Background Note to New Section 9:*

This document is the draft for an entirely new Section in the FAO and WHO Manual on development and use of pesticide specifications. It is based on the discussions and conclusions of two *ad-hoc* meetings between JMPS and industry - the first held in January 2016 at CRA-W in Gembloux, Belgium and the second in October 2016 at WHO in Geneva.

Being designed as a trial edition and stand-alone document, the new Section 9 is self-contained and presents in subsections all procedural and normative documents (e.g. data requirements, specification templates etc) facilitating appropriate review and public consultation. At a later stage and in revised form the Section 9 may be incorporated into the main text body of the Manual.

The terms "MPCA" and "MPCP" stand for microbial pest control agents and - products and are used to differentiate these kind of pesticides from the synthetic chemical ones ("pesticides" in general), botanicals (plant extracts) and semiochemicals (pheromonones). These terms come directly from the OECD Guidance Document¹.

9.1.2 *Scope of specifications*

The term "microbial pesticide" is considered to embrace active ingredients in any form, irrespective of whether, or to what extent, they have been formulated for application. The term is usually associated with materials intended to kill or control pests (insecticides, fungicides, herbicides, etc.) but, for the present purposes, it may also embrace certain materials used to modify the behaviour or physiology of pests or of crops during production or storage.

FAO and WHO specifications for synthetic chemical pesticides apply only to the products of manufacturers whose technical materials have been evaluated as satisfactory by the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS). The corresponding products of other manufacturers must be assessed by the JMPS to ensure that existing FAO/WHO specifications are applicable to them (equivalence process). For microbial pesticides however, no such equivalence process is foreseeable for the moment being, as the identity of microbial pesticide control agents (MPCA) is defined in a different way (see subsection 9.3).

Specifications should encompass the physical appearance of the material, its content of active ingredient² and any relevant impurities, and its physical and chemical properties, and stability in storage.

¹accessible under

<http://www.oecd.org/chemicalsafety/pesticides-biocides/countrydatareviewreportsforbiologicalpesticidesregistration.htm> (December 2018)

² In the context of this Section 9 guideline, the term "active ingredient" refers to all kinds of microbial pest control agents (bacteria, viruses, etc). A definition for active ingredient in relation to microbial pesticides will be included in an updated glossary of terms.

The specifications do not encompass the chemical characteristics of the formulants, other than where they influence the physical characteristics (which are taken to include characteristics such as pH, acidity and alkalinity). The specifications do not include clauses which define the fundamental properties of the active ingredient and this includes the efficacy of the pesticide. Data on the efficacy of pesticides are not evaluated by the JMPS. FAO specifications for agricultural pesticides are developed only after registration by the manufacturer in one or more countries and the efficacy of these pesticides is usually inferred from this evidence. However, the efficacy of the active ingredient and formulations of public health pesticides will be evaluated in laboratory and field trials by formerly WHO Pesticide Evaluation Scheme (WHOPES) and since recently WHO Vector Control Prequalification Team (WHO PQT-VC), usually when the WHO/FAO specification for the technical material has been developed. WHO specifications for formulations are published, following satisfactory evaluation of safety and efficacy. In special cases, where specifications are required during evaluation of the efficacy of a novel product for public health for example, WHO may introduce an interim specification for a formulation and may also introduce an interim guideline specification for the same purpose.

FAO/WHO specifications are intended for quality assurance and risk management. The evaluation of the hazards and risks associated with pesticides for specifications purposes is based primarily on the assessment of the national registration authorities, and is carried out by a WHO designated unit or other international organization. In the absence of evaluation by bodies such as a national registration authority, JMPR/JECFA or WHO/PCS, WHO/FAO arranges a detailed assessment of original studies before the JMPS proceeds with the development of specifications. An important aspect of the assessment of hazards and risks is to determine the links between (i) the hazard and purity/impurity profile data submitted, and (ii) the purity/impurity profile data submitted and the limits for purity/impurities applied in normal manufacturing production. FAO and WHO recognise that generation of replicate data on all potential/actual hazards by each manufacturer of a pesticide may be unnecessary and ethically undesirable. The lack of direct links in (i), above, does not preclude development or extension of a specification but proposers are required to disclose the links, or lack of them, to ensure that JMPS recommendations are based upon a properly informed assessment of hazards and risks.

9.1.3 The JMPS

The JMPS is composed of scientists collectively possessing expert knowledge of the development of specifications. Their opinions and recommendations to FAO/WHO are provided in their individual expert capacities, not as representatives of their countries or organizations. FAO and WHO may also invite academic or government experts with special skills or knowledge to attend the JMPS as special advisors.

In addition, industry experts may be invited for either of two purposes. Firstly, they may be invited to provide explanations or additional information in support of specifications proposed by their own company (there is no access to other companies' information or proposals). Secondly, industry scientists with special skills or knowledge of technical issues (not related to a particular company's

proposals or specifications) may be invited. Industry experts do not, and the other additional experts may not, participate in drafting the recommendations of the JMPS (see also 9.2.3).

The primary function of the JMPS is to produce recommendations to FAO and/or WHO on the adoption, extension, modification or withdrawal of specifications.

9.1.4 Liaison with other international organizations, international conventions and national regulatory authorities

9.1.4.1 Collaborative International Pesticides Analytical Council (CIPAC) and AOAC International (AOAC)

Wherever practicable, the test methods cited in FAO/WHO specifications should have been evaluated by inter-laboratory trials. This holds for analytical methods for the determination of synthetic chemical pesticides, but not for MPCA. Methods to determine the strength or content of MPCA must be peer validated at a minimum (ILV).

CIPAC also validates and publishes methods for the determination of physical-chemical properties of pesticide formulations. Methods to be used in support of FAO and WHO specifications may be validated by other organizations but, with few exceptions, the methods currently in use have been produced by CIPAC and AOAC. Methods for determination of the active ingredient or of a physical property, other than those validated by CIPAC or AOAC, are accepted by the JMPS on a case-by-case basis. In cases of dispute, designated referee methods should be used. Where available, those produced by CIPAC and AOAC will normally be considered the referee methods (unless they have been proven inferior to another method).

9.1.4.2 FAO/WHO Joint Meeting on Pesticide Residues (JMPR)

The principal function of the JMPR is to make recommendations on the acceptable daily intake (ADI), acute reference dose (ARfD) and maximum residue limits (MRLs) for and botanical pesticides, to FAO, WHO and the Codex Committee on Pesticide Residues as a contribution to the WHO and FAO activities on food safety.

Whereas the objectives of JMPR do not formally include or exclude MPCA, it becomes obvious that the *modus operandi* and the published evaluations of pesticides are focused on synthetic chemical and botanical pesticides¹. It is therefore expected, that JMPR evaluations of pesticides do not play a major role for the evaluation of MPCA by JMPS.

9.1.4.3 Rotterdam Convention on Prior Informed Consent (PIC)

¹ Manual on the Submission and Evaluation of Pesticide Residues Data _ Third Edition (2016)

http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/JMPS_Manual_2016/3rd_Amendment_JMPS_Manual.pdf

The Rotterdam Convention focuses on hazardous chemicals and those MPCAs that are intended to be used in agriculture and public health are not expected to fall under Rotterdam Convention and Prior Informed Consent.

9.1.4.4 *Stockholm Convention on Persistent Organic Pollutants (POP)*

The Stockholm Convention focuses on persistent organic pollutants and MPCAs that are intended to be used in agriculture and public health are not expected to fall under the Stockholm Convention.

9.1.4.5 *International Organization for Standardization (ISO)*

English ISO¹ common names, accepted by ISO, are adopted wherever possible for synthetic chemical pesticides, however these are not used for MPCAs. Taxonomy names are used for microbial pesticides. See Section 9.3.1.3 (description of taxonomy)

9.1.4.6 *International Nomenclature for Cosmetic Ingredients (INCI)*

The standard names for insect repellents published by INCI are adopted where appropriate.

9.1.4.7 *Organisation for Economic Co-operation and Development (OECD)*

The OECD references FAO and WHO specifications for active ingredients and formulations in its harmonised recommendations for registration. The data requirements included in Section 9, are taken from the OECD Guidance for Country Data Review Reports on Microbial Pest Control Agents (Monograph Guidance for Microbials), Series on Pesticides No. 22, Health and Safety, Environment Directorate, Appendix 6 and from the FAO Guideline " Guidelines for the registration of microbial, botanical and semiochemical pest control agents for plant protection and public health uses" (FAO Rome, 2017).

9.1.4.8 *United Nations Industrial Development Organization (UNIDO)*

UNIDO co-operates with FAO and WHO in establishing technical specifications for active ingredients and formulations, and uses or recommends the use of such specifications in its technical assistance programmes.

9.1.4.9 *United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS)*

In the assessment of risks of chemicals to the human health and environment. JMPS applies the GHS classification².

9.1.4.10 *National and regional registration authorities*

As far as practicable and without prejudice to the progress of specifications development by any of the organizations, FAO, WHO and the JMPS seek harmonization of principles and specification requirements with registration

¹ International Standard ISO 1750 and amendments - Pesticides and other Agrochemicals - Common Names.

² GHS (Rev.6) (2015), UN New York and Geneva, https://www.unece.org/trans/danger/publi/ghs/ghs_rev07/07files_e.html - c61353 (December 2018)

authorities. Normally, JMPS bases its evaluation of risks and hazards to the health and environment on the detailed evaluations made by national registration authorities.

This cost- and time-efficient approach can be replaced by a full *de novo* evaluation of all data if an up-to-date national registration is not available or the JMPS, for other reasons, recommends this course of action.

The European Community (EC) has harmonized pesticide registration and control systems in member countries and FAO specifications are an important feature of the authorization Regulations. Specification requirements for agricultural pesticides in various developing countries are also being harmonized with those of FAO.

9.1.5 Participation by the pesticide industry

9.1.5.1 Development of specifications

The data on which FAO and WHO specifications are based are provided by the pesticide industry. Pesticide manufacturers are strongly encouraged to submit draft specifications and the supporting data to the JMPS for evaluation.

9.1.5.2 WHO PQT efficacy data requirements

Data on efficacy provided by industry are assessed by WHO PQT in deciding further laboratory and field testing requirements, prior to the development of formulation specifications by the JMPS. Efficacy data are not considered by the JMPS.

9.1.5.3 Changes affecting specifications after adoption by FAO and WHO

It is the responsibility of industry to inform FAO and/or WHO of any changes in manufacturing process which could affect the validity of specifications, and of any changes in manufacturer's name or contact address. Such changes in manufacturing process should be evaluated by the JMPS. Failure to provide this information may lead to withdrawal of the specification.

9.1.5.4 Development of specification guidelines and principles

Industry is strongly encouraged to prepare draft guideline specifications for new formulation types for consideration by the JMPS. Comments on, or suggested amendments to, proposed or existing guidelines may come from industry, experts participating in the JMPS or any other interested party. Guidelines are kept under review by the JMPS. Guidelines and related matters are normally considered at open meetings (see amended Glossary of terms, Appendix C) of the JMPS but are adopted by a closed meeting. As part of a continuing process by FAO and WHO to consider specification principles, representatives of all pesticide manufacturers are strongly encouraged to participate in open meetings of the JMPS. Industry groups (for example, CropLife International¹, AgroCare² and

¹ <https://croplife.org/>

² <http://www.agro-care.org/>

International Biocontrol Manufacturers Association (IBMA)¹) may be invited to provide technical experts as advisers to special consultation sessions of the JMPS, to facilitate a fully informed deliberation of issues. Industry experts are not involved in preparing JMPS recommendations to FAO and WHO.

9.1.6 Purpose and use of specifications

9.1.6.1 Purpose

In general, specifications may be used:

- (i) as part of a contract of sale, so that a buyer may purchase a pesticide with some guarantee of the quality expected; and
- (ii) by the competent authority to check that the quality of the formulation on the market is the same as that registered.

FAO/WHO specifications are intended to enhance confidence in the purchase and use of pesticides and thus to contribute to human and environmental safety, as well as to more sustainable agricultural production and improved public health. FAO/WHO specifications may be used by national authorities as an international point of reference but are not intended to replace national or international registration requirements.

9.1.6.2 Requirements

In order to characterize a pesticide, it is necessary to be able to determine its composition and chemical and physical properties.

It is clearly not practicable to test all possible chemical and physical properties. The parameters critically related to identity and quality are identified and limits for these parameters selected to form the basis of a specification. A specification should be brief but it must be unambiguous and supported by appropriate test methods to determine whether the material conforms with the limits established. The specification itself does not define biological efficacy.

9.1.6.3 Basis of contract

A specification may be used as part of a contract of sale, to ensure delivery of good quality pesticides.

Pesticides should continue to be fit for use after storage for at least 2 years in the unopened, original containers, provided that (i) they have not been unduly exposed to extremes of temperature, humidity and/or light; (ii) that labels (for example, prepared according to FAO labelling guidelines²) do not indicate a shorter shelf-life as e.g. for some biological products based on micro-organisms; and (iii) that any special instructions from the manufacturer have been followed.

9.1.6.4 Official control of pesticides

¹ <http://www.ibma-global.org/>

² Food and Agriculture Organization of the United Nations, Rome (2015). Guidelines on Good Labelling Practice., <http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/code/list-guide-new/en/> (March 2016)

Where appropriate, FAO and WHO specifications should be linked to registration requirements so that they can also be used in the official control of pesticides, to ensure as far as possible that the quality of the pesticide supplied is the same as that registered. The guidelines provided in this Manual may also be used as a framework of criteria and/or parameters for the assessment of technical or formulated pesticides for which FAO or WHO specifications either do not exist or have not yet been assessed by the JMPS as being applicable to the products of a particular manufacturer.

Ultimately the competent authorities decide whether or not a particular pesticide shall be used in their country.

Up to June 2018, WHOPES recommendations and subsequently WHO PQT recommendations on the use of public health pesticides, expedite the local registration of products to be used for the control of vectors and pest of public health importance and minimize requirements for local testing of products that have given satisfactory results in similar circumstances. Reports of WHOPES evaluations and/or WHO PQT for public health pesticides are available on request from the address given in section 9.1.7.

9.1.6.5 Role of specifications in the world market

Harmonization of relevant national and/or international standards through the use of FAO and WHO specifications should facilitate world trade in pesticides.

FAO and WHO specifications are designed to reflect generally acceptable product standards. The specifications provide an international point of reference against which products can be judged, either for regulatory purposes or in commercial dealings, and thus help to prevent the trading of inferior products. They define the essential chemical and physical properties that may be linked to the efficacy and safe use of a product.

9.1.7 Access to FAO and WHO specifications

Users of specifications are advised that these are subject to a continuing process of up-dating and that it is essential that only the most recent version is used. In case of doubt, confirmation of the most recent version may be obtained from FAO or WHO.

Copies of current FAO specifications may be obtained from the Sales & Marketing Group, FAO, Viale delle Terme di Caracalla, 00100 Rome, Italy.

e-mail: publications-sales@fao.org

web site: <http://www.fao.org/publications>

Or accessed at: <http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmps/en/> (all April 2018)

Copies of current WHO specifications may be obtained from WHO Prequalification Team Vector Control Group (PQT-VC), World Health Organization, 1211 Geneva 27, Switzerland.

e-mail: pqvectorcontrol@who.int

9.2 THE PROCESS OF DEVELOPING FAO/WHO SPECIFICATIONS

9.2.1 *Categories of specification and their status*

Prior to 1999, three categories of FAO specifications (tentative, provisional and full) were developed¹, differing in the CIPAC/AOAC status of the analytical methods for the active ingredient. Following a transition period, 1999–2000, only full specifications were adopted, using new procedures² similar to those presented in this Manual. From 2002, full specifications have been adopted according to the procedures given in this Manual.

Prior to the introduction of this Manual, two categories of WHO specifications (interim and full) were developed. The difference in status reflected the extent of peer review of the specifications and the extent of validation of the analytical and physical test methods required to support the specifications. From 2002, WHO has normally developed only full specifications under the new procedure. Exceptionally, where there is an urgent public health requirement and on a case-by-case basis, WHO may develop a time-limited interim specification, if the validation of the methods is in progress but incomplete.

Only manufacturers who have submitted a data package and specification (which have then been evaluated as acceptable) in accordance with current JMPS procedures, may claim that their material complies with the specification. Materials from other manufacturers may not comply, without a detailed evaluation of information provided by the other manufacturers, because FAO/WHO cannot know that the reference specification is appropriate to the material produced by other manufacturers. Under Article 6.2.4 of the FAO International Code of Conduct on the Distribution and Use of Pesticides (2002)³, the pesticide industry is expected to ensure that active ingredients and formulated products conform to the appropriate FAO and WHO specifications.

9.2.2 *Submission of proposals and data*

Proposals for inclusion of specifications for a MPCA and/or its formulations (MPCP) in the JMPS schedule must be sent to FAO or WHO, or both if appropriate⁴. Requests for inclusion in the JMPS future work program must include the list of studies supporting the proposed data submission.

¹ Manual on the Development and Use of FAO Specifications for Plant Protection Products, 4th Edition, FAO Plant Production and Protection Paper 128, FAO, Rome, 1995.

² Manual on the Development and Use of FAO Specifications for Plant Protection Products, 5th Edition, FAO Plant Production and Protection Paper 149, FAO, Rome, 1999.

³ International Code of Conduct on Pesticide Management, FAO, Rome, 2014 and WHO Geneva, 2014.

<http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/code/en/> (March 2016)

⁴ Correspondence, clearly marked “Confidential” if confidential information is included, should be addressed, as required, to:

The Senior Officer (Pesticide Management Group), Plant Production and Protection Division, FAO, Viale delle Terme di Caracalla, 00100 Rome, Italy.

WHO Prequalification Team Vector Control Group (PQT-VC), World Health Organization, 1211 Geneva 27, Switzerland. mail to: pqvectorcontrol@who.int.

Where two or more manufacturers seek specifications for the same active ingredient (same strain) in the same year, they are encouraged to form a task force. Such a task force may be able to harmonize the proposed specification limits, test methods requirements, etc., while preserving data confidentiality for all task force members, before making detailed submissions to the JMPS, thus simplifying and speeding up completion of the specifications. Formation of a task force is not mandatory. If manufacturers are unwilling or unable to work together, independent submissions may be made.

Detailed submissions of proposed specifications and supporting data should be submitted to FAO and/or WHO, as appropriate, according to the timetable outlined in Section 9.2.5.

To facilitate communication, subsequent dialogue and information exchange may occur between the proposer and the designated evaluator but all such communications must be copied, or recorded if verbal, to FAO and/or WHO.

9.2.3 Meetings and functions of the JMPS

FAO and WHO will organize, annually, open and closed meetings of the JMPS. Open meetings can be attended by anyone and are intended for discussion of specifications principles, new guidelines, amendments to the Manual, and so on. Closed meetings are restricted to JMPS members, and others invited by FAO/WHO, because they involve consideration of commercially confidential information. Details are given in the glossary. Prior to these meetings, draft or revised specifications, together with the supporting data, will be evaluated by experts participating in the JMPS, as designated by FAO and/or WHO.

The overall purposes of the annual meetings are:

- to evaluate and confirm (or reject) new and revised specifications and to resolve issues or evaluations in dispute;
- to update and prepare the agenda of the JMPS for the following years, taking into account any developments or emergent information which may necessitate changes in priority; and
- to advise FAO and WHO on specifications, relevant policy and procedures.

In open meetings (see glossary) the JMPS will consider issues of general importance to specifications and, in doing so, will seek the views of all interested parties.

In closed meetings, (see glossary) the JMPS will consider:

- (i) evaluations and proposed specifications, involving commercially confidential data;
- (ii) changes in technical requirements for, and policy on, specifications;
- (iii) priorities for review of specifications in the forthcoming years;

and make appropriate recommendations to FAO and/or WHO.

If required, additional experts from academia, government and/or industry may be invited by FAO/WHO to attend certain sessions of the closed meetings, to provide information or opinion on problematic or contentious issues. All additional experts will be required to respect the confidentiality of the information and discussions, and to sign a declaration of conflict of interest, but their periods of

attendance will be restricted to ensure that confidentiality of commercial information is strictly maintained. Industry experts will not, and the other additional experts may not, be permitted to participate in the development of final recommendations by the appointed experts.

9.2.4 Confidentiality of Information

FAO and WHO will maintain the confidentiality of all confidential information provided in support of proposed specifications¹. By means of a letter of access provided by the proposer, FAO and/or WHO will seek, as a minimum, to establish that the data provided on purity and impurities are similar to those provided to one or more registration authorities in countries in which the proposer indicates that the pesticide is registered. Additional facts about the active ingredient or formulation will be sought only from the proposer. A specification will not be published without agreement between the proposers, the JMPS and FAO/WHO on the content but, irrespective of agreement on the specification, the JMPS evaluation will be published on the internet by FAO, WHO or both.

The manufacturing process and analytical data on the impurity profile of the MPCA (excluding identity and analytical methods for relevant impurities) are always regarded as confidential. In the unusual cases where information on the ingredients and processes involved in preparing formulations is required, this information will also be regarded as confidential. Previously unpublished information which will appear in the published evaluation is regarded as confidential until the evaluation is published. Unpublished confidential reports or correspondence, containing information evaluated by the JMPS, will be treated as confidential but will normally be referenced in the evaluation, to provide an audit trail of decisions.

9.2.5 Timetable and principles for the development of specifications^{2,3}

The procedure and deadlines are scheduled with reference to the annual FAO/WHO JMPS.

- (i) After each JMPS meeting, FAO and WHO will publish a yearly programme for pesticides to be evaluated at the following JMPS meeting and announce the dates of the meeting. Intending proposers may request inclusion of new or revised specifications, by writing to FAO and/or WHO, at any time (See also 9.2.2). Prior to each meeting, FAO and WHO will provide the JMPS with a summary of the requests received. Submission of a request will

¹ A statement of the procedures for handling unpublished proprietary pesticide data and potential conflicts of interest in the development of pesticide specifications by the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS) is provided on page ii of the Manual, 2016 revision.

² Correspondence, clearly marked "Confidential" if confidential information is included, should be addressed, as required, to:
The Senior Officer (Pesticide Management Group), Plant Production and Protection Division, FAO, Viale delle Terme di Caracalla, 00100 Rome, Italy.
WHO Prequalification Team Vector Control Group (PQT-VC), World Health Organization, 1211 Geneva 27, Switzerland.

³ Attendance at closed meetings of the JMPS is at the express invitation of FAO or WHO, only. Attendance at the open meetings is open to all who wish to attend.

not guarantee its inclusion in the yearly programme but the JMPS will consider as many requests as practicable.

Actor	Task	Deadline
Proposers	Proposal	Any time
FAO/WHO	Publication of a yearly programme of work	after JMPS
FAO/WHO	Nomination of evaluator and peer reviewer	after JMPS
Proposer	Draft specification & supporting information	31 Oct
Evaluator	Evaluation and request for additional information if needed	31 Dec
Proposer	Provision of additional information requested	28 Feb
Evaluator, Proposer	Discussion on any open questions	30 April
Evaluator	Sending of draft specification, evaluation and appraisal to peer reviewer and , FAO/WHO	30 April
Peer reviewer	Comments and proposals to evaluator and FAO/WHO	15 May
Evaluator	Sending of draft specification, evaluation report and/or equivalence assessment report with comparison tables to FAO/WHO, JMPS chair and co-chair	20 May
FAO/WHO	Sending of draft specification, evaluation report and/or equivalence assessment report with comparison tables to JMPS panel members	20 May
JMPS	Discussion and decision of the proposal; eventual request of further information from the proposer	1 st week of June
Proposer	Provision of additional information	Agreed at JMPS
FAO/WHO	Publication of the specification	3 months after evaluation completed

- (ii) Following publication of the yearly programme, proposers will be required to provide draft specifications and the supporting data outlined in Sections 9.3.1 or 9.3.2. Proposers who are unable to provide the data required to support specifications, within the timetable given in paragraphs (iii) and (vi) below, must notify FAO and/or WHO as soon as possible, so that the programme may be adjusted accordingly. Where a pesticide is withdrawn from the yearly programme, an alternative pesticide may be brought forward by FAO and WHO.
- (iii) Proposers should submit draft specifications and supporting information to FAO or WHO, as appropriate, by 31 October. One printed copy of the supporting information and draft specification should be submitted, together with an electronic version, using templates available on the FAO¹ and WHO-PQT-VC websites. The guideline specifications provided in this Manual must be used. If appropriate guidelines do not exist, proposers should refer to Section 9.1.5.4. The proposer must confirm whether or not the proposer's data differ from those submitted to WHO, the FAO/WHO JMPS or the registration authorities in the country which the proposer uses as the support of the FAO/WHO specification; and that all relevant information is included in the proposal.
- (iv) On receipt of the draft specification(s) and supporting information for a pesticide, FAO or WHO will allocate it to an expert participating in the JMPS, for preliminary evaluation.

¹ <http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmps/manual/en/> (March 2016)

- (v) If the toxicological and/or ecotoxicological data provided are identical to those submitted to WHO, or the FAO/WHO JMPR, JECFA, their evaluations of the hazards and risks will normally be incorporated into the JMPS evaluation. If the impurity, toxicological and/or ecotoxicological data are identical to those submitted to national authorities for the purposes of registration, registration of the active ingredient and formulations will normally be interpreted by the JMPS as acceptability of the hazards and risks. Registration authorities may be contacted for confirmation of the similarity of the impurity, toxicological or ecotoxicological data, utilizing the proposer's letter authorizing access to the proprietary information. Where the data submitted to JMPS differ from those evaluated by the other organizations, the proposer will be asked for an explanation. Where no national, JMPR/JECFA or WHO evaluation is available, a full assessment of the toxicological and ecotoxicological data will be organized by FAO/WHO before proceeding with the JMPS evaluation.

An important aspect of the assessment of hazards and risks is to determine the links between (i) the hazard and purity/impurity profile data submitted, and (ii) the purity/impurity profile data submitted and the limits for purity/impurities applied in normal manufacturing production. FAO and WHO recognise that generation of replicate data on all potential/actual hazards by each manufacturer of a pesticide may be unnecessary and ethically undesirable. The lack of direct links in (i), above, does not preclude development or extension of a specification but proposers are required to disclose the links, or lack of them, to ensure that JMPS recommendations are based upon a properly informed assessment of hazards and risks.

- (vi) The proposer should be notified of additional information required, if any, by 31 December.
- (vii) The proposer should send additional information, as requested, to the evaluator and FAO/WHO by 28 February, if the proposal and corresponding evaluation are to be considered at the next meeting of the JMPS. The evaluator should send any questions, as soon as they arise, to the company for resolution before the meeting if possible. All communications between the evaluator and proposer, related to the proposal under consideration, will be copied, or reported, to FAO/WHO.
- (viii) The evaluator should consider the information provided and send a completed evaluation to FAO/WHO by 30 April, for circulation to the proposer and the experts participating in the JMPS.
- (ix) The evaluator should send the evaluation and draft appraisal to the assigned peer reviewer by 30 April. It is not necessary to provide the original data to the peer reviewer. The reviewed documents should be returned to the evaluator and FAO or WHO by mid May.
- (x) The peer reviewer should read the draft specifications, evaluation and appraisal and provide comments back to the author.

The peer reviewer should check;

- if wording in the specifications agrees with wording in the Manual;
- if values for the physical properties of the formulations are reasonable;
- if adequate and systematic information is recorded in the data summary tables of physical and chemical properties, toxicology and ecotoxicology;
- if all necessary analytical and test methods are provided and validation is adequate;
- if anything is missing, e.g. a required physical property, a required specification or study references; and
- if the recommendations and appraisal are consistent with the summarised data.

The peer reviewer should also draw to the attention of the author any other point that does not make sense, e.g. references in the reference list that do not appear in the text or tables.

- (xii) The procedure for considering evaluations at meetings of the JMPS will be:
- a presentation by the evaluator and consideration by the JMPS;
 - followed by consideration of the final JMPS recommendation.

Post-meeting amendments involving anticipated subsequent responses from the proposer will be accepted for incorporation into the evaluation report. Depending upon the number and complexity of minor changes, the JMPS may recommend post-meeting circulation of the final draft evaluation and/or specifications, to ensure maintenance of agreement between the experts. Major changes, or unexpected and important emergent information from the proposer, will require that the submission is reconsidered by a future meeting.

Where the JMPS considers draft or revised specifications prepared by multiple proposers for the same pesticide, the proposers may address the JMPS individually or together, according to the proposers' preference.

- (xiii) If the JMPS is unable to reach a consensus, the proposer will be asked to provide data to resolve the outstanding issue(s), within a specified time. Following a recommendation to reject a proposed specification, a specification redrafted by the proposer may be considered at the next meeting, depending upon the priorities and workload of the JMPS.
- (xiv) The basis for recommendations to accept or reject specifications will be recorded in the evaluation.
- (xv) The proposer(s) will be identified in the evaluation, which will be cross-referenced with the specification(s).
- (xvi) The specifications do not apply to the active ingredients or formulations of other manufacturers, nor to those produced by different processes, unless these have been evaluated as equivalent. If the proposer subsequently changes the manufacturing process significantly, re-evaluation by the JMPS will be required to ensure compliance with the specification. The primary specification may be modified to accommodate the additional products, or those produced by the different process, depending upon the outcome of the JMPS evaluation. The reference profile of impurities will normally remain that associated with the specification as initially adopted.

9.2.6 Publication of specifications

Specifications, and the corresponding evaluations, will be published only on the internet. It is intended that publication of the evaluation should be within the calendar year of the meeting at which the specifications were considered by the JMPS. Specifications (dated with month and year) will either be published at the same time or, where appropriate, upon acceptable validation/adoption of the supporting test methods. Only the latest versions of specifications will be available but all evaluations will be made available. Specifications and evaluations will normally be published as a single, two-part document.

The evaluations provide the evidence and rationale upon which JMPS recommendations were based. They do not contain confidential information but decisions based on such information are explained as fully as possible whilst maintaining confidentiality.

The content of evaluation reports, and the nature and style of publications, will be determined by FAO and WHO. Proposers and the owners of data will normally be identified in evaluations. Proposers will not normally be identified in specifications but will be identified, indirectly, by reference to the evaluation. Exceptionally and at the discretion of FAO or WHO, a proposer may be identified in a footnote to a specification, if it is necessary to clarify which specification applies (or does not apply) to that proposer.

CIPAC adopted or accepted methods for testing physical-chemical properties of formulations are usually first published under the pre-published method scheme

before they appear in printed form in CIPAC Handbooks or CD ROM,¹ or the AOAC Handbook² and Journal, and physical test methods are published in the CIPAC Handbooks. Methods in support of WHO specifications developed under the previous procedure are attached to the specifications. It is important to note that CIPAC allocate Code numbers for microbial pesticides, however they do not develop or publish methods of quantitation for microbial pesticides³. CIPAC MTs are applicable to characterisation of physical and chemical properties of microbials unless there is some kind of slow release characteristics together with an assay for the product.

9.2.7 Review of specifications

Specifications will be reviewed at intervals. FAO and WHO will prepare a programme for review of all published specifications, which will be considered by the JMPS. As one of their responsibilities of product stewardship, and as a condition for maintaining an FAO or WHO specification, proposers must inform FAO/WHO of changes in the manufacturing process which have implications for the existing specification, and of changes in company name or address.

Specifications are published on the basis that information on the manufacturing process (confidential), impurity profiles (confidential), the hazard data available to FAO/WHO, and the manufacturer's name and address remain valid. Proposers have a responsibility to inform FAO/WHO of changes in this information. Where the validity of this information is in doubt, the specification(s) may be scheduled for review by the JMPS. The manufacturer of a product evaluated by WHO PQT, and based upon which evaluation the WHO recommendations for use and specifications have been developed, should notify WHO of any changes to the manufacturing process, formulation characteristics and/or formulants that could require re-evaluation of the product and/or review of the specification. Proposers may also request review of specifications.

Specifications under review must be supported by the data indicated in Sections 9.3.1 or 9.3.2 of this Manual (as appropriate).

The JMPS will then:

- (i) confirm that the existing specification is suitable, or
- (ii) recommend an amended specification, or
- (iii) recommend that the specification be withdrawn.

Where national authorities find it necessary to adapt FAO or WHO specifications, FAO and WHO should be informed by the proposer, or the authority, of the

¹ Updated order forms are provided under <http://www.cipac.org/index.php/methods-publications> (March 2016)

² Official Methods of Analysis, 18th edition. Obtainable from AOAC International, Wachovia Bank Lockbox, P.O. Box 7517, Baltimore, Maryland 21275-5198, USA. (tel +1 301 924 7077, fax +1 301-924-7087, e-mail: fulfillment@aoac.org, website: <http://www.aoac.org>).

³ CIPAC codes can be accessed under <https://www.cipac.org/index.php/code-numbers> (December 2018)

changes made and the reasons for them. Such modified specifications cannot be considered to be FAO/WHO specifications but information supporting the changes will assist revisions of the specifications by the JMPS.

Comments and further information relating to specifications are welcomed by FAO and WHO. Proposals for modification of specifications should be supported by evidence to show that the change is pertinent to maintaining or improving the quality/performance, or to reducing the risks, of the technical grade active ingredient or formulation.

9.2.8 Overview of information required for specifications

The following information should be submitted.

- (i) The name, address and contact point of the proposer(s) of the specification.
- (ii) Either the draft new specification or a statement of the specification to be extended.
- (iii) The information described in section 9.3, to support a new specification.
- (iv) If the proposal is for joint FAO/WHO specifications, the proposer must state whether or not the materials used for both areas of application are similar and, unless different formulation specifications are proposed, that the specifications for the formulations are applicable to both agricultural and public health uses.
- (v) Any other relevant information likely to help the JMPS to make sound recommendations.

All clauses in the draft specification should be presented in a standard form (see sections 9.5 and 9.6 of this Manual).

9.2.9 Acceptability of methods of quantitation and physical chemical properties

Assay methods, supporting FAO and WHO specifications, for the quantitation of MPCA in technical and formulated pesticides must be peer validated. MPCA which have assay methods which are acceptable by international pharmacopeia for the quantitation should be considered as peer reviewed.

Methods for the determination of relevant impurities or stabilizers and other additives included in the specification, must be independent laboratory validated.

Where a peer-validated (ILV) of the method of quantitation is still in progress at the date of submitting the proposal, the estimated date of completion must be provided. Specifications will not normally be published prior to the completion of validation of the methods and, if the validation is unlikely to be completed before the next closed meeting of the JMPS, consideration of the proposal may be postponed.

Test methods for physical properties may be validated by CIPAC or ASTM, or according to the requirements of OECD or EC, or, where appropriate, by equivalent pharmaceutical organizations. References to physical test methods in this Manual are prefixed "MT" for CIPAC methods, "EC" for European Community methods, or with the complete acronym for OECD or ASTM methods. These methods may be regarded as definitive as, in many cases, the physical property is defined by the method of measurement. Where more than one method is available, a referee method must be designated. Where a method is specified that has not been adopted by CIPAC, the specification should also define the property as measured by the most appropriate CIPAC method, if there is one.

Unless it is considered to have been superseded, the CIPAC method will normally be considered the referee method.

Validation requirements for methods which determine unstable physical properties¹, which are not amenable to validation by collaborative study, are currently under consideration by CIPAC. Until defined by CIPAC, or equivalent, the validation requirements will be determined by FAO/WHO on a case-by-case basis. It should be noted that CIPAC currently decides on a case by case basis on the validation of methods for unstable properties (e.g. viscosity of non-Newtonian fluids) or methods which cannot be properly validated like pH.

In addition to the emergence of new information on the active ingredient or the specifications, review of an existing specification may be triggered by revocation of the CIPAC/AOAC status of a method.

¹ For example, the distribution of active ingredient in/on slow- or controlled-release products is intended to change with time, temperature and so on. As these conditions are difficult or impossible to control during the distribution of samples for an inter-laboratory validation study, the results may reflect uncontrolled variations in the test parameter more than variations which are inherent in the test method.

9.3 DATA REQUIREMENTS AND PROCEDURES FOR DEVELOPMENT OF FAO/WHO SPECIFICATIONS

9.3.1 *Data requirements for support of the specification for a MPCA active ingredient*

9.3.1.1 *Scope*

These specification guidelines are aimed at providing a framework for development of specifications for technical MPCA and MPCP for both plant protection and public health uses, but semio-chemicals (like pheromones) and macro-organisms are excluded.

MPCA derived from or based-on genetically modified organisms (GMOs), as defined by the OECD¹, (a (...) *micro-organism or virus, which has been genetically engineered or modified..*) are outside of the scope of this guidance as they represent a special consideration and should be addressed separately. Currently, this guideline does not consider MPCA based on so called 'RNA interference' technology.

This document aims to harmonize best practice from guidance available globally for registration of micro-organisms. In this guidance, documents developed by for example OECD, EPA and the EU are considered and recommended.

These guidelines, however, do not consider matters related to access, intellectual property rights and benefit sharing although due attention should be paid to this aspect, though the confidentiality of data submitted has a high priority (see Section 9.2.4).

9.3.1.2 *Introduction to microbial pest control agents (MPCAs)*

MPCAs are some of the newer crop protection agents and have activity against insects, mites, nematodes, plant pathogens, and occasionally weeds for use as stand-alone products and for use in IPM or IVM. Products based on *Bacillus thuringiensis* (*Bt*) are the longest established and best known MPCAs, they are widely used in field vegetables particularly against *Lepidoptera* spp. and in still or running water as vector control agents. Other MPCAs use is greatest in high value protected crops and more recently in high value field crops and some use in broad acre crops, for grain and food storage facilities, and for control of vectors and household pests. MPCAs can be applied for example as foliar or seed treatments, to water courses, household and factory facilities.

The OECD Working document on the evaluation of microbials for pest control² is a useful framework for regulatory considerations that may be needed for MPCA and MPCP.

¹ <https://stats.oecd.org/glossary/detail.asp?ID=1107> (December 2018)

² OECD Environment, Health and Safety Publications Series on Pesticides No. 43

MPCAs are specialist types of crop protection and public health active ingredients and therefore require certain specialist know-how. In some countries, in addition to registration it may be the role of the regulatory organisation to approve the health and safety of a MPCA production facility and to ensure distributors and growers comply with labels. Therefore, it may be necessary to provide suitable training in micro-organisms used in MPCAs to allow pesticide boards to carry out these functions.

Micro-organisms used for MPCAs have the potential to produce secondary compounds (also called metabolites) during fermentation and so can be present in the product and/or they can be produced *in situ*. These metabolites may, or may not, contribute to the activity of the MPCA. These metabolites may, or may not, be of toxicological concern. Metabolites are to be addressed in the dossier only when they are known, from literature or studies, to be of toxicological concern and where there would be exposure (human or environmental) and/or they are the principle mode of action.

Existing testing guidelines for synthetic chemical pesticides may not be directly applicable to testing MPCA and specific guidelines for each test system and type of microbial pesticide to be evaluated, modified as necessary to avoid interference by constituents in the test samples, are usually needed. Test guidelines specific for micro-organisms have been developed by EPA, OECD and the EU.

9.3.1.3 Categories of MPCAs and information on identity considered in this guideline

In the framework of this draft guideline on microbial pest control product specifications, the term Taxon is used as a proxy for the full taxonomic designation of bacteria, viruses etc.

Bacteria:

The following taxonomy for bacteria applies: Order, family, sub-family, Genus, Species, Strain (and associated number), and molecular identification if required.

OECD and EU regulations require that identification is made at the strain level. Techniques to identify at strain level sometimes rely on the taxonomy and morphology (traditional methods of bacterial identification relying on phenotypic identification of the organism using Gram staining, culture and biochemical methods), rather than at the molecular level (such as Real Time PCR (Polymerase Chain Reaction and microarrays), because the technology is not universally available at the present time.

Each MPCA from a manufacturer should carry its own strain number, especially as “appropriate techniques”, may or may not include molecular identification. It is understood that not all manufacturers may have access to molecular identification and that the wording “appropriate techniques” allows for some flexibility in the technique used.

The methods should be the most straightforward and cost effective way possible to confirm the identity. However it is acknowledged that biological methods are

not appropriate to ensure identity in all cases, and molecular techniques are sometimes necessary in order to confirm identity at strain level.

It should be emphasized to also consider the method of manufacture (fermentation) since the production process has an impact on the identity.

Technical equivalence may be possible at a later stage (mainly this will be for Baculovirus), and for that a good understanding of the reference profile will be required.

Fungi:

The taxonomy as outlined for bacteria, also applies to fungi i.e. Order, family, sub-family, Genus, Species, Strain (and associated number), and molecular identification, if required.

Again it is noted that the production process affects the secondary compounds, so the taxonomy identifies the microbial but the specification is linked to the production process due to possible relevant impurities and contaminants.

Viruses:

The same taxonomy as outlined for bacteria, also applies to fungi and viruses, i.e. Order, family, sub-family, Genus, Species, Strain (and associated number), and molecular identification, if required; however, unlike bacteria and fungi, the identification for viruses is linked to its host organism. These host organisms have an order, family, sub family, host species name, then strain name, molecular identification.

OECD are currently developing a guidance document for baculovirus that may give further advice. At time of preparation of this document (Late 2018) that guidance document was not yet available but may be considered for a later version.

Most virus related products on the market are baculoviruses but there are others like mosaic virus. For the moment and near future, the JMPS will restrict the focus to Baculovirus.

Others

Other microbial pesticides are also envisaged in the future, such as protozoa and yeast microbials, however no current examples can be given at the time of writing.

9.3.1.4 Data requirements for microbial pest control agents (MPCAs)

Introductory note: the data requirements are taken from the OECD Guidance for Country Data Review Reports on Microbial Pest Control Agents (Monograph Guidance for Microbials), Series on Pesticides No. 22, Health and Safety, Environment Directorate, Appendix 6 and from the FAO Guideline " Guidelines for the registration of microbial, botanical and semiochemical pest control agents for plant protection and public health uses" (FAO Rome, 2017). However these OECD and FAO data requirements have been modified and shortened. These adaptations seem necessary as the focus of this guidance document is on data supporting FAO and WHO specifications in contrast to registration purposes.

9.3.1.4.1 Minimum data requirements for support of the specification for an MPCA

Preface

As with synthetic chemical pesticides, the identification techniques for MPCA are essential to ensure the taxonomic identity of the active ingredient. In contrast to chemical pesticides, where fairly clear criteria for positive identification and assay methods are established, a more pragmatic view is appropriate with MPCA, as far as possible, stating it is best practice to use simplest and the most cost efficient methods. Traditional methods such as microscopy can be used if acceptable, and more advanced molecular identification procedures such as molecular genetic techniques should be used for identification if required.

This is in line with the OECD monograph¹ which states that industry should employ the best available technology to identify the strain: it is recommended that a detailed taxonomic identification of the microbial active substance by the most appropriate and up-to-date methods, is necessary for the assessors to use properly the data submitted or found in literature (using a micro-organism for comparison purposes, i.e. the same species, but another strain). Such information can be used either to identify potential adverse effects and thus serve as a basis for further inquiries, or to demonstrate the safety of the microbial active substance.

In summary, the identification of the microbial active substance should preferably be performed by at least two independent laboratories using the most up-to-date and standardized techniques available from the scientific community. The technique used will depend on the organism and possibly will also vary from a laboratory to another. Where a microbial active substance relates to different (new/novel) species, additional testing should be undertaken to definitively identify the microbial active substance and relate it to a (existing) species.

A. Data requirements for an MPCA (TK only)

A. 1 Identity of the MPCA (non confidential data)

A.1.1 Scientific name of microorganism to strain level

¹ OECD ENV/JM/MONO(2008)36: Working document on the evaluation of microbials for pest control

- A.1.2 Accession no. of sample in a recognized culture collection
- A.1.3 Test procedures and criteria, using best available technology, to characterize the strain or serotype
- A.1.4 Trade names, common names if any, developmental code names

A.2 Composition of technical grade of MPCA / Active Substance (TK)

- A.2.1 Concentration of microorganism (and relevant impurities and contaminants, if required) in terms of g/kg or g/L (also in % w/w) or another appropriate unit: (non-confidential information)
- A.2.2 Composition of microbial material used for manufacture of end use products in terms of g/kg or g/L for each active ingredient including microbial and non-microbial (confidential information).
- A.2.3 Methods of production and quality criteria for the production and storage of the active microorganism, including quality control measures and information on human/mammalian pathogens (confidential information).
- A.2.4 Quality control data (measures of quality criteria) from 3 - 5 production batches, including storage stability data (confidential information).
- A.2.5 Potential formation, presence and/or impact of unintentional ingredients (confidential information)
- A.2.6 Physical and chemical properties, if MPCA is produced as a manufactured use product (MUP) that is stored prior to formulation of end-use products.

A.3 and A4 Methods for quantification and information on the production process for the MPCA

- A.3.1 Methods for quantification and validation data for the MPCA (non-confidential information). Methods for active ingredient content must be peer-validated (ILV).
- A.4.1 Methods for relevant impurities and validation data (non-confidential information). Methods for relevant impurities content must be independently validated.
 - A.4.1. Method to preserve and maintain the master seed stock; criteria for an acceptable level of consistency and integrity of seed stock (confidential information)
 - A.4.2 Production process for the TK (confidential information)
 - A.4.3 Quality control and monitoring methods
 - A.4.4. Storage stability test, data and determination of shelf life, if MPCA is stored prior to formulation

A.5 Toxicological and Exposure Data on MPCA TK (non confidential data)

- A.5.1 Summary: potential of MPCA to be hazardous to humans with

consideration of its pathogenic potential, its ability to infect and pattern of clearance, and its toxicological effects

A.5.2 Occupational health surveillance report on workers during production and testing of MPCA

A.5.3 Acute oral infectivity, toxicity and pathogenicity

A.5.4 Acute intratracheal/inhalation infectivity, toxicity and pathogenicity

A.5.5 Acute intravenous/intraperitoneal infectivity

A.5.6 Cell culture study, for viruses and viroids or specific bacteria and protozoa with intracellular replication

A.5.7 Genotoxic potential, especially for fungi and actinomycetes

A.5.8 Toxicity studies on toxicologically relevant secondary compounds (metabolites) (especially toxins)

A.5.9 Published reports of adverse effects, especially clinical cases and follow-up studies

A.5.10 Summary of mammalian toxicity and overall evaluation

A.6 Ecotoxicological studies on the MPCA TK (non confidential data)

A.6.1 Avian toxicity

A.6.2 Fish toxicity

A.6.3 Toxicity to aquatic species other than fish and aquatic species field testing

A.6.4 Effects on algal growth and growth rate

A.6.5 Effects on aquatic plants

A.6.6 Effects on terrestrial plants

A.6.7 Effects on bees

A.6.8 Effects on non-target terrestrial arthropods

A.6.9 Effects on earthworms

A.6.10 Effects on soil microorganisms

A.6.11 Other/special studies

9.3.2 Minimum data requirements supporting the specification for an MPCP

B.1 Identity of the MPCP and further information

B.1.1 Declared content of MPCA in MPCP (in terms of g/kg or g/L or other appropriate unit); indicate scientific name and strain designation, and development stage (e.g. spore) (non-confidential information)

B.1.2 Composition of ingredients in MPCP with regard to additives, stabilizers, microbial and non-microbial impurities. (confidential information)

B.1.3 Quality criteria for the production and storage of the MPCP, including product specific tolerance for content of MPCA, presence of human or non-target

animal pathogens, maximum acceptable level for microbial impurities and known mammalian toxins (non-confidential information).

B.1.4 Quality control data (measures of quality criteria) from 3 - 5 production batches, including product stored for duration of shelf life or accelerated storage stability if it is metabolically active (confidential information).

B.1.5 Formation, presence and possible adverse effects of unintentional ingredients (theoretical discussion), (confidential information).

B.2 Physical, chemical and technical properties of the MPCP

B.2.1 Appearance (non-confidential information)

B.2.2 Information on storage stability or shelf-life (non-confidential information)¹

B.2.3 Formulation type of the MPCP² (non-confidential information)

B.2.4 Physical and chemical properties of the MPCP - as appropriate

B.2.5 Information on cold ³and accelerated storage stability tests ⁴and determination of shelf life (methods of analysis) (non-confidential information) – as appropriate.

B.3 Methods for quantification and analysis of the MPCP

B.3.1 Method for quantification and analysis for MPCA content and relevant microbial and chemical contaminants (non-confidential information). Methods for active ingredient and relevant impurities content must be peer-validated.

B.4 Toxicological and Exposure Data on MPCP (non confidential)

¹ For storage stability and shelf life refer to CropLife Monograph Nr. 17, 2nd edition: Guidelines for Specifying the Shelf Life of Plant Protection Products (June 2009) accessible through https://croplife.org/wp-content/uploads/pdf_files/Technical-Monograph-17-2nd-edition-June-2009.pdf

² For formulation codes refer to CropLife Monograph Nr. 2 (March 2017) Catalogue of pesticide formulation types and international coding system, accessible through <https://croplife.org/wp-content/uploads/2017/04/Technical-Monograph-2-7th-Edition-Revised-March-2017.pdf>

³ Cold stability should be considered for solid formulations where cold storage could adversely affect the active ingredient content, and for liquid formulations where cold storage could adversely affect the active ingredient content and the physical and chemical properties. If the information provided by the manufacturer indicates instability under cold storage, then cold temperature storage testing is required.

⁴ The recommended accelerated storage stability test (CIPAC MT 46.3) used for synthetic chemical pesticides is not suitable for microbial pesticides. Therefore, the traditional storage stability clause that contains a requirement to perform an analysis of active ingredient content before and after storage, will be removed from the specification templates for microbial pesticides for the time being. However, a modified accelerated stability clause will be retained in the specification with emphasis on the physical and chemical properties before and after storage. The JMPS notes that there is an onus on industry to come up with a suitable solution that will enable quality control laboratories to monitor the stability of these products, including the stability of active content. The microbial pesticide product should be placed on the market according to the label instructions. For that reason an expiration date and storage conditions will need to be included on the label.

data)¹

B.4.1 Acute toxicity

B.4.2 Acute oral toxicity

B.4.3 Acute percutaneous (dermal) toxicity

B.4.4 Acute inhalation toxicity to rats

B.4.5 Skin irritation

B.4.6 Eye irritation

B.4.7 Skin sensitisation

B.4.8 Summary of mammalian toxicity and overall evaluation

B.5 Ecotoxicological studies on the MPCP (non confidential data)

B.5.1 Effects on birds

B.5.2 Effects on aquatic organisms

B.5.3 Effects on bees

B.5.4 Effects on terrestrial arthropods other than bees

B.5.5 Effects on earthworms

B.5.6 Additional studies

9.3.3 Determination of the relevance or non-relevance of impurities

The following categories of impurities can be considered to be potentially relevant:

- Microbial contaminants
- Chemical impurities (from the manufacturing process)
- Secondary compounds

The OECD guidance published 2011² proposes microbial contaminant limits in microbial pest control products (MPCP). The limits proposed by the OECD are accompanied by rationale such as the virtual absence of human pathogens, aerobic and anaerobic plate counts etc. It is noted that the OECD guidance has some limitations because it only relates to human pathogens and oral exposure, but other exposure routes are also possible. Contaminants are placed into groups such as pathogens, microbial activity, human faecal and environmental contaminants and other tests. It is noted that some limits mentioned in the OECD guideline are even more stringent than the limits set for food.

¹ If the hazard and exposure has not been assessed for MPCA, then B.4 and B.5 are not required for the MPCP.

² OECD Issue Paper On Microbial Contaminant Limits For Microbial Pest Control Products" Series on Pesticides No. 65.

Secondary undesired metabolites that may or may not be formed during production of the MPCA/MPCP need to be controlled on a case-by-case basis and limits set accordingly.

Chemical impurities are considered to be related to the production process and can be evaluated either according to the GHS criteria in the absence of more specific information or based on more detailed information.

9.4 Aims, applicability, and requirements of specification clauses

Introduction

The aims, applicability, and requirements for many of the specification clauses within the Manual (third revision of the First Edition, 2016) remain directly applicable to microbial pesticides. However JMPS notes that there are some relevant exceptions such as active ingredient identity, content and a limited number of physical and chemical properties.

A specification should not require judgement to be exercised by the buyer, so the clauses in it should describe quantifiable parameters and provide limits for them. Apart from the title and description, non-quantifiable elements should be included in the notes attached to, but not forming part of the specification. Such notes may include information on the hazard classification of the MPCA and MPCP, or other properties and characteristics to assist the user, e.g. reference to national and international handling and transport regulations, phytotoxicity and other potential problems relating to the use of the MPCA or formulated product. In addition, the notes may provide supporting information on test conditions or, in some cases, provide details of the test methods for microbial identification and quantification in MPCA and MPCP. It should be noted that the majority of specifications for conventional chemicals simply give references to the test methods to be used. For synthetic chemical pesticides two methods for the identification and one for the quantification are required, but for microbial pesticides, JMPS requires at least one identification method allowing unambiguous identification. This method has to be either published (with a clear reference in the specification) or a full description of the method has to be submitted to FAO/WHO. The method will not be treated as confidential information and will be published as an annex to the specification.

Technical grade active ingredients should be as pure as economically practicable, as this will generally tend to minimize formulation and toxicity problems, as well as those arising from taint, phytotoxicity, etc. In setting standards, the JMPS will take account of the technical problems associated with raising quality but, even where no compelling reasons exist for doing so, the long term advantages of improving quality will often outweigh the disadvantages.

The specification of a formulation takes into account properties which have relevance to, for example, efficacy, operator safety and impact on the environment. Standard tests do not yet exist for all parameters for which specification limits are desirable and, in some cases, the standard tests available are not ideal. Therefore there is a continuing need for new test methods and improvement of existing ones.

Certain clauses in the guidelines presented in Sections 9.5 and 9.6 may be inappropriate, or additional clauses may be necessary, for a particular specification. Where the need for the clause is clearly dependent upon the MPCA, proposers should simply state that it is not relevant. Insertion of a proposed clause, or deletion of a standard clause, in draft specifications must be

supported by a reasoned case, which may range from a simple explanation to a detailed technical argument with supporting information.

Proposals for specification limits that are more stringent than those given in the guidelines are usually acceptable to the JMPS. Proposals for specification limits which are less stringent than those given in the guidelines must be supported by a reasoned case and, where practicable, data to show that the formulation behaves satisfactorily in use.

9.4.1 Title and code

Aim

To provide a brief, unequivocal identification and description of the MPCA or MPCP.

Applicability

All specifications.

Methods

Not relevant.

Requirements

Taxonomy

The following general taxonomy applies to microbials:

Order, family, sub-family, Genus, Species, Strain (and associated number), and molecular identification if required (except viruses which also have a host organism). For bacteria it must also be stated whether they are Gram +ve or -ve.

Common names shall not be included in the taxonomy of microbials.

Codes

CIPAC codes for active ingredients are referenced in Appendix D of the 2016 Manual. CropLife International codes for technical pesticides and formulation types are listed in Appendix E of the 2016 Manual.

9.4.2 Description

Aims

To provide a brief, clear description of properties of the MPCA or MPCP, which can be checked by simple inspection, and statements identifying the active ingredient(s) and the presence of essential additives.

Applicability

All specifications.

Methods

Not relevant.

Requirements

The description of a MPCA or MPCP should include the physical state (e.g. crystals, liquid, hard lumps, etc.), colour, odour (if appropriate) and, where required, declaration of any modifying agents present (e.g. grinding agents). General terms, such as “solid” or “liquid”, must be qualified with suitable adjectives to make them more descriptive. The description should be sufficiently specific to meet the aim of checking by simple inspection, and is preferred to a generic description. Each specification guideline (Sections 9.5 and 9.6) includes a standard clause for the description.-

The taxonomy must also be included in the descriptions for both MPCA and MPCP. The most accurate, current, taxonomic information should be provided to verify the identity of the microorganism based on the strain. The following general taxonomy applies to microbials: order, family, sub-family, genus, species, strain identification (including the accession number), and where appropriate molecular identification. For viruses the identification should also include the host organism. For bacteria it must also be stated whether they are Gram positive or negative (see Section 9.3.1.3).

If the identity and quantity of essential additives are not critical characteristics, information on them may be provided in a Note but they will not be considered to be part of the specification. If they are critical characteristics, an appropriate clause and limit must be inserted, supported by a peer-validated analytical method.

9.4.3 Active ingredient

9.4.3.1 Identity tests

Aim

To provide a proven means for identification of the active ingredient

Applicability

All specifications.

Methods

Must be referenced and, if not already published, a full description provided to FAO and/or WHO. In cases where the method is not published, it will be published as an annex to the specification.

Requirements

It is noted that each microorganism should be identified and named at the strain level. Microorganism’s genus, species, strain etc should be clearly stated in the submitted documents.

The identity should be confirmed using microbiological techniques, with the easiest, most accessible and cost effective way to get unambiguous identification. Where unambiguous identification is not

possible using classical microbiological techniques, more advanced identification techniques based on molecular identification should be used.

For synthetic chemical pesticides two methods for the identification and one for the quantification are required, but for microbial products one unambiguous identification method is sufficient. This method has to be either published (with a clear reference in the specification) or a full description has to be submitted to FAO/WHO. The method will be published as an annex to the specification.

The number of laboratories able to conduct these testings is limited. Even for microscopic methods which are commonly available particular expertise is required with knowledge at strain level.

It is necessary that laboratories other than the company itself is able to conduct the testings; otherwise there is no real quality control. Therefore Independent Laboratory Validation (ILV) testing is required for the chosen identity test. ILV will be defined as a second laboratory that can be in another company or the same company but not under same laboratory management.

The proposer will be requested to propose the independent laboratory, and demonstrate an acceptable level of consistency between the laboratories' validation data. The proposer should prepare a report based on their experience of analysing the particular microbe. The second laboratory must be able to reproduce the validation data from the first laboratory to within acceptable limits.

Laboratories are recommended to have some quality assurance available, such as ISO/IEC 17025 or GLP certification. However, GLP or ISO 17025 is not a mandatory requirement.

9.4.3.2 *Content of active ingredient*

Aims

To ensure that the active ingredient content is described by limits, acknowledging the fact that results of the quantitation method, and actual concentrations are all variable.

Applicability

All specifications.

Methods

Methods for quantification should be peer-validated (ILV). If the method has not yet been published, then full details must be submitted to FAO and/or WHO by the proposer. The methods must be referenced and, if not already published, it will be published as an annex to the specification.

Requirements

The active ingredient content should be declared. Most microbial active substances are processed directly into the final formulation (integrated process), rather than isolated as a TK. A minimum content and (if required) a maximum content should be specified, if required.

The active ingredient content of **technical concentrates (TK) and formulated products** should be expressed as:

“The [taxon] content shall be declared (g/kg, or for liquids only, g/l at 20 ± 2 °C, or insert appropriate unit) and, when determined, the average measured content shall not be less than the declared content.”

The tolerances for formulated products and TK should be declared and are expected to be product-specific.

Depending on the microbial pesticide, the active ingredient content or biopotency may be expressed as e.g. total viable counts, Colony Forming Unit (CFU/g, CFU/mL), International Toxic Unit (ITU/mg) or as content in g/kg or g/L of any relevant primary and/or secondary compound (metabolite). In some justified cases a maximum content may also be specified if there is a risk to human or environmental health through exposure to the microbial pesticide.

The tolerances refer to the average result of the method of quantitation obtained and take into account manufacturing, sampling and analytical variations, except where an overage is required. Positive deviations from the upper limits specified for the product (tolerances will be product specific) may be utilised if the formulation is manufactured with an overage to compensate for degradation in storage. The requirement for an overage must be justified when the draft specification is proposed.

Validation of the method(s) and development of the specification may proceed in parallel, or the former may precede the latter. However, the specification will not be published until validation of the method(s) is completed.

In special cases, an overage relative to the nominal content may be accepted but the need for the overage must be justified by the proposer and the overage should be as low as practicable.

9.4.3.3 *Tablet dose uniformity*

Aim

To ensure that the active ingredient dose is routinely accurate.

Applicability

Water dispersible tablets (WT).

Method

Analysis of a specified number of individual tablets to determine the relative standard deviation of active ingredient content.

Requirements

General limits cannot be given.

9.4.3.4 *Rate of release of active ingredient*

Aim

To ensure that the movement of active ingredient within, or to the surface of, or from a slow/controlled-release product occurs in a defined manner.

Applicability

Slow-release granules (GR).

Methods

Appropriate test methods are not available for slow release granules.

Requirement.

General limits cannot be given.

Comments

The release of active ingredient from slow- or controlled-release formulations is dependent upon the external environment and physical forces placed upon the formulation.

Tests require strict adherence to the method protocol because the active ingredient release or retention characteristics are defined by the method of measurement. The method is intended to distinguish a product having an acceptable release/retention in use from one which releases the active ingredient too rapidly or too slowly. No test can simulate all, or any, of the conditions occurring in normal use but the method is expected to provide a broad indication of whether the release/retention is acceptable when the product is used according to label recommendations.

9.4.4 *Relevant impurities and contaminants*¹

9.4.4.1 *Microbial contaminants, Chemical impurities & Secondary compounds*

Aim

To limit the content of these relevant impurities and contaminants which may otherwise increase the risks associated with handling or use of the MPCA or MPCP, or adversely affect the efficacy of the formulation.

¹ This information should include only relevant impurities or contaminants and the sub-title in the specification should be changed to reflect the name of the relevant impurity or contaminant. Where a published method for identification or quantitation for the relevant impurity or contaminant is applicable, it should be used provided it is officially recognized (e.g ISO, AOAC, OECD, EU, EPA). If the method has not yet been published then full details must be submitted to FAO/WHO by the proposer.

Applicability

All specifications where relevant impurities or contaminants may be associated with the MPCA or MPCP.

Methods

Methods must be peer validated (ILV), as a minimum. Where the method and peer validation data have not been published, they must be submitted to FAO and/or WHO, for evaluation by the JMPS. Unless published, the method should be described as an annex to the specification.

Requirements

The microbial contaminant level should be quoted as Maximum:(insert appropriate unit) of [taxon] content

Chemical impurities & Secondary compounds should be quoted as Maximum: [appropriate unit].

Clauses must be provided only for relevant impurities and contaminants..

Separate clauses must be provided for each relevant impurity. Absence in g or mL or a maximum value. The OECD issue paper No. 65 on Microbial Contaminant Limits for Microbial Pest Control Products (ENV/JM/MONO(2011)43) provides criteria for establishing limits on microbiological contamination in microbial pest control products.

Comments

JMPS decides whether a microbial contaminant or an impurity is relevant or non-relevant and how limits are set for microbial contaminants or an impurity on an ad-hoc basis.

The average measured level of a microbial contaminant and relevant impurities must not exceed its declared maximum limit.

9.4.4.2 **Water**

Aim

To limit the water content where water might adversely affect storage stability or where subsequent formulation of the active ingredient containing too much water could lead to an unacceptable product.

Applicability

MPCA and MPCP if required.

Methods

MT 30.2 : Dean and Stark method

MT 30.6 Water: Karl Fischer method using pyridine-free reagents.

Requirement

The maximum permitted level must be quoted in g/kg of the technical concentrate or formulation.

Comments

This clause is required only where water is directly considered to be a relevant impurity, or it has the potential to become a relevant impurity in products formulated from a TK, and the water is not adequately limited by another clause.

9.4.5 Physical – chemical properties

Introduction

In general, physical-chemical properties as described in the Manual should be applicable in the case of MPCPs and MPCAs, but the limits for the determined properties may not be applicable in all cases. In some cases the limits can deviate from the existing default limits in place for these MT methods. The limits are likely to deviate from product to product. Therefore limits will need to be carefully proposed but they will always be considered taking into account the minimum quality of product that is possible while still having the requirement to be fully safe and functional. For establishing the limits the input by the manufacturers will be considered absolutely necessary.

There are already some notable limits which will be difficult to stay within when testing microbial pesticides. For dispersibility, spontaneity of dispersion and suspensibility cut off of < 60 % is acceptable in justified cases. The residue on wet sieve test > 2 % seems possible based on the larger particle size.

Distribution and adhesion to seeds may be difficult to determine and may show higher variations, as the microbes are not washed easily from the surface of the seeds. In conclusion most of the physical, chemical and technical parameters seem to be applicable to microbial pesticides in the same way as to chemical active ingredients. Most of the likely exceptions have been noted above.

For the purposes of this Section, these properties are broadly grouped and numbered as follows: (i) density properties, (ii) surface properties,; (iii) particulate, fragmentation and adhesion properties,; (iv) dispersion properties, (v) flow properties; These groups are not definitive and some properties could be placed in more than one category.

Tests of physical properties cannot emulate what happens in the field under all circumstances. Instead, the tests provide simple models against which satisfactory/unsatisfactory performance may be judged. Limits for satisfactory performance are based on the experience of manufacturers, WHO PQT and others, in relating physical performance in the field to test results. Test results are therefore indicative of physical performance, they do not define exactly how a product will perform under specific conditions.

For some physico-chemical tests, recommended limits are stated. For example, in the case of suspensibility, not less than 60 % of the active ingredient shall remain in suspension. However, in certain cases, due to the standardized test

conditions (e.g. the test temperature), the test results may not meet the guideline limits, despite the fact that the formulation is fit for its intended purpose. A less stringent limit does not automatically imply that a formulation is not fit for use but, where a proposed limit is less stringent than that given in the guideline, the JMPS requires evidence to demonstrate acceptable behaviour of the formulation in the spray tank or other application equipment.

The physical properties of formulations that are diluted with water before use can be affected by the hardness of the water used for dilution and the water temperature. Test temperatures for determination of certain physical properties have been harmonised at $30 \pm 2^\circ\text{C}$. Not because this represents an “average” field temperature but because it is a temperature which is readily maintained in most laboratories (for example in a water bath, which may be difficult or relatively costly to control at lower temperatures). However, CIPAC has started to apply $25 \pm 5^\circ\text{C}$ as standard temperature range in revised or new MT methods, e.g in MT 47.3 (persistent foam) and MT 197 (disintegration of tablets).

CIPAC Handbook F lists standard waters that may be used in laboratory tests, to simulate naturally occurring waters. With certain exceptions, Standard Water D should be adopted in tests, even where an alternative Standard Water is recommended in the CIPAC method. Exceptions are tests of emulsion stability and dispersion stability where both Standard Waters A and D are to be used.

Test concentrations should relate to the recommended use rates given on the label. Where several use rates are recommended, the highest and lowest concentrations (provided they are in line with the scope and limitations of the test method) should be used, even where other concentrations are indicated in the existing CIPAC method. Recently revised CIPAC methods have taken this into account.

(i) Density properties

9.4.5.1 Bulk (pour and tap) density

Aim

To provide information for packaging, transport and application. Density specifications may have particular utility for solid materials where measurement of dosage is by volume (scoop or other container) rather than by weight.

Applicability

Granulated materials.

Method

MT 186 Bulk density.

Requirement

General limits cannot be given.

Comment

The limits should be justified.

(ii) Surface properties

9.4.5.2 *Wettability*

Aim

To ensure that water dispersible powders and granules are rapidly wetted when mixed with water, e.g. in the tank of a spraying machine.

Applicability

All solid formulations to be dispersed or dissolved in water.

Method

MT 53.3 Wetting of wettable powders.

Requirement

Normally the formulation shall be wetted in 1 min, without swirling.

9.4.5.3 *Persistent foam*

Aim

To limit the amount of foam produced when filling the spray tank.

Applicability

All formulations intended for dilution with water before use.

Method

MT 47.3 Persistent foam.

Requirement

Normally there shall be a maximum of 60 ml of foam after 1 min.

Comments

The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier.

(iii) Particulate, fragmentation and adhesion properties

9.4.5.4 *Wet sieve test*

Aim

To restrict the content of insoluble particles of sizes which could cause blockage of sprayer nozzles or filters.

Applicability

Wettable powders (WP); suspension concentrates including those for seed treatment (SC and FS); water dispersible granules (WG) water dispersible tablets (WT).

Methods

MT 182 Wet sieving using recycled water;

MT 185 Wet sieve test, the preferred method, a revision of the methods MT 59.3 and MT 167.

Requirement

A suitable phrase and values may be:

Maximum 2% retained on a 75 µm test sieve. It should be noted that a value > 2% is highly probable for microbial pesticides and therefore this value will have to be considered on a case by case basis.

Comment

In some specification guidelines, this test is not included because it is effectively included in other tests, e.g. suspensibility.

9.4.5.5 *Nominal size range*

Aim

To ensure that an acceptable proportion of a granule formulation is within an appropriate particle size range, in order to minimize segregation during transport and handling, thus ensuring uniform flow rates through application equipment.

Applicability

Granules (GR) and water dispersible granules (WG).

Methods

MT 170 Dry sieve analysis of water dispersible granules (WG)

MT 187 Particle size analysis by laser diffraction

Requirements

Not less than 85% of the formulation shall be within the nominal size range.

Comment

Size range may affect biological activity and the suitability of application equipment.

9.4.5.6 *Dustiness*

Aim

To restrict the dustiness of granular formulations, which may liberate dust into the air when handled and applied, and hence the risks to users.

Applicability

Granules (GR), and water dispersible granules (WG)

Method

MT 171.1 Dustiness of granular formulations¹.

Requirement

The formulation shall have a maximum collected dust of 30 mg by the gravimetric method or a maximum dust factor of 25 by the optical method of MT 171.1 (essentially non-dusty).

Comments

The revised MT 171.1 describes two ways to measure dustiness: a gravimetric method and an optical method. The optical method usually shows good correlation with the gravimetric method and can, therefore, be used as an alternative, where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute, the gravimetric method shall be used.

9.4.5.7 *Attrition resistance*

Aims

To ensure that granular and tablet formulations remain intact until use, to minimize risks during handling or use from the dust generated by attrition in handling and transport. In the case of granules (GR) and tablet formulations, to avoid generation of dusts and/or fines that may also affect application and efficacy in the field.

Applicability

Granular formulations (GR, and WG) and tablet formulations (WT).

Method

MT 178 Attrition resistance of granules (GR).

MT 178.2 Attrition resistance of granules intended for dispersion in water (WG). This method is also applicable to measure the attrition resistance of tablets (WT)

Requirement

General limits cannot be given.

Comment

The attrition resistance of a tablet is often closely related to the packaging design. If a tablet is packaged in a protective/shock absorbing container, removing it from the container for the purpose of abrasion/integrity testing may not be appropriate for quality control, because it will be subject to impact and abrasion forces greatly

¹ The revised MT 171.1 has been adopted at the CIPAC Meeting in Athens in 2015. MT 171 is no longer supported and should not be used with new specification proposals, but remains valid in support of existing specifications. Results obtained by MT 171.1 are equivalent to results obtained by MT 171.

exceeding those which normally occur during transport, storage and handling of the commercial container.

9.4.5.8 *Tablet integrity*

Aims

To ensure that tablets remain intact until use, ensuring that the intended dose is applied.

Applicability

Tablets (WT).

Method

Visual observation.

Requirements

No broken tablets in at least one pack/package containing multiple tablets.

9.4.5.9 *Adhesion to seeds*

Aims

To ensure that the intended dose remains on seeds, and is not easily removed, which may increase risks in handling and adversely affect efficacy.

Applicability

All seed treatment formulations.

Methods

MT 194 Adhesion to treated seed.

Requirement

General limits cannot be given.

9.4.5.10 *Particle size range*

Aim

To restrict the sizes of suspended particulates to a sufficiently narrow range to ensure optimum efficacy and/or safety of the product.

Applicability

Multiple phase formulations, if appropriate.

Methods

MT 187 Particle size analysis by laser diffraction.

Requirements

Limits are usually product-dependent.

9.4.5.11 *Tablet hardness*

Aim

To ensure that tablets remain intact during handling and application.

Applicability

Tablets which must not crumble before or during application.

Method

No suitable test methods are available for tablet hardness.

Requirements

Limits are usually product-dependent.

(iv) Dispersion properties

9.4.5.12 *Dispersibility and spontaneity of dispersion*

Aim

To ensure that the formulation is easily and rapidly dispersed when diluted with water.

Applicability

Suspension concentrates (SC), and water dispersible granules (WG).

Methods

MT 160 Spontaneity of dispersion of suspension concentrates;

MT 174 Dispersibility of water dispersible granules.

Requirements

For suspension concentrates (SC), normally at least 60% of the active ingredient shall remain in dispersion. For water dispersible granules (WG) the dispersibility shall be at least 60 % by gravimetric analysis. However, Dispersibility may be < 60 % for microorganisms.

Comments

Using method MT 160, gravimetrical assay is deemed acceptable for MPCP to measure the mass of active ingredient still in suspension. Method MT 174 has been validated only for gravimetric determination.

9.4.5.13 *Disintegration time and dispersibility/dissolution*

Aims

To ensure that soluble or dispersible tablets disintegrate rapidly on addition to water and that the formulation is readily dispersed or dissolved.

Applicability

Water dispersible tablets (WT).

Methods

MT 197 Disintegration of tablets

Requirement

General limits cannot be given

9.4.5.14 *Suspensibility*

Aim

To ensure that a sufficient amount of active ingredient is homogeneously dispersed in suspension in the spray liquid to give a satisfactory and effective mixture during spraying.

Applicability

Wettable powders (WP), suspension concentrates (SC), flowable concentrate for seed treatment (FS) which are diluted for use, water dispersible granules (WG) and water dispersible tablets (WT)

Method

MT 184.1 Suspensibility of formulations forming suspensions on dilution in water (a harmonisation of methods MT 15.1, MT 161 and MT 168).

Requirement

For wettable powders, suspension concentrates, and water dispersible granules, normally at least 60% of the active ingredient shall remain in suspension. However, suspensibility may be < 60 % for microorganisms.

Comments

The suspension is prepared by the method given in the instructions for use of the formulation or, if no method is given, by the MT 184.1 method (b), without creaming. The test is normally carried out before and after the test of stability at elevated temperature, using CIPAC Standard Water D. Suspensions are to be tested at the highest and lowest recommended rates of use, provided that they are within the scope of the method (0.1 % to 10%). As explained in the revised MT 184.1, this is usually the case with formulations that are diluted in the low % range. However, FS formulations - if diluted at all before use - have such high use concentrations that they are not in line with the upper limit of MT 184.1 and the suspensibility should not be tested.

(v) Flow properties

9.4.5.15 *Flowability*

Aims

To ensure that granules for direct application will flow freely from application machinery; and that granules for dispersion or dissolution in water will flow freely, rather than clumping, after storage.

Applicability

Water dispersible granules (WG), and granules (GR).

Methods

MT 172.2 Flowability of granular preparations after accelerated storage under pressure.

Requirement

General limits cannot be given.

9.4.5.16 *Pourability*

Aim

To ensure that formulations have characteristics that will enable them to pour readily from containers.

Applicability

Suspension concentrates (SC, and FS).

Methods

MT 148.1 Pourability of suspension concentrates, revised.

Requirement

Maximum "residue": 5 %.

Comments

The "residue" is the proportion of formulation remaining in the cylinder.

The clause does not define the pouring and rinsing characteristics of containers. Pouring characteristics of formulation/container combinations are unique and the test method determines only the performance of the formulation in a test cylinder. Important though the pouring and rinsing characteristics of the formulation/container combination are to the user, methods are not yet available that permit them to be incorporated into FAO or WHO specifications.

Where the proposed limit is high, it will be necessary to demonstrate that the residue can be rinsed readily from containers.

(vi) Solution and dissolution properties

9.4.5.17 *Acidity and/or alkalinity or pH range*

Aim

To minimize potential decomposition of the active ingredient, deterioration of the physical properties of the formulation, or potential corrosion of the container.

Applicability

Specifications for any material where adverse reactions would occur in the presence of excessive acid or alkali.

Methods

MT 31.1 Free acidity or alkalinity

MT 191 Free acidity or alkalinity of formulations, the preferred method for acidity or alkalinity.

MT 75.3 Determination of pH values

Requirements

General limits cannot be given.

Acidity and alkalinity should be expressed as g/kg H₂SO₄ and NaOH, irrespective of the nature of the acid or alkali species present.

pH must be expressed as a range with upper and lower limits.

Comment

The requirement for this clause should be justified by the proposer. For example, it will be justified where acid- or base-catalysed degradation of the active ingredient occurs but not if the active ingredient and formulants are stable over a wide range of pH values.

9.4.6 *Storage stability*

9.4.6.1 *Stability at 0°C*

Aim

To ensure that the properties of formulations are not adversely affected by storage during cold periods, with respect to active ingredient content, dispersion and particulate properties.

Applicability

Solid formulations (active ingredient only) and liquid formulations (active ingredient and relevant physical chemical properties).

Method

MT 39.3 (cone shaped centrifuge tube) or original packaging. Low temperature stability of solid and liquid formulations.

Requirements

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the formulation must continue to comply with the requirements of appropriate clauses for content, and with the requirements for appropriate physical chemical properties. The

permitted normal maximum amount of separated solid and liquid is 0.3 ml.

Comments

Testing of content active substance-after storage at $0 \pm 2^{\circ}\text{C}$ for 7 days should be considered for microbial formulations only in those cases where cold storage may adversely affect the stability of the active substance in the formulation.

9.4.6.2 *Stability at elevated temperature*

It is well known that microorganisms are sensitive to elevated temperatures. For that reason the accelerated storage stability test described in CIPAC MT 46.3 and applied to conventional chemical pesticides cannot be used in the case of microbial pesticides as per normal. The accelerated test clause for MPCPs will only require that the relevant physical and chemical properties are tested before and after the accelerated test.

Comments

Where the formulation is not suitable nor intended for use in hot climates and is adversely affected by high temperature, the test conditions may be modified. Avoidance of temperatures exceeding 50°C is likely to be necessary where the formulation is packed in water soluble bags.

Alternative conditions are: 4 weeks at $50 \pm 2^{\circ}\text{C}$, 6 weeks at $45 \pm 2^{\circ}\text{C}$; 8 weeks at $40 \pm 2^{\circ}\text{C}$, 12 weeks at $35 \pm 2^{\circ}\text{C}$ or 18 weeks at $30 \pm 2^{\circ}\text{C}$.

9.5 SPECIFICATION GUIDELINES FOR MPCA TECHNICAL CONCENTRATES (MICROBIAL TKS)

The generic term “Technical grade active ingredient” is used throughout the Manual, and is generally used to refer to both the technical material (TC) and the technical concentrate (TK) of conventional pesticides. However, only the technical concentrate (TK) is applicable when referring to the “Technical grade active ingredient” for microbial pesticides because microbial technical grade active ingredients do not exist in the form of an isolated TC.

Microbial TKs are referred to as microbial pest control agent (MPCA) in Section 9 of the Manual. The FAO/WHO Joint Meeting on Pesticide Management (JMPM) defines an MPCA as:

“A microorganism (protozoan, fungus, bacterium, virus, or other microscopic self-replicating biotic entity) (revised ISPM Pub. No. 3. IPPC, 2005) and any associated metabolites, to which the effects of pest control are attributed (OECD, 2008). A microorganism active substance may contain viable and/or non-viable microorganisms. It can contain relevant metabolites/toxins produced during cell proliferation (growth), material from the growth medium, provided none of these components have been intentionally altered”.

The FAO/WHO Joint Meeting on Pesticide Management (JMPM) defines an MPCP as:

“Microbial pest control product (MPCP): A product containing an MPCA that is registered or labelled with instructions for direct use or application for pest control purposes”.

It is noted that tablets and formulations for seed treatment are already available.

Therefore it has been decided that specification templates will only be drafted for the main formulation types **WG, WP, GR, WT, SC** and **FS**, as these formulations types are available at the moment. The specification templates will be classified as draft guidelines.

9.5.1 Technical concentrates (TK)

Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those than given in the guidelines, without providing justification. From the “Notes” provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [Taxon] TECHNICAL CONCENTRATE

[CIPAC number]/TK (month & year of publication)

1 Description

The material shall consist of [taxon] together with related manufacturing components, and shall be [physical description] . It may include added modifying agents like diluent and stabilizer, if required.

2 Active ingredient

2.1 Identity tests (Note 1)

The active ingredient shall comply with at least one identity test and, where the identity remains in doubt, shall comply with at least one additional test, if required.

2.2 [Taxon] content (Note 1)

The [taxon] content shall be declared (g/kg, or for liquids only, g/l at 20 ± 2 °C, or insert appropriate unit) and, when determined, the average measured content shall not be less than the declared content

3 Relevant impurities

3.1 Microbial contaminants (Notes 1 & 2), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.2 Secondary compounds (Notes 1 & 2), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.3 **Chemical impurities (from the manufacturing process)** (Note 3), if required

Maximum:(insert chemical name) g/kg

3.4 **Water** (MT 30.6) (Note 3), if required

Maximum: g/kg.

4 **Physical properties**

4.1 **pH range** (MT 75.3), if required

pH range: to

4.2 **Any other clause** (Note 3)

Note 1 Method(s) of analysis must be peer validated. If the methods have not yet been published then full details, with appropriate method validation data, must be submitted to FAO/WHO by the proposer.

Note 2 The clause includes only relevant impurities and the title should be changed to reflect the name of the relevant impurity. Method(s) of analysis must be peer validated.

Note 3 Clauses to be included only if appropriate to the material.

9.6 SPECIFICATION GUIDELINES FOR MPCP

Specification templates are currently only provided for the main formulation types **GR, WP, WG, WT, SC, and FS**, as these formulations types are available at the moment for MPCPs. Additional specification templates can be drafted as amendments to this guideline and considered in a revised version of the guideline if needed.

9.6.1 **WATER DISPERSIBLE GRANULES (WG)**

Introduction

Water dispersible granules are intended for application after disintegration and dispersion in water by conventional spraying equipment.

WGs are formulated in many different ways depending on the properties of the active ingredient and the manufacturing equipment available. This can lead to products of differing appearances and differing particle size ranges. Products with a wide particle size range may give rise to some segregation in the containers. However, since the mixture from which WGs are formed is homogeneous, it is possible to allow a wider particle size range than typically used for GRs.

In order to check the properties of a WG according to a given specification, it is essential that the sample taken is representative. A method of sample

preparation of WG is available (CIPAC MT 166: "Sample preparation for analytical determination of WG") which should be applied.

The properties specified in this guideline are considered to be essential for good field performance. In addition to the properties usually considered for WG, these are dispersibility in water, dustiness, and flow properties.

Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those than given in the guidelines, without providing justification. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [Taxon] WATER DISPERSIBLE GRANULES

(CIPAC number)/WG (month & year of publication)

1 Description

The material shall consist of an homogeneous mixture of technical [taxon], complying with the requirements of the FAO/WHO specification, in the form of together with carriers and any other necessary formulants. It shall be in the form of granules (Note 1) for application after disintegration and dispersion in water. The formulation shall be dry, free-flowing, nearly dust free or essentially non-dusty, and free from visible extraneous matter and hard lumps.

In case there is no TK, the material shall contain [taxon], together with carriers and any other necessary formulants. It shall be in the form of granules (Note 1) for application after disintegration and dispersion in water. The formulation shall be dry, free-flowing, essentially non-dusty, and free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 Identity tests (Note 2)

The active ingredient shall comply with at least one identity test and, where the identity remains in doubt, shall comply with at least one additional test, if required.

2.2 [Taxon] content (Note 2)

The [Taxon] content shall be declared (insert appropriate unit) and, when determined, the average content measured shall not be less than the declared content.

3 Relevant impurities

3.1 Microbial contaminants (Note 3), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.2 Secondary compounds(Note 3), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.3 Chemical impurities (from the manufacturing process) (Note 3), if required

Maximum:(insert chemical name) g/kg

3.4 Water (MT 30.6) (Note 4), if required

Maximum: g/kg.

4 Physical properties

4.1 Acidity and/or **Alkalinity** (MT 191) or **pH range** (MT 75.3) (Note 5), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

4.2 Wettability (MT 53.3)

The formulation shall be completely wetted in min.

4.3 Wet sieve test (MT 185) (Note 6)

Maximum:% retained on a 75 µm test sieve.

4.4 Dispersibility (MT 174)

Dispersibility: minimum% after 1 min of stirring.

4.5 Suspensibility (MT 184.1) (Notes 7 & 8)

A minimum of% shall be in suspension after 30 min in CIPAC Standard Water D at 25 ± 5 °C.

4.6 Persistent foam (MT 47.3) (Note 9)

Maximum: ml after 1 min.

4.7 Dustiness (MT 171.1) (Note 10)

The formulation shall have a maximum collected dust of 30 mg by the gravimetric method or a maximum dust factor of 25 by the optical method of MT 171.1.

4.8 Flowability (MT172.2)

At least% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve.

4.9 Attrition resistance (MT 178.2)

Minimum:% attrition resistance.

5 Storage stability

5.1 **Low temperature stability**, if required (Note 11)

After storage at 0 ± 2 °C for 7 days, the determined average active ingredient content must not be lower than% relative to the determined average content found before storage

5.2 **Stability at elevated temperature** (MT 46.3)

After storage at 54 ± 2 °C for 14 days (Note 12), the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (4.1),
 - wet sieve test (4.3),
 - dispersibility (4.4),
 - suspensibility (4.5),
 - dustiness (4.7),
 - attrition resistance (4.9),
- as required.

Note 1 Depending on the manufacturing conditions, WGs may have different forms and particle size ranges. To describe specific formulations, it is recommended that information about the form (e.g. irregular shape, nearly spherical, cylindrical) is added and the nominal size range stated.

Note 2 Method(s) of identification and quantitation must be peer validated (ILV). If the methods have not yet been published then full details, with appropriate method validation data, must be submitted to FAO/WHO by the proposer.

Note 3 The clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. Method(s) of analysis must be peer validated (ILV).

Note 4 There may be cases where a minimum water content has to be specified.

Note 5 The method to be used shall be stated. If several methods are available, a referee method shall be selected.

Note 6 The wet sieve test detects coarse particles that may block filters and nozzles.

Note 7 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in MT 184.1.

Note 8 MT 184.1 allows gravimetric determination and assay of the active ingredient in the remaining 25 ml. The assay of some microbial active ingredients may be complex, and therefore the gravimetric determination is generally considered acceptable.

Note 9 The mass of sample to be used in the test should be specified at the highest rate recommended by the supplier. The test is to be conducted in CIPAC standard water D.

Note 10 Measurement of dustiness must be carried out on the sample "as received" and, where practicable, the sample should be taken from a newly opened container, because changes in the water content of samples may influence dustiness significantly. The optical method of MT 171.1, usually shows good correlation with the gravimetric method, and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute the gravimetric method shall be used.

Note 11 The cold temperature storage test is to be conducted in glass bottles as for MT 46.3.

Note 12 Unless other temperatures and/or times are specified. Refer to Section 9.4.6.2 of this Manual for alternative storage conditions.

9.6.2 WETTABLE POWDERS (WP)

Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those than given in the guidelines, without providing justification. From the “Notes” provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [Taxon] WETTABLE POWDER

[CIPAC number]/WP (month & year of publication)

1 Description

The material shall consist of an homogeneous mixture of technical [taxon], complying with the requirements of FAO/WHO specification [.....] in the form oftogether with filler(s) and any other necessary formulants. It shall be in the form of a fine powder free from visible extraneous matter and hard lumps.

In case there is no TK, the material shall contain [taxon], in the form oftogether with filler(s) and any other necessary formulants. It shall be in the form of a fine powder free from visible extraneous matter and hard lumps.

2 Active ingredient

2.1 Identity tests (Note 1)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 [Taxon] content (Note 1)

The [taxon] content shall be declared (insert appropriate unit) and, when determined, the average content measured shall not be less than the declared content.

3 Relevant impurities

3.1 Microbial contaminants (Note 2), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.2 Secondary compounds (Note 2), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.3 Chemical impurities (from the manufacturing process) (Note 2), if required

Maximum:(insert chemical name) g/kg

3.4 **Water** (MT 30.6), if required

Maximum: g/kg.

4 **Physical properties**

4.1 **Acidity** and/or **Alkalinity** (MT 191) or **pH range** (MT 75.3) (Note 3), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

4.2 **Wet sieve test** (MT 185)

Maximum:% retained on a 75 µm test sieve.

4.3 **Suspensibility** (MT 184.1) (Note 4)

A minimum of % of the ... [Taxon] content shall be in suspension after 30 min in CIPAC Standard Water D at 25 ± 5 °C (Notes 5).

4.4 **Persistent foam** (MT 47.3) (Note 6)

Maximum: ml after 1 min.

4.5 **Wettability** (MT 53.3)

The formulation shall be completely wetted in min without swirling.

5 **Storage stability**

5.1 **Low temperature stability** (Note 7) if required

After storage at 0 ± 2 °C for 7 days, the determined average active ingredient content must not be lower than% relative to the determined average content found before storage

5.2 **Stability at elevated temperature** (MT 46.3)

After storage at 54 ± 2 °C for 14 days (Note 8), the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (4.1),
 - wet sieve test (4.2),
 - suspensibility (4.3),
 - wettability (4.5),
- as required.
-

- Note 1 Method(s) of identification and quantitation must be peer validated (ILV). If the methods have not yet been published then full details, with appropriate method validation data, must be submitted to FAO/WHO by the proposer.
- Note 2 This clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. Method(s) of analysis must be peer validated (ILV).
- Note 3 The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 4 The formulation should be tested at the highest and lowest rates of use recommended by the supplier, provided this does not exceed the conditions given in method MT 184.1.
- Note 5 MT 184.1 allows for either gravimetric determination or assay of the active ingredient in the remaining 25 ml in the cylinder. As the assay of some microbial active ingredients may be complex, the gravimetric determination is considered acceptable.
- Note 6 The mass of sample to be used in the test should be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.
- Note 7 The cold temperature storage test is to be conducted in glass bottles or commercial packaging as as for MT 46.3.
- Note 8 Unless other temperatures and/or times are specified. Refer to Section 9.4.6.2 of this Manual for alternative storage conditions.

9.6.3 GRANULES (GR)

Introduction

These specifications are intended for granular products to be applied in dry form by machine. Granules formulated on commercially available fertilizers as carriers are excluded, if they are to be applied at full fertilizer rate.

Granules intended to be used in crop protection are formulated in many different ways depending on the physico-chemical properties of the active ingredient(s), the manufacturing equipment available and the nature of the carriers used. This can lead to products of differing physical properties. Furthermore, a wide range of application equipment is available in different parts of the world. In consequence, the establishment of internationally agreed specifications for granules is relatively more difficult than is the case for some other types of formulation.

Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those than given in the guidelines, without referring to section 4. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [Taxon] GRANULES

[CIPAC number]/GR (month & year of publication) (Note 1)

1 Description

The material shall consist of granules containing technical [taxon], complying with the requirements of FAO/WHO specification [.....], in the form of, together with suitable carriers and any other necessary formulants (Note 1). It shall be dry, free from visible extraneous matter and hard lumps, free-flowing, nearly dust-free or essentially non-dusty and intended for application by machine.

In case there is no TK, the material shall contain [taxon], in the form of, together with suitable carriers and any other necessary formulants. It shall be dry, free from visible extraneous matter and hard lumps, free-flowing, nearly dust-free or essentially non-dusty and intended for application by machine.

2 Active ingredient

2.1 Identity tests (Note 2)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 [Taxon] content (Note 2)

The [taxon] content shall be declared (insert appropriate unit) and, when determined, the average content measured shall not be less than the declared content

2.3 Rate of release of active ingredient, if required

Applicable only to slow release granules (GR), appropriate test method not available.

3 Relevant impurities

3.1 Microbial contaminants (Note 3), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.2 Secondary compounds (Note 3), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.3 Chemical impurities (from the manufacturing process) (Note 3), if required

Maximum:(insert chemical name) g/kg

3.4 Water (MT 30.6), if required

Maximum: g/kg.

4 Physical properties

4.1 Acidity and/or **Alkalinity** (MT 191) or **pH range** (MT 75.3) (Note 4), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

4.2 Pour and tap density (MT 186), if required

Pour density: to g/ml.

Tap density: to g/ml.

4.3 Nominal size range (MT 170)

The nominal size range of the formulation shall be declared (Note 5). Normally, the ratio of the lower to the upper limit should not exceed 1:4 (Note 6). Not less than 850 g/kg of the formulation shall be within the nominal declared size range.

4.4 Dustiness (MT 171.1)

The formulation shall have a maximum collected dust of 30 mg by the gravimetric method or a maximum dust factor of 25 by the optical method (Note 7).

4.5 Attrition resistance (MT 178.2)

Minimum% attrition resistance.

5 Storage stability

5.1 Low temperature stability (if required)

After storage at 0 ± 2 °C for 7 days, the determined average active ingredient content must not be lower than% relative to the determined average content found before storage

5.2 Stability at elevated temperature (MT 46.3)

After storage at 54 ± 2 °C for 14 days (Note 8 & 9), and the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (4.1),
- dustiness (4.4),
- attrition resistance (4.5),

as required.

Note 1 Where the specification does not include certain types of granule, the exclusions should be noted in the description.

Note 2 Method(s) of identification and quantitation must be peer validated (ILV). If the methods have not yet been published then full details, with appropriate method validation data, must be submitted to FAO/WHO by the proposer.

Note 3 This clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. Method(s) of analysis must be peer validated (ILV).

Note 4 The method to be used shall be stated. If several methods are available, a referee method shall be selected.

Note 5 e.g. 250 to 500 µm, 500 to 1,200 µm.

Note 6 Higher ratios increase the risk of segregation and adverse effects on the flow rate. This should be checked with the machine to be used. The purchaser should check that the nominal size range is suitable for his requirements, since different size ranges may affect biological activity.

Note 7 The optical method of MT 171.1, usually shows good correlation with the gravimetric method, and can, therefore, be used as an alternative where the equipment is available. Where the correlation is in doubt, it must be checked with the formulation to be tested. In case of dispute the gravimetric method shall be used.

Note 8 Unless other temperatures and/or times are specified. Refer to Section 9.4.6.2 of this Manual for alternative storage conditions.

Note 9 Samples of the formulation taken before and after the storage stability test should be analyzed together after the test in order to reduce the analytical error.

9.6.4 WATER DISPERSIBLE TABLETS (WT)

Introduction

Tablets are preformed solids of uniform shape and dimensions, usually circular, with either flat or convex faces. Their size and weight is determined by manufacturing and/or use requirements. For some physical tests the tablets must be broken and their fragments be used.

Water dispersible tablets (WT) are intended for application after disintegration and dispersion in water by conventional application equipment.

Dispersible tablets are often not coated or highly compacted and possess lower mechanical strength. They require commercial packaging that minimizes or eliminates mechanical stress during normal handling and transport. Selection of physical tests methods must take into account the commercial packaging of tablets.

Certain clauses are not applicable to effervescent tablets. These type of tablets, according to Pharm Eur are: (quote) "uncoated tablets generally containing acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide" (unquote). The excess of acid and base will mask possible acidity or alkalinity that are conveyed by the active ingredient or coformulants in the tablet. For this reason, the clauses for acidity/alkalinity or pH range are not applicable to effervescent tablets.

Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those than given in the guidelines, without referring to Section 4. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [Taxon] WATER DISPERSIBLE TABLETS

[CIPAC number]/WT (month & year of publication)

1 Description

The material shall consist of an homogeneous mixture of technical [taxon], complying with the requirements of FAO/WHO specification [...], in the form of together with carriers and any other necessary formulants. It shall be in the form of tablets for application after disintegration and dispersion in water. The formulation shall be dry, unbroken and free-flowing tablets, and shall be free from visible extraneous matter.

In case there is no TK, the material shall contain [taxon], in the form of together with carriers and any other necessary formulants. It shall be in the form of tablets for application after disintegration and dispersion in water. The formulation shall be dry, of unbroken and free-flowing tablets, and shall be free from visible extraneous matter.

2 Active ingredient (Note 1)

2.1 Identity tests

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2[Taxon] content (Notes 1 and 2)

The [taxon] content shall be declared (insert appropriate unit) and, when determined, the average content measured shall not be less than the declared content.

2.3 Tablet dose uniformity, if required

The [taxon] content, measured separately in ... tablets, shall have a relative standard deviation (RSD) of not more than ...%.

3 Relevant impurities (Note 1)

3.1 Microbial contaminants (Note 3), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.2 Secondary compounds (Note 3), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.3 Chemical impurities (from the manufacturing process (Note 3), if required

Maximum:(insert chemical name) g/kg

3.4 Water (MT 30.6), if required

Maximum: g/kg.

4 Physical properties

4.1 Acidity and/or Alkalinity (MT 191) or pH range (MT 75.3) (Notes 4, 5 and 6), if required (Note 7)

Maximum acidity: ... g/kg calculated as H₂SO₄.

Maximum alkalinity: ... g/kg calculated as NaOH.

pH range: ... to ...

- 4.2 **Disintegration of tablets** (MT 197) (Note 8)
For effervescent tablets (Note 7) or if required for non-effervescent
Maximum: ... % of residue after specified disintegration time
- 4.3 **Wet sieve test** (MT 185) (Note 9)
After complete disintegration of the tablet or a fragment of a tablet follows procedure (b) wet sieving of CIPAC MT 185.
Maximum: ... % retained on a 75 µm test sieve.
- 4.4 **Suspensibility** (MT 184.1) (Notes 5, 10, 11 and 12)
A minimum of ...% shall be in suspension after 30 min in CIPAC Standard water D at 25 ± 5°C.
- 4.5 **Persistent foam** (MT 47.3) (Notes 5 and 13)
Maximum: ... ml after 1 minute.
- 4.6 **Tablet integrity** (Note 14)
No broken, soft or sticky tablets should be present
Fragments: yes/no
Soft/sticky: yes/no
- 4.7 **Attrition resistance of tablets** (MT 178.2) (Notes 15 & 16) if required
Minimum attrition resistance:%.

5 Storage stability

- 5.1 **Low temperature stability** (if required)
After storage at 0 ± 2 °C for 7 days, the determined average active ingredient content must not be lower than% relative to the determined average content found before storage
- 5.2 **Stability at elevated temperature** (MT 46.3)

After storage at $54 \pm 2^{\circ}\text{C}$ for 14 days (Note 17) without pressure (Note 18), the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (4.1),
- disintegration of tablets (4.2)
- wet sieve test (4.3),
- suspensibility (4.4)
- tablet integrity (4.6),
- attrition resistance of of tablets (4.7),

as required.

Note 1 Measuring the active ingredient content or relevant impurities requires a representative sample of the tablet. A representative sample is obtained by grinding one or several tablets and then sampling the homogeneous powder.

Note 2 Method(s) of identification and quantitation must be peer validated (ILV). If the methods have not yet been published then full details, with appropriate method validation data, must be submitted to FAO/WHO by the proposer.

Note 3 The clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. Method(s) of analysis must be peer validated (ILV).

Note 4 The method to be used shall be stated. If several methods are available, a referee method shall be selected.

Note 5 If tests need to be conducted at use-rate a tablet may be broken and fragments be used. The following tests may require breaking tablets:

Point	Property	CIPAC	Rate
4.1	Acidity or alkalinity	MT 191	10 g add 100 ml
	pH range	MT 75.3	1 g make up 100 ml
4.3	Wet sieve	MT 185	Maximum recommended use-rate
4.4	Suspensibility	MT 184.1	
4.5	Persistent foam	MT 47.3	

Tablets or fragments of tablets must be completely disintegrated for the purposes of CIPAC methods MT 191, MT 75.3, MT 185, MT 184.1 and MT 47.3.

Note 6 Before performing the CIPAC test, it is necessary to let the tablet(s) or fragments of a tablet disintegrate completely in a 250 ml beaker containing 50 ml of the water required by the method. A gentle stirring may be needed.

- Note 7 This clause is not applicable to effervescent tablets, as they incorporate an effervescent system.
- Note 8 The determination of an end-point of disintegration for tablets is difficult and subjective as tablets or fragments of tablets are not visible in bubbling and opaque suspensions. Instead of an endpoint of dissolution this method measures a residue after a fixed disintegration time.
- Note 9 Weigh out the appropriate amount of the tablet(s) to prepare 100 to 250 ml of a dispersion of the maximum recommended use rate. Break or cut the tablet if necessary, do not grind. Then add the required tablet(s) or fragment(s) to 100 - 250 ml of CIPAC standard water D at $25 \pm 5^{\circ}\text{C}$ and stir gently at 200 rpm for the time specified by the manufacturer. If the stirring time is not specified by the manufacturer of the tablet, then stir for 10 minutes. Proceed with the method as per (b) Wet sieving.
- Note 10 Before performing the suspensibility test, it is necessary to let the tablet(s) or fragment(s) of a tablet disintegrate completely in a 250 ml beaker containing 50 ml of the water required by the method. Therefore weigh out an appropriate amount of the tablet(s) or fragment(s) required to make 250 ml of a suspension in water. Break or cut the tablet if necessary, do not grind. Add the weighed sample to a 250 ml beaker containing 50 ml CIPAC standard water D at $25 \pm 5^{\circ}\text{C}$ and stir gently with a spatula until the sample is fully dispersed. Fill the suspension carefully in the 250 ml measuring cylinder and rinse the beaker with CIPAC standard water D to get a final volume of 250 ml. Stopper the cylinder and proceed with the method as per (b) Determination of sedimentation.
- Note 11 The formulation should be tested at the maximum use rate recommended by the supplier. If the dimensions of the fragments do not allow exact weighing of the required amount an excess of up to 120 % of the recommended use rate is allowed.
- Note 12 As the assay of some microbial active ingredients may be complex, the gravimetric determination is considered acceptable.
- Note 13 Grind the tablet or fragments of it with a mortar and pestle to a fine powder. Weigh out an appropriate amount of powder required for 200 ml of water. Fill 150 – 180 ml of Standard water D into a 250 ml beaker. Add the powder to the beaker and stir gently with a spatulum until the tablet/fragments is fully dissolved. Fill the solution carefully in the 250 ml measuring cylinder and rinse the beaker with CIPAC standard water D to get a final volume of 200 ml. Stopper the cylinder and follow the method.
- Note 14 This requirement method describes the physical state of the tablet for example whether it is broken or dusty with fragments or soft and sticky. Visual observation only. Unless otherwise indicated, at least one pack/package containing multiple tablets should be inspected for color, texture, fragments and dust.
- Note 15 An attrition test is only required for bulk packaged tablets with a diameter < 1 cm that may exhibit surface wear during transport and handling.
- Note 16 The scope of CIPAC MT 178.2 is to measure attrition resistance of water dispersible granules but the method is considered to be applicable to DT, WT and ST with a diameter of < 1cm as well.
- Note 17 Unless other temperatures and/or times are specified. Alternative conditions are: 6 weeks at $45 \pm 2^{\circ}\text{C}$; 8 weeks at $40 \pm 2^{\circ}\text{C}$; 12 weeks at $35 \pm 2^{\circ}\text{C}$ or 18 weeks at $30 \pm 2^{\circ}\text{C}$. Whole tablets must be stored. After storage tablets may be broken for tests as specified in Note 5.
- Note 18 Without pressure means that the test is performed as specified by CIPAC MT 46.3, but no pressure is applied to the sample during aging.

9.6.5 **SUSPENSION CONCENTRATES (SC)**

Introduction

SC is the designation for a stable suspension of active ingredient(s) in an aqueous continuous phase, intended for dilution with water before use.

The parameters which best describe the performance characteristics are:

- pourability test (to ensure that the SC can be poured from its container);
- water dispersibility (spontaneity of dispersion), suspensibility, wet sieve and persistent foam tests (to ensure the sprayability of the diluted suspension).

Some other physical properties, especially particle size range and viscosity, however, are excluded from the specification for the following reasons:

- particle size range: There is no internationally accepted, simple method for determination of the particle size range of SCs. Moreover, particle size range is described and limited in the specification by a number of easily quantifiable parameters which are influenced by it. These parameters are the wet sieve analysis, suspensibility, pourability and water dispersibility.
- viscosity: Although viscosity is also an important property, it cannot readily be determined by simple means. Since most SCs show non-Newtonian flow characteristics, viscosity is only one part of a much more complex rheology (flow properties). Pourability and water dispersibility parameters included in the specification adequately describe the rheological properties.

Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those than given in the guidelines, without providing justification. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [Taxon] SUSPENSION CONCENTRATE

[CIPAC number]/SC (month & year of publication)

1 Description

The material shall consist of a suspension of fine particles of technical [taxon], complying with the requirements of FAO/WHO specification, , in the form ofin an aqueous phase together with suitable formulants. After gentle agitation the material shall be homogeneous (Note 1) and suitable for further dilution in water.

In case there is no TK, the material shall contain [taxon], in the form ofin an aqueous phase together with suitable formulants. After gentle

agitation the material shall be homogeneous (Note 1) and suitable for further dilution in water.

2 Active ingredient

2.1 Identity tests (Note 2)

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 [Taxon] content (Note 2)

The [taxon] content shall be declared (insert appropriate unit, Note 3) and, when determined, the average content measured shall not be less than the declared content.

3 Relevant impurities

3.1 Microbial contaminants (Note 4), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.2 Secondary compounds (Note 4), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.3 Chemical impurities (from the manufacturing process) (Note 4), if required

Maximum:(insert chemical name) g/kg

4 Physical properties

4.1 Acidity and/or Alkalinity (MT 191) or pH range (MT 75.3) (Note 5), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

4.2 Pourability (MT 148.1)

Maximum "residue":%.

4.3 Spontaneity of dispersion (MT 160) (Note 6)

A minimum of% shall be in suspension after 5 min in CIPAC Standard Water D at 30 ± 2 °C (Note 7).

4.4 Suspensibility (MT 184.1) (Note 6)

A minimum of% of the formulation content shall be in suspension after 30 min in CIPAC Standard Water D at 25 ± 5 °C (Note 7).

4.5 **Wet sieve test** (MT 185) (Note 8)

Maximum:% of the formulation shall be retained on a μm test sieve.

4.6 **Persistent foam** (MT 47.3) (Note 9)

Maximum: ml after 1 min.

4.7 **Particle size distribution** (MT 187), if required

...% of particles shall be in the range ... to ... (Note 10)

5 **Storage stability**

5.1 **Stability at 0 °C** (MT 39.3)

After storage at 0 ± 2 °C for 7 days, the determined average active ingredient content must not be lower than the specified minimum active ingredient content (Note 11) the formulation shall continue to comply with clauses for:

- suspensibility (4.4),
- wet sieve test (4.5),

as required.

5.2 **Stability at elevated temperature** (MT 46.3)

After storage at 54 ± 2 °C for 14 days (Note 11), the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (4.1),
- pourability (4.2),
- spontaneity of dispersion (4.3),
- suspensibility (4.4),
- wet sieve test (4.5),

as required.

Note 1 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or of sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, by gentle shaking of the commercial container (for example by inverting the closed container several times). Large containers must be opened and stirred adequately. After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer ("cake") is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a sample taken after the recommended homogenization procedure.

Note 2 Method(s) of quantitation must be peer validated (ILV). If the methods have not yet been published then full details, with appropriate method validation data, must be submitted to FAO/WHO by the proposer.

Note 3 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre and in calculation of the active ingredient content (in g/l) if methods other than OECD 109 or MT 3.3 are used. If the buyer requires both g/kg and g/l at 20 °C, then in case of dispute the analytical results shall be calculated as g/kg.

- Note 4 The clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. Method(s) of analysis must be peer validated (ILV).
- Note 5 The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6 As the assay of some microbial active ingredients may be complex, the gravimetric determination is considered acceptable.
- Note 7 Unless other temperatures and/or times are specified.
- Note 8 This test detects coarse particles (e.g. caused by crystal growth) or agglomerates (crust formation) or extraneous materials which could cause blockage of spray nozzles or filters in the spray tank.
- Note 9 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D.
- Note 10 Percentages may be specified in one or more ranges, as appropriate to the product. Laser diffraction is not always suitable to measure the particle size distribution of liquid formulations. This should be evaluated by Wet sieve test (MT 185) and Suspensibility (MT 184.1).
- Note 11 Unless other temperatures and/or times are specified. Refer to Section 9.4.6.2 of this Manual for alternative storage conditions.

9.6.6 SUSPENSION CONCENTRATES FOR SEED TREATMENT (FS) (Flowable concentrates for seed treatment)

The guidelines for seed treatment formulations do not apply to formulations intended for film-coating or pelleting of seeds. They include special clauses, related to their use pattern, although some of the corresponding test methods are not yet developed. The influence of treatment on germination is of major importance but it is not the subject of a specification clause because no test method is applicable to all types of seeds. To avoid adverse effects, users should apply the formulation strictly according to the recommendations of the manufacturer and should not treat seeds for which effect on germination is not known. Treated seeds should be stored in a suitable container and should be protected from excessive temperature and moisture.

Note for preparation of draft specifications. Do not omit clauses or insert additional clauses, nor insert limits that are more lax than those than given in the guidelines, without providing justification. From the “Notes” provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [Taxon] SUSPENSION CONCENTRATE FOR SEED TREATMENT (Note 1)

[CIPAC number]/FS (month & year of publication)

2.1 Description

The material shall consist of a suspension of fine particles of technical [taxon], complying with the requirements of FAO specification, in the form of in an aqueous phase together with suitable formulants, including colouring matter (Note 1). After gentle stirring or shaking, the material shall be homogeneous (Note 2) and suitable for further dilution with water if necessary.

In case there is no TK, the material shall contain [taxon], in the form of in an aqueous phase together with suitable formulants, including colouring matter (Note 1). After gentle stirring or shaking, the material shall be homogeneous (Note 2) and suitable for further dilution with water if necessary.

2.2 Active ingredient**2.1 Identity tests (Note 3)**

The active ingredient shall comply with an identity test and, where the identity remains in doubt, shall comply with at least one additional test.

2.2 [Taxon] content (Note 3)

The [taxon] content shall be declared (insert appropriate unit), (Note 4) and, when determined, the average content measured shall not be less than the declared content.

3 Relevant impurities**.1 Microbial contaminants (Note 5), if required**

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Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.2 Secondary compounds (Note 5), if required

Maximum:(insert appropriate unit) of [taxon] content found under 2.2.

3.3 Chemical impurities (from the manufacturing process) (Note 5), if required

Maximum:(insert chemical name) g/kg

4 Physical properties

4.1 Acidity and/or Alkalinity (MT 191) or pH range (MT 75.3) (Note 6), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

4.2 Pourability (MT 148.1)

Maximum "residue":%.

4.3 Wet sieve test (MT 185) (Note 7)

Maximum:% retained on aµm test sieve.

4.4 Persistent foam (MT 47.3) (Note 8) if required

Maximum: ml after 1 min.

4.5 Suspensibility (MT 184.1) (Note 9), if required

A minimum of% of the formulation content shall be in suspension after 30 min in CIPAC Standard Water D at 25 ± 5 °C (Note 10).

4.6 Particle size distribution (MT 187), if required

...% of particles shall be in the range ... to ... (Note 11)

4.7 Adhesion to seeds (MT 194)

The manufacturer shall declare for a representative type of seeds for which the seed treatment formulation is recommended, the minimum percentage of the [taxon] remaining on the seeds after the test.

5 Storage stability

5.1 Stability at 0 °C (MT 39.3)

After storage at 0 ± 2 °C for 7 days, the determined average active ingredient content must not be lower than% relative to the determined average content found before storage and the formulation shall continue to comply with the clause for: wet sieve test (4.3).

5.2 Stability at elevated temperature (MT 46.3)

After storage at 54 ± 2 °C for 14 days (Note 12), the formulation shall continue to comply with the clauses for:

- acidity, alkalinity or pH range (4.1),
- pourability (4.2),

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- wet sieve test (4.3),
 - suspensibility (4.5),
 - adhesion to seeds (4.7),
- as required.
-

Note 1 The influence of treatment on germination is of major importance but it is not the subject of a specification clause because no test method is applicable to all types of seeds. To avoid adverse effects, users should apply the formulation strictly according to the recommendations of the manufacturer and should not treat seeds for which effect on germination is not known. Treated seeds should be stored in a suitable container and should be protected from excessive temperature and moisture.

The formulation is expected contain a dye or pigment that permanently colours the seed after treatment (red is recommended). For special purposes however, the dye/pigment can be added at a later stage. In some countries, there may be a legal requirement that a specific colour shall be used. The same colour must not be used for denaturing seeds intended for use as livestock feeding stuffs.

Note 2 Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, suspension concentrates usually develop a concentration gradient from the top to the bottom of the container. This may even result in the appearance of a clear liquid on the top and/or sediment on the bottom. Therefore, before sampling, homogenize the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, gently shake the commercial container (for example by inverting the closed container several times, large containers must be opened and stirred adequately). After this procedure, the container should not contain a sticky layer of non-dispersed matter at the bottom. A suitable and simple method of checking for a non-dispersed sticky layer ("cake") is by probing with a glass rod or similar device adapted to the size and shape of the container. All the physical and chemical tests must be carried out on a sample taken after the recommended homogenization procedure.

Note 3 Method(s) of quantitation must be peer validated (ILV). If the methods have not yet been published then full details, with appropriate method validation data, must be submitted to FAO/WHO by the proposer.

Note 4 Unless homogenization is carried out carefully, it is possible for the sample to become aerated. This can lead to errors in the determination of the mass per millilitre, and in calculation of the active ingredient content (in g/l) if methods other than OECD 109 or MT 3.3 are used. If the buyer requires both g/kg and g/l at 20 °C, then in case of dispute the analytical results shall be calculated as g/kg.

Note 5 The clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. Method(s) of analysis must be peer validated (ILV).

Note 6 The method to be used shall be stated. If several methods are available, a referee method shall be selected.

Note 7 This test should detect coarse particles (e.g. caused by crystal growth) or extraneous materials which could cause blockage of spray nozzles or filters of the application equipment.

Note 8 The mass of sample to be used in the test should correspond to the highest rate of use recommended by the supplier provided it is within the scope of the method. The test is to be conducted in CIPAC standard water D.

Note 9 Suspensibility is not applicable for FS which are used without dilution and the clause can be removed. In cases where the dilution rate complies with the upper limit of MT 184.1 (10 %), gravimetric assay is deemed acceptable for determination of the mass of active ingredient still in suspension.

Note 10 Unless other temperatures and/or times are specified.

Note 11 Percentages may be specified in one or more ranges, as appropriate to the product. Laser diffraction is not always suitable to measure the particle size distribution of liquid formulations. This should be evaluated by Wet sieve test and Suspensibility or Dispersion stability.

9.13 SPECIFICATION GUIDELINES FOR MICROBIAL PESTICIDES

Note 12 Unless other temperatures and/or times are specified. Refer to Section 9.4.6.2 of this Manual for alternative storage conditions.

Appendix A – H

- Appendix A** Check-list for submission of application for development of FAO and or WHO specifications (refer to 2016 Manual)
- Appendix B** Supply and certification of reference substances (refer to 2016 Manual)
- Appendix C** Glossary of terms, amended 73
- Appendix D** Coding of active ingredients, specifications and method status (refer to 2016 Manual)
- Appendix E** CropLife International codes for technical and formulated pesticides (refer to 2016 Manual)
- Appendix F** Declarations of interests and confidentiality by FAO/WHO experts (refer to 2016 Manual)
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- Appendix J:** Calculation of expanded tolerances for the active ingredient content of mixed solid formulations (refer to 2016 Manual)

GLOSSARY OF TERMS

Term	Definition
Active ingredient(s)	Active ingredient means the part of the product that provides the pesticidal action..
Additive	An ingredient, other than the MPCA, intentionally added to a formulation
Agglomerate	Particles bound firmly together.
Aggregate	Particles adhering loosely together.
ALINA	Asociación Latinoamericana de la Industria Nacional de Agroquímicos
AOAC	AOAC International, formerly the Association of Official Analytical Chemists.
Apparent density	see Density.
Attrition	The wearing away of the surface of a solid by friction or impact, particularly by particle-to-particle interaction. See also Friability.
Batch	A defined quantity of material produced in a single series of operations.
Bt	<i>Bacillus thuringiensis</i>
Bulk density	see Density.
CA	Chemical Abstracts®.
Carrier	A solid formulant added to a technical grade active ingredient as an absorbent or diluent.
CAS® No.	Chemical Abstracts Service® Registry number.
CFU	Colony forming units
CIPAC	Collaborative International Pesticides Analytical Council.
Co-formulant	Co-formulant means a non-active ingredient component of a formulated product.
CropLife International	Formerly known as GCPF and also GIFAP.
Closed meeting	A meeting of the JMPS dealing with confidential information, where participation is confined exclusively to experts appointed by FAO/WHO. Proposers and/or others may be invited by FAO/WHO for consideration of specific issues.
Compatibility	The absence of adverse or unwanted reactions/interactions (physical, chemical or biological) when chemicals or formulations are mixed together.
Contaminant (biological)	For the purposes of this Manual, any unexpected biological entity or parts thereof (other than components which may be considered as chemical contaminants), occurring by any means in a technical or formulated pesticide. See also Impurity.
Contaminant (chemical)	For the purposes of this Manual, an unexpected substance or material, or a mixture, occurring by any means in a technical or formulated pesticide. See also Impurity.
Cream	An opaque layer accumulating at the top or the bottom of an emulsion.
Density	Mass per unit volume of substance at a stated temperature. The units of volume and mass must be stated, e.g. grams per millilitre at 20 ± 2°C. Bulk density of powders and granules refers to their apparent density, including air, etc., incorporated into the bulk. Bulk density values are affected by settling (e.g. by tapping), compaction or pressure.
Device	For the purposes of this Manual, any physical or mechanical entity which is loaded with a quantity of pesticide, ready for immediate use without dilution, mixing, etc.
Dispersibility	The ease with which an insoluble solid or liquid material may be dispersed uniformly in a liquid.
Dust	A fine solid material, potentially airborne, with particle size less than 50 µm.
ECCA	European Crop Care Association

GLOSSARY OF TERMS

Term	Definition
Ecotoxicological profile	A summary of data on ecotoxicological endpoints that may have consequences for aquatic and terrestrial organisms, due to possible exposure dependent on the intended uses, for a particular pesticide.
ELINCS No.	European List of Notified Chemical Substances number (for new chemicals).
EINECS No.	European Inventory of Existing Commercial Chemical Substances number (for existing chemicals).
Equivalence (equivalent)	<p>The FAO/WHO International Code of Conduct on Pesticide Management defines equivalence broadly as: "Equivalence means the determination of the similarity of the impurity and toxicological profile, as well as of the physical and chemical properties, presented by supposedly similar technical material originating from different manufacturers, in order to assess whether they present similar levels of risk."</p> <p>In practice, determination of equivalence by the JMPS involves a comparative assessment of the impurity and toxicological profiles, the manufacturing specification as well as data for the physical and chemical properties of technical grade active ingredients (TC/TK) produced by different manufacturers or by different manufacturing routes or on different manufacturing sites. The comparison is made with the reference profile in each case. If the materials can share a common specification, and if the degree of similarity is such that the material(s) produced by the additional manufacturer(s), or the new manufacturing route(s) or sites, present(s) risks that are considered to be no greater than the TC/TK on which the reference profiles are based, the additional/new material(s) can be considered equivalent to the original TC/TK.</p> <p>Formulations of a particular pesticide are regarded as equivalent if they are prepared from equivalent TCs/TKs and conform to the same specification but this does not imply that they necessarily provide equal efficacy or present identical risks in a particular application.</p>
Endpoint	Measurable physico-chemical, ecological or toxicological characteristic or parameter of the test system (usually an organism) that is chosen as the most relevant assessment criterion (e.g. temperature of decomposition, death in an acute test or tumour incidence in a chronic study).
Evaluator	An expert attending the JMPS, assigned by FAO/WHO to perform the evaluation of data provided in support of a proposed FAO/WHO specification, or of a proposed extension to an existing specification, following the procedural principles laid down in the current edition of this Manual.
FAO	Food and Agriculture Organization of the United Nations.
FAO/WHO specifications	International standards of quality for pesticides evaluated and published by FAO/WHO.
Filler	An inert solid formulant used as a diluent.
Fines	see Undersize particles.
Flammable	Readily ignitable.
Flammable liquid	A liquid having a flash point of not less than 21°C and not more than 55°C, as determined by a closed cup method. See also Highly flammable liquid.
Flash point	The lowest temperature at which a material forms a flammable vapour/air mixture under standard conditions.
Flocculation	Aggregation of particles suspended in a liquid.
Flowability	Ability of materials to flow freely under stated conditions.
Formulant	Any substance, other than a technical grade active ingredient, intentionally incorporated in a formulation.
Formulation	Formulation means the combination of various ingredients designed to render the product useful and effective for the purpose claimed and for the envisaged mode of application.

GLOSSARY OF TERMS

Term	Definition
Friability	The tendency of a solid, such as a granule or tablet, to disintegrate by crumbling. See also Attrition.
GMO	Genetically modified organisms (GMOs) are organisms (i.e. plants, animals or microorganisms) in which the genetic material (DNA) has been altered by genetic engineering.
Hazard	Inherent property of an agent or situation having the potential to cause adverse effects when an organism, system, or (sub)population is exposed to that agent. See also Risk.
Highly flammable liquid	A liquid having a flash point of less than 21°C as determined by a closed cup method. See also Flammable liquid.
Impurity (biological)	A biological entity or parts thereof (other than components which may be considered as chemical contaminants) arising from manufacture of an active ingredient derived from a biological source. For the purposes of this Manual, the definition does not include impurities derived from formulants or other additives. See also Contaminant and Relevant impurity.
Impurity (chemical)	A by-product arising from manufacture of the active ingredient or derived from the active ingredient during formulation or storage. For the purposes of this Manual, the definition does not include impurities derived solely from formulants or other additives, before or during storage. See also Contaminant and Relevant impurity.
INCI No.	International Nomenclature of Cosmetic Ingredients number.
Independent laboratory validation	See peer validation.
Interested parties	Organizations or individuals, such as commercial companies, pesticide registration authorities, non-governmental organizations, and scientists concerned with pesticide specifications.
ISO	International Organization for Standardization, which publishes common names for pesticides which have generally been developed by the British Standards Institution (BSI). E-ISO indicates the English form of the name and F-ISO indicates the French form. French names are identified as masculine (m) or feminine (f) as appropriate.
IUPAC	International Union of Pure and Applied Chemistry.
JMPR	FAO/WHO Joint Meeting on Pesticide Residues. Comprised of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues.
JMPS	FAO/WHO Joint Meeting on Pesticide Specifications. A group of experts appointed by FAO and WHO to deal with pesticide specifications.
Lot	Part or all of a consignment that may comprise part of, all of, one manufacturing batch.
Lump	A macroscopic piece of solid matter without regular shape.
Manual	The current edition or revision of the Manual on the development and use of FAO/WHO specifications for pesticides.
Manufacturer	Manufacturer means a corporation or other entity in the public or private sector (including an individual) engaged in the business or function (whether directly or through an agent or entity controlled by or under contract with it) of manufacturing a pesticide active ingredient

GLOSSARY OF TERMS

Term	Definition
Manufacturing specification	Minimum purity of the active ingredient in a technical grade active ingredient together with the identity and maximum concentrations of all impurities (including "unknowns") produced by a manufacturer using a single process, derived from analysis of representative production batches. In general, the impurities are those with manufacturing specification limits at or above 1 g/kg but lower limits apply to exceptionally hazardous impurities. Where the same active ingredient is produced at different sites by the same manufacturer and manufacturing route, the profile should encompass all sites. Where the manufacturing route differs between sites, or the manufacturers differ, the impurity profiles should be defined separately. Whereas the minimum purity of the active ingredient and on identity and maximum levels of relevant impurities after evaluation are published in the specification, the information on non-relevant impurities is kept confidential.
Metabolites	Metabolites include products resulting from degradative and biosynthetic reactions taking place within the microorganism or other organisms used to produce the microorganism of interest.
Microbial impurity, microbial contaminants,	Microbiological contamination refers to the non-intended or accidental introduction of microbes such as bacteria, yeast, , virus, prions, protozoa or their toxins and by-products into a.MPCA or MPCP
Microbial Pest Control Agents and Products (MPCA and MPCP)	MPCA and MPCP: for microbial pest control agents and -products and are used to differentiate these kind of pesticides from the synthetic chemical ones ("pesticides" in general), botanicals (plant extracts) and semiochemicals (pheromonones). MPCA can be defined as: A microorganism (protozoan, fungus, bacterium, virus, or other microscopic self-replicating biotic entity) (revised ISPM Pub. No. 3. IPPC, 2005) and any associated metabolites, to which the effects of pest control are attributed (OECD, 2008). A microorganism active substance may contain viable and/or non-viable microorganisms. It can contain relevant metabolites/toxins produced during cell proliferation (growth), material from the growth medium, provided none of these components have been intentionally altered MPCP can be defined as: A product containing an MPCA that is registered or labelled with instructions for direct use or application for pest control purposes.
Minimum data requirements	Data required to evaluate proposals for FAO/WHO specifications. Such data are the minimum considered necessary to evaluate all aspects of the specification.
Non-flammable	Not readily ignitable, with a flash point above 55°C as determined by a closed cup method.
Open meeting	A meeting jointly organized by JMPS and CIPAC where, in addition to experts invited by FAO/WHO, participation is open to anyone who wishes to attend.
Oversize particles	Particles of a solid material larger than a specified size.
Peer validation (also known as Independent laboratory validation ILV)	Validation of an analytical method by a (peer) laboratory operating independently from that of the originator of the method. The two laboratories may belong to the same organisation, as long as the analysts, equipment, etc., are distinct and operate separately and without collusion for the validation. The validation process will follow the peer verification procedure of AOAC International (or similar).

GLOSSARY OF TERMS

Term	Definition
Pesticide	<p>Pesticide means any substance, or mixture of substances of chemical or biological ingredients intended for repelling, destroying or controlling any pest, or regulating plant growth.</p> <p>In the context of the Manual, the term includes any substance, or mixture of substances, or micro-organisms including viruses, intended for repelling, destroying or controlling any pest, including vectors of human or animal disease, nuisance pests, unwanted species of plants or animals causing harm during or otherwise interfering with the production, processing, storage, transport, or marketing of food, agricultural commodities, wood and wood products or animal feeding stuffs, or which may be administered to animals for the control of insects, arachnids or other pests in or on their bodies. The term includes substances intended for use as insect or plant growth regulators; defoliants; desiccants; agents for setting, thinning or preventing the premature fall of fruit; and substances applied to crops either before or after harvest to protect the commodity from deterioration during storage and transport. The term also includes pesticide synergists and safeners, where they are integral to the satisfactory performance of the pesticide. The term “technical pesticide” refers to technical materials and technical concentrates. The term “formulated pesticide” refers to any formulation containing a pesticide.</p>
Phytotoxic	<p>Phytotoxicity is the capacity of a compound to cause temporary or long-lasting damage to plants. The damage may be general or restricted to certain species or cultivars of plants. Phytotoxic impurities or contaminants in a herbicide may extend the range of plants damaged beyond that expected.</p>
Proposer	<p>Any manufacturer, group of manufacturers, or interested party, which submits a draft specification and a data package, to FAO/WHO for evaluation, in support of a new specification or for extension of an existing specification.</p>
Reference specification	<p>The current published specification for a pesticide, where this has been developed according to evaluation procedures similar to that given in this Manual (i.e. 1999-on for FAO specifications and 2002-on for WHO specifications). The reference specification is subject to review and may be revised in the light of emergent information, or to incorporate the formulations of a subsequent manufacturer. The reference specification is used as the first criterion in the determination of equivalence of a technical grade active ingredient and/or formulation of a parallel or subsequent manufacturer.</p>
Reference profile	<p>The purity/impurity, toxicological and ecotoxicological profiles upon which the original specification for a technical grade active ingredient is based.</p> <p>The reference profiles are used for the determination of equivalence. A reference profile is not amended by the data supporting additional technical grade active ingredients that are subsequently judged to be equivalent but, following a review of specifications by the JMPS, a new reference profile may supersede an earlier one.</p> <p>Generally, the reference profile of impurities relates to the technical grade active ingredient supported by the most complete toxicological and ecotoxicological profiles.</p>
Release date	<p>The date from which the supplier guarantees a shelf-life of at least 2 years, unless stated otherwise, under actual conditions of storage in the area where the technical grade active ingredient or formulation is to be marketed.</p>

GLOSSARY OF TERMS

Term	Definition
Relevant impurity	A by-product of the manufacture or storage of a pesticide which, compared with the active ingredient, is toxicologically significant to health or the environment, is phytotoxic to treated plants, causes taint in food crops, affects the stability of the pesticide, or causes any other adverse effect. Water may be a relevant impurity if it can adversely affect the stability of the pesticide or the manufacture of a satisfactory formulation. Insoluble material may also be a relevant impurity in a TC/TK if formulations to be prepared from them would block spray filters/nozzles, or fail the wet sieve test, for example. An impurity may be non-relevant in one pesticide or product and relevant in another, even though it occurs in both, because relevance is determined by impurity hazards relative to those of the active ingredient.
Relevant metabolites	Metabolites that are of concern for human or animal health and/or the environment.
Relevant additive/stabilizer	Compounds added to a MPCP in relatively small amounts to effect a desired property (additive) or enhance the stability of the MPCA (stabilizer)
Risk	The probability of an adverse effect in an organism, system, or (sub)population caused under specified circumstances by exposure to an agent.
Sedimentation	The fall of particles in a continuous medium (usually liquid for specification purposes).
Seeds	The term "seeds" as used in this Manual with regard to seed treatment encompasses all kind of plant material that can be sown, e.g. seeds of cereals, "seed" potatoes, stem parts of cassava etc.
Sieving	Separation of particles according to their size by the use of sieves.
Secondary compound	Small organic molecules produced by an organism that are not essential for their growth, development and reproduction.
Seed treatment	Seed treatment refers to the application of fungicide, insecticide, or a combination of both, to seeds so as to disinfect and disinfest them from seed-borne or soil-borne pathogenic organisms and storage insects (cited after ecoport.org).
Size distribution	The mass or numerical frequency distribution of the particles of a solid particulate material.
Size range	Lower and upper limits in size of a particulate material.
Specification	The Code of Conduct on Pesticide Management broadly defines "Specification means the parameters and criteria defining the physical appearance and physical and chemical properties of technical and formulated pesticides linked with hazard and risk profiles". For more details see Section 1.1., Scope of Specifications. FAO and WHO specifications together with the evaluation reports are published on the respective websites of these two organizations.
Subsequent, additional or parallel manufacturer	Any pesticide manufacturer other than the proposer of the original specification.
Surfactant	A formulant which reduces the interfacial tension of two boundary surfaces, thereby increasing the emulsifying, spreading, dispersibility and/or wetting properties of liquids or solids.
Tank mix	Two or more formulations mixed in the spray tank (including non-pesticide formulations e.g. liquid fertilizers) .
Tap density	see Density.
Taxon	In the framework of this guideline on microbial pest control product specifications, the term Taxon is used as a proxy for the full taxonomic designation of bacteria, viruses etc.
Tolerance	Permitted limits of variation for active ingredient content from a given value. Known as "certified limits" in some countries.
Toxicity	Inherent property of an agent to cause an adverse biological effect.

GLOSSARY OF TERMS

Term	Definition
Toxicological profile	A summary of data on toxicological endpoints that may have consequences for human health, due to exposure <i>via</i> various routes, for a particular pesticide.
Undersize particles	Particles of a solid material smaller than a specified size.
Validation	Process by which the reliability and relevance of a particular approach, method, process, or assessment is established for a defined purpose.
WHO	World Health Organization.
WHOPES	WHO Pesticide Evaluation Scheme.
WHO PQT-VC	WHO Prequalification Team Vector Control Group (PQT-VC)