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Manual on the development and use of FAO and WHO specifications for chemical pesticides

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PROCEDURES FOR HANDLING CONFIDENTIAL PROPRIETARY PESTICIDE DATA AND POTENTIAL CONFLICTS OF INTEREST BY THE FAO/WHO JOINT MEETING ON PESTICIDE SPECIFICATIONS

This statement has been prepared to ensure and verify the transparency of the process of data evaluation by the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS) (a process essential for the development of internationally acceptable specifications for pesticides), whilst complying with the legitimate need of industry to protect trade secrets (e.g. the results of their research, confidential business information).

- a) The proposer of a specification is asked to provide all pertinent data specified in Sections 3.1, 3.2 and 3.3 of this Manual, together with any other information justifiably required by the Food and Agriculture Organization of the United Nations (FAO) and/or the World Health Organization (WHO) for the purposes of the JMPS. Confidential information pertaining to the manufacturing process and other trade secrets must be identified clearly by the proposer, so that this information will not be published in the evaluation summary or inadvertently divulged to third parties.
- b) Where a manufacturer makes available confidential proprietary data or information, for the purposes of evaluation by the JMPS, FAO and WHO undertake to respect and safeguard the data from unauthorized release or disclosure and to provide the necessary facilities or safeguard systems, at FAO headquarters in Rome or WHO headquarters in Geneva, to ensure the proper handling and security of the above-mentioned data.
- c) The data package received by FAO or WHO for evaluation will be sent to the expert, participating in the JMPS, to whom the compound has been assigned for evaluation for consideration by the forthcoming closed meeting (see glossary).
- d) When FAO or WHO arranges the sending of or sends confidential proprietary data or information to a nominated expert participating in the JMPS, it will instruct the expert not to make copies of all or parts of the data, nor to share or use the data for any other purpose than evaluation of the proposed specification and the corresponding presentation of the draft evaluation to the closed meeting.
- e) Experts participating in the JMPS will be required to take all appropriate measures to respect the confidentiality of the proprietary data and the restrictions on use, and any discussions pertaining to them. The deliberations of the JMPS will be recorded in the confidential report of the closed meeting, to be held by FAO and WHO.
- f) Experts participating in the JMPS will be required to sign a declaration of their actual or potential interests in the information, proposals or pesticides under consideration. Experts will not take part in discussions in which their declared interest gives rise to a conflict of interest, except to provide the JMPS with information, if required.
- g) Following the closed meeting and completion of the evaluation and specifications, the evaluator should destroy the data package copy or return it to FAO or WHO. Subsequently, the confidential data and information will be accessed only for the purposes of determination of equivalence or review of the specifications, under similar procedures. Confidential data and information do not become the property of FAO or WHO.
- h) In the determination of equivalence, if the existing limit for a relevant impurity is exceeded by the additional technical material (TC) or technical concentrate (TK),

FAO and/or WHO can be expected to request information from the additional proposer about the increased levels of relevant impurities. Where there is a new impurity, or an exceedance of the 50% or 3 g/kg limit for non-relevant impurities, requests for further information from the additional proposer will refer only to the impurity data provided by the second proposer. No reference will be made to the data owned by any other proposer other than that, by inference, it may be concluded that the 50% or 3 g/kg limit has been exceeded. In such cases, every care will be taken to avoid inadvertent release of confidential information.

BACKGROUND TO FAO AND WHO SPECIFICATIONS FOR PESTICIDES

FAO specifications

Acting on the recommendations of the FAO Conference on Pesticides in Agriculture (FAO, 1962a), which were endorsed at the second session of the FAO Committee of Experts on Pesticides in Agriculture (FAO, 1962b), the Director-General of FAO established an FAO Working Party on the Official Control of Pesticides on 25 July 1963 under the provisions of the statutes of the FAO Committee of Experts on Pesticides in Agriculture.

The purpose and terms of reference of the Working Party were to advise and assist the Director-General on all matters related to the official control of pesticides, and to prepare a model licensing and approval scheme; to provide guidance on efficacy and safety in use and transport; and to produce specifications for pesticides used in agriculture.

The Working Party was subsequently divided into two sections: Section A, to prepare a model scheme for the official control of pesticides and to provide guidance on labelling; and Section B, to prepare specifications for pesticides used in plant protection.

In 1975, the Working Party was renamed the FAO Panel of Experts on Pesticide Specifications, Registration Requirements and Application Standards (FAO, 1975). In 1989, the Panel of Experts on Prior Informed Consent was amalgamated with the other groups, to become part of the Panel of Experts on Pesticide Specifications, Registration Requirements, Application Standards and Prior Informed Consent. The FAO Experts on Pesticide Specifications (FAO EPS) held formal meetings in 1977, 1979, 1981, 1992, 1997 and 1998 and, for many years, has held additional (informal) technical meetings in association with the annual meetings of the Collaborative International Pesticides Analytical Council (CIPAC).

The first edition of the FAO Specifications Manual was published in 1971 as *FAO Agricultural Development Paper No. 93*. The second, third and fourth editions were published in 1979, 1987 and 1995, as *FAO Plant Production and Protection Papers No. 13*, *No. 85* and *No. 128*, respectively.

In 1996, a draft plan was prepared by the FAO Group on Specifications, to change the procedures by which specifications were developed and applied. The objectives were (i) to prepare specifications by a formal evaluation procedure that is transparent and analogous to that employed by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR); (ii) to enable JMPR evaluations of pesticide toxicology and residues to be linked to the evaluations of the technical active ingredients; and (iii) to limit the scope of specifications to manufacturers whose technical active ingredients have been evaluated by the FAO EPS. Following extensive consultation and comments from interested parties, the procedures were adopted by the FAO EPS at formal meetings in October 1998, held in Rome. The new procedures were presented in the fifth edition of the manual (*FAO Plant Production and Protection Paper No. 149*, 1999). In addition, the manual was extensively reorganized. Statements of the aim, applicability, methods and requirements were provided for all specification clauses, which were grouped according to broad characteristics. Similarly, for clarity and ease of comparison, the specification guidelines were grouped according to the general features of the products involved. A Spanish version of the 5th edition of the manual was made available in 2001.

Specifications developed under the two procedures are superficially similar in appearance but have a very different basis. Specifications developed under the old procedure could be applied to any manufacturer's product. Specifications developed under the new procedure apply only to the products of manufacturers whose data have been evaluated by the Group on Specifications. Prior to 1999, all specifications were produced in hard copy only. Under the new procedure, specifications are published on the internet and only available in hard copy form on request. Specifications published on the internet are integral with the corresponding evaluations of data, so that users of the specifications can be informed of the data and scientific reasoning which support the specification.

WHO specifications

Prior to 2002, draft specifications proposed by industry were reviewed by the WHO Expert Advisory Panel on Vector Biology and Control and WHO collaborating centres and were then issued as interim specifications. These were then reviewed every five to six years by the WHO Expert Committee on Vector Biology and Control, which could recommend their publication as full WHO specifications. At its meeting in 1999, the Expert Committee on Vector Biology and Control recommended harmonization of the specification development procedures and processes with those of FAO (WHO, 2001). From 2002, all specifications for technical grade active ingredients and most specifications for formulated products have been developed through the JMPS, using the new procedure. As in the case of FAO specifications, a transition period permitted completion of specifications already in development under the old procedure. Under the new procedure, WHO recommendations on use and WHO specifications were restricted to the data package and products evaluated by WHO.

In 2014, WHO made the decision that the responsibility for the evaluation of pesticide-based vector control products under the WHO Pesticide Evaluation Scheme (WHOPES) would be transferred to the Prequalification Unit (PQT). The PQT is within the Department of Regulation and Prequalification. As of 1 June 2018, the WHO evaluation of vector control products was fully transitioned from WHOPES to the WHO Prequalification Unit - Vector Control Product Assessment Team (WHO PQT/VCP). This transition included transferring the role of the WHO Secretariat to the JMPS.

The decision to bring vector control products under the prequalification system was to ensure that the approach to evaluation of these products is similar to other health technology products and focuses on a product lifecycle approach which includes: a pre-market scientific evaluation of safety, quality and efficacy; a review of the product labelling as well as post market updating of product information, monitoring and surveillance of the product when used in the real world; and routine inspections of manufacturing facilities. Aligning the scientific assessment and the quality processes of vector control products with existing prequalification processes also enables enhanced transparency in vector control product evaluation timelines and criteria, strengthened quality management throughout a products life cycle, and facilitate proactive engagement with national regulatory authorities. The goal is to ensure an efficient, predictable, and effective global assessment process to increase the availability of safe, quality-assured vector control products.

Joint FAO/WHO specifications

In December 1999, the WHO Expert Committee on Vector Biology and Control recommended that FAO and WHO should use the same definitions, nomenclatures, format and supporting methodologies for pesticide specifications. The Committee further recommended that WHO and FAO should develop joint specifications for technical materials (TC) and technical concentrates (TK) for those pesticides used in both public health and agricultural applications. In May 2000, the proposal was recommended for adoption by the FAO Panel of Experts (WHO, 2001).

In consequence, to facilitate harmonization of specifications development, in 2001, WHO and FAO signed a Memorandum of Understanding to implement the recommendations and to enable the expert committees of FAO and WHO to work together. When working together, the two expert committees are known as the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS); the first full meeting of the JMPS was held in Rome in June 2002. In future, it is expected that the expert committees will meet separately only where a specifications issue arises that cannot be resolved by the JMPS.

In 2001, a draft of the FAO/WHO manual was circulated widely by FAO and WHO, with comments invited from industry, member governments and any other interested party. In February 2002, a small drafting group of members of the FAO and WHO expert committees and industry technical experts met in York, United Kingdom of Great Britain and Northern Ireland, to consider all the comments received and to produce a draft for adoption by the JMPS in June 2002.

The 1st edition of the FAO/WHO manual was published in 2002. It incorporated guidelines for pesticide formulations for public health use, including those for microbial larvicides, together with new guidelines for agricultural pesticides (dispersible concentrate [DC], oil dispersion [OD], emulsifiable concentrate [EG] and emulsifiable powder [EP]). A Spanish version of the first edition was published in 2004 and a Chinese version was published in 2005.

Revisions of the manual and their status

The manual will continue to evolve to reflect experience and continuing scientific and technological developments in pesticides, formulations and product testing, and in data assessment.

In June 2005, a draft supplement to the manual, containing procedural refinements and clarifications made by the JMPS since publication of the 1st edition of the manual, together with various other proposals for amendments to the manual, was considered by the JMPS in Utrecht, the Netherlands. In November 2005, FAO and WHO organized a consultation with members of the JMPS and other experts in Wädenswil, Switzerland, to consider the comments received and to produce a revised supplement. The 2002 edition of the manual and the supplement were both long and complex documents and, to avoid the problem of cross-referencing between the two, they were merged to form a revised 1st edition of the manual. The revision was agreed by JMPS members and, in February 2006, was adopted by FAO and WHO for publication on their websites.

In 2007, it was proposed that amendments to the manual should be published as addenda to the report of the open meeting and that the manual should be updated every 5 years. Such

amendments should be clearly stated because they become a source of reference for JMPS work until the next revision of the manual.

This approach was based on the JMPS procedure of general reports each year serving as amendments and additions to procedures until the next edition of the manual.

The 2016 revision took into account points reported by the open and closed meetings of 2009 to 2015 and points suggested by JMPS members, CIPAC and industry. The revision was also an opportunity to edit the text and bring it up to date.

This 2021 second edition of the manual takes into account points reported by the open and closed meetings of 2016 to 2020 and points suggested by JMPS members, CIPAC and industry. Furthermore, the former Section 9 was removed and, after major revision and amendment, will be available as a dedicated manual for the development and use of FAO and WHO specifications for microbial pesticides (FAO and WHO, forthcoming). The two manuals – for chemical and microbial pesticides, respectively – are siblings, resembling each other in the more general sections like procedures, but being fairly different where required, e.g. in the sections for data requirements and criteria and especially in the templates for the technical materials and formulated products.

Until a new hard-copy edition of the manual is published, the 2022 second edition of the manual is available only on the internet, in English. For FAO and WHO purposes, the most recent revision published on the internet has the status of the current working version of the manual. Any earlier text which differs is superseded. For this reason, wherever practicable, users of translated versions of the second edition of the manual should check the most recent version published on the internet, to ensure that the text they wish to use remains valid.

1. INTRODUCTION

1.1 SCOPE OF SPECIFICATIONS FOR CHEMICAL PESTICIDES

In the context of this manual, the term “pesticide” is used following the definitions provided in the Article 2 of the *International Code of conduct on pesticide management* (the Code): "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" (FAO and WHO, 2014).

The term of “chemical pesticide” is considered to embrace inorganic and organic-synthetic 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 also embraces certain materials used to modify the behaviour or physiology of pests (e.g. insect repellents and synergists) or of crops during production or storage (herbicide safeners, germination inhibitors).

FAO and WHO specifications apply only to the products of manufacturers whose technical materials have been evaluated as satisfactory by the JMPS. The corresponding products of other manufacturers may be submitted for assessment to ensure that existing FAO/WHO specifications are applicable to them.

The specifications encompass the physical appearance of the material, its content of active ingredient and any relevant impurities, and its physical and chemical properties, and stability in storage.

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 may be assessed by WHO. WHO specifications may be developed for technical materials and formulations prior to any country registration. WHO specifications for formulations are published, in conjunction with the successful prequalification of a formulated product.

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/Joint FAO/WHO Expert Committee on Food Additives (JECFA) or WHO/International Programme on Chemical Safety (IPCS), 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 submitted and the limits for purity/impurities applied in

normal manufacturing production. FAO and WHO recognize 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.

1.2 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. The JMPS is a statutory body of FAO and WHO whose Panel Members are appointed by the two 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 with special skills or knowledge of technical issues (not related to a particular company's proposals or specifications) may be invited to provide advice on certain topics where FAO/WHO deem such advice appropriate. Industry experts do not, and the other additional experts may not, participate in drafting the recommendations of the JMPS (see also Section 2.3).

The primary function of the JMPS is to develop recommendations to FAO and/or WHO on the adoption, extension, modification or withdrawal of specifications based on the scientific evaluation of the applicable data. The JMPS may propose other related work, including the development of operational policies. Such related work must be agreed with the FAO and/or WHO secretariat. FAO and WHO may request the involvement of JMPS in the conduction of other related work, but may also rely on other resources.

The principles, practices and procedures currently applied by FAO and WHO for the provision of scientific advice through the JMPS are also described in the document on *FAO/WHO Framework for the Provision of Scientific Advice on Food Safety and Nutrition* (FAO and WHO, 2018).

1.3 LIAISON WITH OTHER INTERNATIONAL ORGANIZATIONS, INTERNATIONAL CONVENTIONS AND NATIONAL REGULATORY AUTHORITIES

1.3.1 Collaborative International Pesticides Analytical Council and AOAC International

Wherever practicable, the test methods cited in FAO/WHO specifications should have been evaluated by inter-laboratory trials.

CIPAC and AOAC publish methods of analysis which have been adopted after collaborative testing (which includes peer validation of analytical methods for relevant impurities and quantitative stereospecific identity tests). 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).

1.3.2 FAO/WHO Joint Meeting on Pesticide Residues

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 pesticides, to FAO, WHO and the Codex Committee on Pesticide Residues as a contribution to the WHO and FAO activities on food safety.

In its 1999 report, the JMPR proposed that its evaluation of the toxicology and residues of a pesticide should, as far as practicable, be conducted following the development of FAO/WHO specifications for that pesticide. The proposal was accepted by the Codex Committee on Pesticide Residues in 2001. The procedure enables the JMPR to take account of the impurities, especially relevant impurities, in its evaluations. Ideally, the JMPR and JMPS evaluations should be conducted in the same year, because this ensures comparability of data provided and minimises duplication of effort in providing the data. FAO and WHO recognized that it would take several years to harmonize the JMPS and JMPR agendas for this purpose. Because food safety is the main concern of JMPR, it may not always be possible to align the priorities of JMPR and JMPS, especially for pesticides not used in agriculture.

In its 2005 report, the JMPR requested clarification of JMPS activities in the area of hazard and risk evaluation, to avoid possible duplication of effort. JMPS

does not evaluate risks¹ and it does not evaluate hazards of the active ingredient itself. JMPS evaluates toxic and non-toxic hazards: (i) to establish the relevance of impurities; (ii) to assign appropriate limits for relevant impurities; and (iii) to determine the equivalence of technical grade active ingredients produced by different manufacturers, processes, etc. The hazard types assessed vary from case to case. In all cases, the assessments refer only to the products of manufacturers named in the evaluation.

The 2016 *FAO Residue Manual* explains the relevance of pesticide specifications for JMPR evaluations (FAO, 2016). An outline of the procedure for specifications is provided in Chapter 7.2, *Safety Assessment of Pesticides*. Where specifications for a pesticide are already published, JMPR residue evaluations state which specifications have been established and provide the JMPS reference.

1.3.3 Rotterdam Convention on Prior Informed Consent

Existing FAO or WHO specifications for pesticides which are subject to the Rotterdam Convention, or could become subject to the Convention following consideration by the Interim Chemical Review Committee, are prioritized for review, and withdrawal if appropriate, by the JMPS. Such specifications may be retained if by changing the formulation, or control of parameters such as the concentration of relevant impurities, the risks – to those handling or using the pesticide, or to the environment – are thereby acceptably reduced.

1.3.4 Stockholm Convention on Persistent Organic Pollutants

Existing FAO or WHO specifications for pesticides which are subject to the Stockholm Convention are prioritized for review and withdrawal by the JMPS, as required.

If a Persistent Organic Pollutants (POP) compound appears as an impurity or potential impurity in a pesticide, the fact that it is a POP compound is stated and is taken into account in the evaluation.

1.3.5 International Organization for Standardization

English International Organization for Standardization (ISO) common names, accepted by ISO, are adopted wherever possible (ISO, 2021).

1.3.6 International Nomenclature for Cosmetic Ingredients

The standard names for insect repellents published by the International Nomenclature for Cosmetic Ingredients (INCI) are adopted where appropriate.

¹ Although the concentration of a relevant impurity is related to exposure and therefore risks, risks are also application-dependent. So, for the purposes of determining the relevance of an impurity, JMPS considers impurity concentration in the context of its contribution to the overall hazard of a product (Chapter 3, Section D).

1.3.7 Organisation for Economic Co-operation and Development

The Organisation for Economic Co-operation and Development (OECD) references FAO and WHO specifications for active ingredients and formulations in its harmonized recommendations for registration.

1.3.8 United Nations Industrial Development Organization

The United Nations Industrial Development Organization (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.

1.3.9 United Nations Globally Harmonized System of Classification and Labelling of Chemicals

In the assessment of risks of chemicals to the human health and environment, JMPS applies the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) classification (UN, 2019).

1.3.10 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 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 Union has harmonized pesticide registration and control systems in member countries and FAO specifications are an important feature of the authorization directives. Specification requirements for agricultural pesticides in various developing countries are also being harmonized with those of FAO.

1.4 PARTICIPATION BY THE PESTICIDE INDUSTRY

1.4.1 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. As far as practicable, and where applicable, submissions should coincide with corresponding submissions to the JMPS (Section 1.3.2 above).

1.4.2 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.

1.4.3 Development of specification guidelines and principles

Industry is strongly encouraged to prepare draft guideline specifications for new formulation types for submission to the FAO/WHO secretariat for consideration by the JMPS. Comments on, or suggested amendments to, proposed or existing guideline specifications may come from industry, experts participating in the JMPS or any other interested party. Specification guidelines are kept under review by FAO and WHO. Specification guidelines and related matters are normally considered at open meetings (see glossary of terms, Appendix C) of the JMPS but are recommended for adoption in 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 International and AgroCare) may be invited by FAO/WHO 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.

1.5 PURPOSE AND USE OF SPECIFICATIONS

1.5.1 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.

1.5.2 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 nor give information on hazards but this type of information (e.g. flash point, explosive properties) may accompany a specification, even though it does not form a part of the specification.

1.5.3 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 (i) that they have not been unduly exposed to extremes of temperature, humidity and/or light; (ii) that labels (for example, prepared according to FAO/WHO labelling guidelines – see FAO and WHO, 2015) do not indicate a shorter shelf-life as e.g. for biological products based on micro-organisms; and (iii) that any special instructions from the manufacturer have been followed.

1.5.4 Official control of pesticides

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.

1.5.5 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.

1.6 ACCESS TO FAO AND WHO SPECIFICATIONS

Users of specifications are advised that these are subject to a continuing process of updating 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.

The current FAO specifications are published on the FAO website (FAO, 2021) and can be accessed at www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/en

The current WHO specifications (WHO, 2020a) are published on the WHO website and can be accessed at: extranet.who.int/pqweb/vector-control-products/who-specifications-pesticides

2. THE PROCESS OF DEVELOPING FAO/WHO SPECIFICATIONS

2.1 CATEGORIES OF SPECIFICATION AND THEIR STATUS

Prior to 1999, three categories of FAO specifications (tentative, provisional and full) were developed (FAO, 1995), 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 procedures (FAO, 1999) 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.

The specifications developed by both organizations under the old procedures remain in force until they are reviewed. Priorities for review are given in Section 3.6 of this manual.

Specifications prepared according to the earlier procedures were applied to all products which were nominally similar. That is, for a defined active ingredient, the specification applied to all products containing that active ingredient, providing they were of the appropriate formulation type. However, under the “new” procedures the FAO and WHO specifications do not apply to nominally similar products of other manufacturers, nor to those where the active ingredient is produced by other routes by the same manufacturer. The scope of these new specifications may be extended to similar products when the supporting data and assessment have shown that the additional products are equivalent to those which formed the basis of the reference specification (see glossary, Appendix C).

A specification published under the new procedure normally supersedes and cancels any earlier specification for the material involved. Under the new procedure, only manufacturers who have submitted a data package and specification (which have then been evaluated as acceptable) in accordance with current procedures, may claim that their material complies with the specification. Materials from other manufacturers may no longer comply, even if their products met the requirements of the superseded specification because, without a detailed evaluation of information provided by the other manufacturers, FAO/WHO cannot know that the specification is appropriate to them. Under Article 6.2.4 of the *FAO/WHO International Code of Conduct on Pesticide Management* (FAO and WHO, 2014), the pesticide industry is expected to ensure that active ingredients and formulated products conform to the appropriate FAO and WHO specifications. Therefore, manufacturers who have not provided data packages and

specifications to the JMPS under the new procedure should do so at the earliest opportunity, for assessment of equivalence (Section 3.2).

2.2 SUBMISSION OF PROPOSALS AND DATA

Proposals for inclusion of specifications for an active ingredient and/or its formulations in the JMPS schedule must be sent to FAO or WHO, or both if appropriate. Requests for inclusion in the JMPS future work programme must include the list of studies supporting the proposed data submission.

Where two or more manufacturers seek specifications for the same active ingredient 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 2.5.

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 FAO and WHO secretariats, JMPS members, and others invited by FAO/WHO, because they involve consideration of commercially confidential information.² 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 3 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), FAO and WHO will consider issues of general importance to specifications and, in doing so, will seek the views of all interested parties.

² 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.

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

- evaluations and proposed specifications, involving commercially confidential data;
- changes in technical requirements for, and policy on, specifications;
- priorities for review of specifications in the forthcoming 3 years (see Section 3.6);
- 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 relevant 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.

2.4 CONFIDENTIALITY OF INFORMATION

FAO and WHO will maintain the confidentiality of all confidential information provided in support of proposed specifications.³ By means of a letter of access provided by the proposer or a certificate of registration for a formulated product and the active ingredient(s) issued by a national registration authority, 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 a request for agreement between the proposers and FAO/WHO on the content but, irrespective of agreement on the specification, the JMPS evaluation may be published on the internet by FAO, WHO or both.

The manufacturing process and analytical data on the impurity profile of the technical grade active ingredient (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.

³ A statement of the procedures for handling unpublished proprietary pesticide data and potential conflicts of interest in the development of pesticide specifications by the JMPS is provided on page VII.

2.5 TIMETABLE AND PRINCIPLES FOR THE DEVELOPMENT OF SPECIFICATIONS

The procedure and deadlines are scheduled with reference to the annual FAO/WHO JMPS. The timetable, content of evaluation reports, and communications between FAO/WHO secretariat, proposer, evaluator, peer reviewer and editor are presented in Appendix K.

- (i) FAO and WHO will develop 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 Section 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 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	Submit draft specification and 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; potential request of further information from the proposer	1st week of June
Proposer	Provision of additional information	As determined
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 3.1, 3.2 and 3.3. Proposers who are unable to provide the data required to support specifications, within the timetable given in paragraph (iii) 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, using templates available on the FAO and

WHO websites.⁴ Documents should be submitted electronically to FAO and WHO. The guideline specifications provided in this manual must be used. If appropriate guidelines do not exist, proposers should refer to Section 1.4.3. The proposer must confirm whether or not the proposer's data differ from those submitted to WHO, the FAO/WHO JMPR 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.
- (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 reassessment of the toxicological and ecotoxicological data will be organized by FAO/WHO to support 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 recognize 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 proposer 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.

⁴ For specifications templates, see www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/en (FAO) and <https://extranet.who.int/pqweb/vector-control-products/specification-templates-proposers> (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 review the draft specifications, evaluation and appraisal and provide comments back to the evaluator.

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 evaluator any other point that does not make sense, e.g. references in the reference list that do not appear in the text or tables.

- (xi) 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.

- (xii) If there are data gaps or the need for clarifying information, 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.
- (xiii) The basis for recommendations to accept or reject specifications will be recorded in the evaluation.
- (xiv) The proposer(s) will be identified in the evaluation, which will be cross-referenced with the specification(s).

- (xv) 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 established 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.

2.6 PUBLICATION OF SPECIFICATIONS

Specifications, and the corresponding evaluations, will be published on the respective FAO and/or WHO websites. 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.

Specifications developed under the old procedures remain valid until, following review by the JMPS, they are withdrawn by FAO and/or WHO (i.e. they are no longer accessible on the internet). Withdrawn specifications have no status as FAO or WHO specifications and their use for regulatory purposes is strongly discouraged.

CIPAC adopted or accepted methods of analysis are usually first published under the pre-published method scheme before they appear in printed form in CIPAC Handbooks or CD ROM,⁵ or the AOAC Handbook⁶ 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.

⁵ Updated order forms are provided at www.cipac.org/index.php/methods-publications

⁶ Official Methods of Analysis, 21st edition. Obtainable from AOAC International at <https://www.aoac.org/>

2.7 REVIEW OF SPECIFICATIONS

2.7.1 Conversion of specifications developed under FAO "old procedure"

Introduction: this subsection is an interim one and will be removed in future, when all FAO specifications developed and published under the old procedure will be either converted into new procedure ones or withdrawn.

Specifications developed under the FAO "old procedure" (cf. Section "Background to FAO and WHO specifications for pesticides," pp. IX onward) are reviewed at intervals based on suitable criteria like whether the compounds are still in use.

The data requirements as outlined in Section 3.1 applies for conversion of old procedure specifications into new ones. However, some particular aspects different than for the proposal of reference specifications for technical and formulated pesticides are considered by JMPS.

For the conversion process, the manufacturer providing the most complete hazard data package (see Section 3.1 A.9) supporting a recent purity and impurity profile of the technical material produced is considered by JMPS as main data proposer and the specifications developed are considered as reference specifications. In cases where such a firm link between a full hazard data and the purity and impurity profile of a technical material cannot be established by a manufacturer, JMPS will consider a proposal from a manufacturer submitting a data package similar as for an equivalence case (see Section 3.2, Minimum data requirements for extension of an existing TC/TK specification to an additional manufacturer or a new manufacturing route, point E.1 for Tier-1). The JMPS will, in addition to the data submitted, consider the published subchronic, chronic, mutagenicity, neurotoxicity and reproduction toxicity studies on the active ingredient and their results that have been reviewed and evaluated by JMPR. A proposal for a TC or TK is deemed acceptable by JMPS provided that:

- (i) The technical material under evaluation does not produce a response in the *in-vitro* mutagenicity test worse than that for the material whose hazard profile has been evaluated by JMPR;
- (ii) No qualitatively new adverse effect is observed in the repeated dose studies (28 or 90 days repeated dose studies in rodents); and
- (iii) The "no observed adverse effect level" (NOAEL) or bench-mark dose for any toxicity end point is not more than a factor of $10^{-0.5}$ lower than that evaluated for the technical material evaluated and published by JMPR.

2.7.2 Review of specifications developed under new procedure

Specifications will be reviewed at intervals, according to the priorities outlined in Section 3.6 of this manual. 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.

Specifications under review must be supported by the data indicated in Sections 3.1, 3.2 or 3.3 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.

In cases where a specification serves as reference for equivalent products and needs revision, an amendment or modification of a clause may render the hitherto equivalent products non-equivalent. In such a situation, JMPS submits a draft version of the revised specification for consultation to those data proposers having equivalent products. Where new data to support the continued equivalence is needed, an appropriate deadline for submission of the data is conceded. The data is evaluated, discussed at the next meeting if required and appropriate recommendations to FAO and/or WHO are made (see Section 2.3, Meetings and functions of the JMPS).

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 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.

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) Either the information described in Section 3.1, to support a new specification, or the information described in Section 3.2 or 3.3, to support the extension of an existing 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 5 to 8 of this manual).

2.9 ACCEPTABILITY OF ANALYTICAL AND PHYSICAL TEST METHODS

Analytical methods, supporting FAO and WHO specifications, for the determination of active ingredients in technical and formulated pesticides must be collaboratively tested and approved by CIPAC or AOAC.⁷

Analytical methods for the determination of relevant impurities or stabilizers and other additives included in the specification, or for the determination of isomer ratio as part of an identity test, must be peer (independent laboratory) validated (e.g. by the AOAC peer verified methods procedure), as a minimum. Peer-validation data should be submitted to AOAC or CIPAC to support adoption of the method. If the validation data have not yet been considered by CIPAC or AOAC, FAO/WHO may request submission of the data for preliminary review.

Where collaborative study, or peer validation, of the method of analysis 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 the American Society for Testing and Materials (ASTM), or according to the requirements of OECD, ISO or the European Union, or, where appropriate, by equivalent pharmaceutical organizations. References to physical methods of testing in this manual are prefixed "MT" for CIPAC methods, "EU" for European Union methods, or with the 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.

⁷ Methods produced by alternative organizations may be accepted on a case-by-case basis.

CIPAC is continuously reviewing and revising MT methods for improving standardization and covering progress in science and technology. Where a revised CIPAC MT method has been adopted by CIPAC, supersedes a previous version and is deemed to provide equivalent results, the revised MT methods⁸ should preferably be referenced in the specification guidelines and in formulation specifications that are currently being developed wherever possible and appropriate.

Validation requirements for methods which determine unstable physical properties,⁹ 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 potential hydrogen (pH).

Although the level of acceptance of methods within the CIPAC or AOAC systems is not completely critical, preference will be given to “full” or “final action” methods and the methods should normally have achieved a minimum of “provisional” or “first action” status. 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.

⁸ A list of methods declared as ‘obsolete’ or ‘superseded’ and a compilation of revised MT versions is published on the CIPAC website, <https://www.cipac.org/index.php/methods-publications/further-information/no-longer-supported-methods>. Methods which are ‘no longer supported’ by CIPAC may still be considered fit for purposes, however, the use of newer versions of MT methods in support of existing specifications is strongly encouraged in case of revising the specification.

⁹ 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.

3. DATA REQUIREMENTS AND PROCEDURES FOR DEVELOPMENT OF FAO/WHO SPECIFICATIONS

3.1 MINIMUM DATA REQUIREMENTS FOR SUPPORT OF THE REFERENCE SPECIFICATION FOR AN ACTIVE INGREDIENT

General notes

- (i) An electronic template, to assist proposers assemble and submit the data required, is available from FAO or WHO. Proposed specifications for TC/TK, and all formulation types involved, should be submitted in the form presented in the manual.

A checklist for first and subsequent proposers is available in Appendix A of this manual.
- (ii) In general, studies which fulfil the requirements of modern national registration systems will meet the needs for the development of FAO and WHO specifications.
- (iii) In cases where the technical material (TC) is not isolated, the data and information in paragraphs A.4 to A.10 and C1 to C5 may be derived from the technical concentrate (TK).
- (iv) The requirements of Section 3.1 will apply in most cases. Exceptionally, where a proposer believes that a requirement is not appropriate to the proposed specification, or that additional information should be considered by the JMPS, the proposer must submit a reasoned case to support this opinion. In such a case, further progress of the proposed specification will depend on agreement (between the JMPS and the proposer) on the data required for evaluation.
- (v) Data submitted will be maintained on confidential files by FAO and/or WHO, for future determination of equivalence, as required, but the data remain the property of the proposer.
- (vi) Original study reports are required and have to be provided for the physical and chemical properties of the active ingredient, the batch analysis data and mutagenicity data on TC/TK, and the physical-chemical properties of formulations. Study reports for toxicological and ecotoxicological data on TC/TK are normally not required, unless the evaluator or the JMPS are unable to resolve a particular issue without the information. They are required if the corresponding data points constitute a data requirement (e.g. assessment of relevance of a particular impurity (quantitative structure–activity relationship (Q)SAR)). The study report source of data should be summarized in the form of study number, author, year, title, report number and company conducting the study, to allow ease of reference between the proposer and FAO/WHO.
- (vii) If certain data are not available, or if the proposer believes that the specifications must deviate from the guidelines presented in the manual, the proposer should provide a written explanation or supporting case. Such explanations or cases should be brief, simple and clear.

.../cont.

- (viii) To introduce a new formulation specification where the proposer's TC/TK specification has already been accepted, or where a formulator utilizes a TC/TK produced by a manufacturer whose specification has already been accepted, it is not necessary to resubmit (or submit) the complete dossier identified below. In the latter case, the formulator must declare the source of the TC/TK and provide an undertaking (i) that it is the sole source; and (ii) that if an alternative source is subsequently utilized, FAO and/or WHO will be notified immediately. Where a complete dossier is thus considered unnecessary, the proposed specification should be submitted, together with any necessary justification for deviations from the guideline specification.
- (ix) The absence of an agreed and published specification guideline does not preclude submission of a proposed specification. FAO and WHO wish to encourage the development of novel formulations which address pest control problems. Guidelines will not exist for unique formulation types and, in such cases, the manufacturer must define the critical characteristics and provide suitably validated test methods for measurement of the appropriate parameters.

A. DATA REQUIREMENTS FOR PURE AND TECHNICAL GRADE ACTIVE INGREDIENTS (TC/TK)

A.1 Identity of the active ingredient.

ISO English (E-ISO) common name (and its status if not yet accepted) or INCI name (if appropriate).

Any other common name or synonym.

Chemical name (International Union of Pure and Applied Chemistry [IUPAC] and Chemical Abstracts [CA]).

Chemical Abstracts Service (CAS) No. (for each isomer or the mixture of isomers, if appropriate).

CIPAC No.

Structural formula(e) (including stereochemistry of the active isomers, if appropriate and if known).

Isomeric composition, if appropriate.

Molecular formula.

Relative molecular mass.

A.2 Physical and chemical properties of the active ingredient (and the methods and conditions used to generate these data).

Where the active ingredient is a mixture of diastereoisomers, physical and chemical data for each diastereoisomer should be submitted, if available.

Where the biologically active moiety is formed from the active ingredient, physical and chemical data should also be submitted for the active moiety, if available.

Studies and data for pure active ingredient (equivalent in purity to analytical standard purity) are required for:

- vapour pressure;
- melting point;
- temperature of decomposition;

- solubility in water;
- octanol-water partition coefficient;
- dissociation characteristics, if appropriate;
- hydrolysis, photolysis and other degradation characteristics.

Studies and data for technical grade active ingredient are required for:

- melting point (active ingredients that are solids above 0°C).

Studies and data for solubility in organic solvents at room temperature are required for pure or technical grade active ingredient.

A.3 Outline of the route of manufacture, summarizing the conditions and solvents employed (confidential information).

- A list of solvents, intermediates, catalysts used in the process with purities where appropriate is required.
- A comprehensive description of the process (without engineering details) is needed to allow the evaluator to make a plausibility check on purity of the finished technical material, separation of critical components, removal of solvents etc.

A.4 Minimum active ingredient content.

The use of the average of the active ingredient content in 5 batches minus 3 times the standard deviation of the same content is recommended in order to establish the active ingredient minimum content¹⁰ in a TC specification. However other soundly justified proposal may be accepted.

A.5 Manufacturing maximum limits for impurities present at or above 1 g/kg, supported by **batch analysis data** (minimum 5 typical batches) (all confidential data). Recent 5-batch studies are required to be Good Laboratory Practice (GLP) studies.

If the manufacturing process is conducted at more than one site, 5 batch analytical data should be provided from every site and the profile of one site should be identified as reference profile. That reference profile is expected to be covered in the statement as requested below under point A.10.4.

The basis for the manufacturing limits should be explained (for example: maximum level found in practice; average plus 3 standard deviations of levels found in practice; etc.). Proposed relevant impurities¹¹ present at or above 1 g/kg must be identified in the submission. Typically the unidentified and/or unaccountable fraction of the TC/TK should not exceed 20 g/kg (confidential

¹⁰ This way of estimation is borrowed from the work of W.S.Gossett in *Biometrika* 6 (1), 1908: 1-25 "The Probable Error of a Mean", also known as "Student" and "Student's t-distribution" (Gossett, 1908). Briefly, the average minus 3 standard deviations represents a probability of higher than 99.7% that a hypothetical next batch produced and analysed will be equal or higher in content than the estimated minimum content, assuming normal distribution of the content in the individual batches and stable production conditions, so batches used being representative of production conditions.

¹¹ Relevant impurities are defined in the glossary, Appendix C.

information, except for the published specification limits for relevant impurities).

A.6 Manufacturing maximum limits for impurities proposed as relevant at < 1 g/kg.

Maximum limits for these impurities should also be supported with batch analytical data (minimum 5 typical batches) and the proposer should state the basis for the manufacturing limits (confidential information).

A.7 Information on relevant impurities, with explanations of the effects observed (for example, toxicological effects, or effects on the stability of the active ingredient).

Limits set by the JMPR and/or registration authorities should accompany this information, identifying the authority responsible for setting the limit.

In certain cases, impurities that could become relevant at higher concentrations were identified in technical materials, but careful control of manufacturing conditions keep these impurities at a level that renders them non-relevant. However, that impurity could occur in the material of other manufacturers at higher concentrations. In these cases, a footnote is added in the TC or TK specification and the proposer provides FAO and or WHO with a copy of a suitable analytical method for determination of that impurity to national programmes on request. The analytical method needs to be properly validated, but not peer validated.

Note to paragraphs A.6 and A.7

- (i) Relevant impurities must be included in the specification but other impurities (including isomers of low activity) must not be included.

A.8 Identity and nominal content (g/kg) of compounds intentionally added to the TC/TK (confidential data).

A.9 Toxicological summaries (including test conditions and results)

Recent studies are required to be GLP studies and to comply with established study guidelines.

A.9.1 Toxicological profile of the TC/TK based on acute oral, dermal and inhalation toxicity; skin and eye irritation, skin sensitization.

A.9.2 Toxicological profile of the TC/TK based on repeated administration (from sub-acute to chronic) with a description of dosage levels (mg/kg bw per d), NOAEL values and recapitulation of findings at the lowest observed adverse effect level (LOAEL) dose, as well as studies on reproductive and developmental toxicity, genotoxicity, carcinogenicity, developmental and adult neurotoxicity, etc.

- A.9.3 Ecotoxicological profile of the TC/TK based on toxicity to aquatic and terrestrial organisms (e.g. fish, crustaceans, algae, birds, bees), as appropriate to the intended use, and information of persistence.

A.10 Other information

- A.10.1 WHO classification by hazard when they exist.
- A.10.2 References to JMPR evaluations for toxicology and environmental fate should be given, when they exist. The toxicological data supplied to the JMPR for evaluation should be cross-referenced to the batch analysis data of the technical materials used in those studies.
- A.10.3 On request by JMPS, a certificate of registration for a formulated product and the active ingredient(s) issued by a national registration authority with a certified translation into English, in case the language of the certificate is other than English.

At the request of FAO/WHO, the proposer may provide, a letter of authorization (see Appendix G) granting competent FAO/WHO and registration authorities access to registration data on behalf of FAO/WHO. This is to enable FAO/WHO to assess whether or not:

- (i) the technical material for which a FAO/WHO specification is proposed is equivalent to that registered by the authority, as assessed by a comparison between the data submitted to FAO/WHO and those submitted for registration; or
- (ii) a decision that technical materials from different manufacturers are equivalent was based on data similar to those provided to FAO/WHO.

If the data are known to differ from those submitted by the proposer for registration, the relevance of the data provided to FAO/WHO should be explained.

At the request of FAO/WHO, the proposer may provide a written undertaking that the data submitted to FAO/WHO are identical to those submitted for registration to a specified national authority. Any deviations between the two data sets must be described in detail.

- A.10.4 Statements to identify the links between purity/impurity data and the hazard information and risk assessments.
- (i) Normally, the data provided are expected to have been generated from the proposer's material. Identify which, if any, of the hazard data were not generated from the proposer's technical grade active ingredient and formulated products, state the source of the information and explain the relevance of the data.

- (ii) Identify any toxicological/ecotoxicological data generated from batches of material which were either specially purified, or in which the impurity concentrations exceeded the limits identified in Sections A.4, A.5 and A.6. Explain the relevance of the data.
- (iii) Confirm that current production complies with the limits identified in Sections A.4, A.5 and A.6.

B. DATA REQUIREMENTS FOR FORMULATIONS (see also general note viii, above)

- B.1 Identify if the formulations are for public health or agriculture uses, or both.
- B.2 In the case of public health pesticides, confirm that the formulation and manufacturing process are the same as those employed for the materials evaluated by WHO PQT/VCP.
- B.3 List the main formulation types available and identify those for which specifications are sought.
- B.4 List the main countries where these formulations are registered and sold or, if there are very many, give the number of countries in each region or continent.
- B.5 A data package covering the physical-chemical properties of the formulated products where specifications are proposed for development, as required in Sections 5 to 8 of this manual. GLP or ISO 17025 is not mandatory for studies supporting specifications for formulations. If necessary, briefly explain why it is proposed that certain clauses should be deleted, new clauses should be inserted, or less stringent limits should be adopted compared with those given in the guideline specifications. Limits should be correctly specified in order to represent acceptable quality of the formulations.

C. METHODS FOR THE ANALYSIS AND TESTING OF TC/TK AND FORMULATIONS

- C.1 At least two methods for testing identity of the active ingredient and one for testing the identity of the counter-ion or other derivative, if appropriate.
- C.2 Method for determination of active ingredient content. If the method has not yet been validated by CIPAC or AOAC or equivalent, or has not been validated for the particular formulation, indicate the expected year of completion of the validation.
- C.3 Methods of analysis for relevant impurities, in detail, including validation data, if not published. Give the principle of the methods of analysis used for non-

relevant impurities in the TC/TK (gas chromatography, with flame ionization detector, for example).

- C.4 Reference test methods for physical properties. If a particular method intended for testing compliance with the specification has not yet been validated by CIPAC, or has not been validated for the particular formulation, indicate the expected year of completion of the validation.
- C.5 Information on validation completed, in progress or planned for methods listed under C.2, C.3 and C.4.

Note to paragraphs C.1 to C.5

- (i) The methods used to generate data submitted in fulfilment of the requirements of Sections A.4, A.5, A.6 and B.5 of Section 3.1 must be referenced, if they differ from those intended only for checking compliance with the specification.
- (ii) Methods required to assess compliance with a specification must be independently validated and must be published or otherwise made publicly available. Where independent laboratory validation (collaborative study of the method of analysis for the active ingredient, or peer validation of a method for a relevant impurity) is in progress at the date of submitting the proposal, the estimated year of completion must be provided. With the exception of certain WHO interim specifications, specifications will not normally be published prior to the completion of validation of the methods.
- (iii) In cases where a bridging between a CIPAC, AOAC or equivalent analytical method and an in-house validated method is required, details on the bridging study and acceptance criteria are provided in Appendix J.

D. DETERMINATION OF THE RELEVANCE AND ESTABLISHING SPECIFICATION LIMITS OF IMPURITIES

D.1 Principles

Any impurity capable of creating an adverse effect, above or beyond that of the active ingredient, is potentially **relevant** and may therefore have to be controlled by the specification. The adverse effects may include toxic or non-toxic hazards (see definition of relevant impurity in the glossary of terms, Appendix C). Relevance is not determined only by the hazards presented by an impurity. For potentially relevant impurities, a compound may be designated as non-relevant in a technical material under consideration if the available evidence indicates no significant likelihood of its hazards being manifested in practice.

Relevance is dependent upon the relative hazards of the active ingredient and impurity and therefore an impurity which happens to occur in two different active ingredients may be designated as relevant in one and non-relevant in the other or may have different maximum acceptable limits applied.

In assessing the relevance of impurities which have an additive effect with the active ingredient, JMPS applies the dose-additivity model (European Union, 2011). This model is also used for impurities with more loosely defined similar effect and same end-point – independent of the mode of action. The reasoning is that: 1) synergistic effects leading to more than additive effect are exceptional at low exposure levels; and 2) IPCS recommendation is that, even for response-additive effects, the model of dose additivity should be used as the worst-case scenario (Meek *et al.*, 2011).

The model of dose-additivity is not used for end-points such as carcinogenicity, mutagenicity, teratogenicity, or eye and skin irritation, and sensitization. For these end-points, the default approach is the application of the GHS classification criteria for mixtures.

D.2 Allocation of limits for relevant impurities

The limits adopted are the result of case-by-case scientific judgement. Expert advice from WHO or another authoritative source will always be taken into account in deciding the most appropriate limit for toxic relevant impurities.

D.2.1 Maximum acceptable limits

In the absence of data or other information permitting a more refined approach, the JMPS will normally adopt the GHS classification criteria (UN, 2019) for mixtures as default maximum acceptable limits for relevant impurities. Examples of GHS limits for skin and eye irritants, sensitizing chemicals, mutagens, carcinogens, and reproductive toxicants are provided hereafter:

- (i) for skin and eye irritants : 10 g/kg for Cat. 1;
- (ii) for sensitizing chemicals : 1 g/kg for Cat. 1A, 10 g/kg for Cat. 1 and 1B;
- (iii) for mutagens and carcinogens : 1 g/kg for Cat. 1A/B, 10 g/kg for Cat. 2;
- (iv) for reproductive toxicants : 3 g/kg for Cat. 1A/B, 30 g/kg for Cat. 2.

The GHS acknowledges that deviations from the guidelines may be necessary or justifiable in some cases. Where the data required are available to the JMPS a maximum acceptable limit, corresponding to a negligible contribution to the overall hazards, will be estimated by the JMPS and used in preference to the GHS limit.

For impurities posing a similar type of toxic hazard to that of the active ingredient [additive effects], the maximum acceptable limit adopted by the JMPS normally corresponds to a concentration which would lead to a calculated 10% increase in the overall hazard presented by the active ingredient. The same cut-off value of 10% is also applied in cases, when the full toxicity profile of both the active ingredient and impurity are known, and appropriate ADI/ARfD values

can be compared. The cut-off value of 10% is arbitrary but is considered to represent a negligible increase in hazard. An increase in hazard up to 10% is still deemed acceptable, but an increase exceeding 10% is not. Example calculations are given in Appendix H. Where no comparable numeric toxicity values are available, the determination of the maximal acceptable concentration limit will be made on a case-by-case basis.

D.2.2 Specification limits for relevant impurities

If a limit below the maximum acceptable for the relevant impurity has been shown to be practical for routine manufacturing (Section 3.1, paragraphs A.5 or A.6), the JMPS will normally adopt it in preference.

D.3 Criteria for designating impurities as relevant or non-relevant

The decision on the relevance of an impurity is the result of case-by-case scientific judgement.

As a default, an impurity becomes relevant when its concentration in the TC equals or exceeds 10% of the maximal acceptable limit as outlined in Section D.2.1. Therefore, the threshold for relevance for skin and eye irritants, sensitizing chemicals, mutagens, carcinogens, and reproductive toxicants depend on the GHS Category. Examples of threshold limits for relevance are provided hereafter:

- (i) for skin and eye irritants : 1 g/kg for Cat. 1;
- (ii) for sensitizing chemicals : 0.1 g/kg for Cat. 1A, 1 g/kg for Cat. 1 and 1B;
- (iii) for mutagens and carcinogens : 0.1 g/kg for Cat. 1A/B, 1 g/kg for Cat. 2;
- (iv) for reproductive toxicants : 0.3 g/kg for Cat. 1A/B, 3 g/kg for Cat. 2.

For chemicals with organ toxicity – as defined e.g. by lethal dose (LD₅₀), LOAEL, NOAEL, benchmark dose (BMD) lower confidence limit (BMDL), ADI – relevance is determined as 10% of the maximal acceptable concentration as shown in Appendix H.

Whereas the considerations for the relevance or non-relevance of an impurity in technical materials and formulated products is based on hazard considerations and the possible contribution of an impurity to the overall hazard, a different consideration may be required for very diluted formulations and/or for relevant impurities where the limit in the TC is already very low. It is understandable that with lower concentrations of the active ingredient a certain impurity assessed as relevant according to the above hazard assessment might become negligible when diluted according to reasoned risk assessment. Furthermore, the effort and technical difficulty to develop and peer-validate an analytical method to determine the concentration of an impurity increases significantly with decreasing concentrations of the active ingredient in the formulation.

In such cases, the proposer may explain in a reasoned case why, in the diluted formulation, a particular relevant impurity may become non-relevant. This reasoned case should consider a low concentration of an impurity and resulting low expected exposure. This reasoned case has to be based on accepted risk assessment and exposure models and dose-effect considerations. It has to be demonstrated that the impurity at the specified level can become non-relevant. As examples, WHO has developed generic risk assessment models for the safety of insecticidal nets, indoor residual spraying and other public health pesticides that could be used for such a purpose.¹²

As a consequence, the analytical method for the impurity in the formulation has to be developed and validated to at least the limit defined for the relevant impurity in the TC. Additionally, when the relevant impurity increases upon storage or during manufacture of the formulated product, the method has to be applied to the formulated product before and after storage for safety assessment.

¹² See <https://extranet.who.int/pqweb/vector-control-products/dossier-preparation> (WHO, 2020b).

3.2 MINIMUM DATA REQUIREMENTS FOR EXTENSION OF AN EXISTING TC/TK SPECIFICATION TO AN ADDITIONAL MANUFACTURER OR A NEW MANUFACTURING ROUTE

General notes

- (i) Applicants who wish to add an alternate or additional manufacturing site should consult with FAO/WHO to determine if a submission is required.
- (ii) An electronic template, to assist proposers assemble and submit the data required, is available from FAO or WHO and will be sent by e-mail upon request.
- (iii) Data submitted for the determination of equivalence are expected to correspond to the same form (i.e. TC or TK) of the technical grade active ingredient upon which the reference specification is based.
- (iv) The requirements of this Section 3.2 will apply in most cases. Exceptionally, where a proposer believes that a requirement is not appropriate to the proposed extension of the specification, or that additional information should be considered by the JMPS, the proposer must provide a reasoned case to support this opinion. In such a case, further consideration of the proposed extension of specification will depend on agreement (between the JMPS and the proposer) on the data required for evaluation.
- (v) Data submitted will be maintained on confidential files by FAO and/or WHO, for future determination of equivalence, if required, but the data remain the property of the proposer.
- (vi) Original study reports are required and have to be provided for the batch analysis data and mutagenicity data on TC/TK. Study reports for toxicological and ecotoxicological data on TC/TK are normally not required, unless the evaluator or the JMPS are unable to resolve a particular issue without the information. They are required if the corresponding data points constitute a data requirement (e.g. equivalence determination, assessment of relevance of a particular impurity ((Q)SAR)). The study report source of data should be summarized in the form of study number, author, year, title, report number and company conducting the study, to allow ease of reference between the proposer and FAO/WHO.
- (vii) If certain data are not available, or if the proposer believes that the specifications must deviate from the guidelines presented in the manual, the proposer should provide a written explanation or supporting case. Such explanations or cases should be brief, simple and clear.

Specific notes on physical and chemical properties when data are submitted for determination of equivalence (see also Section 3.1 A.2)

- (i) Studies and data on the physical and chemical properties of a pure active ingredient are required only where its composition is presumed to be different from the composition of the pure reference material (e.g. different or variable ratio of isomers).
- (ii) The composition of pure active ingredient is accepted as the same in both reference material and the proposed material when it is a single non-chiral compound, a single enantiomer or a chiral compound as a racemate of an enantiomeric pair. If the pure active ingredient is a mixture, apart from a racemate of an enantiomeric pair, the composition of the pure active ingredient is presumed to be different in the reference material and proposed material without evidence that the compositions are the same.

.../cont.

Specific notes on physical and chemical properties ...(cont.)

- (iii) Physical and chemical property data available for the reference material on the pure individual isomers of an isomer-mixture are accepted as applying to the pure individual isomers of the proposed material.
- (iv) In addition, studies and data are required where the measured value of a property is not in reasonable agreement with the recorded value in the evaluation supporting the reference specification.
- (v) Studies and data for solubility in organic solvents at room temperature are required for pure or technical grade active ingredient. However, if solvent solubility data for pure active ingredient are already recorded in the evaluation supporting the reference specification, solvent solubility data are not required for the pure (or technical) active ingredient of the proposed material, provided it has the same composition as the reference pure material.

Specific notes on toxicological properties when data are submitted for determination of equivalence

- (i) Acute oral, inhalation and dermal studies are no longer mandatory requirements from the second manufacturer equivalence for his TC. Nevertheless, if they are available, they should be submitted. This does not change of course the requirement of these studies from an initial manufacturer M1 for the establishment of the hazard profile of that compound. This is in agreement with the objective of Animal Health and Welfare that is also well recognized by OECD and many national authorities.
- (ii) (Q)SAR models may be used to provide information on impurities of unknown toxicity. They must be scientifically valid and in order to maximise the sensitivity and specificity of the prediction, at least two independent (Q)SAR models, where possible, (e.g. based on different training sets and/or algorithms such as knowledge based and statistical-based models) should be applied (EFSA, 2016).

E. DATA REQUIREMENTS FOR THE DETERMINATION OF EQUIVALENCE

E.1 Tier-1 data requirements for technical grade active ingredients include the information required in Section 3.1, paragraphs A.1, A.2 (see also notes (i) to (v) above – Specific notes on physical and chemical properties when data are submitted for determination of equivalence), A.3 to A.8, A.10.3, A.10.4 (iii), and mutagenicity (bacteria *in vitro*) test data.

Tier-2 data requirements for technical grade active ingredients include the toxicological profile of the TC/TK based on skin and eye irritation,¹³ and skin sensitization. Furthermore, when deemed necessary by JMPS,¹⁴ additional

¹³ Acute eye and skin irritation is required only in cases where the proposed minimum purity of the TC/TK is less than 990 g/kg and the hazard classification of the reference material is not Category 1 eye or skin irritant.

¹⁴ Qualitative and quantitative differences in the second manufacturer's impurity profile may indicate additional or increased hazards in the TC/TK under consideration not covered by the acute toxicity studies. These suspected hazards need to be addressed by suitable toxicological studies.

toxicological studies, e.g. 28 days or 90 days repeated dose¹⁵ studies in rodents are required as well as the information required in Section 3.1, paragraphs A.10.4(i) and A.10.4(ii).

E.2 Additional toxicological summaries

The following additional information may be required, in cases where the equivalence cannot be determined from the data required by paragraph E.1.

E.2.1 Studies on reproductive and developmental toxicity, genotoxicity other than that required at Tier-1, carcinogenicity, developmental and adult neurotoxicity, etc.

E.2.2 Ecotoxicological profile corresponding to that of Section 3.1, paragraph A.9.3.

F. DETERMINATION OF EQUIVALENCE

Equivalence is determined in a two-tiered approach.

TIER 1 (F.1 – F.4)

F.1 Technical grade active ingredients from different manufacturers or manufacturing processes are deemed to be equivalent if:

F.1.1 the materials meet the requirements of the existing FAO/WHO specifications; and

F.1.2 assessments of the manufacturing process used, the impurity profile and results of mutagenicity (bacteria, *in vitro*) testing have been carried out with the result that the profiles meet the requirements of paragraph F.3 below.

F.2 Where a producer changes the manufacturing process for a technical grade active ingredient which has previously been evaluated and incorporated into a specification, equivalence may be determined on the basis of paragraphs F.1.1 and F.1.2, above.

F.3 Equivalence of the impurity profiles of technical grade active ingredients, determined by comparison of the manufacturing specification limits.¹⁶

¹⁵ OECD Guideline for the testing of chemicals: *Repeated Dose 28-Day Oral Toxicity Study in Rodents (Test No. 407)* and *Repeated Dose 90-day Oral Toxicity Study in Rodents (Test No. 408)*, respectively (OECD, 2008, 2018). The choice of study guideline is governed by the analogue study available for the reference material. When a novel study is performed for the equivalence determination, the animal species and strain shall be the same as in the study for the reference technical material. The dose spacing shall include the LOAEL, NOAEL, and NOAEL/10^{-0.5} as established for the reference profile.

¹⁶ Note. Although this procedure may be used by anyone with legitimate access to the data required, for the purposes of FAO and WHO specifications, equivalence must be determined by the JMPS.

- F.3.1 Where (i) the maximum level (manufacturing limit) of non-relevant impurity is not increased by more than 50% (relative to the maximum level in the reference profile), or the maximum absolute level (manufacturing limit) is not increased by more than 3 g/kg (whichever represents the greater increase); (ii) there are no new relevant impurities; and (iii) the maximum level of the relevant impurities is not increased; the technical grade active ingredients will normally be considered equivalent.
- F.3.2 Where these limits for differences in maximum non-relevant impurity concentration are exceeded, the proposer will be asked to provide a reasoned case, with supporting data as required, as to why the particular impurities remain “non-relevant”. The JMPS will evaluate the case to decide whether or not the technical active ingredient is considered to be equivalent.
- F.3.3 Where new impurities are present at ≥ 1 g/kg, the proposer will be asked to provide a reasoned case, with supporting data if available, as to why these impurities are “non-relevant”. The JMPS will evaluate the case to decide whether or not the technical active ingredient is equivalent.
- F.3.4 The mutagenicity (bacteria, *in vitro*) profile is considered equivalent to that of the reference material if the assessment compares endpoint to endpoint and the outcome is not worse for the material under consideration.
- F.3.5 Information about the assessment of the proposed material by a competent registration authority is taken into account in Tier-1.
- F.3.6 Where relevant impurities are increased in maximum concentration and/or where new relevant impurities are present, appropriate toxicological, ecotoxicological or other information on the technical grade active ingredient or the impurities in question should be submitted, if available, for evaluation in Tier-2.
- F.4 Where the Tier-1 information is insufficient to decide on equivalence or is insufficient to decide on non-equivalence, further evaluation should proceed with information and data available under Tier-2.

Technical grade active ingredients from different manufacturers or manufacturing processes are deemed to be equivalent if Tier-1 non-equivalence is uncertain and the Tier-2 assessments of the toxicological/ecotoxicological profiles have been carried out with the result that the profiles meet the requirements of paragraph F.5 and F.6, below.

TIER 2 (F.5 – F.6)**F.5 Equivalence of the toxicological profiles of a technical grade active ingredient**

F.5.1 The toxicological profile will be considered equivalent to that of the reference profile, where the data required by paragraph E.1 above (referring to the requirements of Section 3.1, paragraph A.9.1) do not differ by more than a factor of 2 compared to the reference profile (or by a factor greater than that of the appropriate dosage increments, if more than 2). There should be no change in the assessment in those studies which produce categorical results (e.g. Category 1, 2, or 3 skin irritant, not a skin irritant).

- (i) Studies which produce categorical results (e.g. Category 1, 2, or 3 skin irritant, not a skin irritant) do not lead to a more serious classification than the reference product.
- (ii) No qualitatively new adverse effect is observed in the repeated dose studies (28 or 90 days repeated dose studies in rodents).
- (iii) The NOAEL or bench-mark dose for any toxicity endpoint is not more than a factor of $10^{-0.5}$ lower than that for the reference product.

F.5.2 Where necessary (see paragraph E.2), additional toxicological data (see paragraph E.2.1) will be assessed by the criterion applied in paragraph F.5.1, provided that, where appropriate, the organs affected are the same. The bench-mark dose should not differ by more than a factor of two, or the “no observable effect levels” (NOELs) or NOAELs should not differ by more than the differences in the dose levels used.

F.6 Equivalence of the ecotoxicological profiles for the technical active ingredient (as appropriate to the intended use of the active ingredient).

Where required (see paragraph E.2), the ecotoxicological profile (paragraph E.2.2) will be considered equivalent to that of the reference profile if the data do not differ by more than a factor of 5 compared to the reference profile (or by a factor more than that of the appropriate dosage increments, if greater than 5), when determined using the same species.

Note to paragraphs F.3.1, F.5.1, F.5.2 and F.6

Reference profiles are defined by the information provided for the reference specification, according to the requirements of paragraphs A.4, A.5, A.6, A.8 and A.9 of Section 3.1.

F.7 Where a technical active ingredient proposed for inclusion in an existing specification does not comply strictly with the tests for equivalence given in this Section 3.2, but it is otherwise considered by the JMPS to be of acceptable or improved quality, a modification of the existing specification will be considered. This procedure may follow evaluation of the data required under paragraph E.1 and/or E.2, above.

3.3 MINIMUM DATA REQUIREMENTS FOR EXTENSION OF AN EXISTING FORMULATION SPECIFICATIONS TO AN ADDITIONAL MANUFACTURER

General notes

- (i) To introduce a new formulation specification where the proposer's TC/TK specification has already been accepted, or where a formulator utilizes a TC/TK produced by a manufacturer whose specification has already been accepted, it is not necessary to resubmit (or submit) the complete dossier identified below. In the latter case, the formulator must declare the source of the TC/TK and provide an undertaking: (i) that it is the sole source; and (ii) that if an alternative source is subsequently utilized, FAO and/or WHO will be notified immediately. Where a complete dossier is thus considered unnecessary, the proposed specification should be submitted, together with any necessary justification for deviations from the guideline specification.
- (ii) Original study reports are required and have to be provided for the physical-chemical properties of formulations. The study report source of data should be summarized in the form of study number, author, year, title, report number and company conducting the study, to allow ease of reference between the proposer and FAO/WHO.
- (iii) The absence of an agreed and published specification guideline does not preclude submission of a proposed specification. FAO and WHO wish to encourage the development of novel formulations which address pest control problems. Guidelines will not exist for unique formulation types and, in such cases, the manufacturer must define the critical characteristics and provide suitably validated test methods for measurement of the appropriate parameters.

G. DATA REQUIREMENTS FOR THE DETERMINATION OF EQUIVALENCE OF CLASSICAL FORMULATIONS

For the purposes of FAO/WHO specifications, formulations may be evaluated by JMPS and generally considered to be equivalent if: (i) the TC/TK has been judged equivalent and (ii) the formulations comply with the same specification.¹⁷

H. DATA REQUIREMENTS FOR THE DETERMINATION OF EQUIVALENCE OF SLOW OR CONTROLLED RELEASE FORMULATIONS

In special cases, for example slow-release formulations such as capsule suspensions (CS), additional evidence may be required to determine equivalence of the formulations and they are likely to be non-equivalent if unique technology, specification limits or test methods are involved.

¹⁷ Equivalent products are not necessarily suitable for the same uses, or provide equal efficacy, etc. Equivalence means only that they comply with similar basic quality criteria.

Unlike most other formulation types, apparently similar slow or controlled release formulations like some CS and granule (GR) products, may be based on different technologies, with the result that a specification developed for one manufacturer's product may not provide a reliable means for testing the acceptability of another manufacturer's product. For this reason, additional information is required to extend existing specifications for slow release products to additional products (i.e. to determine their equivalence) or, where appropriate, to develop separate specifications.

3.4 EVALUATION REPORTS

Evaluation reports have the following general structure. They contain no confidential information on the manufacturing process or impurity profile, other than the minimum required to identify relevant impurities and their limits. In special cases, it may be necessary to explain why a particular impurity is considered to be non-relevant.

The timetable, content of evaluation reports, and communications between FAO/WHO secretariat, proposer, evaluator, peer reviewer and editor are presented in Appendix K.

TITLE [ISO name of compound]

CIPAC code/year of evaluation by JMPS

3.4.1 Recommendations

Provides recommendations regarding withdrawal/retention of existing FAO/WHO specifications, if necessary.

Provides recommendations regarding adoption by FAO/WHO of proposed new specifications, or of proposed modifications/extensions to existing specifications. Recommendations may be conditional in some cases, subject to satisfactory validation of analytical or physical test methods by the manufacturer, for example.

May identify additional information required from the manufacturer (or other source), to enable the JMPS to complete the evaluation.

May provide recommendations to FAO/WHO on general principles for pesticide specifications development, where these emerge from the evaluation.

3.4.2 Appraisal

Identifies the active ingredient and its patent status, the proposed and any existing specifications, the manufacturers/proposers and the year in which the data package was originally submitted. Provides a brief history and explains if the evaluation is in response to unresolved or open points.

Provides an evaluation of all information supporting the recommendations. In general, it does not provide evaluations of the same, or related, data made by other organizations, except where they have a bearing on the JMPS recommendations. However, evaluations made by WHO with regards to WHO specifications and/or prequalified products are always summarized, with the essential arguments fully explained.

Provides the outcome and rationale for JMPS conclusions on the relevance of impurities and the equivalence of technical and formulated products. An indication is provided of whether the impurity profile data correspond to those submitted for registration in a particular country. No confidential data are included, other than those incorporated into the specification to be published.

Identifies gaps in, or problems with, the data submitted. Explains why a proposed specification or the data profile may be considered unacceptable.

3.4.3 Supporting information

Uses. The main uses of the active ingredient (or formulation, in special cases) are summarized briefly. This information is not evaluated for the appraisal.

Identity of the active ingredient. Provides the ISO (or other) common name; synonyms; IUPAC and CA chemical names; CAS Registry number; CIPAC number; structural formula; empirical formula; molecular weight; identity tests. Where the active ingredient defined by the specification has no common name, or where definition differs from that implied by the common name, or where there is any other potential ambiguity, this is fully explained in the appraisal.

Physical and chemical properties of pure active ingredient. Usually provides data on vapour pressure; melting point; decomposition temperature; water solubility; log P K_{ow} ; hydrolysis; photolysis; pKa; and any other characteristic relevant to the proposed specifications. These data are evaluated and, where the properties have a bearing on decisions made by the JMPS, an explanation is provided in the appraisal.

Chemical composition and properties of the technical grade active ingredient. Usually provides data on mass balances observed in 5-batch analyses of purity/impurities; minimum content of active ingredient (including tolerance for TK); maximum levels of relevant impurities; identities and limits for the content of stabilizers or other essential additives; melting point, boiling point and/or decomposition temperature. These data are evaluated and, where they have a bearing on decisions made by the JMPS, an explanation is provided in the appraisal.

Background information on toxicology/ecotoxicology. Provides a brief summary of toxicology evaluations conducted by other organizations. This information is not evaluated for the appraisal unless, exceptionally, it has a bearing on JMPS decisions. Includes the manufacturer's statement on the relationship between the data provided on chemical composition of the technical grade active ingredient (previous paragraph) and the materials used

to produce the data on toxicity and ecotoxicity (proposer's hazard summary, 3.4.4).

Formulations. The main formulation types available are identified and a summary of countries where the formulations are registered and sold is provided.

Methods of analysis and testing. Methods used to produce data on physico-chemical properties are summarized briefly. Methods for determination of active ingredient identity (at least 2 independent techniques), active ingredient content, content of relevant impurities, and physical test methods are summarized. Methods for identification of the counter-ion, etc., are stated in cases where the active ingredient is present in the form of a specific salt or other derivative. The validation status of methods supporting the specification is stated, incompletely validated methods are identified, and the information is provided in the appraisal.

Containers and packaging. A brief indication of special requirements for containers and packaging, if required, but the information is not evaluated.

Expression of the active ingredient. Where the active ingredient is present in the form of a salt, ester, or other derivative, the moiety determined by the analytical method is stated, together with the form of expression of results.

3.4.4 Hazard summary provided by the proposer

Provides a summary of information on acute and sub-acute to chronic toxicity (including carcinogenicity and teratogenicity); genotoxicity, and ecotoxicology, derived from technical grade active ingredient manufactured by the proposer. Provides information on the toxicity of relevant impurities, if available. Where data from this section have been evaluated by WHO, for example to assist in the determination of equivalence, the evaluation is summarized in the appraisal, otherwise the information is neither evaluated nor summarized in the appraisal.

3.4.5 References

Published and unpublished documents, containing data or other information presented or mentioned in the report, are referenced. A reference section at the end of the evaluation of the confidential data should include the relevant studies and documents. A second reference section should be included at the end of the evaluation of non-confidential data for the relevant studies and documents there. Unpublished documents are referenced by study number (or document number), authors, year and title and document number allocated by the sponsor. E-mails are referenced by author, date, sender's organization and FAO/WHO recipient.

FAO and WHO, before publication and during the final editorial process, will remove source details from the toxicological studies (e.g. author names) to protect the authors and laboratories from extremists.

The example shows the format for references.

References (sorted by study number)			
Study number	Author(s)	year	Study title. Study identification number. Report identification number. GLP [if GLP]. Company conducting the study. Title and journal reference for published documents.
	Cambon J-P and Bastide J.	1996	Hydrolysis kinetics of thifensulfuron-methyl in aqueous buffer solutions. <i>J. Agric. Food Chem.</i> 44:333-337.
	FAO/WHO	2021	Manual on development and use of FAO and WHO specifications for chemical pesticides. Second edition. https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/en/ and https://extranet.who.int/pqweb/vector-control-products/manual-amendments
	Martijn A and Dobrat W	2000	CIPAC Handbook Volume J. Analysis of Technical and Formulated Pesticides.
XX-nnn	Author AB and Writer CD	2007	Determination of melting point of pure and technical grade xoo6. Study XX-nnn. Report XX-nnn.03. GLP. XYZ Contract Laboratories, XXland. Unpublished.

3.5 MAKING A RECOMMENDATION AND ACTION PROCEDURES FOR DEALING WITH SUBMISSIONS FROM INITIAL AND SUBSEQUENT PROPOSERS

Scenario 3.5.1

No FAO/WHO specification exists for the pesticide.

- A proposer or group of proposers submits a draft specification, supported by information in accordance with the requirements of Section 3.1.
- The JMPS assesses the impurity, toxicological and ecotoxicological profiles, to determine which impurities are relevant and must be specified.
- FAO/WHO agree the text of the evaluation and specification and the proposer checks it for factual accuracy.
- FAO/WHO publish the evaluation and specification, including the name(s) of the proposer(s) of the specifications for technical grade active ingredient(s) or formulation(s) recommended for adoption in the evaluation.

Scenario 3.5.2

Incorporation of a subsequent manufacturer's technical grade active ingredient or formulation(s) into an existing evaluation and the list of evaluations.

- (a) The subsequent proposer(s) provide(s) information in accordance with the requirements of Sections 3.2 and/or 3.3 (manufacturing process, impurity profile, short term toxicity and, where equivalence cannot be determined with this information, any additional toxicity data requested by the JMPS).
- (b) The JMPS compares the new impurity, toxicological and ecotoxicological profiles with the original one(s), and recommends that FAO/WHO take actions as indicated below.

Case (i) Insufficient data are provided or the quality of the material is unacceptable.

Action: Rejection of the new submission.

Case (ii) Submission and quality of the material are acceptable and no change of the specification is needed.

Action: Add the name(s) of the subsequent proposer(s) to the evaluation and the list of evaluations to be published by FAO/WHO.

Case (iii) The quality of the material is acceptable but the specification must be changed to accommodate the additional material.

Action: Involve the proposer(s) already listed to develop a mutually agreed draft of a revised specification. If the listed proposer(s) do not wish to comment on, or cannot agree to, changes in the specification, the JMPS will recommend options for appropriate action by FAO/WHO.

3.6 PRIORITIZATION CRITERIA FOR DEVELOPMENT AND REVIEW OF SPECIFICATIONS

FAO and WHO will prioritize the 3-year programme according to the following criteria, which are not presented in strict order of priority.

- Development of specifications for new active ingredients and/or formulations required by FAO or WHO for use in international programmes, e.g. for locust control and for control of major vector-borne diseases.
- Review of existing specifications for active ingredients or impurities with newly discovered serious health or environmental hazards and/or a rejection of re-registration at national/regional review for this reason.
- Review or development of specifications for active ingredients under evaluation or re-evaluation by JMPS.
- Development of specifications for new active ingredients or formulation types, as chosen by the proposer.
- Extension of existing specifications to encompass products manufactured by additional producers.
- Review of existing specifications where changes to the manufacturing process have occurred.

- Review of existing specifications where the active ingredients are, or are expected to become, subject to international agreements on Prior Informed Consent or Persistent Organic Pollutants.
- Review of existing specifications where active ingredients are subject to withdrawal of national or regional registration, due to lack of supporting data.
- Review of existing specifications where active ingredients being reviewed by the European Union, the United States of America, Japan and other regulatory authorities, under re-registration programmes.
- Review of existing specifications which are tentative, provisional or interim.
- Review of existing specifications older than 10 years where the pesticides are still marketed.
- Review of existing specifications where the pesticides are no longer marketed.
- The three-year programme will be reviewed annually.

4. AIMS, APPLICABILITY AND REQUIREMENTS OF CLAUSES

Note

Certain additional clauses for household insecticides appear in Section 8. In these cases, the aims, applicability and requirements are generally evident from the context of the clauses.

Introduction

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 active ingredient and formulations, such as the flash point, 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 technical or formulated product. In addition, the notes may provide supporting information on test conditions or, in some cases, provide details of the test methods. However, in most cases, the specifications simply give references to the test methods to be used.

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 5 to 8 may be inappropriate, or additional clauses may be necessary, for a particular specification. Where the need for the clause is clearly dependent upon the active ingredient, 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.

With the exception of tolerances on active ingredient content, 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.

Formulation specifications normally refer only to a single active ingredient. Where two or more active ingredients are co-formulated,

- 1) the specified minimum purity and the maximum content of all relevant impurities for every active ingredient are expected to apply;
- 2) the analytical methods referred to in the specifications may no longer apply without modification. It is the duty of the manufacturer to submit adequate information.
- 3) For the physical properties
 - where limits are recommended under “Requirements” in Section 4.5 of this manual, these limits are expected to apply.
 - where no limits are recommended, the suitable value of the “mixed” specifications should apply.

Examples of applying these procedures:

Specification for product of active ingredient 1	Specification for product of active ingredient 2	Specification for product of mixed active ingredients 1 and 2
70% suspensibility	95% suspensibility	60% suspensibility
70% suspensibility	no specification	60% suspensibility
Pourability 1%	Pourability 3%	Pourability 5%
Pourability 1%	no specification	Pourability 5%
pH 3 ... 6	pH 4 ... 8	pH 4 ... 6
pH 3 ... 6	no specification	pH 3 ... 6

In exceptional cases a specification may be accepted for a co-formulated product but the manufacturer must explain the basis for the requirement.

FAO/WHO specifications do not apply to mixtures prepared in the spray tank, etc.

As far as practicable, a sample taken for testing for compliance with a specification must be representative of the entire lot of the pesticide under scrutiny.

Recommendations for sampling are presented in Section 8, in the Notes to the guideline specifications.

Whereas the majority of specification clauses are deemed to be applicable to all possible cases, some other clauses are conditional and therefore are necessary for certain particular cases only. These conditional requirements carry the wording "if required". It is up to the proposer to justify whether a clause that is marked with "if required" in a particular specification is necessary. As an exhaustive coverage of all possible cases is difficult and even unnecessary, some selected examples from recently published specifications and their justifications are presented in Appendix L and illustrate the underlying principles for these conditional specification clauses. These

examples of specifications with "if required" clauses provide a justification why such a particular "if required" clause was deemed acceptable by the Meeting.

Generally speaking, an "if required" clause is justified in cases where it carries essential information not available otherwise (e.g. a stabilizer or a particular isomeric composition in a TC), or if a clause and its limit or acceptable range is needed to control certain adverse effects e.g. an increase in hazard of a TC through the presence of a relevant impurity, degradation reactions catalysed by water or an unsuitable pH-range.

4.1 TITLE AND CODE

Aim

To provide a brief, unequivocal identification and description of the technical or formulated pesticide.

Applicability

All specifications.

Methods

Not relevant.

Requirements

Names

The E-ISO (or INCI for repellents, etc.) common name of the active ingredient should be used, indicating the status of the name. If an ISO or INCI name does not exist then the trivial name, or the chemical name according to IUPAC or CA conventions, may be used. If a trivial name is used, the IUPAC or CA chemical name should be given in addition.

Codes

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

Comments

Codes for FAO specifications developed under former procedures included a status code. The previous system is explained in Appendix B of the *Manual on the Development and Use of FAO Specifications for Plant Protection Products*, 4th edition, Plant Production and Protection Paper 128, 1995, FAO, Rome. These status codes will be superseded when the earlier specifications are reviewed.

Codes developed under former procedures for WHO *full specifications* included a status code and type of pesticide product, followed by a number allocated to each compound and formulated product. Codes for *interim specifications* included a status code and a number referring to the year of publication and file number. As part of the transition to the new procedure, codes for more recent WHO interim specifications have included the product type, CIPAC number and year of publication.

4.2 DESCRIPTION

Aim

To provide a brief, clear description of properties of the technical grade active ingredient or formulation, 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 technical grade active ingredient or formulation should include physical state (e.g. crystals, liquid, hard lumps, etc.), colour, odour (if appropriate, and taste for products intended for use in potable water) 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 5 to 8) includes a standard clause for the description.

Where the active ingredient may exist in various chemical forms, the description must fully identify the form. For example, in the case of 2,4-D, the active ingredient must be described as 2,4-D sodium salt, 2,4-D free acid, 2,4-D *iso*-octyl ester, etc., as appropriate. If the same specification is to be applied to more than one salt, ester, etc., the clause should identify them. For example, “...as the sodium, potassium or ammonium salt...” or “...as the mixed sodium and potassium salts...”. The phrase must be deleted from the description (Sections 5 to 8) if it does not apply. The title must include CIPAC code for the salt or derivative.

In most cases, a specification will apply only to one active ingredient, whether or not it may be formulated with others. Where it is essential to include more than one active ingredient in a single specification, the description must identify all active ingredients present.

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.

4.3 ACTIVE INGREDIENT

4.3.1 Identity tests

Aim

To provide a proven means for identification of the active ingredient(s).

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 techniques involved are non-standard, the description should appear as a note at the end of the specification.

Requirements

At least two identity tests are required for the active ingredient, or its active component, to enable a clear decision to be made if one test produces ambiguous results.

Where the active ingredient is in the form of a salt (etc.) and the counter ion (etc.) is not identified by the test for the active component, a separate identity test may be required for the counter ion (etc.). Such a test is usually more important for TC/TK specifications, so that formulators can be sure of their starting materials. However, if the identity of the counter-ion is important for reasons of product stability, safety, efficacy, etc., the test may also be required for formulations. The identity test for the counter-ion may be simpler than, or part of, the identity test for the active component. For example, melting point may be used or, if an active ingredient identity test is based on IR, a band specific to the salt may be sufficient. A single identity test is usually sufficient for the counter-ion (etc.).

Where the active ingredient is a mixture of isomers and its ISO common name defines the mixture, the specification does not require a clause to define the mixture. If the mixture is not defined by an ISO common name, the specifications for technical and formulated products will normally include a clause for isomer ratio. In the latter case, JMPS consideration of manufacturer's proposals will take into account current regulatory practice in countries where the active ingredient is registered. In both cases, the analytical method to determine isomer ratio must be peer-validated, as a minimum.

4.3.2 Content of active ingredient

Aim

To ensure that the active ingredient content is described by limits, acknowledging the fact that both analytical results and actual concentrations are variable.

Applicability

All specifications.

Methods

The method(s) of analysis must be adopted by CIPAC or AOAC (provisional method as a minimum) prior to publication of the specification. If the method has not yet been published, then full details must be submitted to FAO and/or WHO by the proposer.

Requirements

For solids, liquid technical pesticides, volatile liquids (of maximum boiling point 50°C) and viscous liquids (with minimum kinematic viscosity of $1 \times 10^{-3} \text{ m}^2/\text{s}$ at $20 \pm 2^\circ\text{C}$) the content must be expressed on a g/kg basis.

For other liquids the active ingredient content may be declared in terms of g/kg or g/l at $20 \pm 2^\circ\text{C}$.

The active ingredient content of **technical materials (TC)** should be expressed as:

“The [ISO common name] content shall be declared (not less than g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.”

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

“The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$) and, when determined, the average measured content shall not differ from that declared by more than the following tolerances:”

The tolerances for formulated products and TK should be expressed in the form of the table below, including only the appropriate content and tolerance entries.

Declared content in g/kg or g/l at $20 \pm 2^\circ\text{C}$	Tolerance
up to 25	\pm 15% of the declared content for “homogeneous” formulations (EC, SC, SL, etc.), or \pm 25% for “heterogeneous” formulations (GR, WG, etc.)
above 25 up to 100	\pm 10% of the declared content
above 100 up to 250	\pm 6% of the declared content
above 250 up to 500	\pm 5% of the declared content
above 500	\pm 25 g/kg or g/l
Note: In each range the upper limit is included.	

Comments

The tolerances are by intention generic in nature and refer to the average analytical result obtained. The dependence of the tolerances from the declared content broadly follow the relationship between the nominal content of an active ingredient in a TK or formulated product and the repeatability relative standard deviation (RSD_R) similar as expressed in the Horwitz equation (Horwitz, Kamps and Boyer, 1980). For practicability reasons, the dependence has been aggregated in concentration classes where, with the lowest concentration heterogeneous concentrations, are allowed a higher tolerance

than homogeneous ones. These tolerances represent the combined variations that may occur in manufacturing, packaging, storage, sampling and analytical assays despite best effort, except where an overage is required.

Technical concentrates or formulations will be considered to comply with the specification if the average analytical result lies within the tolerance range of the declared content.

In cases of dispute, the following should be kept in mind:

- if a specification provides limits in both g/kg and g/l, the analytical results must be determined and expressed as g/kg. Conversion of g/kg data to g/l should be based on measurement of the actual mass per millilitre of the formulation at a specific temperature, not on a nominal value.
- when an analytical result (expressed as average of two or more measurements) and its associated confidence interval overlaps or is outside a limit according to the nominal content, a generally accepted approach for settling conflicting results obtained in one laboratory with that responsible for the released consignment is encouraged (see e.g. CropLife International Technical Monograph No. 1, *Use of Tolerances in the Determination of Active Ingredient Content in Specifications for Plant Protection Products* [CropLife International, 2005]).

Positive deviations from the upper limits given in the table 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 and the overage should be as low as practicable.

Technical materials (TC) do not have an upper limit given for content because it is desirable that their purity should be as high as practicable. An increase in active ingredient content above the minimum specified will have no measurable risk consequences but the consequential decrease in impurity content may reduce risks and will minimize the dispersal of the impurities into the environment.

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.

The table of tolerances should include only those formulation concentrations which are available in the market and, in the case of WHO specifications, those which have been evaluated by WHO PQT/VCP.

Where the method for determination of active ingredient content is based on detection of only the active component of a salt (etc.) and not the complete salt (etc.), the specification must define the exact basis for calculation and expression of active ingredient content. The same applies where the active ingredient content is determined indirectly.

4.3.3 Expanded tolerances for active ingredient content of mixed solid formulations

Aim

To allow for the fact that solids cannot be mixed to produce the degree of homogeneity achievable with liquid mixtures.

Applicability

Mixtures of solid products prepared post-formulation.

Methods

An example calculation is given in Appendix I. Limits for active ingredient content (Section 4.3.2) within each component formulation are expanded by applying a corresponding tolerance to the content of the formulation within the mixture, as follows.

Formulation a.i. upper or lower limit, g/kg (A)
= declared content of a.i. in component, g/kg \pm tolerance

Component upper or lower limit, g/kg (B)
= declared content of component in the mixture, g/kg \pm tolerance

Expanded a.i. upper or lower limit, g/kg = (A x B)/1000
where:

a.i. = active ingredient;

component = the formulation containing the a.i.;

tolerance = value obtained from the table of tolerances (4.3.2), according to the declared value for a.i. content or component. The tolerance is added or subtracted to calculate the upper or lower limit values, respectively, for A and B.

Requirements

The size of sample to be analysed (test portion) must be stated.

Comments

Values for B are not intended as tolerances for addition of components to the mixture. They provide a simple, empirical approach to the calculation of expanded tolerances and reflect limits achievable with good practice in manufacturing.

4.3.4 Tablet dose uniformity

Aim

To ensure that the active ingredient dose is routinely accurate.

Applicability

Tablet for direct application (DT), water soluble tablets (ST), water dispersible tablets (WT).

Methods

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

Requirements

General limits cannot be given.

4.3.5 Rate of release or wash resistance index 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- or controlled-release granules (GR), slow-release capsule suspensions (CS), multi-character liquid formulation (ZC, ZW, ZE), long-lasting storage bags (LB), matrix release (MR).

Methods

Appropriate test methods are not available except for long-lasting insecticidal nets (LN) and LB. Test methods for CS, GR, multi-character formulations and MR are product-specific. CIPAC has developed a method to determine the wash resistance index of active ingredient for insecticide treated nets and LB. The wash resistance index is determined by analysing net samples in triplicate representing wash points 0 and 4 for total active ingredient content and calculating the average wash resistance index per wash.

MT 195 Wash resistance index of LN.

Requirements

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 capsules, granules or resin formulations. Encapsulated granules and capsules are usually subjected to a more or less consistent environment after application and the tests reflect this.

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.

4.3.6 “Free” active ingredient

Aim

To limit the proportion of active ingredient that can be regarded as non-encapsulated in an encapsulated formulation, in order to limit the risks of dermal exposure to users (the formulation may be rinsed from skin before significant penetration occurs).

Applicability

Slow-release capsule suspensions (CS), multi-character liquid formulation (ZC, ZW, ZE).

Methods

Test methods are product specific. Appropriate test methods need to be available.

Requirements

General limits cannot be given.

Comments

“Free” active ingredient may be in solution, emulsion or adhering to the outside of capsule walls. The active ingredient within slow release capsules is usually in dynamic equilibrium with the external environment and it follows that any measurement which disturbs the equilibrium will change the distribution. Use of the methods therefore requires strict adherence to the extraction protocol because “free” active ingredient is defined by the method of measurement.

4.4 RELEVANT IMPURITIES

4.4.1 By-products of manufacture or storage

Aim

To limit the content of impurities (other than water or insolubles) which may otherwise increase the risks associated with handling or use of the technical material or formulation, or adversely affect the efficacy of the formulation.

Applicability

All specifications where relevant impurities may be associated with the active ingredient.

Methods

Analytical methods must be peer validated, as a minimum. Where the analytical 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 analytical method should be described in a note to the specification. CIPAC

has issued a guideline¹⁸ on requirements for peer validation of relevant impurity methods.

Requirements

The maximum permitted level should be quoted as g/kg of the active ingredient content. The maximum permitted level may be quoted as g/kg of formulated product only in unusual cases where evidence is provided to show that its concentration relative to the active ingredient is affected by the formulation, dilution, etc.

Clauses must be provided only for relevant impurities (see comments, below).

Separate clauses must be provided for each relevant impurity.

Comments

Section 3.1, D describes how the JMPS decides whether an impurity is relevant or non-relevant and how limits are set for relevant impurities.

Relevant impurities can occur in formulants and unintended contamination with other chemicals can occur during preparation of a formulation. Formulants and their impurities, and formulation contaminants, are not within the scope of FAO and WHO specifications. In exceptional cases, where an impurity in a formulant is capable of increasing the content of a relevant impurity produced by synthesis or degradation of the active ingredient, the maximum content of the relevant impurity may be specified on a formulation basis (as opposed to the usual active ingredient basis). In all other cases where hazardous compounds could be present in formulants, manufacturers of formulations must ensure that risks from these sources are minimized and acceptable.

The average measured level of a relevant impurity must not exceed its declared maximum limit.

4.4.2 Water

Aim

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

Applicability

Technical materials, technical concentrates and non-aqueous formulations.

¹⁸ CIPAC Guideline for analytical methods for the determination of relevant impurities referred to in FAO/ WHO specifications for pesticide technical grade active ingredients and formulations; rev. 7. Available at www.cipac.org/index.php/guidelines (CIPAC, 2009).

Methods

MT 30.2 Dean and Stark method.

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

Requirements

The maximum permitted level must be quoted in g/kg of the active ingredient 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 TC/TK, and the water is not adequately limited by another clause. Water is usually accepted as a relevant impurity in a TC/TK if it is to be used to prepare water-sensitive formulations, such as emulsifiable concentrate (EC), ultra-low volume liquid (UL), dispersible concentrate (DC), oil miscible liquid (OL) and oil dispersion (OD).

4.4.3 Insolubles

Aims

To limit materials that are insoluble in specified solvents. This is to enable producers of formulations to quantify impurities that, when the formulation is used in the field, may block filters and nozzles, or may otherwise adversely affect the physical properties of the formulation. Insolubles must be shown to be relevant to be included in a specification.

Applicability

Technical materials and technical concentrates, if required.

Methods

MT 7 Ethanol insoluble material;

MT 71 Sodium hydroxide insoluble material;

MT 10 Water insoluble material;

MT 11 Xylene insoluble material;

MT 27 Acetone insoluble material;

MT 35 Oil insoluble material.

Requirements

The maximum permitted level must be quoted in g/kg of the active ingredient. The method to be used must be stated.

Comments

If none of the existing methods is suitable, reasons should be given and alternatives referenced together with information supporting their validation.

4.5 PHYSICAL PROPERTIES

Introduction

For the purposes of this manual, these properties are broadly grouped and numbered as follows: (i) density properties, 1-10; (ii) surface properties, 11-20; (iii) volatilization properties, 21-30; (iv) particulate, fragmentation and adhesion properties, 31-40; (v) dispersion properties, 41-50; (vi) flow properties, 51-60; (vii) solution and dissolution properties, 61-70. 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/VCP 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 physical-chemical tests, recommended limits are stated. For example, in the case of suspensibility, it shall be at least 60% after 30 min. 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 had been harmonized 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), MT 184.1 (suspensibility of formulations forming suspensions on dilution in water) and MT 197 (disintegration of tablets).

CIPAC MT 18 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 which is assumed to cover the whole range of the use rates. However, where a fixed concentration is indicated in a CIPAC method this concentration should be used.

(i) **Density properties**

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

Granules (GR).

Methods

MT 186 Bulk density, the preferred method.

Requirements

General limits cannot be given.

Comments

The limits should be justified.

(ii) **Surface properties**

4.5.11 Wettability

Aim

To ensure that water dispersible/soluble powders and granules, and emulsifiable 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.

Methods

MT 53.3 Wetting of wettable powders.

Requirements

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

4.5.12 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.

Methods

MT 47.3 Persistent foam.

Requirements

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 provided it is within the scope of the method.

Except for formulations packed in water soluble bags, persistent foaming is not tested after storage at elevated temperature.

(iii) Volatilization properties¹⁹**4.5.21 Volatility****Aim**

To ensure that application of ultra-low volume formulations does not lead to unacceptable drift due to too rapid evaporation of the sprayed droplets.

Applicability

Ultra-low volume liquids (UL).

Methods

No suitable test methods are available for volatility of UL.

Requirements

Dependent upon the method of measurement.

Comments

The evaporation rate of droplets is dependent on their size, composition and air temperature. Initial droplet size is partly a function of the application equipment used. In the absence of a standard test for evaporation rate, the method adopted for the specification must be made available to FAO and/or WHO, together with data supporting its validity. Supporting information should

¹⁹ Flash point is an important safety characteristic of many liquid formulations. Under the FAO/WHO old procedure, clauses to limit flash point were included in certain guideline specifications but they were withdrawn under the new procedure. Flash point is usually determined by the solvents used for formulation and is therefore under manufacturing control. However, flash point is a measure of hazard, not of performance, and, as in the case of the active ingredient, the risks are application-dependent. As with other hazards, the JMPS cannot undertake risk assessments and relies upon assessments made by national registration authorities, WHO/PCS, IPCS and FAO/WHO JMPR. Risk assessments relating to the active ingredient can usually be adopted freely* because hazard characteristics such as toxicity are not greatly influenced by climate. In contrast, the risks associated with flash point are dependent upon both climate and the specific uses which are registered and it is difficult to provide global specifications for this characteristic. In cases where flash point is of major concern, a "Note" may be inserted into a specification, drawing attention to the need to adhere to national requirements, but FAO/WHO specifications cannot provide a single, universal limit for flash point.

*Note. A criterion for development of an FAO/WHO specification is current registration by one or more competent authorities, implying that the risks associated with one or more uses of the product have been assessed as acceptable in one or more countries. The existence of an FAO/WHO specification does not diminish the need for other registration authorities to assess the risks associated with uses of the product in areas for which they are responsible.

be provided on the correlation between the volatility specified and droplet size reduction and consequential increased drift potential.

(iv) **Particulate, fragmentation and adhesion properties**

4.5.31 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 and oil-based (SC and FS), oil dispersions (OD); water dispersible granules (WG) and water dispersible powder for slurry seed treatment (WS); capsule suspensions (CS); dispersible concentrates (DC); suspo-emulsions (SE); water soluble and dispersible tablets (ST and WT); emulsifiable granules and powders (EG and EP), multi-character liquid formulations (ZC, ZW, ZE).

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.

Requirements

A suitable phrase and values may be:

Maximum 2% retained on a 75 µm test sieve.

Comments

In some specification guidelines, this test is not included because it is effectively included in other tests, e.g. solution stability, see 4.5.64.

4.5.32 Dry sieve test

Aim

To restrict the content of particles of unwanted sizes.

Applicability

Dustable powders (DP), Powders for dry seed treatment (DS).

Methods

MT 170 Dry sieve analysis of water dispersible granules.

Requirements

General limits cannot be given.

4.5.33 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).

Methods

MT 170 Dry sieve analysis of water dispersible granules.

MT 187 Particle size analysis by laser diffraction.

Requirements

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

Comments

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

4.5.34 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), water dispersible granules (WG), emulsifiable granules (EG) and water soluble granules (SG).

Methods

MT 171.1 Dustiness of granular products.

Requirements

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.

Comments

Method 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.

4.5.35 Attrition resistance or degree of attrition

Aim

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 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, WG, SG and EG) and tablet formulations (DT, WT, ST, depending upon their intended mode of use).

Methods

MT 178 Attrition resistance of granules (GR).

MT 178.2 Attrition resistance of dispersible granules and tablets (smaller than 1 cm diameter).

Requirements

General limits cannot be given.

Comments

MT 178.2 is also applicable to measure the attrition resistance of tablets with a diameter ≤ 1 cm.

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

4.5.36 Tablet integrity

Aim

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

Applicability

Tablets (DT, ST and WT).

Methods

Visual observation.

Requirements

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

4.5.37 Adhesion to seeds

Aim

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 seeds.

Requirements

General limits cannot be given.

4.5.38 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.

4.5.39 Tablet hardness

Aim

To ensure that tablets remain intact during handling and application.

Applicability

Tablets which must not crumble before or during application.

Methods

No suitable test methods are available for tablet hardness.

Requirements

Limits are usually product-dependent.

(v) Dispersion properties

4.5.41 Dispersibility and spontaneity of dispersion

Aim

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

Applicability

Suspension concentrates (SC), capsule suspensions (CS), mixed formulations of CS and SC (ZC) 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), capsule suspensions (CS), and mixed formulations of CS and SC (ZC), the spontaneity of dispersion shall be at least 60% after 5 min.

For water dispersible granules (WG), the dispersibility shall be at least 60% after 1 min of stirring.

Comments

Using method MT 160, chemical assay is the only fully reliable technique to measure the mass of active ingredient still in suspension. Simpler measurements such as gravimetric and solvent extraction determination may be used routinely, provided that they have been shown to give equal results to those of the chemical assay method. In cases of dispute, chemical assay shall be the referee measurement. The test is normally carried out using CIPAC standard water D at $25 \pm 5^\circ\text{C}$. Method MT 174 has been validated only for gravimetric determination.

4.5.42 Disintegration time and dispersibility/dissolution

Aim

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

Applicability

Soluble tablets (ST) and water dispersible tablets (WT).

Methods

MT 196 Solution properties of water soluble tablets (ST).

MT 197 Disintegration of tablets.

Requirements

General limits cannot be given.

4.5.43 Suspensibility

Aim

To ensure that the active ingredient remains homogeneously dispersed in the spray liquid to give a satisfactory and effective mixture during spraying.

Applicability

Capsule suspensions (CS), flowable concentrate for seed treatment (FS) which are diluted for use, suspension concentrates (SC), mixed formulations of CS and SC (ZC), water dispersible granules (WG), wettable powders (WP), and water dispersible tablets (WT).

The suspensibility test is not required for formulations or formulation types where the concentration for use is not in line with the upper limit of MT 184.1. This may be the case e.g. for FS formulations.

Methods

MT 184.1 Suspensibility of formulations forming suspensions on dilution in water (superseding MT 184, MT 168, MT 161, MT 15.1).

Requirements

Suspensibility of the active ingredient(s) shall be 60% - 105% after 30 min. Otherwise, a re-suspensibility test according to MT 184.1 should be performed and re-suspensibility of the active ingredient(s) shall be 95%-105%.

Comments

The suspension is prepared according to MT 184.1. Unless specified otherwise, e.g. in label instructions, samples of solid formulation types are prepared without pre-slurrying. The test is normally carried out before and after the accelerated storage test at elevated temperature, using CIPAC standard water D at $25 \pm 5^\circ\text{C}$ at the highest and lowest recommended rates of use, provided these are within the scope of the method.

4.5.44 Dispersion stability

Aim

To ensure that the active ingredient is homogeneously dispersed in suspension and emulsion in the spray liquid to give a satisfactory and effective mixture throughout spraying.

Applicability

Suspo-emulsions (SE), emulsifiable granules (EG), emulsifiable powders (EP), dispersible concentrates (DC), oil dispersions (OD), and mixed formulations of CS and emulsion, oil in water (EW) (ZW), mixed formulations of CS and EW (ZW), mixed formulations of CS and SE (ZE).

Methods

MT 180 Dispersion stability of suspo-emulsions.

Requirements

The formulation, when diluted at $23 \pm 2^\circ\text{C}$ with CIPAC standard waters A and D, shall continue to comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	initial dispersion complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml
24 h	re-dispersion complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml

Comments

The test should be carried out at 2% dilution.

4.5.45 Emulsion stability and re-emulsification**Aim**

To ensure that the active ingredient is uniformly dispersed in emulsion to give a satisfactory and effective mixture throughout spraying.

Applicability

Emulsifiable concentrates (EC), emulsions, oil in water (EW), emulsions for seed treatment (ES) and microemulsions (ME).

Methods

MT 36.3 Emulsion characteristics and re-emulsification properties.

Requirements

The formulation, when diluted with CIPAC standard waters A and D at the temperature recommended in the method MT 36.3, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	initial emulsification complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
2.0 h	"cream", maximum: ml
	"free oil", maximum: ml
24 h	re-emulsification complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml

Note: tests after 24 h are required only where results at 2 h are in doubt.

Comments

The test is normally carried out before and after the heat stability test, using CIPAC standard waters A and D at a temperature of either $30 \pm 2^\circ\text{C}$ or $25 \pm 5^\circ\text{C}$. The test should be carried out at the highest and lowest recommended rates of use and being within the scope of the method.

(vi) Flow properties**4.5.51 Flowability****Aim**

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), water soluble granules (SG), granules (GR) and emulsifiable granules (EG).

Methods

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

Requirements

General limits cannot be given.

4.5.52 Pourability**Aim**

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

Applicability

Suspension concentrates (SC, FS and OD), capsule suspensions (CS), suspo-emulsions (SE) emulsions, oil-in-water (EW), multi-character liquid formulation (ZC, ZW, ZE) and similarly viscous formulations.

Methods

MT 148.1 Pourability of suspension concentrates.

Requirements

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.

4.5.53 Viscosity

Aim

To ensure that single-phase formulations, e.g. UL, have viscosity properties suitable for purpose.

Applicability

Ultra-low volume liquids (UL).

Methods

MT 192 Viscosity of liquids by rotational viscometry.

MT 22 Viscosity, kinematic (suitable for Newtonian products).

Requirements

Limits are usually product-dependent.

(vii) Solution and dissolution properties

4.5.61 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 Free acidity or alkalinity, the preferred method for TC/TK and formulations that do not contain surfactants, e.g. some UL.

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

MT 75.3 Determination of pH values.

Requirements

General limits cannot be given.

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

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

Comments

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.

4.5.62 Miscibility with hydrocarbon oil

Aim

To ensure that when a formulation is diluted with oil, an homogeneous mixture is produced.

Applicability

Any specification for a formulation intended to be diluted with oil before use (e.g. OL).

Methods

MT 23 Miscibility with hydrocarbon oil.

Requirements

General limits cannot be given.

4.5.63 Dissolution of water soluble bags

Aim

To ensure that formulations packed in water soluble bags, when dispersed or dissolved, will not block filters or nozzles of application equipment.

Applicability

All formulations packaged in water soluble bags.

Methods

MT 176 Dissolution rate of water soluble bags.

Requirements

A suitable figure may be a maximum of 30 sec.

4.5.64 Degree of dissolution and/or solution stability

Aim

To ensure that: (i) water soluble formulations dissolve readily and when diluted, produce stable solutions without precipitation, flocculation, etc.; (ii) soluble concentrates produce stable solutions on dilution.

Applicability

Specifications for all water soluble formulations.

Methods

MT 179.1 Degree of dissolution and solution stability.

MT 41.1 Dilution stability of aqueous solution.

MT 196 Solution properties of water soluble tablets (ST).

Requirements

Maximum 2% retained on a 75 µm test sieve (MT 179.1, MT 196).

Trace of sediment after 30 min (MT 41.1).

Comments

MT 179.1 has been tested for water soluble granules (SG), but it has been agreed by CIPAC that it is also applicable to water soluble powders (SP).

MT 41.1 is applicable to aqueous solutions in general.

4.6 STORAGE STABILITY

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 dispersion and particulate properties.

Applicability

Specifications for liquid formulations.

Methods

MT 39.3 Low temperature stability of 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 initial dispersion, stability of emulsion or suspension, and wet sieve test. The permitted normal maximum amount of separated solid and liquid is 0.3 ml.

Comments

The main problems with low temperature storage are related to the possible precipitation or separation of liquid phases. The original properties of the formulation must be restored on warming and mixing, otherwise application in the field is likely to be unsatisfactory. The test may be conducted at a lower temperature, if required and if agreed between buyer and seller.

In certain cases (e.g. CS) it may be important to assess the effect of freezing and thawing cycles on the formulation. Adverse effects on retention of the active ingredient by capsules may occur.

Method MT 39.3 is suitable for formulations consisting of a solution of a pesticide in water or organic solvent (e.g. solution concentrates and emulsifiable concentrates). It may be used for certain liquid formulations that consist of a dispersion in an aqueous or non-aqueous continuous phase but, in these cases, the applicability of the method must be established before the clause and limit are based upon it.

4.6.2 Stability at elevated temperature

Aim

To ensure that the properties of formulations are not adversely affected by storage at high temperature, and to provide means for an early prediction of their long-term storage stability at more moderate temperature, with respect to content of active ingredient (and a possible consequent increase in relevant impurities) and certain physical properties.

Applicability

Specifications for all formulation types unless storage at elevated temperature is excluded by conditions recommended for the product (e.g. for biological products based on micro-organisms).

Methods

MT 46.4 Accelerated storage procedure (superseding all previous versions of MT 46 for accelerated storage).

Requirements

After storage at $54 \pm 2^{\circ}\text{C}$ for 14 days, the formulation must continue to comply with the requirements of appropriate clauses for content of active ingredient, relevant impurities, and relevant physical parameters.

The average active ingredient content should not decline to less than 95% of the average content measured prior to the accelerated storage stability test, and relevant physical properties should not change to an extent that might adversely affect the application and/or safety.

Where the formulation is not suitable nor intended for use in hot climates and is adversely affected by very 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 and this may also be necessary in the case of certain household insecticides, such as aerosols (AE).

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 $30 \pm 2^{\circ}\text{C}$.

Comments

Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently, after the test, in order to reduce the analytical error.

Further information must be provided if the degradation of the active ingredient exceeds 5% or a physical property is adversely affected. For example, the degradation products must be identified and quantified. In formulations with concentrations of 1% or below, there may be analytical challenges in identifying the degradation products that may only be at 0.1 % level. In such cases available evidence and scientific argument on the likely degradation products should be provided.

Formulation labels must be marked with the release date (month and year) of the lot or batch. The date shown on the label must be the start date from which the supplier guarantees the quality of the formulation. The term “release date” should be used rather than “formulation date”, which may lead to confusion between supplier and buyer (see also *International Code of Conduct on Pesticide Management – Guidelines on Good Labelling Practice for Pesticides* [FAO and WHO, 2015]).

Formulations of chemical pesticides and in contrast to biological pesticides, are generally expected to continue to be satisfactory in use after storage for at least 2 years from the release date in the unopened original containers, provided that these have been stored according to the instructions given on the label. Information on the storage stability of the formulation must be provided on the label if the intended shelf-life is less than 2 years.

FAO and WHO do generally not recommend storage of formulations for more than 2 years and the specifications are not intended to apply to longer periods of storage. Where a formulation has been subjected to prolonged storage or adverse conditions during storage, analysis and testing are recommended to assess its suitability for use.

The rate at which products undergo chemical and/or physical changes depends on the nature of the active ingredient(s), the formulation, the packaging, and the storage conditions. The product remains fit for use as long as the changes do not adversely affect the application, the biological performance, or the safety of operators, consumers or environment. However, such adverse effects cannot be assessed routinely by the buyer and – excepting biological products – the test of storage at elevated temperature provides an economic means for demonstrating that they should not occur if the product is stored according to the label recommendations.

Reaction kinetics (Arrhenius equation) are not linear with respect to temperature and therefore, storage at constant temperature t_C is not equal to storage at variable temperatures with an arithmetic mean of t_C . Estimation of average air/surface temperatures is problematic, even where accurate measurements of daily maxima and minima are available. In addition, the main

bulk of a product is not usually subjected to the extremes of temperature reached by the packaging. Therefore, calculation of the impact of a particular storage regime on the stability of a product may be misleading. The recommended test of storage stability at the conditions recommended for storage is expected to provide a more reliable indicator.

The clause for stability at elevated temperature provides limits for the active ingredient content and physical properties of the product. It is generally accepted that deviations of $\pm 10\%$ of the nominal active ingredient content²⁰ of a chemical pesticide do not significantly influence the biological performance. Where the active ingredient is unavoidably subject to degradation during recommended storage, an overage $\leq 10\%$ of the nominal content may be applied to compensate for degradation. Alternatively, a limit $< 95\%$ for active ingredient content after the storage stability test may be proposed. In either case, the manufacturer will normally be asked to provide supporting evidence for the requirement.

A more detailed consideration of shelf life and storage stability matters is given in the CropLife International Technical Monograph No. 17, *Guidelines for Specifying and Managing Shelf Life and Expiry Date of Crop Protection Products*, 3rd edition (CropLife International, 2021). See also the *International Code of Conduct on Pesticide Management* (FAO and WHO, 2014).

²⁰ This is not to be confused with the standard tolerances given in the table in Section 4.3.2, which do not include an allowance for degradation or overage.

5. SPECIFICATION GUIDELINES FOR TECHNICAL MATERIALS AND TECHNICAL CONCENTRATES

Introduction

A technical material (TC) is an active ingredient isolated (as far as is practicable) from the starting materials, solvents, etc., used to produce it. The isolation process may be simple, for example filtration and drying of a precipitate, or relatively complex. A TC may be prepared from a TK but it may also be diluted, with or without conversion to a salt or other derivative, to prepare a TK. A TC is formulated before use as a pesticide and a salt or other derivative may be formed during the formulation process. A TC is traded between manufacturers and formulators.

A technical concentrate (TK) may be an active ingredient which has not been isolated from the materials, solvents, etc., used to produce it, or it may be a minimally diluted TC intended for use in preparing formulations. In some cases it is necessary or advantageous to manufacture formulations from a TK, rather than from a TC. For example, the active ingredient may be unstable in a pure form or an isolation process may introduce unnecessary cost and complexity, especially if the only impurity removed is water. A salt or other derivative may be formed during the formulation process or in the preparation of the TK.

Where a TC/TK is intended for application by the end user, it should comply with the formulation specifications appropriate to its physical state.

If necessary, TC and TK materials can usually be reworked by manufacturers, to ensure compliance with specifications prior to formulation, and therefore storage stability clauses are not included in these specifications.

TC and TK specifications may also appear to be very simple because very few physical properties are likely to affect the stability and performance of the active ingredient in this form. The simplicity of the TC/TK specifications may appear to contrast with the volume of data evaluated in support them but it should be remembered that TC/TK specifications form the starting point for all formulation specifications.

“Technical grade active ingredient” is used in this manual as a generic term, referring to both TC and TK.

5.1 TECHNICAL MATERIALS

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.

..... [ISO common name] TECHNICAL MATERIAL

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

5.1.1 Description

The material shall consist of [ISO common name] together with related manufacturing impurities, in the form of (see Section 4.2), and shall be [physical description] free from visible extraneous matter and added modifying agents, except stabilizers if required.

5.1.2 Active ingredient

5.1.2.1 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.

5.1.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (not less than g/kg) and, when determined, the average measured content shall not be lower than the declared minimum content.

5.1.2.3 Any other relevant clause (Note 1), if required

Such as isomer ratio.

5.1.3 Relevant impurities

5.1.3.1 By-products of manufacture or storage (Note 2), if required

Maximum: g/kg.

5.1.3.2 Water (MT 30.6) (Note 3), if required

Maximum: g/kg.

5.1.3.3 Insolubles (Notes 3 & 4), if required

Maximum: g/kg.

5.1.4 Physical properties

5.1.4.1 **Acidity** and/or **alkalinity** (MT 191) or pH range (MT 75.3)
(Notes 3 & 4), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

5.1.4.2 **Any other clause** (Notes 3 & 4), if required

Such as a sieve test, kinematic viscosity range, specific gravity, etc.

<u>Note 1</u>	Method(s) of analysis must be CIPAC, AOAC or equivalent. 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..
<u>Note 2</u>	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.
<u>Note 3</u>	Clauses to be included only if appropriate to the material.
<u>Note 4</u>	The method to be used shall be stated. If several methods are available, a referee method shall be selected.

5.2 TECHNICAL CONCENTRATES

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.

..... **[ISO common name] TECHNICAL CONCENTRATE**

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

5.2.1 Description

The material shall consist of [ISO common name] together with related manufacturing impurities, in the form of (see Section 4.2), and shall be [physical description] free from visible extraneous matter and added modifying agents except for the diluent and stabilizer, if required.

5.2.2 Active ingredient

5.2.2.1 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.

5.2.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg or, for liquids only, g/l at $20 \pm 2^\circ\text{C}$) and, when determined, the average measured content shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

5.2.2.3 Any other clause (Note 1), if required

Such as isomer ratio.

5.2.3 Relevant impurities

5.2.3.1 By-products of manufacture or storage (Note 2), if required

Maximum:% of the [ISO common name] content found under 5.2.2.2.

5.2.3.2 Water (MT 30.6) (Note 3), if required

Maximum: g/kg.

5.2.3.3 Insolubles (Notes 3 & 4), if required

Maximum: g/kg.

5.2.4 Physical properties

5.2.4.1 Acidity and/or alkalinity (MT 191) or pH range (MT 75.3) (Notes 3 & 4), if required

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

5.2.4.2 Any other clause (Notes 3 & 4)

Such as a sieve test, kinematic viscosity range, specific gravity, etc.

Note 1 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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

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

6. SPECIFICATION GUIDELINES FOR SOLID FORMULATIONS

SOLID FORMULATIONS FOR DIRECT USE

- 6.1 Dustable powders (DP)
- 6.2 Powders for dry seed treatment (DS)
- 6.3 Granules (GR)
- 6.4 Tablets for direct application (DT)

SOLID FORMULATIONS FOR DISPERSION

- 6.11 Wettable powders (WP)
- 6.12 Wettable powders in sealed water soluble bag (WP-SB)
- 6.13 Water dispersible powders for slurry seed treatment (WS)
- 6.14 Water dispersible granules (WG)
- 6.15 Water dispersible granules in sealed water soluble bag (WG-SB)
- 6.16 Water dispersible tablets (WT)
- 6.17 Emulsifiable granules (EG)
- 6.18 Emulsifiable powders (EP)

SOLID FORMULATIONS FOR DISSOLUTION

- 6.21 Water soluble powders (SP)
- 6.22 Water soluble powders for seed treatment (SS)
- 6.23 Water soluble granules (SG)
- 6.24 Water soluble tablets (ST)

Introduction

In the following subsections, an open numbering system has intentionally been chosen to differentiate the formulation types according to their application mode and to allow later addition of newly developed specification templates.

6.1 DUSTABLE POWDERS

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.

..... [ISO common name] DUSTABLE POWDER

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

6.1.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification [.....], in the form of (see Section 4.2), together with carriers and any other necessary formulants. It shall be in the form of a fine, free-flowing powder, free from visible extraneous matter and hard lumps.

6.1.2 Active ingredient

6.1.2.1 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.

6.1.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.1.3 Relevant impurities

6.1.3.1 By-products of manufacture or storage (Note 2), if required

Maximum:% of the [ISO common name] content found under 6.1.2.2.

6.1.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.1.4 Physical properties

6.1.4.1 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

6.1.4.2 Dry sieve test (MT 170) (Note 4)

If appropriate, maximum y% of the formulation shall be retained on a test sieve, the mesh size of which must be specified.

Maximum: y% retained on a ... µm test sieve.

Alternatively, not more than (0.00y x X)% of the mass of the sample used for the determination shall be present as ... [ISO common name]

in the residue on the sieve, where X is the ... [ISO common name] content (g/kg) found under 6.1.2.2.

6.1.5 Storage stability

6.1.5.1 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 5), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 6) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.1.3.1),
 - acidity/alkalinity/pH range (6.1.4.1),
 - dry sieve test (6.1.4.2),
- as required.

Note 1 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

Note 3 The method to be used shall be stated. If several methods are available, a referee method shall be selected.

Note 4 Method MT 170, together with relevant methods of analysis for active ingredient, see Note 1.

Note 5 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 6 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.2 POWDERS FOR DRY SEED TREATMENT

Introduction

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 referring to Section 4. From the “Notes” provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [ISO common name] POWDER FOR DRY SEED TREATMENT (Note 1)

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

6.2.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification [.....], in the form of (see Section 4.2), together with suitable fillers and any other necessary formulants including colouring matter (Note 1). It shall be in the form of a fine free-flowing powder, free from visible extraneous matter and hard lumps.

6.2.2 Active ingredient

6.2.2.1 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.

6.2.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.2.3 Relevant impurities

6.2.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 6.2.2.2.

6.2.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.2.4 Physical properties

6.2.4.1 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

6.2.4.2 Dry sieve test (MT 170)

If appropriate, maximum y% of the formulation shall be retained on a test sieve, the mesh size of which must be specified.

Maximum: y% retained on a ... µm test sieve.

Alternatively, not more than (0.00y x X)% of the mass of the sample used for the determination shall be present as ... [ISO common name] in the residue on the sieve, where X is the ... [ISO common name] content (g/kg) found under 6.2.2.2.

6.2.4.3 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 [ISO common name] remaining on the seeds after the test.

6.2.5 Storage stability**6.2.5.1 Stability at elevated temperature (MT 46.4)**

After storage at 54 ± 2 C for 14 days (Note 6), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 7) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.2.3.1),
 - acidity/alkalinity/pH range (6.2.4.1),
 - dry sieve test (6.2.4.2),
 - adhesion to seeds (6.2.4.3),
- 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 to 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 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

.../cont.

- Note 4** The method(s) to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 5** MT 170, together with relevant methods of analysis for active ingredient, see Note 2.
- Note 6** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

6.3 GRANULES

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 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.

..... [ISO common name] GRANULES

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

6.3.1 Description

The material shall consist of granules containing technical [ISO common name], complying with the requirements of FAO/WHO specification [.....], in the form of (see Section 4.2), 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.

6.3.2 Active ingredient

6.3.2.1 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.

6.3.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.3.2.3 Release rate of active ingredient (applicable only for slow- or controlled release formulations), if required

The release rate measured shall comply with the following criteria:
.....

6.3.3 Relevant impurities

6.3.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 6.3.2.2.

6.3.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.3.4 Physical properties

6.3.4.1 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

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

Pour density: to g/ml.

Tap density: to g/ml.

6.3.4.3 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.

6.3.4.4 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).

6.3.4.5 **Flowability** (MT 172.2)

At least% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve (Note 8).

6.3.4.6 **Attrition resistance** (MT 178)

Minimum% attrition resistance.

6.3.5 Storage stability

6.3.5.1 **Stability at elevated temperature** (MT 46.4)

After storage at 54 ± 2 C for 14 days (Note 9), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 10) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.3.3.1),
 - acidity/alkalinity/pH range (6.3.4.1),
 - dustiness (6.3.4.4),
 - attrition resistance (6.3.4.6),
- 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 analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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 The flowability test (MT 172.2) includes the accelerated storage conditions to be used.

Note 9 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 10 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.4 TABLETS FOR DIRECT APPLICATION

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. Tablets for direct application (DT) are intended for application in the field (e.g. rice paddies) without prior dispersal or dissolution in water.

Tablets for direct application are often not coated or highly compacted and possess lower mechanical strength. Such tablets 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 types of tablets, are defined by the European Pharmacopoeia as "uncoated tablets generally containing acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide" (EDQM, 2022). 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.

..... [ISO common name] TABLETS FOR DIRECT APPLICATION

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

6.4.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification [.....], in the form of (see Section 4.2), together with carriers and any other necessary formulants. It shall be in the form of tablets for application without prior disintegration and dispersion/dissolution in water. The formulation shall consist of dry, unbroken, free-flowing tablets and shall be free from extraneous matter.

6.4.2 Active ingredient (Note 1)

6.4.2.1 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.

6.4.2.2 **[ISO common name] content** (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.4.2.3 **Tablet dose uniformity**, if required

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

6.4.3 Relevant impurities (Note 1)

6.4.3.1 **By-products of manufacture or storage** (Note 3), if required

Maximum: % of the [ISO common name] content found under 6.4.2.2.

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

Maximum: g/kg.

6.4.4 Physical properties

6.4.4.1 **Acidity** and/or **alkalinity** (MT 191) or **pH range** (MT 75.3) (Notes 4, 5 & 6), if required (Note 7)

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

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

pH range: ... to ...

6.4.4.2 **Tablet integrity** (Note 8)

No broken, soft or sticky tablets should be present.

Fragments: yes/no

Soft/sticky: yes/no

6.4.4.3 **Attrition resistance of tablets** (MT 178.2) (Notes 9 & 10) if required

Minimum attrition resistance:%.

6.4.5 Storage stability

6.4.5.1 **Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 11) without pressure (Note 12) the determined average active ingredient content must not be lower than ... % relative to the determined average content found before storage (Note 13) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.4.3.1),

- acidity/alkalinity/pH range (6.4.4.1),

- tablet integrity (6.4.4.2),

- attrition resistance of tablets (6.4.4.3),

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 analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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

Note 5 The following tests may require breaking tablets to adjust the test concentration:

Point	Property	CIPAC	Rate
6.4.4.1	Acidity or alkalinity	MT 191	10 g add 100 ml
	pH range	MT 75.3	1 g make up 100 ml

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

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 This requirement 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 9 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 10 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 < 1 cm as well.

Note 11 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions. Whole tablets must be stored. After storage tablets may be broken for tests as specified in Note 8.

Note 12 Without pressure means that the test is performed as specified by CIPAC MT 46.4, but no pressure is applied to the sample during its aging.

Note 13 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.11 WETTABLE POWDERS

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.

..... [ISO common name] WETTABLE POWDER

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

6.11.1 Description

The material shall consist of a homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification [.....], in the form of (see Section 4.2), together 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.

6.11.2 Active ingredient

6.11.2.1 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.

6.11.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.11.3 Relevant impurities

6.11.3.1 By-products of manufacture or storage (Note 2), if required

Maximum:% of the [ISO common name] content found under 6.11.2.2.

6.11.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.11.4 Physical properties

6.11.4.1 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

6.11.4.2 Wet sieve test (MT 185)

Maximum:% retained on a 75 µm test sieve.

6.11.4.3 Suspensibility (MT 184.1) (Note 4)

Suspensibility: minimum% after 30 min in CIPAC standard water D at 25 ± 5°C (Notes 5 & 6).

6.11.4.4 Persistent foam (MT 47.3) (Note 7)

Maximum: ml after 1 min.

6.11.4.5 Wettability (MT 53.3)

The formulation shall be completely wetted in min without swirling.

6.11.5 Storage stability**6.11.5.1 Stability at elevated temperature** (MT 46.4)

After storage at 54 ± 2 C for 14 days (Note 8), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.11.3.1),
- acidity/alkalinity/pH range (6.11.4.1),
- wet sieve test (6.11.4.2),
- suspensibility (6.11.4.3),
- wettability (6.11.4.5),

as requested.

Note 1 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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 Unless another temperature is specified.

Note 6 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 7 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 at 25 ± 5°C.

.../cont.

Note 8 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 9 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.12 WETTABLE POWDERS IN SEALED WATER SOLUBLE BAG

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.

..... [ISO common name] WETTABLE POWDER IN SEALED WATER SOLUBLE BAG

(CIPAC Number)/WP-SB (month & year of publication)

6.12.1 Description

The material shall consist of a defined quantity of a homogeneous mixture of technical [ISO common name], complying with the requirements of the FAO/WHO, in the form of (see Section 4.2) together 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, contained in a sealed water soluble bag (Note 1).

6.12.2 Active ingredient

6.12.2.1 Identity tests (Notes 2 & 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.

6.12.2.2 [ISO common name] content (Notes 2 & 3)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.12.3 Relevant impurities (Note 2)

6.12.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 6.12.2.2.

6.12.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.12.4 Physical properties (Note 2)**6.12.4.1 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

6.12.4.2 Wettability (MT 53.3)

The formulation shall be completely wetted in min without swirling.

6.12.4.3 Wet sieve test (MT 185)

Maximum:% retained on a 75 µm test sieve.

6.12.4.4 Suspensibility (MT 184.1) (Notes 6 & 7)

The suspensibility shall be tested on a suspension containing the WP and the bag material in the actual ratio of application, prepared according to the procedure described in Note 8.

Suspensibility: minimum% after 30 min in CIPAC standard water D at 25 ± 5°C (Note 9).

6.12.4.5 Persistent foam (MT 47.3) (Note 10)

The persistent foam shall be tested on a suspension containing the WP and the bag material in the actual ratio of application in CIPAC standard water D, prepared according to the procedure described in Note 8.

Maximum: ml after 1 min.

6.12.4.6 Dissolution of the bag (MT 176) (Notes 2 & 11)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag together with an appropriate proportion of the WP in CIPAC standard water D taken according to the procedure described in Note 11.

Flow time of the suspension: maximum sec.

6.12.5 Storage stability**6.12.5.1 Stability at elevated temperature** (MT 46.4)

The package should be enclosed in a watertight sachet, box or any other container at 54 ± 2°C for 14 days (Note 12 & 13). The determined average active ingredient content must not be lower than% relative to the determined average content found before storage

(Note 14) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.12.3.1),
- acidity/alkalinity/pH range (6.12.4.1),
- wettability (6.12.4.2),
- wet sieve test (6.12.4.3),
- suspensibility (6.12.4.4),
- persistent foam (6.12.4.5),
- dissolution of the bag (6.12.4.6),

as required.

None of the bags tested should show signs of leakage or rupture during normal handling, before and after storage.

Note 1 For record keeping purposes, the suffix "SB" should be added to the formulation code (WP-SB).

Note 2 Sub-sampling.

Lay the bag on a bench and carefully open one side of the bag with a cutter, taking care not to damage the seals. Transfer the contents of the bag into a suitable flask. This material shall be used to carry out the tests for:

- active ingredient identity (2.1),
- active ingredient content (2.2),
- by-products of manufacture or storage (3.1),
- water content (3.2),
- acidity/alkalinity/pH range (4.1),
- wettability (4.2),
- wet sieve test (4.3),
- suspensibility (4.4),
- persistent foam (4.5),
- dissolution of the bag (4.6).

The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction and weighed to the nearest 0.01 g. Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (4.4) and persistent foam (4.5) tests.

In the case of delay of the above tests, the bag shall be stored in a watertight container (glass bottle or equivalent) to avoid any change in its properties.

Note 3 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.

Note 4 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.

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

Note 6 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.

.../cont.

Note 7 Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.

Note 8 The procedure for adding the bag material to the solution for the suspensibility and persistent foam tests should be as follows:

Prepare a stock solution of the bag material (1 mg/ml) by weighing a sample (\underline{n} mg) of the bag (excluding sealed parts). Dissolve this sample by stirring in the standard water used for the tests to give a final volume of \underline{n} ml. Store the stock solution in a stoppered bottle before use.

Calculate the volume (\underline{V} ml) of the stock solution of the bag to be added to the test suspension of the water dispersible granule according to the following equation:

$$V(\text{ml}) = X \times \frac{1000B}{W}$$

Where: B (g) = weight of the emptied and cleaned bag
 W (g) = nominal weight of the WP contained in the bag
 X (g) = weight of the WP sample used in the test

Note 9 Unless another temperature is specified.

Note 10 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 at 25 ± 5 °C..

Note 11 The sampling of the bag for the dissolution test should be as follows:

Lay the empty cleaned bag in its original configuration (double layer). Delineate and then cut up a test sample including part of the upper seal (5 cm) and symmetrically including the vertical seal (10 cm). If the size of the bag is less than this dimension, use the whole bag.

Carry out the dissolution test immediately to avoid any modification of the sample.

Note 12 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 13 If irreversible changes in the characteristics of the bag material are known to occur when stored at elevated temperatures, refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 14 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.13 WATER DISPERSIBLE POWDERS FOR SLURRY SEED TREATMENT

Introduction

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 referring to Section 4. From the “Notes” provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [ISO common name] **WATER DISPERSIBLE POWDER
FOR SLURRY SEED TREATMENT** (Note 1)

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

6.13.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification [.....], in the form of (see Section 4.2), together with carriers and any other necessary formulants, including colouring matter (Note 1). It shall be in the form of a powder free from visible extraneous matter and hard lumps.

6.13.2 Active ingredient

6.13.2.1 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.

6.13.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.13.3 Relevant impurities

6.13.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 6.13.2.2.

6.13.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.13.4 Physical properties

6.13.4.1 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

6.13.4.2 Wet sieve test (MT 185) (Note 5)

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

6.13.4.3 Persistent foam (MT 47.3) (Note 6), if required

Maximum: ml after min.

6.13.4.4 Wettability (MT 53.3)

The formulation shall be completely wetted in min without swirling.

6.13.4.5 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 [ISO common name] remaining on the seeds after the test.

6.13.5 Storage stability**6.13.5.1 Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 7) the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 8) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.13.3.1),
- acidity/alkalinity/pH range (6.13.4.1),
- wet sieve test (6.13.4.2),
- adhesion to seeds (6.13.4.5),

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 should not be used for denaturing seeds to be used as livestock feeding stuffs.

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

.../cont.

- Note 4** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 5** This test should detect coarse particles or extraneous materials which could cause blockage of spray nozzles or filters of the application equipment.
- Note 6** The mass of sample to be used in the test should be specified at the highest rate of use recommended by the supplier, provided it is within the scope of the method. For MT 47.3, the implicit upper limit is approximately 10 % w/v. In case the highest use rate exceeds 10 %, testing persistent foam using MT 47.3 is not possible and the clause should be omitted.
- Note 7** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 8** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.14 WATER DISPERSIBLE GRANULES

Introduction

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

WGs are formulated in many different ways depending on the physico-chemical 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 WP, 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 referring to Section 4. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [ISO common name] WATER DISPERSIBLE GRANULES

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

6.14.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of the FAO/WHO specification, in the form of (see Section 4.2), 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.

6.14.2 Active ingredient

6.14.2.1 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.

6.14.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.14.3 Relevant impurities

6.14.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 6.14.2.2.

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

Maximum: g/kg.

6.14.4 Physical properties

6.14.4.1 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

6.14.4.2 Wettability (MT 53.3) (Note 6)

The formulation shall be completely wetted in min.

6.14.4.3 Wet sieve test (MT 185)

Maximum:% retained on a 75 µm test sieve.

6.14.4.4 Dispersibility (MT 174)

Dispersibility: minimum% after 1 min of stirring.

6.14.4.5 **Suspensibility** (MT 184.1) (Notes 7 & 8)

Suspensibility: minimum% after 30 min in CIPAC standard water D at $25 \pm 5^\circ\text{C}$ (Note 9).

6.14.4.6 **Persistent foam** (MT 47.3) (Note 10)

Maximum: ml after 1 min.

6.14.4.7 **Dustiness** (MT 171.1) (Note 11)

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.

6.14.4.8 **Flowability** (MT 172.2)

At least% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve (Note 12).

6.14.4.9 **Attrition resistance** (MT 178.2)

Minimum:% attrition resistance.

6.14.5 Storage stability

6.14.5.1 **Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 13), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 14) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.14.3.1),
- acidity/alkalinity/pH range (6.14.4.1),
- wet sieve test (6.14.4.3),
- dispersibility (6.14.4.4),
- suspensibility (6.14.4.5),
- dustiness (6.14.4.7),
- attrition resistance (6.14.4.9),

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 analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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

.../cont.

- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6** The method to be used shall be stated, either with or without swirling.
- 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 method MT 184.1.
- Note 8** Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.
- Note 9** Unless another temperature is specified.
- Note 10** 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 at $25 \pm 5^\circ\text{C}$.
- Note 11** 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 12** The flowability test (MT 172.2) includes the accelerated storage conditions to be used.
- Note 13** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 14** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.15 WATER DISPERSIBLE GRANULES IN SEALED WATER SOLUBLE BAG

Introduction

Water dispersible granules in sealed water soluble bag (WG-SB) are intended for application after disintegration and dispersion in water by conventional spraying equipment. A defined quantity of the granules are included in a closed bag which dissolves quickly once applied in water allowing the granules to be disintegrated and dispersed in water.

WGs are formulated in many different ways depending on the physico-chemical 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.

Samples of intact bags for analysis and testing should be taken from a *freshly* opened commercial container, if practicable.

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

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.

**..... [ISO common name] WATER DISPERSIBLE GRANULES
IN SEALED WATER SOLUBLE BAG**

[CIPAC number]/WG-SB (month & year of publication)

6.15.1 Description

The material shall consist of a defined quantity of a homogeneous mixture of technical [ISO common name], complying with the requirements of the FAO/WHO, in the form of (see Section 4.2) together with carriers and any other necessary formulants. It shall be in the form of granules (Note 1), contained in a sealed water soluble bag (Note 2), 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.

6.15.2 Active ingredient

6.15.2.1 Identity tests (Notes 3 & 4)

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

6.15.2.2 [ISO common name] content (Notes 3 & 4)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.15.3 Relevant impurities (Note 3)

6.15.3.1 By-products of manufacture or storage (Note 5), if required

Maximum:% of the [ISO common name] content found under 6.15.2.2.

6.15.3.2 Water (MT 30.6) (Note 6), if required

Maximum: g/kg.

6.15.4 Physical properties (Note 3)

- 6.15.4.1 **Acidity** and/or **alkalinity** (MT 191) or **pH range** (MT 75.3) (Note 7), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

- 6.15.4.2 **Wettability** (MT 53.3) (Note 8)

The formulation shall be completely wetted in min.

- 6.15.4.3 **Wet sieve test** (MT 185)

Maximum:% retained on a 75 µm test sieve.

- 6.15.4.4 **Dispersibility** (MT 174)

Dispersibility: minimum% after 1 min of stirring.

- 6.15.4.5 **Suspensibility** (MT 184.1) (Notes 9 & 10)

The suspensibility shall be tested on a suspension containing the WG and the bag material in the actual ratio of application, prepared according to the procedure described in Note 11.

Suspensibility: minimum% after 30 min in CIPAC standard water D at 25 ± 5°C (Note 12).

- 6.15.4.6 **Persistent foam** (MT 47.3) (Note 13)

The persistent foam shall be tested on a suspension containing the WG and the bag material in the actual ratio of application, prepared according to the procedure described in Note 11.

Maximum: ml after 1 min.

- 6.15.4.7 **Dustiness** (MT 171) (Note 14)

Nearly dust free or essentially non-dusty. 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.

- 6.15.4.8 **Flowability** (MT 172.2)

At least% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve (Note 15).

- 6.15.4.9 **Attrition resistance** (MT 178.2)

Minimum:% attrition resistance.

- 6.15.4.10 **Dissolution of the bag** (MT 176) (Notes 3 & 16)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag together with an appropriate proportion of the WG in CIPAC standard water D taken according to the procedure described in Note 16.

Flow time of the suspension: maximum sec.

6.15.5 Storage stability

6.15.5.1 Stability at elevated temperature (MT 46.4)

The package should be enclosed in a watertight sachet, box or any other container at $54 \pm 2^\circ\text{C}$ for 14 days (Notes 17 & 18). The determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 19) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.15.3.1),
- acidity/alkalinity/pH range (6.15.4.1),
- wet sieve test (6.15.4.3),
- dispersibility (6.15.4.4),
- suspensibility (6.15.4.5),
- persistent foam (6.15.4.6),
- dustiness (6.15.4.7),
- attrition resistance (6.14.4.9),
- dissolution of the bag (6.14.4.10),

as required.

None of the bags tested should show signs of leakage or rupture during normal handling, before and after storage.

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 For record keeping purposes, the suffix "SB" should be added to the formulation code (WG-SB).

Note 3 Sub-sampling.

Lay the bag on a bench and carefully open one side of the bag with a cutter, taking care not to damage the seals. Transfer the contents of the bag into a suitable flask. This material shall be used to carry out the tests for:

- active ingredient identity (2.1),
- active ingredient content (2.2),
- by-products of manufacture or storage (3.1),
- water content (3.2),
- acidity/alkalinity/pH range (4.1),
- wettability (4.2),
- wet sieve test (4.3),
- dispersibility (4.4),
- suspensibility (4.5),
- persistent foam (4.6),
- dustiness (4.7),
- flowability (4.8),
- attrition resistance (4.9),
- dissolution of the bag (4.10).

The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction and weighed to the nearest 0.01 g. Aliquots of an aqueous solution of the bag material shall be used in the suspensibility (4.5) and persistent foam (4.6) tests.

In the case of delay of the above tests, the bag shall be stored in a watertight container (glass bottle or equivalent) to avoid any change in its properties.

.../cont.

- Note 4** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 5** 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.
- Note 6** There may be cases where a minimum water content has to be specified.
- Note 7** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 8** The method to be used shall be stated, either with or without swirling.
- Note 9** 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 10** Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.
- Note 11** The procedure for adding the bag material to the solution for the suspensibility and persistent foam tests should be as follows:
- Prepare a stock solution of the bag material (1 mg/ml) by weighing a sample (\underline{n} mg) of the bag (excluding sealed parts). Dissolve this sample by stirring in the standard water used for the tests to give a final volume of \underline{v} ml. Store the stock solution in a stoppered bottle before use.
- Calculate the volume (\underline{V} ml) of the stock solution of the bag to be added to the test suspension of the water dispersible granule according to the following equation:
- $$V(\text{ml}) = X \times \frac{1000B}{W}$$
- Where: B (g) = weight of the emptied and cleaned bag
W (g) = nominal weight of the WG contained in the bag
X (g) = weight of the WG sample used in the test
- Note 12** Unless another temperature is specified.
- Note 13** 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 at $25 \pm 5^\circ\text{C}$.
- Note 14** 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 15** The flowability test (MT 172.2) includes the accelerated storage conditions to be used.
- Note 16** The sampling of the bag for the dissolution test should be as follows:
- Lay the empty cleaned bag in its original configuration (double layer). Delineate and then cut up a test sample including part of the upper seal (5 cm) and symmetrically including the vertical seal (10 cm). If the size of the bag is less than this dimension, use the whole bag.
- Carry out the dissolution test immediately to avoid any modification of the sample.
- Note 17** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 18** If irreversible changes in the characteristics of the bag material are known to occur when stored at elevated temperatures, refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 19** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.16 WATER DISPERSIBLE TABLETS

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. This type of tablets, according to Pharm Eur are "uncoated tablets generally containing acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide". 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 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.

..... [ISO common name] WATER DISPERSIBLE TABLETS

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

6.16.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification [...], in the form of (see Section 4.2), 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.

6.16.2 Active ingredient (Note 1)

6.16.2.1 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.

6.16.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.16.2.3 Tablet dose uniformity, if required

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

6.16.3 Relevant impurities (Note 1)**6.16.3.1 By-products of manufacture or storage** (Note 3), if required

Maximum: % of the [ISO common name] content found under 6.16.2.2.

6.16.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.16.4 Physical properties**6.16.4.1 Acidity** and/or **alkalinity** (MT 191) or **pH range** (MT 75.3) (Notes 4, 5 & 6), if required (Note 7)

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

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

pH range: ... to ...

6.16.4.2 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.

6.16.4.3 Wet sieve test (MT 185) (Notes 5 & 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.

6.16.4.4 Suspensibility (MT 184.1) (Notes 5, 10, 11 & 12)

Suspensibility: minimum% after 30 min in CIPAC standard water D at 25 ± 5°C.

6.16.4.5 Persistent foam (MT 47.3) (Notes 5 & 13)

Maximum: ... ml after 1 minute.

6.16.4.6 Tablet integrity (Note 14)

No broken, soft or sticky tablets should be present.

Fragments: yes/no

Soft/sticky: yes/no

6.16.4.7 Attrition resistance of tablets (MT 178.2) (Notes 15 & 16) if required

Minimum attrition resistance:%.

6.16.5 Storage stability**6.16.5.1 Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 17) without pressure (Note 18), the determined average active ingredient content must not be lower than ... % relative to the determined average content found before storage (Note 19) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.16.3.1),
- acidity/alkalinity/pH range (6.16.4.1),
- disintegration of tablets (6.16.4.2)
- wet sieve test (6.16.4.3),
- suspensibility (6.16.4.4),
- tablet integrity (6.16.4.6),
- attrition resistance of tablets (6.16.4.7),

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 analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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
6.14.4.1	Acidity or alkalinity	MT 191	10 g add 100 ml
	pH range	MT 75.3	1 g make up 100 ml
6.14.4.3	Wet sieve	MT 185	Maximum recommended use-rate
6.14.4.4	Suspensibility	MT 184	
6.14.4.5	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.

.../cont.

- 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** Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.
- 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 < 1 cm as well.
- Note 17** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions. 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 46.4, but no pressure is applied to the sample during aging.
- Note 19** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.17 EMULSIFIABLE GRANULES

Introduction

An emulsifiable granule (EG) is a formulation consisting of granules to be applied as a conventional O/W emulsion of the active ingredient(s), either solubilized or diluted in an organic solvent, after disintegration and dissolution in water.

Emulsifiable granules comprise one or several active ingredient(s), either solubilized or diluted in a suitable organic solvent which is (are) absorbed in a water soluble polymeric shell or some other type of soluble or insoluble matrix. The formulation may contain other formulants as necessary.

Emulsifiable granules are treated in a similar fashion to water dispersible granules (WG) and emulsifiable concentrates (EC) as they disintegrate and emulsify on dilution into water.

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.

..... [ISO common name] EMULSIFIABLE GRANULES

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

6.17.1 Description

The material shall consist of granules (Note 1) containing technical [ISO common name] in the form of (see Section 4.2), complying with the requirements of FAO/WHO specification, which may be dissolved in an organic solvent, together with other suitable formulants. The material shall be homogeneous, dry, free-flowing, free from visible extraneous matter and hard lumps and provide an emulsion upon dilution in water.

6.17.2 Active ingredient

6.17.2.1 Identity tests (Note 2)

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

6.17.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.17.3 Relevant impurities

6.17.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 6.17.2.2.

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

Maximum: g/kg.

6.17.4 Physical properties

6.17.4.1 **Acidity** and/or **alkalinity** (MT 191) or **pH range** (MT 75.3) (Notes 4 & 5), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

6.17.4.2 **Wettability** (MT 53.3) (Note 6)

The formulation shall be completely wetted in min.

6.17.4.3 **Dispersion stability** (MT 180) (Note 7)

The formulation, when diluted at $23 \pm 2^\circ\text{C}$ with CIPAC standard waters A and D, shall comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	initial dispersion complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml
24 h	re-dispersion complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml

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

Maximum:% retained on a 75 μm test sieve.

6.17.4.5 **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.

6.17.4.6 **Attrition resistance** (MT 178.2)

Minimum:% attrition resistance.

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

Maximum ml after 1 min.

6.17.4.8 **Flowability** (MT 172.2)

At least% of the formulation shall pass through a 5 mm test sieve after 20 drops of the sieve (Note 10).

6.17.5 Storage stability

6.17.5.1 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 11), the determined average active ingredient content must not be lower than ...% relative to the determined average content found before storage (Note 12) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.17.3.1),
- acidity, alkalinity or pH range (6.17.4.1),
- dispersion stability (6.17.4.3),
- wet sieve test (6.17.4.4),
- dustiness (6.17.4.5),
- attrition resistance (6.17.4.6),

as required.

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

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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

Note 5 In case of drifting pH values, the reading on the pH-meter is taken as constant and valid if the deviation in value is less than 0.1 pH unit over a period of 10 min (without stirring).

Note 6 The method to be used shall be stated, either without or with swirling (MT 53.3.1 or MT 53.3.2).

Note 7 The formulation should be tested at 2% dilution.

Note 8 The test will detect any coarse particle which could cause blockage of nozzles and filters.

Note 9 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 at $25 \pm 5^\circ\text{C}$.

Note 10 The flowability test (MT 172.2) includes the accelerated storage conditions to be used.

Note 11 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 12 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.18 EMULSIFIABLE POWDERS

Introduction

An emulsifiable powder (EP) is applied as a conventional oil-in-water emulsion of the active ingredient(s), after dispersion in water. The active ingredient(s) may be solubilized or diluted in organic solvent(s).

Emulsifiable powders contain one or more active ingredient(s), either solubilized or diluted in suitable organic solvent(s) which is (are) absorbed in a water soluble polymer powder or some other type of soluble or insoluble powder. The formulation may contain other formulants, as necessary.

Emulsifiable powders are treated in a similar fashion to wettable powders (WP), emulsifiable granules (EG) and emulsifiable concentrates (EC), as they disperse and emulsify on dilution in water.

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.

..... [ISO common name] EMULSIFIABLE POWDER

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

6.18.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification [.....], in the form of (see Section 4.2), together with any other necessary formulants. The material shall be dry, free flowing, free from visible extraneous matter and hard lumps and provide an emulsion upon dilution in water.

6.18.2 Active ingredient

6.18.2.1 Identity tests (Note 1)

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

6.18.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.18.3 Relevant impurities

- 6.18.3.1 **By-products of manufacture or storage** (Note 2), if required
Maximum:% of the [ISO common name] content found under 6.16.2.2.
- 6.18.3.2 **Water** (MT 30.6), if required
Maximum: g/kg.

6.18.4 Physical properties

- 6.18.4.1 **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
- 6.18.4.2 **Wettability** (MT 53.3) (Note 4)
The formulation should be completely wetted in min.
- 6.18.4.3 **Dispersion stability** (MT 180) (Note 5)
The formulation, when diluted at 23 ± 2°C with CIPAC standard waters A and D, shall comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	initial dispersion complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml
24 h	re-dispersion complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml

- 6.18.4.4 **Wet sieve test** (MT 185) (Note 6)
Maximum:% retained on a 75 µm test sieve.
- 6.18.4.5 **Persistent foam** (MT 47.3) (Note 7)
Maximum ml after 1 min.

6.18.5 Storage stability

- 6.18.5.1 **Stability at elevated temperature** (MT 46.4)
After storage at 54 ± 2°C for 14 days (Note 8), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.18.3.1),
 - acidity, alkalinity or pH range (6.18.4.1),
 - dispersion stability (6.18.4.3),
 - wet sieve test (6.18.4.4),
- as required.

- Note 1** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.
- Note 3** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 4** The method to be used shall be stated, either without or with swirling (MT 53.3.1 or MT 53.3.2).
- Note 5** The formulation should be tested at 2% dilution.
- Note 6** The test will detect any coarse particle which could cause blockage of nozzles and filters.
- Note 7** 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 at $25 \pm 5^\circ\text{C}$.
- Note 8** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 9** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.21 WATER SOLUBLE POWDERS

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.

..... [ISO common name] WATER SOLUBLE POWDER

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

6.21.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), together with any necessary formulants. It shall be in the form of a powder to be applied as a true solution of the active ingredient after solution in water, but which may contain insoluble inert ingredients.

Where the material is packaged in sealed water soluble bags, the description shall be as follows (Note 1):

The material shall consist of a defined quantity of a [ISO common name] water soluble powder complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), contained in a sealed water soluble bag.

6.21.2 Active ingredient

6.21.2.1 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.

6.21.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.21.3 Relevant impurities

6.21.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 6.21.2.2.

6.21.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.21.4 Physical properties

6.21.4.1 Acidity and/or alkalinityalkalinity (MT 191) or pH range (MT 75.3) (Note 4), if required

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

6.21.4.2 Wettability (MT 53.3)

The formulation shall be completely wetted in min without swirling.

6.21.4.3 Degree of dissolution and solution stability (MT 179.1) (Note 5)

Residue of formulation retained on a 75 μm test sieve after dissolution in CIPAC standard water D at $25 \pm 5^\circ C$ (Note 6):

Maximum:% after 5 min.

Maximum:% after 24 h.

In the case of water soluble bag packaging, the provisions of clause 6.21.6.3 should be applied.

6.21.4.4 Persistent foam (MT 47.3) (Note 7)

Maximum: ml after 1 min

In the case of water soluble bag packaging, the provisions of clause 6.21.6.3 should be applied.

6.21.5 Storage stability**6.21.5.1 Stability at elevated temperature (MT 46.4)**

After storage $54 \pm 2^\circ\text{C}$ for 14 days (Note 8), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.21.3.1),
- acidity/alkalinity/pH range (6.21.4.1),
- wettability (6.21.4.2),
- degree of dissolution and solution stability (6.21.4.3),

as required.

In the case of water soluble bag packaging, the package should be enclosed in a watertight sachet, box or any other container at $^\circ\text{C}$ (Note 10) for 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 clauses for:

- by-products of manufacture or storage (6.21.3.1),
- acidity/alkalinity/pH range (6.21.4.1),
- wettability (6.21.4.2),
- dissolution of the bag (6.21.6.1),
- degree of dissolution and solution stability (6.21.6.2),
- persistent foam (6.21.6.3),

as required.

None of the bags tested should show signs of leakage or rupture during normal handling, before and after storage.

6.21.6 Material packaged in a sealed water soluble bag (Notes 11, 11 & 13)**6.21.6.1 Dissolution of the bag (MT 176)**

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag in CIPAC standard water D taken according to the procedure described in Note 12, together with an appropriate proportion of the SP.

Flow time of the suspension: maximum sec.

6.21.6.2 **Degree of dissolution and solution stability** (MT 179.1) (Note 5)

The degree of dissolution and solution stability shall be tested on a solution containing the SP and the bag material in the actual ratio of application, prepared according to the procedure described in Note 13.

Residue of formulation retained on a 75 µm test sieve after dissolution in CIPAC standard water D at 25 ± 5°C (Note 6).

Maximum:% after 5 min.

Maximum:% after 24 h.

6.21.6.3 **Persistent foam** (MT 47.3) (Note 7)

The persistent foam shall be tested on a solution containing the SP and the bag in the actual ratio of application, prepared according to the procedure described in Note 13.

Note 1 For record keeping purposes, the suffix "SB" should be added to the formulation code (SP-SB).

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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

Note 5 This test will detect coarse particles which arise from impurities in the technical material and/or are present as inert ingredients, which could cause blockage of nozzles or filters in the application equipment.

Note 6 Unless another temperature and/or water is specified.

Note 7 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 at 25 ± 5°C.

Note 8 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 9 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

Note 10 If, due to irreversible changes in the characteristics of the bag material when stored above 50°C, the test temperature should not exceed 45°C; refer to Section 4.6.2 of this manual for alternative storage conditions.

.../cont.

Note 11 Sub-sampling

Lay the bag on a bench and carefully open one side of the bag with a cutter, taking care not to damage the seals.

Transfer the contents of the bag into a suitable flask. This material shall be used to carry out the tests for:

- active ingredient identity (6.21.2.1),
- active ingredient content (6.21.2.2),
- by-products of manufacture or storage (6.21.3.1),
- water content (6.21.3.2),
- acidity/alkalinity/pH range (6.21.4.1),
- wettability (6.21.4.2),
- dissolution of the bag (6.21.6.1),
- degree of dissolution and solution stability (6.21.6.2),
- persistent foam (6.21.6.3),

as required.

The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction and weighed to the nearest centigram. Aliquots of an aqueous solution of the bag material shall be used in the degree of dissolution and solution stability (6.21.6.2) and persistent foam (6.21.6.3) tests.

In the case of delay of the above tests, the bag shall be stored in a watertight container (glass bottle or equivalent) to avoid any change in its properties.

Note 12 The sampling of the bag for the dissolution test should be as follows:

Lay the empty cleaned bag in its original configuration (double layer). Delineate and then cut up a test sample including part of the upper seal (5 cm) and symmetrically including the vertical seal (10 cm). If the size of the bag is less than this dimension, use the whole bag.

Carry out the dissolution test immediately to avoid any modification of the sample.

Note 13 The procedure for adding the bag material to the solution for the degree of dissolution and solution stability and the persistent foam tests should be as follows:

Prepare a stock solution of the bag material (1 mg/ml) by weighing a sample (\underline{n} mg) of the bag (excluding sealed parts). Dissolve this sample by stirring in the standard water used for the tests to give a final volume of \underline{v} ml. Store the stock solution in a stoppered bottle before use.

Calculate the volume (\underline{V} ml) of the stock solution of the bag to be added to the test solution of the water soluble powder according to the following equation:

$$V(\text{ml}) = X \times \frac{1000B}{W}$$

Where: B (g) = weight of the emptied and cleaned bag
 W (g) = nominal weight of the WG contained in the bag
 X (g) = weight of the WG sample used in the test

6.22 WATER SOLUBLE POWDERS FOR SEED TREATMENT

Introduction

The guidelines for seed treatment (SS) 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 referring to Section 4. From the “Notes” provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

**..... [ISO common name] WATER SOLUBLE POWDER
FOR SEED TREATMENT (Note 1)**

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

6.22.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name]), complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), together with any necessary formulants including colouring matter (Note 1). It shall be in the form of a water soluble powder, free from visible extraneous matter and hard lumps.

6.22.2 Active ingredient

6.22.2.1 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.

6.22.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.22.3 Relevant impurities

6.22.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 6.22.2.2.

6.22.4 Physical properties

6.22.4.1 Acidity and/or alkalinityalkalinity (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

6.22.4.2 Degree of dissolution and solution stability (MT 179.1)

Residue of formulation retained on a 75 µm test sieve after dissolution in CIPAC standard water D at 25 ± 5°C:

Maximum residue after 5 min:%.

Maximum residue after 24 h:%.

6.22.4.3 Persistent foam if required (MT 47.3) (Note 5), if required

Maximum: ml after min.

6.22.4.4 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 [ISO common name] remaining on the seeds after the test.

6.22.5 Storage stability**6.22.5.1 Stability at elevated temperature** (MT 46.4)

After storage at 54 ± 2°C for 14 days (Note 6), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 7) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.22.3.1),
- acidity/alkalinity/pH range (6.22.4.1),
- degree of dissolution and solution stability (6.22.4.2),
- adhesion to seeds (6.22.4.4),

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. 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 should not be used for denaturing seeds to be used as livestock feeding stuffs.

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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

.../cont.

- Note 5** 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. For MT 47.3, the implicit upper limit is approximately 10 % w/v. In case the highest use rate exceeds 10 %, testing persistent foam using MT 47.3 is not possible and the clause should be omitted.
- Note 6** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 7** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

6.23 WATER SOLUBLE GRANULES

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.

..... [ISO common name] WATER SOLUBLE GRANULES

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

6.23.1 Description

The material shall consist of granules containing technical [ISO common name] complying with the requirements of the FAO/WHO specification, in the form of (see Section 4.2), and, if required, suitable carriers and/or necessary formulants. It shall be homogeneous, free from visible extraneous matter and/or hard lumps, free flowing, and nearly dust free or essentially non-dusty. The active ingredient shall be soluble in water. Insoluble carriers and formulants shall not interfere with compliance with 6.23.4.2.

Where the material is packaged in sealed water soluble bags, the description shall be as follows (Note 1):

The material shall consist of a defined quantity of [ISO common name] water soluble granules complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), contained in a sealed water soluble bag.

6.23.2 Active ingredient

6.23.2.1 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.

6.23.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.23.3 Relevant impurities**6.23.3.1 By-products of manufacture or storage** (Note 3), if required

Maximum:% of the [ISO common name] content found under 6.23.2.2.

6.23.3.2 Water (MT 30.6), if required

Maximum: g/kg.

6.23.4 Physical properties**6.23.4.1 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

6.23.4.2 Degree of dissolution and solution stability (MT 179.1)

Residue of formulation retained on a µm test sieve after dissolution in CIPAC standard water D at 25 ± 5°C (Note 5).

Maximum:% after 5 min.

Maximum:% after 24 h.

In the case of water soluble bag packaging, the provisions of clause 6.21.6.3 should be applied.

6.23.4.3 Persistent foam (MT 47.3) (Note 6)

Maximum ml after 1 min.

In the case of water soluble bag packaging, the provisions of clause 6.23.6.3 should be applied.

6.23.4.4 Dustiness (MT 171.1) (Note 7)

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.

6.23.4.5 Attrition resistance (MT 178.2)

Minimum:% attrition resistance.

6.23.4.6 Flowability (MT 172.2)

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

6.23.5 Storage stability

6.23.5.1 Stability at elevated temperatures (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 8) the determined average active ingredient content shall not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.23.3.1),
- acidity/alkalinity/pH range (6.23.4.1),
- degree of dissolution and solution stability (6.23.4.2),
- dustiness (6.23.4.4),
- attrition resistance (6.23.4.5),

as required.

In the case of water soluble bag packaging, the package should be enclosed in a watertight sachet, box or any other container at °C (Note 11) for 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 clauses for:

- by-products of manufacture or storage (6.23.3.1),
- acidity/alkalinity/pH range (6.23.4.1),
- dissolution of the bag (6.23.6.1),
- degree of dissolution and solution stability (6.23.6.2),
- persistent foam (6.23.6.3),

as required.

None of the bags tested should show signs of leakage or rupture during normal handling, before and after storage.

6.23.6 Material packaged in a sealed water soluble bag (Notes 11, 12 & 13)

6.23.6.1 Dissolution of the bag (MT 176)

The dissolution of the bag shall be tested on a sample of the emptied and cleaned bag in CIPAC standard water D taken according to the procedure described in Note 12, together with an appropriate proportion of the SG.

Flow time of the solution: maximum sec.

6.23.6.2 Degree of dissolution and solution stability (MT 179.1)

The degree of dissolution and solution stability shall be tested on a solution containing the SG and the bag material in the actual ratio of application, prepared according to the procedure described in Note 13.

Residue of formulation retained on a μm test sieve after dissolution in CIPAC standard water D at $25 \pm 5^\circ\text{C}$ (Note 5).

Maximum:% after 5 min.

Maximum:% after 24 h.

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

The persistent foam shall be tested on a solution containing the SG and the bag in the actual ratio of application, prepared according to the procedure described in Note 13.

- Note 1** For record keeping purposes, the suffix "SB" should be added to the formulation code (SG-SB).
- Note 2** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.
- Note 4** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 5** Unless other temperatures or waters are specified.
- 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 at $25 \pm 5^\circ\text{C}$.
- 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 4.6.2 of this manual for alternative storage conditions.
- Note 9** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.
- Note 10** If, due to irreversible changes in the characteristics of the bag material when stored above 50°C , the test temperature should not exceed 45°C , refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 11** Sub-sampling
- Lay the bag on a bench and carefully open one side of the bag with a cutter, taking care not to damage the seals.
- Transfer the contents of the bag into a suitable flask. This material shall be used to carry out the tests for:
- active ingredient identity (6.23.2.1),
 - active ingredient content (6.23.2.2),
 - by-products of manufacture or storage (6.23.3.1),
 - water content (6.23.3.2),
 - acidity/alkalinity/pH range (6.23.4.1),
 - dissolution of the bag (6.23.6.1),
 - degree of dissolution (6.23.6.2),
 - persistent foam (6.23.6.3),
- as required.
- The bag is then opened on three sides, completely cleaned from adhering powder by brushing or suction and weighed to the nearest 0.01 g. Aliquots of an aqueous solution of the bag material shall be used in the degree of dissolution and solution stability (6.23.6.2) and persistent foam (6.23.6.3) tests. In the case of delay of the above tests, the bag shall be stored in a watertight container (glass bottle or equivalent) to avoid any change in its properties.

.../cont.

Note 12 The sampling of the bag for the dissolution test should be as follows:

Lay the empty cleaned bag in its original configuration (double layer). Delineate and then cut up a test sample including part of the upper seal (5 cm) and symmetrically including the vertical seal (10 cm). If the size of the bag is less than this dimension, use the whole bag.

Carry out the dissolution test immediately to avoid any modification of the sample.

Note 13 The procedure for adding the bag material to the solution for the degree of dissolution and solution stability and the persistent foam tests should be as follows:

Prepare a stock solution of the bag material (1 mg/ml) by weighing a sample (\underline{n} mg) of the bag (excluding sealed parts). Dissolve this sample by stirring in the standard water used for the tests to give a final volume of \underline{n} ml. Store the stock solution in a stoppered bottle before use.

Calculate the volume (\underline{V} ml) of the stock solution of the bag to be added to the test solution of the water soluble granules according to the following equation:

$$V(\text{ml}) = X \times \frac{1000B}{W}$$

Where: B (g) = weight of the emptied and cleaned bag
 W (g) = nominal weight of the WG contained in the bag
 X (g) = weight of the WG sample used in the test

6.24 WATER SOLUBLE TABLETS

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 soluble tablets (ST) are intended for use with conventional application equipment. The active ingredient of STs is soluble in water at use rate. However, water soluble tablets may contain insoluble inerts that disperse in the spray liquid. Soluble tablets are often not coated or highly compacted and possess lower mechanical strength. Such tablets 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. This type of tablets, according to Pharm Eur are "uncoated tablets generally containing acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide". 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.

..... [ISO common name] WATER SOLUBLE TABLETS

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

6.24.1 Description

The material shall consist of an homogeneous mixture of technical [ISO common name], complying with the requirements of FAO/WHO specification [.....], in the form of (see Section 4.2), together with carriers and any other necessary formulants. It shall be in the form of tablets for application after disintegration and dissolution in water. The formulation shall be of dry, of unbroken, free-flowing tablets and shall be free from extraneous matter.

6.24.2 Active ingredient (Note 1)**6.24.2.1 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.

6.24.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

6.24.2.3 Tablet dose uniformity, if required

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

6.24.3 Relevant impurities (Note 1)**6.24.3.1 By-products of manufacture or storage** (Note 3), if required

Maximum: % of the [ISO common name] content found under 6.24.2.2.

6.24.3.2 Water (MT 30.5), if required

Maximum: g/kg

6.24.4 Physical properties**6.24.4.1 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 ...

6.24.4.2 **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.

6.24.4.3 **Solution properties of water soluble tablets** (MT 196) (Note 5)

Maximum: ... % retained after 2 hours on a 75 µm test sieve.

6.24.4.4 **Persistent foam** (MT 47.3) (Notes 5 and 9)

Maximum: ... ml after 1 minute

6.24.4.5 **Tablet integrity** (Note 10)

No broken, soft or sticky tablets should be present.

Fragments: yes/no

Soft/sticky: yes/no

6.24.4.6 **Attrition resistance of tablets** (MT 178.2) (Notes 11 & 12) if required

Minimum attrition resistance:%.

6.24.5 Storage stability

6.24.5.1 **Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 13) without pressure (Note 14) the determined average active ingredient content must not be lower than ... % relative to the determined average content found before storage (Note 15) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (6.24.3.1),
 - acidity/alkalinity/pH range (6.24.4.1),
 - disintegration of tablets (6.24.4.2),
 - solution properties of water soluble tablets (6.24.4.3),
 - tablet integrity (6.24.4.5),
 - attrition resistance of tablets (6.24.4.6),
- 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 analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

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

.../cont.

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
6.24.4.1	Acidity or alkalinity	MT 191	10 g add 100 ml
	pH range	MT 75.3	1 g make up 100 ml
6.24.4.3	Solution properties	MT 196	Maximum recommended use-rate
6.24.4.4	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, MT196 and MT 47.3.

Note 6 Before performing the CIPAC test covering the physical properties, 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 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 CIPAC 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 10 This requirement 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 11 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 12 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 < 1 cm as well.

Note 13 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions. Whole tablets must be stored. After storage tablets may be broken for tests as specified in Note 5.

Note 14 Without pressure means that the test is performed as specified by CIPAC MT 46.4, but no pressure is applied to the sample during aging.

Note 15 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7. SPECIFICATION GUIDELINES FOR LIQUID FORMULATED PESTICIDES

SIMPLE SOLUTIONS

- 7.1 Soluble concentrates (SL)
- 7.2 Solutions for seed treatment (LS)
- 7.3 Oil miscible liquids (OL)
- 7.4 Ultra-low volume liquids (UL)
- 7.5 Gel for direct application (GD)

SOLUTIONS FOR DISPERSION

- 7.11 Emulsifiable concentrates (EC)
- 7.12 Dispersible concentrates (DC)

EMULSIONS

- 7.21 Emulsions, oil in water (EW)
- 7.22 Emulsions for seed treatment (ES)
- 7.23 Micro-emulsions (ME)

SUSPENSIONS

- 7.31 Suspension concentrates (SC)
- 7.32 Flowable concentrate for seed treatment (FS)
- 7.33 Capsule suspensions (CS)
- 7.34 Oil dispersions (OD)

MULTI-CHARACTER LIQUID FORMULATIONS

- 7.41 Suspo-emulsions (SE)
- 7.42 Mixed formulations of CS and SC (ZC)
- 7.43 Mixed formulations of CS and EW (ZW)
- 7.44 Mixed formulations of CS and SE (ZE)

Introduction

In the following subsections, an open numbering system has intentionally been chosen to differentiate the formulation types according to their application mode and to allow later addition of newly developed specification templates.

7.1 SOLUBLE CONCENTRATES

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.

..... [ISO common name] SOLUBLE CONCENTRATE

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

7.1.1 Description

The material shall consist of technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a clear or opalescent liquid, free from visible suspended matter and sediment, to be applied as a true solution of the active ingredient in water.

7.1.2 Active ingredient

7.1.2.1 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.

7.1.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 2) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.1.3 Relevant impurities

7.1.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 7.1.2.2.

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

Maximum: g/kg.

7.1.4 Physical properties

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

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

7.1.4.2 Dilution stability (MT 41.1)

The formulation, following dilution (Note 6) with CIPAC standard water D and standing at $30 \pm 2^\circ\text{C}$ for 24 h, shall give a clear or opalescent solution, free from more than a trace of sediment and visible solid particles. Any visible sediment or particles produced shall pass through a 75 μm test sieve.

7.1.4.3 Persistent foam (MT 47.3) (Note 7)

Maximum: ml after 1 min.

7.1.5 Storage stability**7.1.5.1 Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

7.1.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 8), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.1.3.1),
- acidity/alkalinity/pH range (7.1.4.1),
- solution stability (7.1.4.2),

as required.

- Note 1** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 2** 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 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.
- Note 4** This clause is not appropriate for formulations formulated in water.
- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6** The concentration 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.
- Note 7** 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 at $25 \pm 5^\circ\text{C}$.
- Note 8** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 9** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.2 SOLUTIONS FOR SEED TREATMENT

Introduction

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 referring to Section 4. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [ISO common name] SOLUTION FOR SEED TREATMENT (Note 1)

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

7.2.1 Description

The material shall consist of technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), dissolved in suitable solvents, together with any other necessary formulants, including colouring matter (Note 1). It shall be in the form of a clear or opalescent liquid, free from visible suspended matter and sediment.

7.2.2 Active ingredient

7.2.2.1 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.

7.2.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.2.3 Relevant impurities

7.2.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 7.2.2.2.

7.2.3.2 **Water** (MT 30.6) (Note 5), if required

Maximum: g/kg.

7.2.4 Physical properties7.2.4.1 **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

7.2.4.2 **Solution stability** (MT 41.1)

The formulation, following dilution (Note 7) with CIPAC standard water D and standing at 30 ± 2°C for 24 h, shall give a clear or opalescent solution, free from more than a trace of sediment and visible solid particles. Any visible sediment or particles produced shall pass through a 75 µm test sieve.

7.2.4.3 **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 [ISO common name] remaining on the seeds after the test.

7.2.5 Storage stability7.2.5.1 **Stability at 0°C** (MT 39.3)

After storage at 0 ± 2°C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

7.2.5.2 **Stability at elevated temperature** (MT 46.4)

After storage at 54 ± 2°C for 14 days (Note 8) the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.2.3.1),
- acidity/alkalinity/pH range (7.2.4.1),
- solution stability (7.2.4.2),
- adhesion to seeds (7.2.4.3),

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 to contain a dye that permanently colours the seed after treatment (red is recommended) and cannot be removed by washing with water. 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** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 3** 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** 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.
- Note 5** Only for non-aqueous solutions.
- Note 6** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 7** The concentration should be within the range of concentrations recommended in the instructions for use, provided that they are within the scope of the method. If concentration of use is high, solution stability should be tested at the upper limit of MT 41.1. The solution stability test is not applicable for LS which are used without dilution and the clause can be removed.
- Note 8** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 9** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.3 OIL MISCIBLE LIQUIDS

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.

..... **[ISO common name] OIL MISCIBLE LIQUID**

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

7.3.1 Description

The material shall consist of a solution of technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), together with any other necessary formulants. It shall be free from visible suspended matter and sediment.

7.3.2 Active ingredient

7.3.2.1 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.

7.3.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 2) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.3.3 Relevant impurities

7.3.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 7.3.2.2.

7.3.3.2 Water (MT 30.6), if required

Maximum: g/kg.

7.3.4 Physical properties

7.3.4.1 Miscibility with hydrocarbon oil (MT 23)

If required, the formulation shall be miscible with the appropriate hydrocarbon oil (Note 4).

7.3.5 Storage stability

7.3.5.1 Stability at 0°C (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

7.3.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 5), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 6) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.3.3.1),
 - miscibility with hydrocarbon oil (7.3.4.2),
- as required.

- Note 1** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 2** 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 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.
- Note 4** The concentration should not be higher than the highest concentration recommended in the instructions for use.
- Note 5** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 6** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.4 ULTRA LOW VOLUME LIQUIDS

Introduction

In addition to the characteristics identified in the guideline below, the potential for loss of droplet mass by volatilization may also be critical for ultra low volume liquid (UL) formulations. If droplet evaporation is too rapid, the proportion of the spray which drifts from the target, and the distance over which drift occurs, may be increased to unacceptable levels. The volatilization and drift that occur in practice are dependent upon the initial droplet size spectrum and the height through which droplets fall, the air temperature and wind speed. Even if the other parameters are reasonably consistent, wind speed, in particular, is usually highly variable even over short distances and periods of time. A degree of volatilization which may be unacceptable for one type of application may be of little or no consequence in another case. It is desirable that a clause to limit losses by volatilization should be included in the specification but, at present, it is difficult to relate a simple measurement of loss by volatilization to the potential increase in drift produced. Industry is requested to produce a method, together with data obtained under controlled conditions, that will allow a meaningful relationship to be established between the results produced and the potential increase in drift in various scenarios.

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.

..... [ISO common name] ULTRA LOW VOLUME LIQUID

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

7.4.1 Description

The material shall consist of technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), together with any necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment.

7.4.2 Active ingredient

7.4.2.1 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.

7.4.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 2) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.4.3 Relevant impurities

7.4.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 7.4.2.2.

7.4.3.2 Water (MT 30.6), if required

Maximum: g/kg.

7.4.4 Physical properties

7.4.4.1 Viscosity, if required (MT 22.1)

The viscosity shall be in the range: to

7.4.5 Storage stability

7.4.5.1 Stability at 0°C (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

7.4.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 4), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 5) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.4.3.1),
as required.

- Note 1** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 2** 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 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.
- Note 4** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 5** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.5 GEL FOR DIRECT APPLICATION

Introduction

Gel for direct application (GD) is the designation for a gel-like preparation, intended to be applied undiluted. A gel for direct application consists of one or more active ingredients, a structuring agent and other formulants if appropriate.

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.

... [ISO common name] (AGROCHEMICAL) GEL FOR DIRECT APPLICATION

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

7.5.1 Description

The material shall consist of technical[ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), homogenized in suitable solvents, together with any other necessary formulants. It shall be in the form of a clear or opalescent gel, free from visible suspended matter and sediment, to be applied directly (without prior dilution in water).

7.5.2 Active ingredient

7.5.2.1 Identity tests (Note 1)

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

7.5.2.2 [ISO common name] content (Notes 1)

The ... [ISO common name] content shall be declared (g/kg or g/L at $20 \pm 2^\circ\text{C}$, Note 2) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance given in the table of tolerances, Section 4.3.2.

7.5.3 Relevant impurities**7.5.3.1 By-products of manufacture or storage** (Note 3), if required

Maximum: ...% of the ... [ISO common name] content found under 7.5.2.2.

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

Maximum: g/kg.

7.5.4 Physical properties**7.5.4.1 Appearance**

Homogeneous formulation, no phase separation is observed.

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

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH .

pH range to

7.5.5 Storage stability**7.5.5.1 Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 mL

7.5.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 6), the determined average active ingredient content shall not be lower than ... relative to the determined average content found before storage (Note 7) and the product shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.5.3.1),
- appearance: no phase separation (7.5.4.1),
- acidity/alkalinity/pH range (7.5.4.2),

as required.

- Note 1** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 2** 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 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.
- Note 4** This clause is not appropriate for formulations formulated in water.
- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 7** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.11 EMULSIFIABLE CONCENTRATES

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.

..... [ISO common name] EMULSIFIABLE CONCENTRATE

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

7.11.1 Description

The material shall consist of technical [ISO common name], complying with the requirements of FAO/WHO specification , in the form of (see Section 4.2), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as an emulsion after dilution in water.

7.11.2 Active ingredient

7.11.2.1 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.

7.11.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg or g/l at 20 ± 2°C, Note 2) and, when determined, the average content

measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.11.3 Relevant impurities

- 7.11.3.1 **By-products of manufacture or storage** (Note 3), if required
Maximum:% of the [ISO common name] content found under 7.11.2.2.
- 7.11.3.2 **Water** (MT 30.6), if required
Maximum: g/kg.

7.11.4 Physical properties

- 7.11.4.1 **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
- 7.11.4.2 **Emulsion stability and re-emulsification** (MT 36.3)

The formulation, when diluted at 25 ± 5°C (Notes 5 & 6) with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	initial emulsification complete
0.5 h	"cream", maximum: ml
2.0 h	"cream", maximum: ml "free oil", maximum: ml
24 h	re-emulsification complete
24.5 h	"cream", maximum: ml "free oil", maximum: ml
Note: tests after 24 h are required only where results at 2 h are in doubt.	

- 7.11.4.3 **Persistent foam** (MT 47.3) (Note 7)
Maximum: ml after 1 min.

7.11.5 Storage stability

- 7.11.5.1 **Stability at 0°C** (MT 39.3)
After storage at 0 ± 2°C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.
- 7.11.5.2 **Stability at elevated temperature** (MT 46.4)
After storage at 54 ± 2 °C for 14 days (Note 8), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.11.3.1),
 - acidity, alkalinity, pH range (7.11.4.1),
 - emulsion stability and re-emulsification (7.11.4.2),
- as required.

- Note 1** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 2** 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 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.
- Note 4** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 5** Unless another temperature is specified.
- Note 6** As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.
- Note 7** 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 at 25 ± 5°C.
- Note 8** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 9** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.12 DISPERSIBLE CONCENTRATES

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.

..... **[ISO common name] DISPERSIBLE CONCENTRATE**

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

7.12.1 Description

The material shall consist of technical [ISO common name], complying with the requirements of FAO/WHO specification , in the form of (see Section 4.2), dissolved in suitable solvents, together with any other necessary formulants. It shall be in the form of a stable homogeneous liquid, free from visible suspended matter and sediment, to be applied as a dispersion after dilution in water.

7.12.2 Active ingredient

7.12.2.1 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.

7.12.2.2 [ISO common name] content (Note 1)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 2) and, when determined, the content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.12.3 Relevant impurities

7.12.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 7.12.2.2.

7.12.3.2 Water (MT 30.6), if required

Maximum: g/kg.

7.12.4 Physical properties

7.12.4.1 Acidity and/or alkalinity (MT 191) or pH range (MT 75.3) (Note 4), if required

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH .

pH range: to

7.12.4.2 Dispersion stability (MT 180) (Note 5)

The formulation, when diluted at $23 \pm 2^\circ\text{C}$ with CIPAC standard waters A and D, shall comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	initial dispersion complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml
24 h	re-dispersion complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml

7.12.4.3 Wet sieve test (MT 185)

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

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

Maximum: ml after min.

7.12.5 Storage stability

7.12.5.1 **Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

7.12.5.2 **Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 7), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 8) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.12.3.1),
- acidity, alkalinity or pH range (7.12.4.1),
- dispersion stability (7.12.4.2),

as required.

- Note 1 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 2 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 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.
- Note 4 The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 5 The formulation should be tested at 2% dilution.
- 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 at $25 \pm 5^\circ\text{C}$.
- Note 7 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 8 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.21 EMULSIONS, OIL IN WATER

Introduction

Emulsions, oil in water (EW) is the designation for a stable emulsion of active ingredient(s) in an aqueous phase, intended for dilution with water before use. The active ingredient is normally a liquid and forms the dispersed oil phase, but it is also possible to emulsify a solid or liquid active ingredient dissolved in a water immiscible solvent.

Emulsions, like suspension concentrates, are metastable systems. Therefore, after transportation and storage, it may be necessary to re-homogenize the formulation, either by shaking small containers or by stirring the contents of large containers.

Emulsions may be non-Newtonian liquids, with complex rheology. Although the rheology can influence the dilution characteristics, these are checked indirectly by the emulsion stability test.

These guideline specifications apply to aqueous macro-emulsions only and not to other formulations such as suspo-emulsions (SE), emulsions, water in oil (EO) or micro-emulsions (ME).

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.

..... [ISO common name] EMULSION, OIL IN WATER

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

7.21.1 Description

The formulation shall consist of an emulsion of technical [ISO common name], complying with the requirements of FAO/WHO specification , in the form of (see Section 4.2), in an aqueous phase together with suitable formulants. After gentle agitation, the formulation shall be homogeneous (Note 1) and suitable for dilution in water.

7.21.2 Active ingredient

7.21.2.1 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.

7.21.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.21.3 Relevant impurities

7.21.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 7.21.2.2.

7.21.4 Physical properties

7.21.4.1 **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

7.21.4.2 **Pourability** (MT 148.1)

Maximum "residue":%.

7.21.4.3 **Emulsion stability and re-emulsification** (MT 36.3)

The formulation, when diluted at 25 ± 5°C (Notes 6 & 7) with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	initial emulsification complete
0.5 h	"cream", maximum: ml
2.0 h	"cream", maximum: ml "free oil", maximum: ml
24 h	re-emulsification complete
24.5 h	"cream", maximum: ml "free oil", maximum: ml
Note: tests after 24 h are required only where results at 2 h are in doubt.	

7.21.4.4 **Persistent foam** (MT 47.3) (Note 8)

Maximum: ml after 1 min.

7.21.5 Storage stability

7.21.5.1 **Stability at 0°C** (MT 39.3)

After storage at 0 ± 2°C for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml.

7.21.5.2 **Stability at elevated temperature** (MT 46.4)

After storage 54 ± 2°C for 14 days (Note 9), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 10) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.21.3.1),
 - acidity/alkalinity/pH range (7.21.4.1),
 - emulsion stability and re-emulsification (7.21.4.3),
- as required.

- Note 1** All physical and chemical tests listed in this specification are to be performed with a sample taken after the recommended homogenization procedure.
- Before sampling to verify the formulation quality, the commercial container must be inspected carefully. On standing, emulsions may develop a concentration gradient which could even result in the appearance of a clear liquid on the top (sedimentation of the emulsion) or on the bottom (creaming up of the emulsion). Therefore, before sampling, the formulation must be homogenized 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.
- Note 2** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 3** 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** 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.
- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6** Unless another temperature is specified.
- Note 7** As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.
- Note 8** 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 at $25 \pm 5^\circ\text{C}$.
- Note 9** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 10** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.22 EMULSIONS FOR SEED TREATMENT

Introduction

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 referring to Section 4. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [ISO common name] EMULSION FOR SEED TREATMENT (Note 1)

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

7.22.1 Description

The material shall consist of a water-based emulsion containing technical [ISO common name], complying with the requirements of FAO specification, in the form of (see Section 4.2), together with any necessary formulants including colouring matter (Note 1). It shall be easy to homogenize (i.e. after gentle shaking of small commercial containers or stirring of the contents of large containers, the material shall be homogeneous), and suitable for dilution with water if necessary.

7.22.2 Active ingredient

7.22.2.1 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.

7.22.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.22.3 Relevant impurities

7.22.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 7.22.2.2.

7.22.4 Physical properties

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

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

7.22.4.2 Emulsion stability on dilution with water (MT 36.3), if required

The formulation, when diluted at $25 \pm 5^\circ\text{C}$ (Notes 6 and 7) with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	initial emulsification complete
0.5 h	"cream", maximum: ml
2.0 h	"cream", maximum: ml "free oil", maximum: ml
24 h	re-emulsification complete
24.5 h	"cream", maximum: ml "free oil", maximum: ml
Note: tests after 24 h are required only where results at 2 h are in doubt.	

7.22.4.3 Persistent foam (MT 47.3) (Note 7), if required

Maximum: ml after 1 min.

7.22.4.4 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 [ISO common name] remaining on the seeds after the test.

7.22.5 Storage stability**7.22.5.1 Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the volume of separation of particulate or oily matter shall not be more than 0.3 ml.

7.22.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 8), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.22.3.1),
- acidity/alkalinity/pH range (7.22.4.1),
- emulsion stability on dilution with water (7.22.4.2),
- adhesion to seeds (7.22.4.4),

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 should not be used for denaturing seeds intended as livestock feeding stuffs.
- Note 2** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 3** 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** 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.
- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6** As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommendations for use provided they are within the scope of the method.
- Note 7** The mass of sample to be used in the test should be specified at the highest rate of use recommended by the supplier, provided it is within the scope of the method. For MT 47.3, the implicit upper limit is approximately 10% w/v. In case the highest use rate exceeds 10%, testing persistent foam using MT 47.3 is not possible and the clause should be omitted.
- Note 8** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 9** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.23 MICRO-EMULSIONS

Introduction

A micro-emulsion (ME) is a mixture of water, water insoluble and water soluble components forming a visually homogeneous, transparent liquid. One or more active ingredients may be present in either the aqueous phase, the non-aqueous phase, or in both phases. A variety of micro-emulsion formulations may be prepared in which the aqueous phase can be considered the dispersed phase, the continuous phase or, alternatively, where the two phases are considered to be bicontinuous. In all cases micro-emulsions will disperse into water to form either conventional emulsions or dilute micro-emulsions.

One of the major benefits of micro-emulsions is that they, unlike other conventional dispersion formulations, are thermodynamically stable. In this respect they are somewhat similar to soluble concentrate (SL) formulations. However, micro-emulsions are often only stable within limited temperature ranges. For this reason particular attention should be given to the directions for formulation storage.

Given that they form emulsions or dilute micro-emulsions on dilution into water, micro-emulsions are treated in a similar fashion to emulsifiable concentrate (EC) formulations, with some additional modifications to take account potential use problems relating to storage and use at high and low temperatures.

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.

..... [ISO common name] MICRO-EMULSION

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

7.23.1 Description

The material shall consist of technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), combined with water and other suitable formulants to give a stable, transparent liquid, free from visible suspended matter and sediment (Note 1).

7.23.2 Active ingredient

7.23.2.1 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.

7.23.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.23.3 Relevant impurities

7.23.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 7.23.2.2.

7.23.4 Physical properties

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

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

7.23.4.2 Persistent foam (MT 47.3) (Note 6)

Maximum ml after 1 min.

7.23.4.3 Emulsion stability and re-emulsification (MT 36.3) (Note 7)

The formulation, when diluted at $25 \pm 5^\circ\text{C}$ (Notes 6 & 7) with CIPAC standard waters A and D, shall comply with the following:

Time after dilution	Limits of stability, MT 36.3
0 h	initial emulsification complete
0.5 h	"cream", maximum: ml
2.0 h	"cream", maximum: ml "free oil", maximum: ml
24 h	re-emulsification complete
24.5 h	"cream", maximum: ml "free oil", maximum: ml
Note: tests after 24 h are required only where results at 2 h are in doubt.	

7.23.5 Storage stability**7.23.5.1 Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the volume of solid and/or liquid which separates shall not be more than 0.3 ml. (Note 9).

7.23.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Notes 9 and 10), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 11) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.23.3.1),
 - acidity/alkalinity/pH range (7.23.4.1),
 - emulsion stability and re-emulsification (7.23.4.3),
- as required.

Note 1 Before sampling a commercial container to verify formulation quality, inspect it carefully to ensure that no phase separation has taken place. If the formulation has been subjected to a temperature extreme, the recovery to a transparent, visually homogeneous liquid may require some gentle agitation of the container before the sample is taken.

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.

Note 3 In certain cases, micro-emulsion formulations may be quite viscous. In such a case, 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 active ingredient content in g/l. It is preferable, therefore, to determine the content in g/kg and, if necessary, to determine the mass per millilitre in g/ml, to calculate the active ingredient content in g/l.

.../cont.

- Note 4** 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.
- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- 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 at $25 \pm 5^\circ\text{C}$.
- Note 7** Unless another temperature is specified.
- Note 8** As outlined in CIPAC MT 36.3, the test concentrations should be based on those in the recommended directions for use supplied with the product. Where several concentrations are recommended, the highest and lowest concentrations within the scope of the method should be used.
- Note 9** In certain circumstances, phase separation may occur at high or low temperatures. The formulation shall be deemed to be acceptable if the recovery to a single phase is as rapid as the thermal equilibrium with ambient or use temperatures.
- Note 10** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 11** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.31 SUSPENSION CONCENTRATES

Introduction

Suspension concentrate (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. Pourability and water dispersibility parameters included in the specification adequately describe the flow (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 referring to Section 4. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [ISO common name] SUSPENSION CONCENTRATE

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

7.31.1 Description

The material shall consist of a suspension of fine particles of technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), in an aqueous phase together with suitable formulants. After gentle agitation the material shall be homogeneous (Note 1) and suitable for further dilution in water.

7.31.2 Active ingredient

7.31.2.1 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.

7.31.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.31.3 Relevant impurities

7.31.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 7.31.2.2.

7.31.4 Physical properties

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

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

7.31.4.2 Pourability (MT 148.1)

Maximum "residue":%.

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

Spontaneity of dispersion: minimum% after 5 min in CIPAC standard water D at $30 \pm 2^\circ\text{C}$.

7.31.4.4 Suspensibility (MT 184.1) (Note 6)

Suspensibility: minimum% after 30 min in CIPAC standard water D at $25 \pm 5^\circ\text{C}$.

7.31.4.5 **Wet sieve test** (MT 185) (Note 7)

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

7.31.4.6 **Persistent foam** (MT 47.3) (Note 8)

Maximum: ml after 1 min.

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

...% of particles shall be in the range ... to ... (Note 9).

7.31.5 Storage stability7.31.5.1 **Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the formulation shall continue to comply with clauses for:

- suspensibility (7.31.4.4),
 - wet sieve test (7.31.4.5),
- as required.

7.31.5.2 **Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 10), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 11) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.31.3.1),
 - acidity/alkalinity/pH range (7.31.4.1),
 - pourability (7.31.4.2),
 - spontaneity of dispersion (7.31.4.3),
 - suspensibility (7.31.4.4),
 - wet sieve test (7.31.4.5),
- 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.

.../cont.

- Note 2** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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** 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.
- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6** Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.
- Note 7** 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 8** 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 at $25 \pm 5^\circ\text{C}$.
- Note 9** Percentages may be specified in one or more ranges, as appropriate to the product. The determination of particle size range by laser diffraction is not an ideal criterion to ensure the suitability of liquid formulations. This should be evaluated by Wet sieve test (MT 185) and Suspensibility (MT 184.1) or Dispersion stability (MT 180).
- Note 10** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 11** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.32 FLOWABLE CONCENTRATES FOR SEED TREATMENT

Introduction

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 referring to Section 4. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

**..... [ISO common name] FLOWABLE CONCENTRATE FOR
SEED TREATMENT (Note 1)**

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

7.32.1 Description

The material shall consist of a suspension of fine particles of technical [ISO common name], complying with the requirements of FAO specification, in the form of (see Section 4.2), 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.

7.32.2 Active ingredient

7.32.2.1 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.

7.32.2.2 [ISO common name] content (Note 3)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 4) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.32.3 Relevant impurities

7.32.3.1 By-products of manufacture or storage (Note 5), if required

Maximum:% of the [ISO common name] content found under 7.32.2.2.

7.32.4 Physical properties

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

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

7.32.4.2 Pourability (MT 148.1)

Maximum "residue":%.

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

Maximum:% retained on a μm test sieve.

7.32.4.4 Persistent foam (MT 47.3) (Note 8), if required

Maximum: ml after 1 min.

7.32.4.5 **Suspensibility** (MT 184.1) (Note 9), if required

Suspensibility: minimum% after 30 min in CIPAC standard water D at $25 \pm 5^\circ\text{C}$.

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

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

7.32.4.7 **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 [ISO common name] remaining on the seeds after the test.

7.32.5 Storage stability

7.32.5.1 **Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the formulation shall continue to comply with the clause for: wet sieve test (7.32.4.3).

7.32.5.2 **Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 11), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 12) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.32.3.1),
- acidity, alkalinity or pH range (7.32.4.1),
- pourability (7.32.4.2),
- wet sieve test (7.32.4.3),
- suspensibility (7.32.4.5),
- adhesion to seeds (7.32.4.7),

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.

.../cont.

- 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 analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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** 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.
- 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 be specified at the highest rate of use recommended by the supplier, provided it is within the scope of the method. For MT 47.3, the implicit upper limit is approximately 10 % w/v. In case the highest use rate exceeds 10 %, testing persistent foam using MT 47.3 is not possible and the clause should be omitted.
- Note 9** Suspensibility is not applicable for FS which are used without dilution or at a dilution rate higher than the scope of the method MT 184.1 (10 %), and the clause can therefore be omitted. In MT 184.1, chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.
- Note 10** Percentages may be specified in one or more ranges, as appropriate to the product. The determination of particle size range by laser diffraction is not an ideal criterion to ensure the suitability of liquid formulations. This should be evaluated by Wet sieve test (MT 185) and Suspensibility (MT 184.1) or Dispersion stability (MT 180).
- Note 11** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 12** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.33 CAPSULE SUSPENSIONS

Introduction

Capsule suspension (CS) is the designation for a stable suspension of micro-encapsulated active ingredient in an aqueous continuous phase, intended for dilution with water before use.

The parameters which best describe the performance characteristics are as follows.

- Active ingredient, determined and expressed as “total”, “free” and “release rate” (“total” is required in all cases, “free” and “release rate” are dependent upon the intended application);
- Pourability test (to ensure that the CS can be poured from its container);
- Spontaneity of dispersion, suspensibility, wet sieve and persistent foam tests (to ensure the sprayability of the diluted suspension);
- Stability to freezing/thawing. Freezing of a micro-encapsulated formulation may result in capsule failure through crystallization or by other mechanisms, with the result that the properties of the formulation may be drastically changed, including release of the active ingredient into the aqueous medium.

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.

..... [ISO common name] CAPSULE SUSPENSION

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

7.33.1 Description

The material shall consist of a suspension of micro-capsules containing technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), in an aqueous phase, together with suitable formulants. After agitation, the material shall appear homogeneous (Note 1) and suitable for further dilution in water.

7.33.2 Active ingredient

7.33.2.1 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.

7.33.2.2 [ISO common name] content

7.33.2.2.1 Total content (Note 2)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 3) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.33.2.2.2 Free (non-encapsulated) content (Notes 2 and 4), if required

The free [ISO common name] average content measured shall not exceed% of the determined total content.

7.33.2.2.3 **Release rate** (Note 4) (for slow- or controlled release formulations), if required

The release rate measured shall comply with the following criteria:

7.33.3 Relevant impurities

7.33.3.1 **By-products of manufacture or storage** (Note 5), if required

Maximum:% of the [ISO common name] content found under 7.33.2.2.1.

7.33.4 Physical properties

7.33.4.1 **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

7.33.4.2 **Pourability** (MT 148.1)

Maximum "residue":%.

7.33.4.3 **Spontaneity of dispersion** (MT 160) (Note 7)

Spontaneity of dispersion: minimum% after 5 min in CIPAC standard water D at 30 ± 2°C.

7.33.4.4 **Suspensibility** (MT 184.1) (Note 7)

Suspensibility: minimum% after 30 min in CIPAC standard water D at 25 ± 5°C.

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

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

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

Maximum: ml after 1 min.

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

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

7.33.5 Storage stability

7.33.5.1 Freeze/thaw stability (Note 11)

After undergoing freeze/thaw cycles and following homogenization, the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (7.33.4.1),
- pourability (7.33.4.2),
- spontaneity of dispersion (7.33.4.3),
- suspensibility (7.33.4.4),
- wet sieve test (7.33.4.5),

as required.

An increase in the free [ISO common name] content shall be allowed, with the maximum concentration after the test corresponding to% of that found for total content under 7.33.2.2.1.

7.33.5.2 **Stability at elevated temperature** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 12), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 13) and the formulation shall continue to comply with the clauses for:

- release rate (7.33.2.2.3)
- by-products of manufacture or storage (7.33.3.1),
- acidity/alkalinity/pH range (7.33.4.1),
- pourability (7.33.4.2),
- spontaneity of dispersion (7.33.4.3),
- suspensibility (7.33.4.4),
- wet sieve test (7.33.4.5),

as required.

An increase in the free [ISO common name] content shall be allowed, with the maximum concentration after the test corresponding to% of that found for total content under 7.33.2.2.1.

Note 1 All physical and chemical tests listed in this specification are to be performed with a sample taken after the recommended homogenization procedure.

Before sampling to verify formulation quality, the commercial container must be inspected carefully. On standing, suspensions 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, the formulation must be homogenized 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.

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.

.../cont.

- 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** A clause for release rate is usually required for slow- or controlled-release CS. A clause for free active ingredient is usually required where the CS is intended to have slow- or controlled-release properties, or is intended to enhance operator safety. Test methods for CS free content and release rate may be product-specific.
- Note 5** 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.
- Note 6** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 7** Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.
- Note 8** This test detects coarse particles (e.g. oversize capsules, crystals) or agglomerates (of capsules or from 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 be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at $25 \pm 5^\circ\text{C}$.
- Note 10** Percentages may be specified in one or more ranges, as appropriate to the product. The determination of particle size range by laser diffraction is not an ideal criterion to ensure the suitability of liquid formulations. This should be evaluated by wet sieve test (MT 185) and suspensibility (MT 184.1) or dispersion stability (MT 180).
- Note 11** After manufacture and during shipping it is often impossible for buyer or seller to guarantee that the formulation has not been exposed to freezing temperatures. As freezing of a capsule suspension may result in undesirable, irreversible changes, including (but not limited to) capsule failure caused by crystallization of the active ingredient, the ability of the formulation to successfully withstand repeated freezing and thawing is an important property. Unless otherwise agreed, the freeze/thaw stability test shall cycle the formulation between room temperature (e.g. $20 \pm 2^\circ\text{C}$) and $-10 \pm 2^\circ\text{C}$ on 18-hour-freeze/6-hour-melt cycles for a total of 4 cycles.
- Note 12** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 13** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.34 OIL DISPERSIONS

Introduction

An oil dispersion (OD) is a stable suspension of active ingredient(s) in an organic fluid, which may contain other dissolved active ingredient(s), intended for dilution with water before use.

OD formulations are metastable systems, like emulsions, oil-in-waters (EW) and suspension concentrates (SC). Therefore, after transportation and storage it may be necessary to re-homogenise the formulation, either by shaking or by stirring.

OD, like SC formulations, do not disperse as spontaneously as EC formulations upon dilution in water. Therefore, the spray solution has to be stirred in order to obtain a homogeneous dispersion before application.

The parameters which best describe the performance characteristics are:

- Pourability (to ensure that the OD can be poured from its container);
- Dispersion stability, wet sieve and persistent foam tests (to ensure the sprayability and stability of the diluted suspension);
- Storage at elevated temperature (to ensure the absence of crystal growth upon storage).

Information about other properties may also be given, e.g. acidity or alkalinity and stability at 0°C, but these parameters do not normally constitute essential parts of the specification.

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.

..... [ISO common name] OIL DISPERSION

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

7.34.1 Description

The material shall consist of a stable suspension of fine particles of technical [ISO common name], complying with the requirements of FAO/WHO specification, in the form of (see Section 4.2), in a non-aqueous fluid together with suitable formulants. After shaking or stirring of the sample, the material shall be homogeneous (Note 1).

7.34.2 Active ingredient

7.34.2.1 Identity tests (Note 2)

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

7.34.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 3) and, when determined, the content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

7.34.3 Relevant impurities

7.34.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 7.34.2.2.

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

Maximum: g/kg.

7.34.4 Physical properties7.34.4.1 **Acidity** and/or **alkalinity** (MT 191) or **pH range** (MT 75.3) (Note 5), if requiredMaximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

7.34.4.2 **Pourability** (MT 148.1)

Maximum "residue":%.

7.34.4.3 **Dispersion stability** (MT 180) (Note 6)

The formulation, when diluted at $23 \pm 2^\circ\text{C}$ with CIPAC standard waters A and D, shall comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	initial dispersion complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml
24 h	re-dispersion complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml

7.34.4.4 **Wet sieve test** (MT 185) (Note 7)Maximum:% of the formulation shall be retained on a μm test sieve.7.34.4.5 **Persistent foam** (MT 47.3) (Note 8)

Maximum: ml after 1 min.

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

...% of particles shall be in the range ... to ... (Note 9)

7.34.5 Storage stability7.34.5.1 **Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the formulation shall continue to comply with the clauses for:

- dispersion stability (7.34.4.3),
- wet sieve test (7.34.4.4),

as required.

7.34.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 10), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 11) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.34.3.1),
- acidity, alkalinity or pH range (7.34.4.1),
- pourability (7.34.4.2),
- dispersion stability (7.34.4.3),
- wet sieve test (7.34.4.4),

as required.

- Note 1** Before sampling to verify the formulation quality, inspect the commercial container carefully. On standing, oil dispersions (OD) 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, homogenise the formulation according to the instructions given by the manufacturer or, in the absence of such instructions, by gently 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 homogenisation procedure.
- Note 2** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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** 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.
- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6** The formulation should be tested at 2% dilution.
- Note 7** This test detects coarse particles (e.g. oversize capsules, crystals) or agglomerates (of capsules or from crust formation), or extraneous materials which could cause blockage of spray nozzles or filters in the spray tank.
- Note 8** 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 at $25 \pm 5^\circ\text{C}$.
- Note 9** Percentages may be specified in one or more ranges, as appropriate to the product. The determination of particle size range by laser diffraction is not an ideal criterion to ensure the suitability of liquid formulations. This should be evaluated by wet sieve test (MT 185) and suspensibility (MT 184.1) or dispersion stability (MT 180).

..../cont.

Note 10 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 11 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.41 SUSPO-EMULSIONS

Introduction

A suspo-emulsion (SE) is a fluid heterogeneous formulation consisting of a stable dispersion of active ingredient(s) in the form of solid particles and of water-non-miscible fine globules in a continuous water phase. The formulation is intended for dilution into water prior to spray application. Mixtures of active ingredients are often used to provide a broader spectrum of pest control. Formulating the active ingredients together eliminates the need for tank mixing (which can lead to incompatibilities). Like other aqueous liquid formulations, suspo-emulsions are easy to handle and measure, dust free, non-flammable and offer good miscibility with water.

Suspo-emulsions are not stable indefinitely and therefore it is necessary to ensure that, after transportation and storage, the formulation remains suitable for use.

Quantification of the following parameters, particularly after high and low temperature stability tests, serves this purpose.

- Active ingredient identity tests and active ingredient content determination (related to biological efficacy);
- Impurities;
- Pourability test (to ensure that the SE can be poured from its container);
- Dispersion stability and wet sieve tests (to ensure the sprayability of the diluted suspo-emulsion).

Information about other properties may also be given, but these parameters do not normally constitute essential parts of the specification.

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.

..... [ISO common name] SUSPO-EMULSION

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

7.41.1 Description

The material shall consist of a suspension of fine particles of technical [ISO common name] complying with the requirements of the FAO/WHO specification, in the form of (see Section 4.2), combined with an

emulsion of fine droplets of technical [ISO common name] complying with the requirements of the FAO/WHO specification, in the form of (see Section 4.2), in an aqueous phase together with suitable formulants. After gentle agitation the material shall appear homogeneous (Note 1) and be suitable for further dilution in water.

7.41.2 Active ingredients

7.41.2.1 Identity tests (Note 2)

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

7.41.2.2 and [ISO common names] content (Note 2)

The and [ISO common names] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 3) and, when determined, the average contents measured shall not differ from those declared by more than the appropriate tolerances, given in the table of tolerances, Section 4.3.2.

7.41.3 Relevant impurities

7.41.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 7.41.2.2.

7.41.4 Physical properties

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

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

7.41.4.2 Pourability (MT 148.1)

Maximum "residue":%.

7.41.4.3 Dispersion stability (MT 180) (Note 6)

The formulation, when diluted at $23 \pm 2^\circ\text{C}$ with CIPAC standard waters A and D, shall comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	initial dispersion complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml
24 h	re-dispersion complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml

7.41.4.4 Wet sieve test (MT 185)

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

7.41.4.5 Persistent foam (MT 47.3) (Note 7)

Maximumml after 1 min.

7.41.5 Storage stability**7.41.5.1 Stability at 0°C** (MT 39.3)

After storage at $0 \pm 2^\circ\text{C}$ for 7 days, the formulation shall continue to comply with the clauses for:

- dispersion stability (7.41.4.3),
- wet sieve test (7.41.4.4),

as required.

7.41.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 8), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 9) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (7.41.3.1),
- acidity/alkalinity/pH range (7.41.4.1),
- pourability (7.41.4.2),
- dispersion stability (7.41.4.3),
- wet sieve test (7.41.4.4),

as required.

Note 1 Before sampling to verify formulation quality, inspect the commercial container carefully. On standing, suspo-emulsions usually develop a concentration gradient which may result in the appearance of a clear layer at either the top or the bottom of the container. A sediment layer may also form at the bottom of the container, which can be detected by probing with a glass rod. 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). After this procedure the container should not contain a sticky layer of non-dispersed matter at the bottom (if the suspo-emulsion has flocculated it may not be possible to re-disperse this sticky layer). All the physical and chemical tests must be carried out on a sample taken after the recommended homogenization procedure.

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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 active ingredient content in g/l. It is preferable, therefore, to determine the content in g/kg and, if necessary, to determine the mass per millilitre, to calculate the active ingredient content in g/l.

.../cont.

- Note 4** 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.
- Note 5** The method to be used shall be stated. If several methods are available, a referee method shall be selected.
- Note 6** The formulation should be tested at 2% dilution.
- Note 7** 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 at $25 \pm 5^\circ\text{C}$.
- Note 8** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.
- Note 9** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.42 MIXED FORMULATIONS OF CS AND SC

Introduction

A mixed formulation of CS and SC is ZC and is a stable suspension of microcapsules and solid fine particles, each of which contains one or more active ingredients. The formulation is intended for dilution into water prior to spray application. Formulating the active ingredients together eliminates the need for tank mixing, which can lead to incompatibility, and facilitates control of a wider range of pests with fewer applications. Like other aqueous liquid formulations, ZC formulations are easy to handle and measure, dust free, non-flammable and offer good miscibility with water.

One or more of the active ingredients is encapsulated for various purposes, such as to increase the residual biological activity, or to reduce the acute toxicity, or to obtain a physical or chemically stable water-based formulation. The purpose determines whether the “free” active ingredient and the “release rate” are relevant properties of a specific product.

Mixed formulations of CS and SC are not stable indefinitely and it is necessary to ensure that, after transportation and storage, the formulation remains suitable for use. Quantification of the following parameters, particularly after high and low temperature stability tests, serves this purpose.

- Active ingredient, determined and expressed as “total”, “free” and “release rate”, as required;
- Pourability;
- Spontaneity of dispersion and wet sieve tests (to ensure the sprayability of the diluted ZC).

Information about other properties may also be given, but these parameters do not constitute essential parts of the specification.

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.

..... [ISO Common name] MIXED FORMULATION OF CS AND SC

[CIPAC numbers]/ZC (month & year of publication)

7.42.1 Description

The material shall consist of a suspension of fine particles of technical [ISO common name] complying with the requirements of the FAO/WHO specification [.... /TC (date)], in the form of [derivative, if appropriate], combined with a suspension of microcapsules of technical [ISO common name] complying with the requirements of FAO/WHO specification [.... /TC (date)], in the form of [derivative, if appropriate], in an aqueous phase together with suitable formulants. After gentle agitation the material shall appear homogeneous (Note 1) and be suitable for dilution in water.

7.42.2 Active ingredients

7.42.2.1 Identity tests (Note 2)

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

7.42.2.2 [ISO common names] content

7.42.2.2.1 Total [ISO common names] content (Notes 2 & 3)

The [ISO common names] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 4) and, when determined, the average content measured shall not differ from those declared by more than the appropriate tolerances, given in the table of tolerances, Section 4.3.2.

7.42.2.2.2 Free, non-encapsulated [ISO common name] content (Notes 2 & 3), if required

The free [ISO common name] average content measured shall not exceed ...% of the determined total content.

7.42.2.2.3 [ISO common name] release rate (Notes 2 & 3), if required

The [ISO common name] release rate measured shall comply with the following criteria:

7.42.3 Relevant impurities

7.42.3.1 By-products of manufacture or storage (Notes 3 & 5), if required

Maximum: ...% of the [ISO common name] content measured.

7.42.4 Physical properties

7.42.4.1 **Acidity** and/or **alkalinity** (MT 191) or **pH range** (MT 75.3), if required

Maximum acidity: g/kg calculated as H₂SO₄.

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

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

...% of particles shall be in the range ... to ... (Note 6)

7.42.4.3 **Pourability** (MT 148.1)

Maximum "residue":%

7.42.4.4 **Spontaneity of dispersion** (MT 160) (Notes 7 & 8)

Spontaneity of dispersion: minimum% after 5 min in CIPAC standard water D at 30 ± 2°C.

7.42.4.5 **Suspensibility** (MT 184.1) (Notes 7 & 8)

Suspensibility: minimum% after 30 min in CIPAC standard water D at 25 ± 5°C.

7.42.4.6 **Wet sieve test** (MT 185) (Note 9)

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

7.42.4.7 **Persistent foam** (MT 47.3) (Note 10)

Maximum: ... ml after 1 min.

7.42.5 Storage stability

7.42.5.1 **Freeze/thaw stability** (Note 11)

After undergoing freeze/thaw cycles and following homogenization, the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (7.42.4.1),
- pourability (7.42.4.3),
- spontaneity of dispersion (7.42.4.4),
- suspensibility (7.42.4.5),
- wet sieve test (7.42.4.6),

as required.

An increase in free ...[ISO common name] content (7.42.2.2.2) shall be permitted, to a maximum of ...% of the total content determined under 7.42.2.2.1.

7.42.5.2 **Stability at elevated temperature** (MT 46.4)

After storage at 54 ± 2°C for 14 days (Note 12), the determined average total active ingredient content must not be lower than ...% relative to the determined average content found before storage

(Note 13) and the formulation shall continue to comply with the clauses for:

- ...[ISO common name] release rate (7.42.2.2.3),
- by-products of manufacture or storage (7.42.3.1),
- acidity/alkalinity/pH range (7.42.4.1),
- pourability (7.42.4.3),
- spontaneity of dispersion (7.42.4.4),
- suspensibility (7.42.4.5),
- wet sieve test (7.42.4.6),

as required.

An increase in free ...[ISO common name] content (7.42.2.2.2) shall be permitted, to a maximum of ...% of the total content determined under 7.42.2.2.1

Note 1 All physical and chemical tests listed in this specification are to be performed with a sample taken after the recommended homogenization procedure. Before sampling to verify formulation quality, inspect the commercial container carefully. On standing mixed formulation of CS and SC usually develop a concentration gradient from the top to the bottom of the container. This may result in the appearance of a clear liquid on the top and/or sediment on the bottom. Therefore, before sampling, the formulation must be homogenized 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). After this procedure the container shall not contain a sticky layer of non-dispersed matter at the bottom (if the ZC has flocculated it may not be possible to re-disperse this sticky layer). 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.

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.

Note 3 Separate tolerances for total content must be provided for each active ingredient, as defined in Section 4.3.2. Separate clauses must be provided for each relevant impurity.

Clauses for free active ingredient content and release rate of the active ingredient are required only for the encapsulated active ingredient(s) and only if appropriate to the intended properties of the capsules. A clause to control release rate is usually required for capsules intended to possess slow- or controlled-release properties. A clause to control free active ingredient is usually required where encapsulation is intended to control the release or stability of the active ingredient, or to decrease the risk to users from accidental exposure to the active ingredient. If more than one active ingredient is encapsulated, limits must be provided for each. Methods for determination of free active ingredient and release rate may be product-specific.

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 ml, 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 This clause should include only relevant impurities. Method(s) of analysis must be peer validated.

.../cont.

- Note 6** Percentages may be specified in one or more ranges, as appropriate to the product. The determination of particle size range by laser diffraction is not an ideal criterion to ensure the suitability of liquid formulations. This should be evaluated by wet sieve test (MT 185) and suspensibility (MT 184.1) or dispersion stability (MT 180).
- Note 7** Chemical assay is the only fully reliable method to measure the mass of active ingredient still in suspension. However, where the same limit applies to all active ingredients in the formulation, the simpler gravimetric method may be used on a routine basis provided that it has been shown to give equal results to those of chemical assay. In case of dispute, chemical assay shall be the referee method.
- Note 8** Limits for spontaneity of dispersion and suspensibility must be provided for each active ingredient.
- Note 9** This test detects coarse particles (e.g. oversize capsules, crystals) or agglomerates (of capsules or from crust formation). or extraneous materials which could cause blockage of spray nozzles or filters in the spray tank.
- Note 10** 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 at $25 \pm 5^\circ\text{C}$.
- Note 11** After manufacture and during shipping it is often impossible for buyer or seller to guarantee that the formulation has not been exposed to freezing temperatures. As freezing of a ZC formulation may result in undesirable, irreversible changes, including (but not limited to) capsule failure caused by crystallization of the active ingredient, the ability of the formulation to successfully withstand repeated freezing and thawing is an important property. Unless otherwise agreed, the freeze/thaw stability test shall cycle the formulation between room temperature (e.g. $20 \pm 2^\circ\text{C}$) and $-10 \pm 2^\circ\text{C}$ on 18-hour-freeze/6-hour-melt cycles for a total of 4 cycles.
- Note 12** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 for alternative storage conditions.
- Note 13** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.43 MIXED FORMULATIONS OF CS AND EW

Introduction

A mixed formulation of CS and EW is ZW and is a stable aqueous dispersion of microcapsules and emulsion droplets, each of which contains one or more active ingredients. The formulation is intended for dilution into water prior to spray application. Formulating the active ingredients together eliminates the need for tank mixing, which can lead to incompatibility, and facilitates control of a wider range of pests with fewer applications. Like other aqueous liquid formulations, ZW formulations are easy to handle and measure, dust free, non-flammable and offer good miscibility with water.

One or more of the active ingredients is encapsulated for various purposes, such as to increase the residual biological activity, or to reduce the acute toxicity, or to obtain a physical or chemically stable water-based formulation. The purpose determines whether the “free” active ingredient and the “release rate” are relevant properties of a specific product.

Mixed formulations of CS and EW are not stable indefinitely and it is necessary to ensure that, after transportation and storage, the formulation remains suitable for use.

Quantification of the following parameters, particularly after high and low temperature stability tests, serves this purpose.

- Active ingredient, determined and expressed as “total”, “free” and “release rate”, as required;
- Pourability;
- Dispersion stability and wet sieve tests (to ensure the sprayability of the diluted ZW).

Information about other properties may also be given, but these parameters do not constitute essential parts of the specification.

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.

..... [ISO Common name] MIXED FORMULATION OF CS AND EW

[CIPAC numbers]/ZW (month & year of publication)

7.43.1 Description

The material shall consist of an emulsion of fine droplets of technical [ISO common name(s)] complying with the requirements of the FAO/WHO specification [.../TC (date)], in the form of [derivative, if appropriate], combined with a suspension of a microcapsules of technical [ISO common name] complying with the requirements of FAO/WHO specification [.../TC (date)], in the form of [derivative, if appropriate], in an aqueous phase together with suitable formulants. After gentle agitation the material shall appear homogeneous (Note 1) and be suitable for dilution in water.

7.43.2 Active ingredients

7.43.2.1 Identity tests (Note 2)

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

7.43.2.2 [ISO common names] content

7.43.2.2.1 Total [ISO common names] content (Notes 2 & 3)

The [ISO common names] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 4) and, when determined, the average content measured shall not differ from those declared by more than the appropriate tolerances, given in the table of tolerances, Section 4.3.2.

7.43.2.2.2 **Free, non-encapsulated [ISO common name] content**
(Notes 2 & 3), if required

The free [ISO common name] average content measured shall not exceed ...% of the determined total content.

7.43.2.2.3 **[ISO common name] release rate** (Notes 2 & 3), if required

The [ISO common name] release rate measured shall comply with the following criteria:

7.43.3 Relevant impurities

7.43.3.1 **By-products of manufacture or storage** (Notes 3 & 5), if required

Maximum: ...% of the [ISO common name] content measured.

7.43.4 Physical properties

7.43.4.1 **Acidity and/or alkalinity (MT 191) or pH range (MT 75.3)**, if required

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

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

...% of particles shall be in the range ... to ... (Note 6)

7.43.4.3 **Pourability** (MT 148.1)

Maximum "residue":%

7.43.4.4 **Dispersion stability** (MT 180) (Note 7)

The formulation, when diluted at $23 \pm 2^\circ C$ with CIPAC standard waters A and D, shall comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	initial dispersion complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml
24 h	re-dispersion complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml

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

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

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

Maximum ... ml after 1 min.

7.43.5 Storage stability

7.43.5.1 Freeze/thaw stability (Note 10)

After undergoing freeze/thaw cycles and following homogenization, the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (7.43.4.1),
- pourability (7.43.4.3),
- dispersion stability (7.43.4.4),
- wet sieve test (7.43.4.5),

as required.

An increase in free ...[ISO common name] content (7.43.2.2.2) shall be permitted, to a maximum of ...% of the total content determined under 7.43.2.2.1.

7.43.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 11), the determined average total content of each active ingredient must not be lower than ...%, relative to the determined average content found before storage (Note 12), and the formulation shall continue to comply with the clauses for:

- ... [ISO common name] release rate (7.43.2.2.3)
- by-products of manufacture or storage (7.43.3.1),
- acidity/alkalinity/pH range (7.43.4.1),
- pourability (7.43.4.3),
- dispersion stability (7.43.4.4),
- wet sieve test (7.43.4.5),

as required.

An increase in free ...[ISO common name] content (7.43.2.2.2) shall be permitted, to a maximum of ...% of the total content determined under 7.43.2.2.1.

Note 1

All physical and chemical tests listed in this specification are to be performed with a sample taken after the recommended homogenization procedure. Before sampling to verify formulation quality, inspect the commercial container carefully. On standing ZW formulations usually develop a concentration gradient from the top to the bottom of the container. This may result in the appearance of a clear liquid on the top and/or sediment on the bottom. Therefore, before sampling, the formulation must be homogenized 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). After this procedure, the container shall not contain a sticky layer of non-dispersed matter at the bottom (if the ZW has flocculated it may not be possible to re-disperse this sticky layer). 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.

.../cont.

- Note 2** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 3** Separate tolerances for total content must be provided for each active ingredient, as defined in Section 4.3.2. Separate clauses must be provided for each relevant impurity.
- Clauses for free active ingredient content and release rate of the active ingredient are required only for the encapsulated active ingredient(s) and only if appropriate to the intended properties of the capsules. A clause to control release rate is usually required for capsules intended to possess slow- or controlled-release properties. A clause to control free active ingredient is usually required where encapsulation is intended to control the release or stability of the active ingredient, or to decrease the risk to users from accidental exposure to the active ingredient. If more than one active ingredient is encapsulated, limits must be provided for each. Methods for determination of free active ingredient and release rate may be product-specific.
- 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** This clause should include only relevant impurities and should be omitted if there is none. Method(s) of analysis must be peer validated.
- Note 6** Percentages may be specified in one or more ranges, as appropriate to the product. The determination of particle size range by laser diffraction is not an ideal criterion to ensure the suitability of liquid formulations. This should be evaluated by wet sieve test (MT 185) and suspensibility (MT 184.1) or dispersion stability (MT 180).
- Note 7** The formulation should be tested at 2% dilution.
- Note 8** This test detects coarse particles (e.g. oversize capsules, crystals) or agglomerates (of capsules or from crust formation) or extraneous materials that 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 be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at $25 \pm 5^\circ\text{C}$.
- Note 10** After manufacture and during shipping it is often impossible for buyer or seller to guarantee that the formulation has not been exposed to freezing temperatures. As freezing of a ZW formulation may result in undesirable, irreversible changes, including (but not limited to) capsule failure caused by crystallization of the active ingredient, the ability of the formulation to successfully withstand repeated freezing and thawing is an important property. Unless otherwise agreed, the freeze/thaw stability test shall cycle the formulation between room temperature (e.g. $20 \pm 2^\circ\text{C}$) and $-10 \pm 2^\circ\text{C}$ on 18-hour-freeze/6-hour-melt cycles for a total of 4 cycles.
- Note 11** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 for alternative storage conditions.
- Note 12** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

7.44 MIXED FORMULATIONS OF CS AND SE

Introduction

A mixed formulation of CS and SE is ZE and is a stable aqueous dispersion of microcapsules, solid fine particles and emulsion droplets, each of which contains one or more active ingredients. The formulation is intended for dilution into water prior to spray application. Formulating the active ingredients together eliminates the need for tank mixing, which can lead to incompatibility, and facilitates control of a wider range of pests with fewer applications. Like other aqueous liquid formulations, ZE formulations are easy to handle and measure, dust free, non-flammable and offer good miscibility with water.

One or more of the active ingredients is encapsulated for various purposes, such as to increase the residual biological activity, or to reduce the acute toxicity, or to obtain a physical or chemically stable water-based formulation. The purpose determines whether the “free” active ingredient and the “release rate” are relevant properties of a specific product.

Mixed formulations of CS and SE are not stable indefinitely and it is necessary to ensure that, after transportation and storage, the formulation remains suitable for use. Quantification of the following parameters, particularly after high and low temperature stability tests, serves this purpose.

- Active ingredient, determined and expressed as “total”, “free” and “release rate”, as required;
- Pourability;
- Dispersion stability and wet sieve tests (to ensure the sprayability of the diluted ZE formulation).

Information about other properties may also be given, but these parameters do not constitute essential parts of the specification.

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.

..... [ISO common names] MIXED FORMULATION OF CS AND SE

[CIPAC numbers]/ZE (month & year of publication)

7.44.1 Description

The material shall consist of an emulsion of fine droplets of technical [ISO common name(s)] complying with the requirements of the FAO/WHO specification [..../TC (date)], in the form of [derivative, if appropriate]; and a suspension of fine particles of technical [ISO common name(s)] complying with the requirements of the FAO/WHO specification [..../TC (date)], in the form of [derivative, if appropriate]; combined with a suspension of microcapsules of technical [ISO common name(s)] complying with the

requirements of FAO/WHO specification [.../TC (date)], in the form of [derivative, if appropriate], in an aqueous phase, together with suitable formulants. After gentle agitation, the material shall appear homogeneous (Note 1) and be suitable for dilution in water.

7.44.2 Active ingredients

7.44.2.1 Identity tests (Note 2)

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

7.44.2.2 [ISO common names] content

7.44.2.2.1 Total [ISO common names] content (Notes 2 & 3)

The [ISO common names] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 4) and, when determined, the average content measured shall not differ from those declared by more than the appropriate tolerances, given in the table of tolerances, Section 4.3.2.

7.44.2.2.2 Free, non-encapsulated [ISO common name] content (Notes 2 & 3), if required

The free [ISO common name] average content measured shall not exceed ...% of the determined total content.

7.44.2.2.3 [ISO common name] release rate (Notes 2 & 3), if required

The [ISO common name] release rate measured shall comply with the following criteria:

7.44.3 Relevant impurities

7.44.3.1 By-products of manufacture or storage (Notes 3 & 5), if required

Maximum: ..% of the [ISO common name] content measured.

7.44.4 Physical properties

7.44.4.1 Acidity and/or alkalinity (MT 191) or pH range (MT 75.3), if required

Maximum acidity: g/kg calculated as H_2SO_4 .

Maximum alkalinity: g/kg calculated as NaOH.

pH range: to

7.44.4.2 Particle size distribution (MT 187), if required

...% of particles shall be in the range ... to ... (Note 6)

7.44.4.3 Pourability (MT 148.1)

Maximum "residue":%

7.44.4.4 Dispersion stability (MT 180) (Note 7)

The formulation, when diluted at $23 \pm 2^\circ\text{C}$ with CIPAC standard waters A and D, shall comply with the following:

Time after allowing the dispersion to stand	Limits of stability
0 h	initial dispersion complete
0.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml
24 h	re-dispersion complete
24.5 h	"cream", maximum: ml
	"free oil", maximum: ml
	sediment, maximum: ml

7.44.4.5 Wet sieve test (MT 185) (Note 8)

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

7.44.4.6 Persistent foam (MT 47.3) (Note 9)

Maximum ... ml after 1 min.

7.44.5 Storage stability**7.44.5.1 Freeze/thaw stability** (Note 10)

After undergoing freeze/thaw cycles and following homogenization, the formulation shall continue to comply with the clauses for:

- acidity/alkalinity/pH range (7.44.4.1),
- pourability (7.44.4.3),
- dispersion stability (7.44.4.4),
- wet sieve test (7.44.4.5),

as required.

An increase in free ...[ISO common name] content (7.44.2.2.2) shall be permitted, to a maximum of ...% of the total content determined under 7.44.2.2.1.

7.44.5.2 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 11), the determined average total content of each active ingredient must not be lower than ...%, relative to the determined average content found before storage (Note 12), and the formulation shall continue to comply with the clauses for:

- ... [ISO common name] release rate (7.44.2.2.3)
- by-products of manufacture or storage (7.44.3.1),
- acidity/alkalinity/pH range (7.44.4.1),
- pourability (7.44.4.3),

- dispersion stability (7.44.4.4),
 - wet sieve test (7.44.4.5),
- as required.

An increase in free ...[ISO common name] content (7.44.2.2.2) shall be permitted, to a maximum of ...% of the total content determined under 7.44.2.2.1.

- Note 1** All physical and chemical tests listed in this specification are to be performed with a sample taken after the recommended homogenization procedure. Before sampling to verify formulation quality, inspect the commercial container carefully. On standing ZE formulations usually develop a concentration gradient from the top to the bottom of the container. This may result in the appearance of a clear liquid on the top and/or sediment on the bottom. Therefore, before sampling, the formulation must be homogenized 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). After this procedure the container shall not contain a sticky layer of non-dispersed matter at the bottom (if the ZE has flocculated it may not be possible to re-disperse this sticky layer). 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.
- Note 2** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 3** Separate tolerances for total content must be provided for each active ingredient, as defined in Section 4.3.2. Separate clauses must be provided for each relevant impurity.
- Clauses for free active ingredient content and release rate of the active ingredient are required only for the encapsulated active ingredient(s) and only if appropriate to the intended properties of the capsules. A clause to control release rate is usually required for capsules intended to possess slow- or controlled-release properties. A clause to control free active ingredient is usually required where encapsulation is intended to control the release or stability of the active ingredient, or to decrease the risk to users from accidental exposure to the active ingredient. If more than one active ingredient is encapsulated, limits must be provided for each. Methods for determination of free active ingredient and release rate may be product-specific.
- 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** This clause should include only relevant impurities and should be omitted if there is none. Method(s) of analysis must be peer validated.
- Note 6** Percentages may be specified in one or more ranges, as appropriate to the product. The determination of particle size range by laser diffraction is not an ideal criterion to ensure the suitability of liquid formulations. This should be evaluated by wet sieve test (MT 185) and suspensibility (MT 184.1) or dispersion stability (MT 180).
- Note 7** The formulation should be tested at 2% dilution.
- Note 8** This test detects coarse particles (e.g. oversize capsules, crystals) or agglomerates (of capsules or from crust formation) or extraneous materials that 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 be at the highest rate of use recommended by the supplier. The test is to be conducted in CIPAC standard water D at 25 ± 5°C.

.../cont.

Note 10 After manufacture and during shipping it is often impossible for buyer or seller to guarantee that the formulation has not been exposed to freezing temperatures. As freezing of a ZE formulation may result in undesirable, irreversible changes, including (but not limited to) capsule failure caused by crystallization of the active ingredient, the ability of the formulation to successfully withstand repeated freezing and thawing is an important property. Unless otherwise agreed, the freeze/thaw stability test shall cycle the formulation between room temperature (e.g. $20 \pm 2^{\circ}\text{C}$) and $-10 \pm 2^{\circ}\text{C}$ on 18-hour-freeze/6-hour-melt cycles for a total of 4 cycles.

Note 11 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 for alternative storage conditions.

Note 12 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

8. SPECIFICATION GUIDELINES FOR PESTICIDES FORMULATED AND/OR PREPARED AS DEVICES

SYSTEMS FOR THERMAL VAPORIZATION OF ACTIVE INGREDIENT

- 8.1 Mosquito coils (MC)
- 8.2 Vaporizing mats (MV)
- 8.3 Liquid vaporizers (LV)

SYSTEMS FOR SPRAYING SOLUTIONS AND OTHER LIQUIDS

- 8.11 Aerosol dispensers (AE)

BARRIER AND CONTROLLED RELEASE SYSTEMS

- 8.21 Insecticide treated nets
- 8.22 Matrix release (MR)
- 8.23 Long-lasting storage bag (LB)

Introduction

In the following subsections, an open numbering system has intentionally been chosen to differentiate the formulation types according to their application mode and to allow later addition of newly developed specification templates.

8.1 MOSQUITO COILS

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.

..... [ISO common name] MOSQUITO COILS

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

The material, sampled from any part of the consignment in accordance with the procedure described in Note 1 or any other acceptable procedure, shall comply with the specification.

8.1.1 Description

The product shall consist of technical [ISO common name] complying with the requirements of the WHO specification(s), in the form of (see Section 4.2), together with organic fillers capable of smouldering well, a binder and additives such as synergists, dye and fungicide, formulated in the form of a coil. The coil must burn without producing any flame except at the beginning, and should be readily extinguishable after ignition of the coil.

8.1.2 Active ingredient

8.1.2.1 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.

8.1.2.2 [ISO common name] content (Note 2)

The [ISO common name] content shall be declared (g/kg) and, when determined on a dry weight basis, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

8.1.3 Relevant impurities

8.1.3.1 By-products of manufacture or storage (Note 3), if required

Maximum:% of the [ISO common name] content found under 8.1.2.2.

8.1.3.2 Water (CIPAC MT 30.2) (Note 4), if required

Maximum: ... g/kg.

8.1.4 Physical properties

8.1.4.1 Average weight of coils (Note 5)

The average weight of the coils shall be declared (in g) and when determined on 20 single coils, the average weight shall not differ from that declared by more than $\pm 10\%$.

8.1.4.2 Burning time (Note 6)

The average burning time determined from five single coils, which must burn continuously in a draught-free atmosphere, shall not be less than that declared.

8.1.4.3 Strength of coil (Note 7)

Every coil of 20 single coils shall be able to withstand a minimum load of 120 g without breaking.

8.1.4.4 Separation of "twin" coils (Note 8)

The mosquito coil, if in "twin" form, shall be properly made so as to facilitate easy separation. When 50 twin coils are separated, not more than 3 coils shall break.

8.1.5 Storage stability**8.1.5.1 Stability at elevated temperature (in original twin coil packaging)** (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 9), the determined average active ingredient content must not be lower than% of the determined average content found before storage (clause 8.1.2.2) (Note 10) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (8.1.3.1),
- burning time (8.1.4.2),
- strength of coil (8.1.4.3),
- separation of "twin" coils (8.1.4.4).

as required.

Note 1 Sampling*General requirements*

- a) Samples shall be stored in such a manner that there is no deterioration of the material.
- b) The sampling instrument shall be clean and dry.
- c) Samples shall be protected against contamination.

Sampling, testing and acceptance

- a) In any consignment, all the master cartons containing containers of the same type shall constitute a lot.
- b) Samples shall be drawn from each lot and individually tested to ascertain whether the material complies with the specified requirements.
- c) Any sample failing to comply with the specified requirements shall be termed as defective. The acceptance number shall be the maximum number of defective samples permissible for a lot to be accepted.
- d) The number of containers to be drawn from the lot and the acceptance number shall be as shown in the following Table.

Total number of containers in lot	Number of containers to be tested	Acceptance number
300 or less	3	0
301 to 1200	6	1
1201 to 2000	13	2
2001 to 7000	21	3
7001 to 15000	29	4
15001 to 24000	48	6
24001 to 41000	84	9
over 41000	126	13

.../cont.

- e) Each of the containers to be tested shall be drawn from a different master carton which shall be selected at random. In order to ensure randomness of selection, random number tables shall be used. If such tables are not available, the following procedure may be adopted.

Starting from any master carton, count the master cartons as 1, 2, 3..... r in a systematic manner. Every r^{th} carton shall be drawn, r being the integral part of N/n , where N is the total number of master cartons in the lot and n the number of master cartons to be selected.

Preparation of test samples

- a) A sufficient quantity of samples is selected by taking at random a twin-form coil from each individual box of the reduced sample. From the total number of selected coils, sufficient coil samples are reserved for examination for compliance with the requirements of physical characteristics in 8.1.4.1, 8.1.4.2, 8.1.4.3 and 8.1.4.4.
- b) The remainder of the coils are ground in a hammer-mill to pass a 1-mm mesh-screen and reserved for test for compliance with 8.1.2.2, 8.1.3.1 and 8.1.3.2. These groups of samples constitute the test samples. Each set of test samples shall be packed and labelled, taking into account the general requirements of Note 1.

Note 2 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and 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.

Note 4 Normally, the water content should not exceed 120 g/kg.

Note 5 Typical average weight per coil is 12 g.

Note 6 A typical burning time should be 7.5 h in order to ensure that the coil burns for a length of time approximately equivalent to the normal duration of sleep. However, in special circumstances to be stated on the label, the burning time may be increased or reduced accordingly.

Note 7 Method for determination of the breaking load/tensile strength of mosquito coil (an alternative, acceptable method may be used).

Apparatus

Plastic device (Figure 1 below).

Spring Scale (e.g. Attonic MP-2) with a range 0 to 500 \pm 5 g, accurately calibrated (Figure 2 below).

Sampling

Select 20 boxes of mosquito coils randomly, pick one single coil from each box. Discard single coils that are broken or cracked due to careless separation in the selection process. Subject all the 20 single coils of the breaking load test.

Procedure

A piece of mosquito coil is placed within the plastic device supported by opposite grooves so that on one side the groove only supports 2 cm of the coil from the tip. The coil and plastic device is then placed on the flat platform of the 500 g scale register. The pointed end of the screw is lowered and adjusted to fit into the head/eye of the coil. The screw is then turned gently and gradually in a clockwise direction depressing the mosquito coil downwards until it breaks. The register on the scale is recorded at the breaking point. The minimum specification for the standard coil is 120 g. Repeat the above procedure for the remaining 19 single coils.

.../cont.

Note 8 Method for separation of twin mosquito coils.

Procedure

- a) Break the connecting points at the ends of the coils, then hold both heads/eyes of the double coils with thumbs and forefingers.
- b) Gently push the heads or eyes in the opposite direction and pull them apart to displace into single coils. Gentle twisting may be done if necessary.

Results

Satisfactory separation of twin coils is considered achieved if no breakage occurs.

Note 9 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 10 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

Note 11 A typical unit container contains 5 double coils.

Note 12 Each unit container shall contain at least one mosquito coil stand/holder.

Note 13 The mosquito coil stand/holder must be made of suitable non-flammable materials which can hold the burning coil stably.

Figure 1. A single mosquito coil supported by plastic device in position

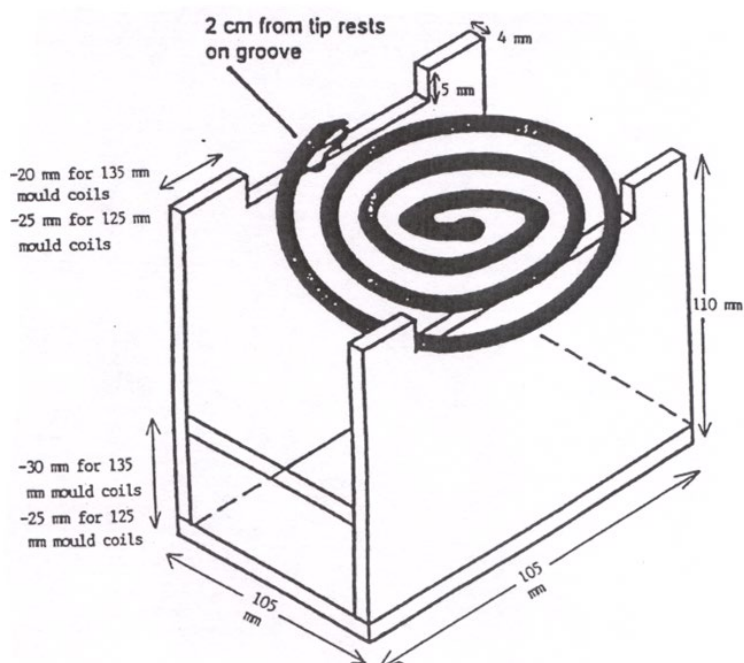
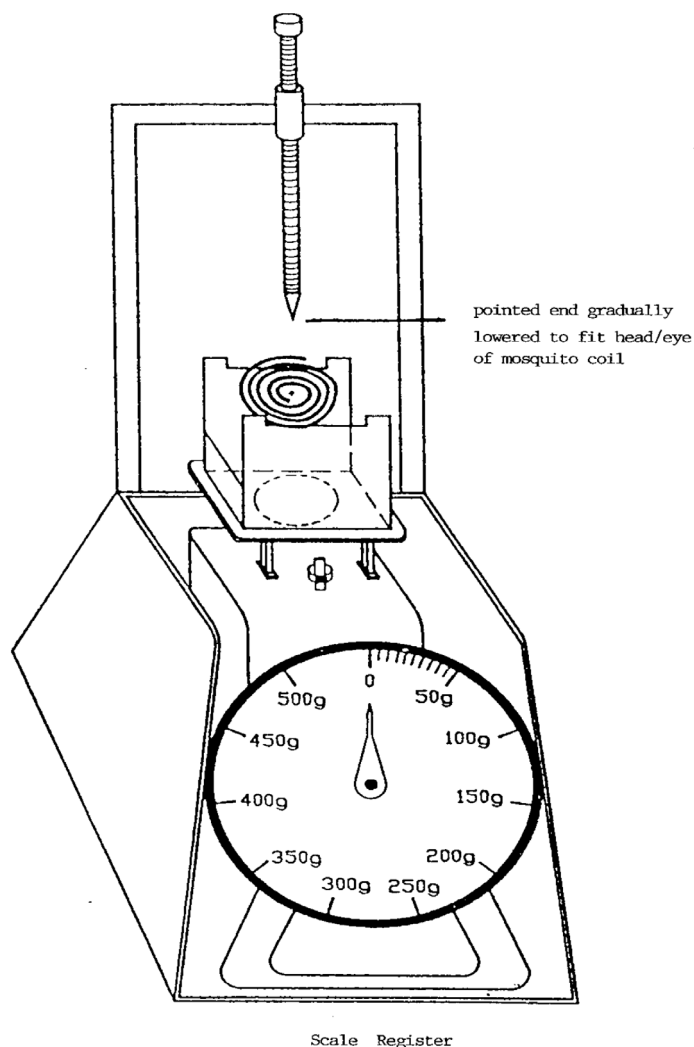


Figure 2. Method for determination of the breaking load/tensile strength of mosquito coil



8.2 VAPORIZING MATS

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.

..... [ISO common name] VAPORIZING MATS

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

The material, sampled from any part of the consignment in accordance with the procedure described in Note 1 or any other acceptable procedure, shall comply with the specification.

8.2.1 Description

The vaporising mat shall consist of a pulp-made mat, or a mat made of other suitable inert materials, impregnated with an insecticide. Stabilisers, synergists, slow-release agents, perfumes and colouring agents may be added. The mat is intended for use in a heating unit (Note 2) designed to produce slow volatilisation of the active ingredient. The [ISO common name] technical material used in the manufacture of the mat shall comply with the requirements of WHO specification

8.2.2 Active ingredient

8.2.2.1 Identity tests (Note 3)

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

8.2.2.2 [ISO common name] content (Note 3)

The [ISO common name] content shall be declared (mg/mat) and, when determined, the average content measured shall not differ from that declared by more than $\pm 15\%$.

8.2.3 Relevant impurities

8.2.3.1 By-products of manufacture or storage (Note 4), if required

Maximum:% of the [ISO common name] content found under 8.2.2.2.

8.2.4 Physical properties

8.2.4.1 Size of mat (Note 5)

The size of the mat should be compatible with the associated heater.

8.2.4.2 Evaporation rate

Suitable evaporation rate may be determined after 4 hours. After heating the mat on the appropriate heating unit for 4 hours, a minimum of 20% of the active ingredient content found under 8.2.2.2 should remain.

8.2.5 Storage stability

8.2.5.1 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 6), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 7) and the formulation shall continue to comply with the clause for:

- by-products of manufacture or storage (8.2.3.1) as required.

Note 1 Sampling*General requirements*

- a) Samples shall be stored in such a manner that there is no deterioration of the material.
- b) The sampling instrument shall be clean and dry.
- c) Samples shall be protected against contamination.

Sampling, testing and acceptance

- a) In any consignment, all the master cartons containing mats of the same type shall constitute a lot.
- b) Samples shall be drawn from each lot and individually tested to ascertain whether the material complies with the specified requirements.
- c) Any sample failing to comply with the specified requirements shall be termed as defective. The acceptance number shall be the maximum number of defective samples permissible for a lot to be accepted.
- d) The number of mats to be drawn from the lot and the acceptance number shall be as shown in the following Table.

Total number of containers in lot	Number of mats to be tested	Acceptance number
300 or less	3	0
301 to 1200	6	1
1201 to 2000	13	2
2001 to 7000	21	3
7001 to 15000	29	4
15001 to 24000	48	6
24001 to 41000	84	9
over 41000	126	13

- e) Each of the mats to be tested shall be drawn from a different master carton which shall be selected at random. In order to ensure randomness of selection, random number tables shall be used. If such tables are not available, the following procedure may be adopted. Starting from any master carton, count the master cartons as 1, 2, 3..... r in a systematic manner. Every r^{th} carton shall be drawn, r being the integral part of N/n , where N is the total number of master cartons in the lot and n the number of master cartons to be selected.

Note 2 The heating unit must comply with all relevant national safety standards.

Note 3 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.

Note 4 This clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. The method(s) of analysis must be peer validated.

Note 5 This clause is to ensure easy insertion and removal of the mat. Typical size of the mat is 35 mm by 22 mm, 2.6 mm thick.

Note 6 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 7 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

8.3 LIQUID VAPORIZERS

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.

..... [ISO common name] LIQUID VAPORIZERS

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

The material, sampled from any part of the consignment in accordance with the procedure described in Note 1 or any other acceptable procedure, shall comply with the specification.

8.3.1 Description

The product shall consist of a liquid insecticide formulation in a cartridge/bottle (Figure 1), designed to fit a suitable heater unit (Note 2), and the formulation shall be effective as it passes up the heated wick and evaporates at a suitable rate, over the period claimed by the manufacturer. The cartridge/bottle shall be designed to minimise the risk of accidental ingestion of the contents. The [ISO common name] technical material used in the manufacture of the liquid vaporizer shall comply with the requirements of WHO specification

8.3.2 Active ingredient

8.3.2.1 Identity tests (Note 3)

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

8.3.2.2 [ISO common name] content (Note 3)

The [ISO common name] content shall be declared (g/kg or g/l at $20 \pm 2^\circ\text{C}$, Note 4) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerance, given in the table of tolerances, Section 4.3.2.

8.3.3 Relevant impurities

8.3.3.1 By-products of manufacture or storage (Note 5), if required

Maximum:% of the [ISO common name] content found under 8.3.2.2.

8.3.4 Physical properties

8.3.4.1 Cartridge/bottle

The cartridge/bottle:

- a) shall be made of a suitable heat-resistant material;
- b) shall be of a suitable shape and size to fit the heater unit for which it was designed;
- c) shall hold the wick firmly, with a stopper preventing spillage should the cartridge/bottle be inverted with the covering cap;
- d) shall have a child-proof cap.

8.3.4.2 Wick

The wick:

- a) shall be made of a suitably porous heat-resistant material;
- b) shall draw up sufficient insecticide formulation, when heated at one end, for vaporisation to provide a suitable level of protection against mosquitoes;
- c) shall be of material and design such that it can vaporise the total content of the insecticide formulation in the bottle/cartridge to which it is attached.

8.3.4.3 Vaporization rate

The wick and cartridge/bottle shall be designed and constructed such that the insecticide formulation vaporizes from the heated end of the wick at a constant, or close to constant, rate to enable a constant rate of active ingredient emission throughout the minimum effective period (8.3.4.4). (Note 6)

8.3.4.4 Minimum effective period (Note 6)

The minimum effective period shall be declared and the cartridge/bottle shall hold sufficient formulation to enable the product to function for not less than the minimum effective period declared.

8.3.5 Storage stability

8.3.5.1 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 7), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 8) and the formulation shall continue to comply with the clauses for:

- by-products of manufacture or storage (8.3.3.1),
- minimum effective period (8.3.4.4).

as required.

Note 1 Sampling*General requirements*

- a) Samples shall be stored in such a manner that there is no deterioration of the material.
- b) The sampling instrument shall be clean and dry.
- c) Samples shall be protected against contamination.

Sampling, testing and acceptance

- a) In any consignment, all the master cartons containing liquid vaporizer refill bottles of the same type shall constitute a lot.
- b) Samples shall be drawn from each lot and individually tested to ascertain whether the material complies with the specified requirements.
- c) Any sample failing to comply with the specified requirements shall be termed as defective. The acceptance number shall be the maximum number of defective samples permissible for a lot to be accepted.
- d) The number of refill bottles to be drawn from the lot and the acceptance number shall be as shown in the following Table.

Total number of containers in lot	Number of containers to be tested	Acceptance number
300 or less	3	0
301 to 1200	6	1
1201 to 2000	13	2
2001 to 7000	21	3
7001 to 15000	29	4
15001 to 24000	48	6
24001 to 41000	84	9
over 41000	126	13

- e) Each of the refill bottles to be tested shall be drawn from a different master carton which shall be selected at random. In order to ensure randomness of selection, random number tables shall be used. If such tables are not available, the following procedure may be adopted.

Starting from any master carton, count the master cartons as 1, 2, 3..... r in a systematic manner. Every r^{th} carton shall be drawn, r being the integral part of N/n , where N is the total number of master cartons in the lot and n the number of master cartons to be selected.

Note 2 The heating unit must comply with all relevant national safety standards.

Note 3 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.

Note 4 If the buyer requires both g/kg and g/l at $20 \pm 2^\circ\text{C}$, then in case of dispute the analytical results shall be calculated as g/kg.

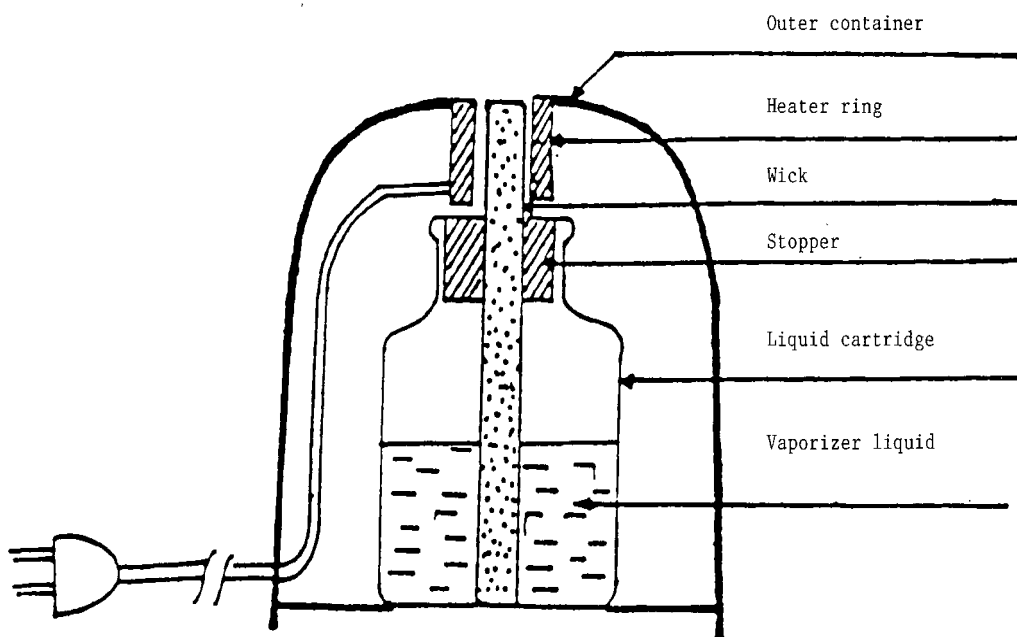
Note 5 This clause should include only relevant impurities and the title should be changed to reflect the name of the relevant impurity. The method(s) of analysis must be peer validated.

Note 6 Determination of the minimum effective period of a refill bottle of a liquid vaporizer. No suitable test methods are available.

Note 7 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 8 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

Figure 1. Diagram of the structure of mosquito electric liquid vaporizer (refill bottle and its heating device)



8.11 AEROSOL DISPENSERS

Introduction

Not all characteristics which define the acceptability of aerosol dispensers (AE) are incorporated in the specification guideline given below.

The flammability and ignition distance of the spray produced by the dispenser and formulation are of potentially great importance to the user but they must be dealt with by appropriate labelling of the dispensers.

The spray droplet size distribution is relevant to operator risk and may influence efficacy. At present, the measurement is complex and interpretation of the results is not straightforward, and therefore no clause is included.

Aerosol dispensers are expected to withstand corrosion for a minimum of 2 years from the date of release by the manufacturer. Ideally, specifications would include a clause to define the corrosion resistance of the dispenser. At present, no practical method is available to predict whether or not the structural integrity of dispenser could be compromised within 2 years and therefore a clause cannot be included. Manufacturers, users of aerosols and/or other interested parties are invited to develop and propose simple methods based on standard conditions, so that this important omission can be rectified.

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.

..... [ISO common name] AEROSOL DISPENSERS

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

The material, sampled from any part of the consignment in accordance with the procedure described in Note 1 or any other acceptable procedure, shall comply with the specification.

8.11.1 Description

The product shall consist of a liquid formulation in a pressurised, non-refillable aerosol dispenser, containing propellant(s), synergist(s) and other formulants (see Note 2, for restrictions on solvents and propellants), as required, intended for release of the active ingredient into the air in the form of an aerosol. The technical (ISO common name(s)), in the form(s) of (see Section 4.2), used in the manufacture of the formulation shall comply with the requirements of WHO specification(s)

8.11.2 Active ingredient and synergist

8.11.2.1 Identity tests (Notes 3 & 4)

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

8.11.2.2 [Active ingredient ISO common name] content (Notes 3 & 4)

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from that declared by more than the appropriate tolerances, given in the table of tolerances, Section 4.3.2.

8.11.2.3 [Synergist ISO common name] content (Notes 3 & 4), if required

The [ISO common name] content shall be declared (g/kg) and, when determined, the average content measured shall not differ from those declared by more than the appropriate tolerances, given in the table of tolerances, Section 4.3.2.

8.11.3 Relevant impurities

8.11.3.1 By-products of manufacture or storage (Notes 4 and 5), if required

Maximum:% of the [active ingredient ISO common name] content found under 8.11.2.2.

8.11.4 Physical properties

8.11.4.1 Net content of formulation

The minimum net content shall be declared (g) and, when determined, the average net content shall not be lower than that declared.

8.11.4.2 Internal pressure (Note 6 and Figure 1)

The pressure of the filled dispenser shall be declared on the label and, when measured at $30 \pm 2^\circ\text{C}$, the internal pressure shall not exceed MPa.

8.11.4.3 Discharge rate (Note 7)

The discharge rate of the filled dispenser shall be within the range to g formulation/sec.

8.11.4.4 pH range (applicable to water-based formulations only) (MT 75.3) (Note 8)

pH range: to

8.11.4.5 Clogging of aerosol dispenser valves

No clogging shall occur when the aerosol dispenser valves are tested in accordance with the procedure as described in Note 9 or any other acceptable method.

8.11.5 Storage stability

8.11.5.1 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 14 days (Note 10), the determined average active ingredient content must not be lower than% relative to the determined average content found before storage (Note 11) and the formulation shall continue to comply with the clause for:

- by-products of manufacture or storage (8.11.3.1); and
- the combined weight of the container and contents shall not be less than ...% of the original weight,

as required.

Note 1 Sampling*General requirements*

- a) Samples shall be stored in such a manner that there is no deterioration of the material.
- b) The sampling instrument shall be clean and dry.
- c) Samples shall be protected against contamination.

Sampling, testing and acceptance

- a) In any consignment, all the master cartons containing containers of the same type shall constitute a lot.
- b) Samples shall be drawn from each lot and individually tested to ascertain whether the material complies with the specified requirements.
- c) Any sample failing to comply with the specified requirements shall be termed as defective. The acceptance number shall be the maximum number of defective samples permissible for a lot to be accepted.
- d) The number of containers to be drawn from the lot and the acceptance number shall be as shown in the following table.

Total number of containers in lot	Number of containers to be tested	Acceptance number
300 or less	3	0
301 to 1200	6	1
1201 to 2000	13	2
2001 to 7000	21	3
7001 to 15000	29	4
15001 to 24000	48	6
24001 to 41000	84	9
over 41000	126	13

- e) Each of the containers to be tested shall be drawn from a different master carton which shall be selected at random. In order to ensure randomness of selection, random number tables shall be used. If such tables are not available, the following procedure may be adopted.

Starting from any master carton, count the master cartons as 1, 2, 3..... r in a systematic manner. Every r^{th} carton shall be drawn, r being the integral part of N/n , where N is the total number of master cartons in the lot and n the number of master cartons to be selected.

Note 2 Solvents not permitted for use in aerosols:

- benzene
- 2-butoxyethanol (ethylene glycol monobutyl ether)
- 2-butoxyethylacetate (ethylene glycol monobutyl ether acetate)
- carbon tetrachloride
- chlorobenzene
- chloroform
- 1,2-dichloroethane (ethylene dichloride)
- 2-ethoxyethanol (ethylene glycol monoethyl ether)
- 2-ethoxyethylacetate (ethylene glycol monoethyl ether acetate)
- n-hexane
- 2-hexanone (methyl n-butyl ketone)
- 2-methoxyethanol (ethylene glycol monomethyl ether)
- n-hexane
- 2-hexanone (methyl n-butyl ketone)

.../cont.

- 2-methoxyethanol (ethylene glycol monomethyl ether)
- 2-methoxyethylacetate (ethylene glycol monomethyl ether acetate)
- tetrachloroethylene
- trichloroethylene.
- Propellants. The Montreal Protocol and European Union¹ directive on the withdrawal of chlorofluorocarbons (CFCs) from aerosols were noted. Hydrocarbon propellants are recommended for insecticide aerosols, provided international safety standards are met by the aerosol producer. Industry should be encouraged to develop alternative and safer propellants and delivery systems.

Note 3 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.

Note 4 To remove the contents of the dispenser it should be weighed (to ± 0.01 g, at room temperature so that it is dry on the outside) and either immersed in dry ice (solid carbon dioxide) for a minimum of 1 h or placed in deep freezer (-18°C or below) overnight. The container should then be removed to a fume hood and, using a suitable shield, the container should be punctured towards the top with a sharp implement, making a hole or holes that will be sufficiently large for the subsequent introduction and removal of extraction solvent. Allow the propellant to evaporate by allowing the contents to rise to room temperature without applying additional warming. Using a suitable solvent (appropriate to the active ingredient and synergist), thoroughly rinse the contents of the dispenser into a volumetric flask, make to volume with the solvent. If possible, use a solvent that will not remove paint or other external coatings. Using a suitable analytical method, determine the mass of active ingredient and synergist in the rinsate. Dry the rinsed dispenser and re-weigh it to determine the mass of formulation it contained. Use this value to express the content of active ingredient and synergist on a g/kg basis.

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

Note 6 Determination of pressure in finished aerosol packs².

Introduction

The determination of the pressure existing in the finished aerosol packs is necessary to verify that the true pressure is compatible with the pressure limitations of the pack, and in accordance with the regulations in force.

True pressure is the relative pressure given by an accurate manometer, at a given temperature.

Objective

The determination of the true pressure in the finished aerosol pack:

- a) in such a way that the measurement affects as little as possible the value of the real pressure;
- b) in such a way that the manometer will not be polluted by the product under pressure present in the pack.

Scope

The method is recommended for determination of the true pressure of all filled aerosol packs.

Apparatus

The following are required:

- a) a source of reference gas (nitrogen for instance) from which the pressure can be regulated by means of a control valve;
- b) a manometer of high accuracy, if possible cushioned by an oil-bath and adapted to fit the aerosol container on which the measurement will be effected (Figure 1).

.../cont.

The apparatus must be assembled in such a way that, in the state of rest, the manometer is connected to the reference gas (the pressure of this gas being slightly higher than the actual pressure in the pack) and, for taking the measurement, the manometer is connected to the interior of the pack to show the actual pressure.

Working operation

- a) Make sure that the aerosol dispenser is thoroughly equilibrated to $30 \pm 2^\circ\text{C}$.
- b) The measuring apparatus must be fitted with an appropriate adaptor for the valve employed.
- c) The pressure of the reference gas must be regulated to a value slightly higher than the anticipated pressure of the dispenser.
- d) Apply the measuring apparatus to the valve and press lightly in order to open the valve and the slide of the apparatus.
- e) Read the true pressure on the manometer, when the needle has stabilized.

Accuracy of measurement

The measurement of the true pressure will be the more accurate:

- a) with larger aerosol dispenser sizes;
- b) with only a small difference in pressure between the reference gas and the true pressure of the dispenser (if required, measurements can be made on additional dispensers after adjusting the reference gas pressure to a value very close to the true pressure);
- c) if the dead volume of the manometer is small (less than 2 ml).

Test report

The test report must indicate, in addition to the results and test conditions, any relevant working details not specified in the method, especially if they are suspected of having influenced the results.

Notes

1. It is necessary to recalibrate the manometer frequently, for example with the aid of a manometric balance.
2. A non-return valve can be inserted in the apparatus to avoid the aerosol product penetrating the manometer if the pressure of the reference gas is inadvertently much lower than the true pressure in the dispenser.

Note 7 Evaluation of discharge rate of filled aerosol dispensers.¹

Scope

The method is applicable to the majority of aerosols marketed at present. It may be used, with discretion, for dispenser fitted with vapour-phase taps where there will be a continually changing composition as the contents are discharged. It is not suitable for use in the inverted position for dispensers with vapour phase taps, as there will be an erratic discharge dependent upon the liquid content of the dip tube. Where dispensers are intended to be used in an inverted position, it is vital that the test shall be done in that way. It is important that discharge tests follow the instructions for use given on the dispenser. The method is not intended for use with metering valves.

Principle

The discharge rate of an aerosol dispenser is determined by measuring the quantity of material expelled through the valve in the given time. The exact duration of discharge, normally 10 sec, and the temperature of the dispenser must be carefully controlled for good reproducibility. Normally the test is repeated three times to give three determinations but, in the case of products filled with vapour phase tap valves, it is preferable to reduce the discharge interval to 5 sec and the number of determinations to two. This is to minimise the variation in composition that will occur as the contents are sprayed off. There will be some loss of accuracy using the shorter duration of discharge.

.../cont.

Alternatively, the discharge rate may be determined at different stages in the emptying of the dispenser (e.g. 90%, 70%, 50%, 30% and 10% fill) which then allows the values to be plotted graphically. Where the composition changes with the emptying of the dispensers, this offers a particularly convenient way of showing the effect of this change. In the case of storage test samples, a single test is normally performed at each examination to conserve the contents.

Apparatus

A water bath at $25\text{ }^{\circ}\text{C} \pm 0.5\text{ }^{\circ}\text{C}$, a stopwatch accurate to 0.2 sec, a balance weighing to 0.1 g and a pressure gauge accurate to 2 psig (0.1 kg.cm^{-2}) are required.

Procedure

- a) The valve of the aerosol dispenser shall be handled according to label instructions and the valve shall be operated for five sec to remove material in the dip tube which may not be homogenous with the bulk of the filling.
- b) The aerosol dispenser shall be immersed in a water bath maintained at $25\text{ }^{\circ}\text{C} \pm 0.5\text{ }^{\circ}\text{C}$ for half an hour, or for sufficiently long for the contents to attain the temperature of the water bath.
- c) The aerosol dispenser shall be removed from the water bath, wiped completely dry, the valve operated for one second to remove any water in the valve, the internal pressures of the dispenser shall be measured, and the dispenser shall be weighed to within 0.1g.
- d) The aerosol dispenser shall then be shaken for 3 sec by hand or other suitable means and the valve shall be operated fully open for 10 sec, timed by the stopwatch. During the discharge, the dispenser shall be positioned as indicated in the instructions for use.
- e) The aerosol dispenser shall be wiped clean of any liquid and re-weighed to within 0.1 g.

Procedures (b) to (d) shall be repeated twice or more and the internal pressure of the dispensers shall be measured again.

Calculation

The difference in weights derived from procedure (e) and procedure (c) shall be divided by 10 (sec). Results should not differ by more than 0.1 g from the mean of the three results. If a greater difference is found at least two more readings should be taken.

Reporting

Report valve discharge rates as g.sec^{-1} at the measured mean pressure of the dispenser. The method, e.g. 3 x 10 sec, 2 x 5 sec or 1 x 5 sec (90%...50%...10%) spraying, etc., shall be quoted.

Notes

- a) Where discharge rates are to be determined at various stages of dispenser emptying it is advisable to allow the dispenser to reach equilibrium at $25\text{ }^{\circ}\text{C}$ in the water bath, shake and spray for 5 sec, re-shake vigorously and re-spray for another 5 sec and replace in water bath. This procedure may then be repeated until the correct dispenser content is reached. This rather tedious procedure avoids errors arising from the fall in temperature of the contents of the dispenser during prolonged spraying.
- b) Results may show variations from sample to sample that are greater than might be expected from normal manufacturing tolerances. This may be due variations in the valve orifice diameter.
- c) The discharge rate of freshly prepared aerosol dispensers will not normally be the same as for samples allowed to "mature", due to the effect of solvents on the gasket.

Note 8 The pH may be determined by any acceptable method.

Note 9 Testing of valves of filled aerosol dispensers for clogging

Apparatus

- a) Fume hood
- b) Protective clothing and mask.

.../cont.

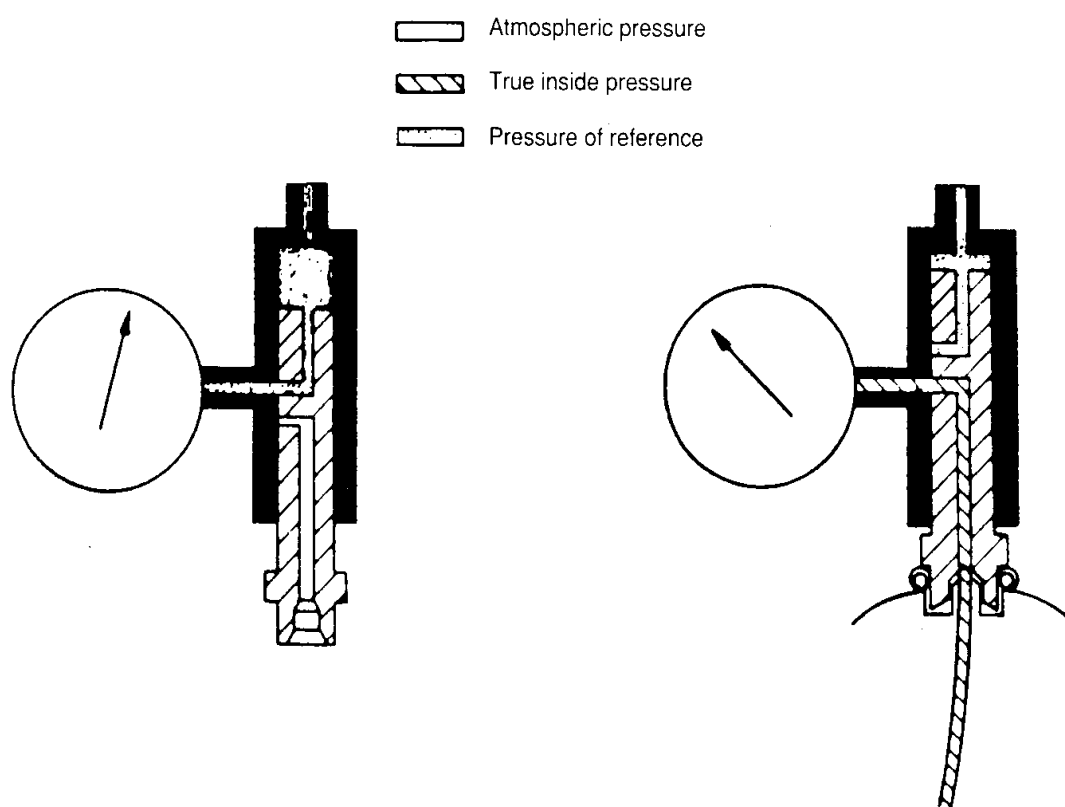
Procedure

Shake the aerosol dispensers thoroughly and, keeping them in an upright position, disperse the contents of each into the fume hood. Actuate the valve in a series of cycles (30 sec on, 30 sec off) until the dispenser is emptied. Examine the valves for clogging.

Note 10 Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions.

Note 11 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

Figure 1. Manometric measurement of internal pressure



8.21 INSECTICIDE TREATED NETS

Introduction

WHO is responsible for the establishment of product specifications for insecticide treated nets. Such specifications are included in the prequalification evaluation process conducted by WHO PQT/VCP. The template specification reflected below is the same as the 2016 template version.

WHO is currently re-evaluating the attributes and methods included in this template and will update this section upon completion of its review.

..... [ISO common name] **LONG-LASTING INSECTICIDAL NET
OR NETTING** (Note 1)

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

8.21.1 Description (Note 1)

The product shall be formed from (or in the form of) netting, consisting of [denier (Note 2), mono-/multi-filament, polymer type] fibres, treated with/incorporating, technical/formulated [ISO common name] complying with the requirements of FAO/WHO specification [CIPAC number/technical or formulation code (date)], and technical/formulated [ISO common name] (synergist, if required) complying with the requirements of FAO/WHO specification [CIPAC number/technical or formulation code (date)], together with any necessary other formulants. The product shall appear clean and shall be free from visible extraneous matter (Note 3), visible damage (such as splitting or tearing) and visible manufacturing defects (such as poorly made seams or a weave that is either not uniform or too loose to remain uniform in use), and shall be suitable for use as/in an insecticidal net with long-lasting activity (Note 4).

8.21.2 Active ingredient and synergist

8.21.2.1 Identity tests (Note 5)

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

8.21.2.2 [Active ingredient ISO common name] content (Notes 5, 6 & 7)

The [ISO common name] content shall be declared (..... g/kg) and, when determined, the average content shall not differ from that declared by more than the appropriate value given in the table of tolerances, Section 4.3.2.

8.21.2.3 [Active ingredient ISO common name] isomer ratio (Notes 5, 6 & 8), if required

The ratio of [ISO common name] isomers shall be in the range to

8.21.2.4 [Active ingredient ISO common name] wash resistance index (MT 195)

The wash resistance index of [ISO common name] from the netting, when determined, shall be within the range to

8.21.2.5 [Synergist ISO common name] content (Notes 5, 6, 7 & 8), if required

The [ISO common name] content shall be declared (..... g/kg) and, when determined, the average content shall not differ from that declared by more than the appropriate value given in the table of tolerances, Section 4.3.2.

8.21.2.6 [**Synergist ISO common name**] **wash resistance index** (MT 195)

The wash resistance index of [ISO common name] from the netting, when determined, shall be within the range to

8.21.3 Relevant impurities

8.21.3.1 **By-products of manufacture or storage** (Notes 6, 8 & 9), if required

Maximum:% of the [active ingredient ISO common name] content found under 8.21.2.2.

8.21.4 Physical properties (Notes 6 & 18)

8.21.4.1 **Fabric weight (mass per m²)** (ISO 3801 / EN 12127)

The mass per unit area shall be declared (..... g/m²), and when determined, shall not differ from that declared by more than ± [appropriate figure] %.

8.21.4.2 **Netting mesh size**

When counted by the method given in Note 10, the average number of complete holes per unit area (holes/cm²), shall be not less than and the lowest value shall be not less than

8.21.4.3 **Dimensional stability of netting to washing** (Note 11)

Not more than 10% shrinkage and not more than 5% expansion in both directions.

8.21.4.4 **Bursting strength** (ISO 13938-2) (Note 12)

The bursting strength of the fabric shall be declared (not less than kPa) and, when determined, the average shall be not less than that declared.

If seams are present, their average bursting strength shall be not less than the average for the fabric.

8.21.4.5 **Flammability** (EN 1102) (Note 13)

Tested according to EN 1102 the following requirements should be achieved*:

After removing the ignition source the following fire phenomena should not occur:

- ignition
- propagation of the flame or glow.
- flaming debris
- ignition of the filter paper

* Fulfilling the requirements above means that the flame speed rate is 0 mm/s, i.e., no flame or glow achieves first and third marker threads.

Formation of holes is allowed provided that the burnt or melted width and length of the holes does not exceed 50 mm and 150 mm, respectively.

8.21.5 Storage stability

8.21.5.1 Stability at elevated temperature (MT 46.4)

After storage at 54 ± 2 C for 14 days (Note 14), the determined active ingredient content shall not be lower than%, and the determined synergist content shall not be lower than% (Note 8), relative to the determined average content found before storage (Note 15) and the product shall continue to comply with the clauses for:

- active ingredient isomer ratio (8.21.2.3),
- wash resistance index (8.21.2.4 and 8.21.2.6) (Note 16),
- by-products of manufacture or storage (8.21.3.1) (Note 17),
- dimensional stability to washing (8.21.4.3),
- bursting strength (8.21.4.4),

as required.

Note 1 The specification may apply to manufactured nets only, to bulk netting only or to both, as required. The title and description clause should be modified accordingly. In contrast with other formulations, an extension of a specification to nominally similar LN of other manufacturers is not possible with the data currently available and the manufacturer and the product should therefore be named in a footnote or in the specification.

Note 2 The linear density (denier) of the fibres cannot be measured in the manufactured net but should be identified on the packaging.

Note 3 Occasional short lengths of loose thread present in the netting are not considered to be extraneous matter.

Note 4 Long-lasting insecticidal netting is expected to retain its insecticidal activity during its lifespan and through a number of washes (public health products) or in worst-case expected climatic conditions (agricultural products).

Note 5 Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.

Note 6 Samples should be taken according to Figure 1 or on a convenient diagonal across the width of bulk material. Samples must be sufficiently large to conduct all tests required and representative of the net or netting. Except where seams are to be tested, do not test material within 10 cm of seams or selvages. Where a final product is made from more than one type of netting, each type of netting should be sampled and tested separately.

.../cont.

Use sharp scissors, or equivalent, to minimize damage to the fibres and fabric and thus avoid any consequential bias in the results of certain tests. Roll up the strips or squares and place them in labelled, new, clean aluminium foil prior to analysis. Samples should be kept cool, avoiding heat sources (including direct sunlight) or freezing, and analysed/tested with minimum delay. Representative portions (sub-samples) for testing should be taken as described in each test method.

For the purposes of chemical analysis, the analytical method and the number and size of test portions analysed should be designed to provide results with a relative standard deviation (RSD) $\leq 5\%$ or as applicable in certain justifiable cases. Test portion and replication requirements for physical test methods are defined in the methods or Notes referenced.

Note 7 If the netting is manufactured under different denier, the active ingredient (and synergist) content has to be specified for each type of denier. If the active ingredient content is also specified as mg/m² of netting, this should be calculated from values for active ingredient in g/kg and mass of net/m². Mass of net/m² should be determined according to ISO 3801 / EN 12127. In cases of dispute, g/kg values shall be used.

Note 8 This clause or sub-clause is required only if appropriate to the product specified. Isomer ratio is specified only where the active ingredient is defined as a particular isomer ratio. A synergist is specified only where required. An impurity is specified only where it is relevant, as defined in the glossary of terms (Appendix C).

Note 9 The method of analysis must be peer-validated, as a minimum. If it is not published, full details of the method and the peer-validation data must be provided.

Note 10 In the absence of a simple or standard method to determine the size of holes, which may have complex shapes, in highly flexible fabrics, mesh size is determined by counting the number of holes in a square of the fabric. Counting may be done directly on the fabric or indirectly by taking a picture/photocopy of the fabric. Indirect methods may ease counting and provide a permanent record. The number of holes per measured area is converted in holes/cm². Before counting, the fabric should be conditioned according to ISO 139 (4 h, 20°C, 65% relative humidity).

Use a template to define the square of netting, taking care not to stretch or distort the fabric. The template should be a 1-2 mm thick rigid sheet, in/on which an accurately calibrated ($\pm 1\%$ in each dimension) square (e.g. 1 x 1 in or 5 x 5 cm) has been cut/marked.

Appropriate template size depends on each LN. Note the suitable template size. If a template is not available and a ruler must be used, great care is required to ensure that the area counted is square. Where practicable, one edge of the square to be counted should be aligned with a row of complete holes in the fabric.

Incomplete holes $\geq \frac{1}{2}$ are counted as complete holes, whereas those $< \frac{1}{2}$ are not counted. Count 5 replicate squares selected according to Note 6, calculate the average and note the lowest value.

Another suitable method is the use of a stereomicroscope with an image analyser software, where the number of holes in a defined area is counted. In case of discrepancy between the netting mesh size using stereomicroscopic method and direct or indirect counting method, the stereomicroscopic method shall be the referee method.

Note 11 Method of preparation, marking and measuring: ISO 3759. Method of washing: ISO 6330. Method of calculation: ISO 5077. Size of test portions: 500 mm x 500 mm; mark off 350 mm x 350 mm within each test portion. Test a total of 4 replicate portions, 2 washed in each of 2 separate loads. Type of washing machine: ISO type A (front loading). Washing programme: 30°C Mild programme. Fill the washer with fabrics and ballast Type III (polyester ballast) up to 2 kg (according to the ISO 6330 standard). Drying: flat drying.

.../cont.

Note 12 Test method: ISO 13938 part 2 with conditioning of the fabric as specified in the ISO standard. The declared bursting strength, and testing for compliance with it, should be based on tests of 7.3 cm² areas of fabric. Proposed specifications based on tests of 50 cm² area must be supported by data showing the suitability of the proposed value and its relationship to minimum of 250 kPa (which is based on 7.3 cm² area). Five replicate tests should be conducted on samples taken at approximately equal distances on a diagonal across the netting, taking no sample within 10 cm of a border or seam. In made up rectangular nets, the "diagonal" may correspond to Figure 1. The average of the 5 measurements is calculated.

The method to test seam bursting strength is identical to that used to test the fabric, except that 5 replicate tests should be made, with the seam centred on the test head. Up to 5 seams may be tested but, if there are < 5 seams, replicate measurements should be made on 1 or more seams, to provide a total of 5 measurements.

Note 13 Flammability test according to EN 1102, using the surface ignition method (position the burner perpendicular to the surface of the specimen).

The following observations shall be reported: the afterflame time, the afterglow time, the maximum burnt or damage width and length, whether or not flame reaches vertical edge of the specimen, whether or not a hole is burnt or melted in the sample, whether or not any flaming debris falls below the bottom edge of the sample and ignition of the filter paper.

Definitions according to ISO 4880:1997 (not included in EN 1102:2016 and EN ISO 6941:1995):

Ignition: initiation of combustion.

Combustion: exothermic reaction of a combustible substance with an oxidizer, accompanied by flames and/or glowing and/or emission of smoke.

Procedure for measuring burnt or damage width and length dimensions of each sample:

Remove the sample from the sample holder and place it on a flat horizontal surface. Place a rule on top of the test sample along the line of maximum damage and parallel with the length side of the test specimen. Measure the maximum length in millimetres from the lowest point of burnt or damage to the end of the hole. To measure the burnt or damage width, proceed in the same way but with the ruler parallel to the width side of the test sample. Proceed in the same way for the other 5 samples.

Note 14 Unless other temperatures and times are specified. Refer to Section 4.6.2 for alternative storage conditions.

Note 15 Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.

Note 16 If justified by the supporting data, an increase or decrease in the limit(s) applying after the storage stability test may be specified in the sub-clause.

Note 17 This sub-clause is required only if the relevant impurity concentration is capable of increasing during storage.

Note 18 Normative references for physical tests:

Currently the following standards are the latest versions of the documents to be used for physical tests. The updated version of the standard should always be used when available.

ISO 139:2005/Amd.1:2011 - Textiles - Standard atmospheres for conditioning and testing.- Amendment 1.

ISO 3801:1977 - Textiles - Woven fabrics - Determination of mass per unit length and mass per unit area.

EN 12127:1997 - Textiles - Fabrics - Determination of mass per unit area using small samples.

.../cont.

ISO 3759:2011 - Textiles - Preparation, marking and measuring of fabric specimens and garments in tests for determination of dimensional change.

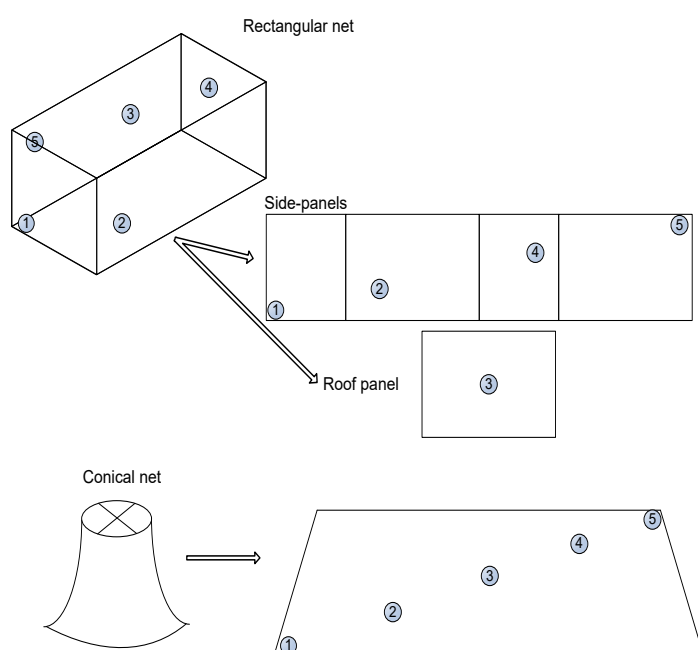
ISO 6330:2012 - Textiles - Domestic washing and drying procedures for textile testing.

ISO 5077:2007 - Textiles - Determination of dimensional change in washing and drying.

ISO 13938-2:2019 - Textiles - Bursting properties of fabrics - Part 2: Pneumatic method for determination of bursting strength and bursting distension.

EN 1102:2016 - Textiles and textile products. Burning behaviour. Curtains and drapes. Detailed procedure to determine the flame spread of vertically oriented specimens.

Figure 1. Recommended positions for 5 pieces of netting to form a representative sample



Note: Recommended positions from which 5 pieces of netting should be taken from a made-up bed net and combined to form a representative sample. In the case of combination LN, an appropriate sampling figure should be provided.

8.22 MATRIX RELEASE

Introduction

Matrix release (MR) in this guideline is mainly for public health protection uses but could potentially also be used in agricultural applications in the future. This formulation type can be classified into the following two basic forms.

- 1) One or more active ingredient(s) are either incorporated into a polymer, or coated onto the surface of a polymer.

- 2) In some cases, both methods (coating and incorporation) are applied for the preparation of a finished MR formulation (combination type).

Combination matrix formulation is composed of different types of formulations such as coated and incorporated, which are produced by different preparation methods.

For combination type MR it is advisable to split the specification into one specification for each polymer preparation type and another for the finished product. The specifications and footnotes should be modified accordingly to cover the clauses properly. For such a product, two specifications which refer to each preparation method are then combined into a specification for a finished product.

A matrix release consists of one or more active ingredients, polymer and formulants if appropriate. Its size and weight is defined by manufacturing and/or use requirements. It is intended for direct application into a body of water.

Generally, for public health protection, this formulation shall realize long lasting pest efficacy by controlled release of active ingredient(s) after application into the habitat of harmful pests, for example, a water source, pond, water jar or well.

Therefore, selection of active ingredient(s), content of active ingredient(s), product design (shape or size) and retention/release rate of active ingredient(s) are important parameters for defining the quality of this formulation type.

These parameters can be optimized by the manufacturing process and/or customer needs.

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. For combination MR, specifications must be separated into one specification for each material and one for the finished product. From the "Notes" provided at the end of this guideline, incorporate only those which are applicable to the particular specification.

..... [ISO common name] MATRIX RELEASE

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

The material, sampled from any part of the consignment in accordance with the procedure described in Note 1 or any other acceptable procedure, shall comply with the specification.

8.22.1 Description

The product shall be formed mainly from polymer treated with, technical/formulated ... [ISO common name] complying with the requirements of FAO/WHO specification ... [CIPAC number/technical or formulation code (date)], and ... [ISO common name and/or chemical name and CAS number] (synergist, if required) complying with the requirements of FAO/WHO specification ... [CIPAC number/technical or formulation code (date)], together with any necessary other formulants. The product shall appear clean and shall

be free from visible extraneous matter, visible damage (such as splitting or tearing) and visible manufacturing defects, and shall be suitable for use as/in a pesticidal formulation with controlled release activity (Note 2).

8.22.2 Active ingredient

8.22.2.1 Identity tests (Note 3)

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

8.22.2.2 [Active ingredient ISO common name] content (Notes 3 & 4)

The ... [ISO common name] content shall be declared (... g/kg) and, when determined, the average content shall not differ from that declared by more than the appropriate value given in the table of tolerances, Section 4.3.2.

8.22.2.3 [Active ingredient ISO common name] isomer ratio (Notes 3, 4 & 5), if required

The ratio of ... isomers shall be in the range ... to

8.22.2.4 Retention/release rate of ... [active ingredient ISO common name] (Notes 3 & 4)

The retention/release rate of ... [ISO common name] from the polymer, when measured, shall comply with the following criteria:

8.22.2.5 [Synergist ISO common name] content (synergist) (Notes 3, 4 & 5), if required

The ... [ISO common name] content shall be declared (... g/kg) and, when determined, the average content shall not differ from that declared by more than the appropriate value given in the table of tolerances, Section 4.3.2.

8.22.2.6 Retention/release rate of ... [synergist ISO common name] (Notes 3, 4 & 5)

The retention/release rate of ... [ISO common name] from the polymer, when measured, shall comply with the following criteria:

8.22.3 Relevant impurities

8.22.3.1 By-products of manufacture or storage (Notes 4 & 6), if required

Maximum: ...% of the ... [active ingredient ISO common name] content found under 8.22.2.2.

8.22.4 Physical properties

8.22.4.1 Floating or sinking ability (Note 7)

The product, when used, should [sink or float] in water.

8.22.5 Storage stability

8.22.5.1 Stability at elevated temperature (MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 2 weeks (Note 8 & 9), the determined total active ingredient content shall not be lower than ...%, and the determined total synergist content shall not be lower than ...% (Note 5), relative to the determined average content found before storage (Notes 10 & 11) and the product shall continue to comply with the clauses for:

- active ingredient isomer ratio (8.22.2.3),
 - retention/release rate (8.22.2.4 and 8.22.2.6),
 - by-products of manufacture or storage (8.22.3.1) (Note 12),
- as required.

Note 1 Sampling

General requirements

- a) Samples shall be stored in such a manner that there is no deterioration of the material.
- b) The sampling instrument shall be clean and dry.
- c) Samples shall be protected against contamination.

Sampling, testing and acceptance

- a) In any consignment, all the master cartons containing matrix formulation products of the same type shall constitute a lot. Each master carton contains several containers.
- b) Samples shall be drawn from each lot and individually tested to ascertain whether the material complies with the specified requirements.
- c) Any sample failing to comply with the specified requirements shall be termed as defective. The acceptance number shall be the maximum number of defective samples permissible for a lot to be accepted.
- d) The number of containers/samples to be drawn from the lot and the acceptance number shall be as shown in the following table.

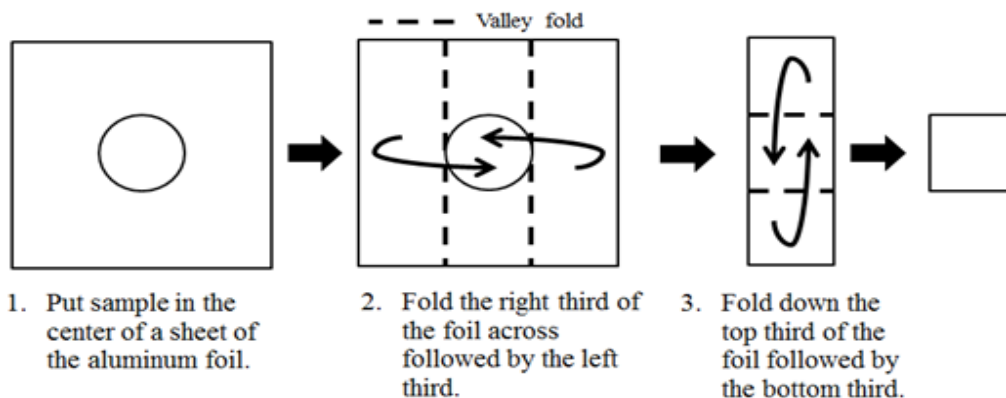
Total number of containers / samples in lot	Number of containers / samples to be tested	Acceptance number
300 or less	3	0
301 to 1200	6	1
1201 to 2000	13	2
2001 to 7000	21	3
7001 to 15000	29	4
15001 to 24000	48	6
24001 to 41000	84	9
over 41000	126	13

- e) Each of the containers/samples to be tested shall be drawn from a different master carton which shall be selected at random. In order to ensure randomness of selection, random number tables shall be used. If such tables are not available, the following procedure may be adopted.

Starting from any master carton, count the master cartons as 1, 2, 3 r in a systematic manner. Every r^{th} carton shall be drawn, r being the integral part of N/n , where N is the total number of master cartons in the lot and n the number of master cartons to be selected.

.../cont.

- Note 2** The product weight and shape should be described in a Note to distinguish it from others.
- Note 3** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer.
- Note 4** Samples must be sufficiently large to conduct all tests required and representative of the product. A sufficient quantity of samples must be selected by taking at random and in some cases the total amount of product must be used. Where a final product is made from more than one type of polymer preparation method (e.g. coating and incorporation), then each type should be sampled and tested separately.
- Use sharp scissors, or equivalent, to minimize damage to the product and thus avoid any consequential bias in the results of certain tests. Put the small portion in a labelled, new, clean screw glass bottle prior to analysis. Samples should be kept cool, avoiding heat sources (including sun heat) or freezing, and analysed/tested with minimum delay.
- For the purposes of chemical analysis, the analytical method and the number and size of test portions analysed should be designed to provide applicable results. Test portion and replication requirements for physical test methods should be defined in the methods or Notes referenced.
- Methods for determination of retention/release rate and the criteria to be met for product retention/release rate may be product specific.
- Note 5** This clause or sub-clause is required only if appropriate to the product specified. Isomer ratio is specified only where the active ingredient is defined as a particular isomer ratio. A synergist is specified only where required. An impurity is specified only where it is relevant, as defined in the glossary of terms (Appendix C).
- Note 6** The method of analysis must be peer-validated, as a minimum. If it is not published, full details of the method and the peer-validation data must be provided.
- Note 7** Whether a final product, when used, sinks or floats on water depends on the type of polymer. It closely relates to application method and must be specified.
- Drop one piece of the product in a sufficiently large beaker containing CIPAC standard water D. Stir thoroughly using a glass rod to ensure complete wetting. Check to confirm that air bubbles are completely removed. After 1 min, state the test result. Possible results are: "sinking" or "floating".
- Note 8** Unless other temperatures and/or times are specified. Refer to Section 4.6.2 of this manual for alternative storage conditions. Whole product must be stored.
- Note 9** MT 46.4 allows for storage of MR in sales packs or individual MR wrapped in aluminium foil (see Note 5 therein). Wrapping in aluminium foil is recommended and shown in Figure 1 below.
- Note 10** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error.
- Note 11** When the whole product is used to analyse the active ingredient/synergist, the tolerance of the product should be examined and described.
- Note 12** This sub-clause is required only if the relevant impurity concentration is capable of increasing during storage.

Figure 1. Recommended wrapping in aluminium foil for individual MR storage (MT 46.4)

8.23 LONG-LASTING STORAGE BAGS

Introduction

A “long-lasting storage bag” (LB) is a woven polymer fibre bag with a pesticide active ingredient incorporated into the fibre or coated on the surface of the fibre. The storage bag is intended for postharvest storage of commodities including cereal grains, pulses and seeds and provides control of pests before they can infest the stored commodities. The pesticide is released to the surface of the material in a sustained manner so that the commodities stored in the bags are continuously protected against pest infestation over a certain time period (at least 2 years, over multiple seasons).

To evaluate the migration of the active ingredient the proposed methodology lends itself from the CIPAC method MT195 (Wash resistance index of LN’s). Whilst it is understood that the bags are unlikely to be washed, it provides a validated method for release and migration properties of the active ingredient to the surface of the polymer material.

Accelerated storage clauses were divided into two sub sections as sampling and sub sampling for chemical and physical tests require different schemes (8.23.5.1 and 8.23.5.2).

In case the fibre material is a polyolefin (high-density polyethylene [HDPE], polypropylene [PP]), an anti-slip weave in the weaving pattern is recommended. Storage bags made of e.g. polypropylene tend to slip when stacked and therefore present a hazard. The anti-slip weave increases the frictional force between stacked bags and reduces the hazard of falling bags. The presence of an anti-slip weave may be checked by a visual inspection counting ends versus picks and comparison with known anti-slip weaving patterns. The anti-slip weave should be noted on the label of the storage bag.

Food contact material

The polymer material used to produce the yarn must be virgin (non-recycled) polymer and comply with international regulations concerning food contact material.

These are:

- **Migration of polyolefins.** If the polymer is a polyolefin (HDPE, PP) migration of polyolefin shall be tested as per the United States of America's Food and Drug Administration (FDA) 21 Code of Federal Regulations Part 177-1520 or European Union Directive 10/2011 for food contact substances.
- **Migration of heavy metals.** Migration of heavy metals shall be tested as per BS EN (British standard implementations of English language versions of European standard) 1186:2002 or TIS-656-2529 (1986) or other suitable ASTM method wherein the sum concentration levels of lead, cadmium, mercury and hexavalent chromium shall not exceed 100 ppm.
- **Residues of pesticide on the stored commodity.** The residues of the pesticide(s) incorporated or coated in the bag on the stored commodity should be determined and should comply with the CODEX Alimentarius MRLs for the pesticide and commodity combinations.

These parameters are not part of the specification but should be covered in the supporting documentation of the proposer for establishment of a LB specification.

Distribution of the active ingredient over the bag material

Manufacturers should control and minimize the within-product heterogeneity of active ingredient and provide a sub-sampling scheme to represent the active ingredient of the product unit. The example sampling scheme given in this specification is a suggested method.

Physical properties

The ISO standard 23560:2015 (Woven polypropylene sacks for bulk packaging of foodstuffs) describes "the construction of the sacks, their dimensions, and test methods suitable for ensuring the long-term storage and transportation of foodstuffs in the sacks" (end of quote). The properties and testing of long-lasting storage bags in this LB guideline are harmonized with the requirements in this standard. In particular, the average breaking strength and elongation at break (clause 8.23.4.1), the breaking strength of bottom seam (clause 8.23.4.2) before and after accelerated storage test and resistance to ultraviolet radiation (UV) and weathering (clause 8.23.6) are adopted from that ISO standard. Table 1 in ISO 23560:2015 (Required construction parameters of fabric and sacks) summarizes parameters and requirements with tolerances together with test methods to be used.

Storage stability

Empty or full storage bags may or may not be protected from sunlight. An additional storage stability clause for UV stability of the fabric has therefore been introduced. If a claim for UV stability is made then the clause for UV stability must be included (clause 8.23.6).

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.

..... [ISO common name] (INCORPORATED/COATED ONTO FILAMENT)
LONG-LASTING STORAGE BAG

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

8.23.1 Description (Note 1)

The product shall be formed from (or in the form of) a storage bag suitable for agricultural commodities, consisting of mono-/poly-filament, [polymer type] fibres, having a width of mm, woven/non-woven coating/incorporating technical/formulated [ISO common name] complying with the requirements of FAO specification [CIPAC number/technical or formulation code (date)], together with any other necessary formulants, if required. The product shall appear clean and shall be free from visible extraneous matter, visible damage (such as splitting or tearing) and visible manufacturing defects (such as poorly made seams or a weave that is either not uniform or too loose to remain uniform in use) (Note 2), and shall be suitable for use as storage bag with long-lasting activity and with/without UV resistance (Notes 3 & 4).

8.23.2 Active ingredient

8.23.2.1 Identity tests (Note 5)

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

8.23.2.2 [ISO common name] content (Notes 5 & 6)

The [ISO common name] content shall be declared (..... g/kg) and, when determined, the average measured content shall not differ from that declared by more than the appropriate tolerance, Section 4.3.2.

8.23.2.3 [ISO common name] isomer ratio (Notes 5, 6 & 7), if required

The ratio of [ISO common name] isomers shall be in the range to

8.23.2.4 [ISO common name] wash resistance index (MT 195)

The wash resistance index of [ISO common name] from the bag material, when determined, shall be within the range to

8.23.3 Relevant impurities

8.23.3.1 By-products of manufacture or storage (Note 8), if required

Maximum:% of the [ISO common name of active ingredient] content found under 8.23.2.2.

8.23.4 Physical properties

8.23.4.1 **Average breaking strength and elongation at break** (ISO 23560:2015, Table 1)

The average breaking strength lengthwise and width wise shall not be less than 918 N for a 50 kg bag and 816 N for a 25 kg bag, respectively. The elongation at break of fabric lengthwise and width wise should comply with ISO 23560:2015, as per Table 1.

8.23.4.2 **Breaking strength of bottom seam** (ISO 23560:2015, Table 1)

The minimum average breaking strength of the bottom seam of the bag shall not be less than 377 N for a 50 kg bag and 337 N for a 25 kg bag, respectively.

8.23.5 Storage stability

8.23.5.1 **Chemical stability at elevated temperature** (CIPAC MT 46.4)

After storage at $54 \pm 2^\circ\text{C}$ for 2 weeks (Note 9), the determined active ingredient content shall not be lower than 95%, relative to the determined average content found before storage (Note 10) and the product shall continue to comply with the clauses for:

- isomer ratio (8.23.2.3),
 - wash resistance index (8.23.2.4),
 - relevant impurities (8.23.3.1),
- as required.

8.23.5.2 **Physical stability of bags at elevated temperature** (MT 46.4) (Note 11)

After storage at $54 \pm 2^\circ\text{C}$ for 2 weeks, the product shall continue to comply with the clauses for physical properties:

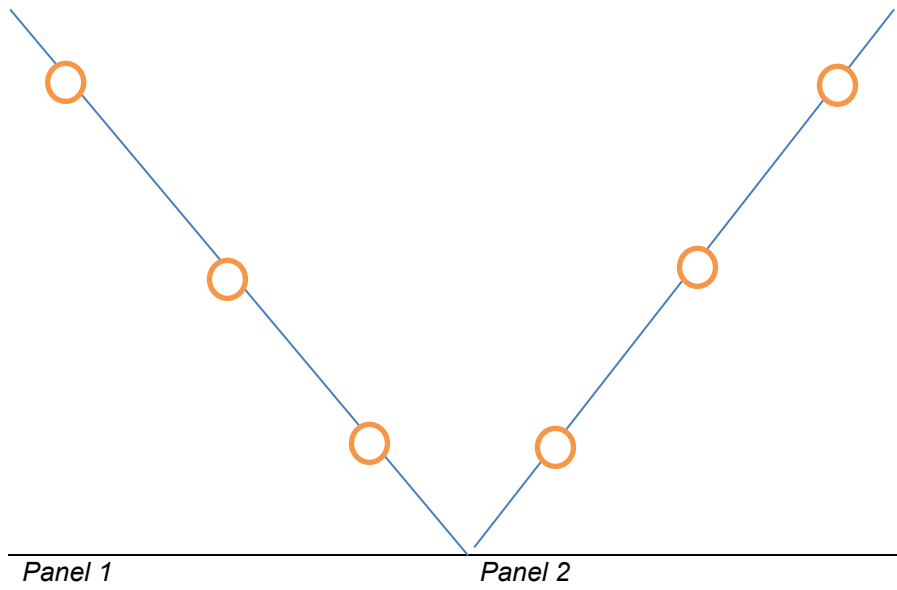
- average breaking strength and elongation at break (8.23.4.1),
 - breaking strength of bottom seam (8.23.4.2),
- as required.

8.23.6 Ultraviolet Resistance (ISO 4892-3: 2013, Table 4, Method A, Cycle No.1) (Note 12), if required

Bags shall retain at least% of active ingredient when tested after exposure to UV radiation and weathering for 144 h and the breaking strength of bottom seam shall not be lower than 50% of the original measure without UV exposure.

- Note 1** The specification may apply to bags in bulk or made-up bags which may be of different capacity made up of woven crushed tapes or non-woven. The bags must be made up of virgin polymer e.g. polypropylene or HDPE and may be white or coloured. These bags are expected to last in the warehouse for at least 2 years.
- Note 2** Occasional short lengths of loose yarns present in made up bags are not considered to be extraneous matter.
- Note 3** Long-lasting storage bags are expected to retain their biological activity and tensile strength during the lifespan and through an exposure to UV over a specified number of hours when tested as per Note 12.
- Note 4** Flammability of the product is not part of the specification, but it should be measured by the manufacturer, according to 16 CFR Part 1610, and the result presented on the package.
- Note 5** Method(s) of analysis must be CIPAC, AOAC or equivalent. Where methods have not yet been published, full details and appropriate method validation data must be submitted to FAO/WHO by the proposer. The sampling scheme should consider the within-product variation. For active ingredient content, homogenization of sample before taking portions before and after storage and keeping the sample in a capped bottle are recommended.
- Note 6** A recommended sampling scheme is presented in Figure 1 below. Samples must be sufficiently large to conduct all tests required and representative of the fabric. Except where seams are to be tested, do not test material within 10 cm of seams or selvedge.
- Use sharp scissors, or equivalent, to minimize damage to the fibres and fabric and thus avoid any consequential bias in the results of certain tests. Roll up the strips or squares and place them in labelled, new, clean aluminium foil prior to analysis. Samples should be kept cool, avoiding heat sources (including direct sunlight) or freezing, and analysed/tested with minimum delay. Representative portions (sub-samples) for testing should be taken as described in each test method.
- Note 7** This clause or sub-clause is required only if appropriate to the product specified. Isomer ratio is specified only where the active ingredient is defined as a particular isomer ratio.
- Note 8** Methods for determination of relevant impurities must be peer validated, as a minimum. If it is not published, full details of the method and the peer-validation data must be provided.
- Note 9** Unless other temperatures and times are specified. Refer to Section 4.6.2 for alternative storage conditions.
- Note 10** Samples of the formulation taken before and after the accelerated storage stability test may be analysed concurrently after the test in order to reduce the analytical error. The manufacturer shall demonstrate the sub-sampling design provides homogenized analytical portions for before and after storage stability test.
- Note 11** The CIPAC method MT 46.4 is used where the entire bag is stored at $54 \pm 2^\circ\text{C}$ for 2 weeks in order to test the physical properties and appropriate samples are taken after the storage from the bag.
- Note 12** UV radiation and weathering test to be conducted as per procedure given in ISO 4892-3:2013, Table 4, Method A, Cycle No.1.

Figure 1. Recommended sampling scheme for a LB product unit



Note: Recommended 6 positions, 3 from each side, cut along the diagonal with at least 10 cm from any edge to make up a representative sample for a product unit.

APPENDIX A

CHECKLIST FOR SUBMISSION OF APPLICATION FOR DEVELOPMENT OF FAO AND WHO SPECIFICATIONS

FAO and WHO welcome submission of requests for development of pesticide specifications or for extension of existing FAO and WHO specifications to products of other manufacturers. A formal application with supporting data should be submitted electronically to FAO and/or WHO. For further information on secure methods for submission of sensitive information, please contact the appropriate secretariat. The data package requirements, as specified in Section 3 of this manual shall be strictly followed.

A covering letter is required and shall include the following information:

- The name, address and contact point of the proposer(s) of the specification.
- A statement if the application is for development of a new specification or for extension of an existing specification. Specify if the proposal is for joint FAO/WHO specifications or for FAO or WHO specifications only. For extension of existing specifications, the source of TC/TK, as the sole source, shall be declared.
- Confirm that current production complies with the limits identified in specifications as it relates to content of active ingredient and relevant impurities. Confirm that current production complies with manufacturing maximum limits for impurities.
- Any other information that can facilitate review and assessment of the application.

Enclose:

- Completed electronic proposer's data entry form (available at <https://www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/en> (Accessed June 2021) and <https://extranet.who.int/pqweb/vector-control-products/specification-templates-proposers> (Accessed June 2021) and specifications in "standard format" and in Word file (**not pdf**). See also the checklist enclosed.
- Original study reports for physical and chemical properties of active ingredient, batch analysis data (with method validation data), mutagenicity data and / or toxicological data when needed.
- Study reports in support of each and every criteria (parameter) of the specifications for a formulated product.
- Validated test method for measurement of specification parameters of a new specification where FAO/WHO guideline specifications do not exist.
- A certificate of registration for a formulated products and the active ingredient issued by a national registration authority or a letter of authorization granting FAO/WHO and a registration authority to access the national registration data for comparison of confidential data (manufacturing process and purity/impurity profile).
- A brief description with necessary data/information of manufacturers internal quality assurance and control schemes.

The following checklist is to facilitate the collation of the data package. In case of doubt or questions, please refer to the relevant sections of this manual. Please provide a copy of the checklist with your application and check (✓) the information/documents that are included with your submission.

A. DATA REQUIREMENTS FOR PURE AND TECHNICAL GRADE ACTIVE INGREDIENTS (TC/TK)

Y = data required; (Y) = conditional data requirement; and N = not required.

Chapter 3, Manual	Requirements	For reference specification	For equivalence (extension of specifications for a TC or TK)	Check (✓) if included in the submission
A.1	Identity of the active ingredient (information only)			
	ISO English (E-ISO) common name and status	Y	Y	
	Any other common name or synonym	Y	Y	
	Chemical name (IUPAC and CA)	Y	Y	
	CAS No. (for each isomer or the mixture of isomers, if appropriate)	Y	Y	
	CIPAC No.	Y	Y	
	Structural formula(e) (including stereochemistry of the active isomers)	Y	Y	
	Isomeric composition, if appropriate	Y	Y	
	Molecular formula	Y	Y	
	Relative molecular mass	Y	Y	
A.2	Physical and chemical properties of the active ingredient (studies and end points), pure active			
	Melting point	Y	(Y)	
	Temperature of decomposition	Y	(Y)	
	Vapour pressure	Y	(Y)	
	Solubility in water	Y	(Y)	
	Octanol-water partition coefficient	Y	(Y)	
	Dissociation characteristics, if appropriate	Y	(Y)	
	Hydrolysis, photolysis and other degradation characteristics	Y	(Y)	
	Melting point of TC (active ingredients that are solids above 0°C).	Y	(Y)	

Chapter 3, Manual	Requirements	For reference specification	For equivalence (extension of specifications for a TC or TK)	Check (✓) if included in the submission
	Studies and data for solubility in organic solvents at room temperature for pure or technical grade active ingredient.	Y	(Y)	
A.3	Outline of the route of manufacture.	Y	Y	
A.4	Minimum active ingredient content.	Y	Y	
A.5	Manufacturing maximum limits for impurities present at or above 1 g/kg, supported by batch analysis data (minimum 5 typical batches) (all confidential data).	Y	Y	
A.6	Manufacturing maximum limits for impurities proposed as relevant at < 1 g/kg.	Y	Y	
A.7	Information on relevant impurities, with explanations of the effects observed (for example, toxicological effects, or effects on the stability of the active ingredient). Limits set by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR) and/or registration authorities should accompany this information, identifying the authority responsible for setting the limit.	Y	Y	
A.8	Identity and nominal content (g/kg) of compounds intentionally added to the TC/TK (confidential data).	Y	Y	
A.9	Toxicological summaries (including test conditions and results).	Y	(Y)	
A.9.1	Toxicological profile of the TC/TK based on acute oral, dermal and inhalation toxicity; skin and eye irritation, skin sensitization.	Y	(Y)	
A.9.2	Toxicological profile of the TC/TK based on repeated administration (from sub-acute to chronic) with a description of dosage levels (mg/kg bw per d), NOAEL values and recapitulation of findings at the LOAEL dose, as well as studies on reproductive and developmental toxicity, genotoxicity, carcinogenicity, developmental and adult neurotoxicity, etc.	Y	(Y)	
A.9.2	<u>Equivalence</u> : Data on <i>in-vitro</i> mutagenicity (<i>Bacterial Reverse Mutation Test, OECD test guideline 471 or equivalent</i>) required in all cases including Tier-1 equivalence.	Y	Y	
A.9.3	Ecotoxicological profile of the TC/TK based on toxicity to aquatic and terrestrial organisms (e.g. fish, Daphnia, algae, birds, bees), as appropriate to the intended use, and information of persistence.	Y	N	
A.10.1	WHO classification by hazard where they exist.	Y	N	

Chapter 3, Manual	Requirements	For reference specification	For equivalence (extension of specifications for a TC or TK)	Check (☐) if included in the submission
A.10.2	References to JMPR evaluations for toxicology and environmental fate should be given, where these exist	Y	N	
A.10.3	A certificate of registration for a formulated product and the active ingredient issued by a national registration authority or a letter of authorization granting competent FAO/WHO and registration authorities access to registration data on behalf of FAO/WHO.	Y	Y	
A.10.4	Statements to identify the links between purity/impurity data and the hazard information and risk assessments.	Y	(Y)	

B. DATA REQUIREMENTS FOR FORMULATIONS

Chapter 3, Manual	Requirements	Check (✓) if included in the submission
B.1	Identify if the formulations are for public health or agriculture uses, or both.	
B.2	In the case of public health pesticides, confirm that the formulation and manufacturing process are the same as those employed for the materials evaluated by WHO PQT/VCP.	
B.3	List the main formulation types available and identify those for which specifications are sought.	
B.4	List the main countries where these formulations are registered and sold or, if there are very many, give the number of countries in each region or continent.	
B.5	Studies on physical-chemical properties, as required in Sections 5 to 8 of this manual. If necessary, briefly explain why it is proposed that certain clauses should be deleted, new clauses should be inserted, or less stringent limits should be adopted compared with those given in the guideline specifications.	

In case of an equivalence determination, formulations are generally considered to be equivalent if (i) the source of starting material (TC/TK) is supported by a current evaluation report confirming compliance with the established specification and (ii) the formulations comply with the same specification. In special cases, for example slow-release formulations such as CS, additional evidence may be required to determine equivalence of the formulations and they are likely to be non-equivalent if unique technology, specification limits or test methods are involved.

C. METHODS FOR THE ANALYSIS AND TESTING OF TC/TK AND FORMULATIONS INGREDIENTS (TC/TK)

Y = data required; (Y) = conditional data requirement; and N = not required.

Chapter 3, Manual	Requirements	For reference specification	For equivalence (extension of specifications for a TC or TK)	Check (✓) if included in the submission
C.1	At least two methods for testing identity of the active ingredient and one for testing the identity of the counter-ion or other derivative, if appropriate	Y	(Y)	
C.2	Method for determination of active ingredient content. The method needs to be collaboratively validated.	Y	(Y)	
C.3	Methods of analysis for relevant impurities. The methods need to be peer-validated, e.g. through CIPAC. Methods of analysis for non-relevant impurities in the TC/TK, including validation data, The methods needs to be validated, e.g. using EU SANCO 3030	Y	Y	
C.4	Reference test methods for physical-chemical properties	Y	Y	
C.5	Information on validation completed, in progress or planned for methods listed under C.2, C.3 and C4	Y	Y	

The following table provides the list of original study reports to be provided in support of FAO/WHO specifications and the Quality Assurance requirements.

Y = study report required; (Y) = conditional study report requirement; and N = not required.

GLP = certified according to the OECD Principles of Good Laboratory Practice.

ISO 17025 = accredited according to the ISO 17025 requirements.

Study	Study report for reference specification	Study report for equivalence	Quality Assurance requirements
Physical and chemical properties of the active ingredient	Y	N	GLP
Batch analysis data on TC/TK: active ingredient and relevant impurities with methods validation data if not collaboratively validated or peer validated, non-relevant impurities with methods validation data	Y	Y	GLP

Mutagenicity data on TC/TK	Y	Y	GLP
Toxicological and ecotoxicological data on TC/TK	(Y)	(Y)	GLP
Physical-chemical properties of formulations	Y	Y	GLP / ISO 17025 not mandatory

APPENDIX B

SUPPLY AND CERTIFICATION OF REFERENCE SUBSTANCES OF PESTICIDE ACTIVE INGREDIENTS

INTRODUCTION

Reference substances of known content are often essential for the quantitative determination of pesticide active ingredients in different types of sample and at various concentration levels. They are available from various sources. It is important that the active ingredient content is declared and certified (Note 1).

1. SUPPLY OF REFERENCE SUBSTANCES

There are two sources for the supply of certified reference substances:

- the manufacturer of the active ingredient in question;
- standards institutions or companies selling reference substances.

1.1 Supply by the manufacturer

The manufacturer of a pesticide technical grade active ingredient, or its formulations, is obliged to supply a certified reference substance in the following cases:

1.1.1 Trade relations between customer and manufacturer

The customer, or an independent laboratory, might want to check the active ingredient content of material delivered by the manufacturer. This is to be done on the basis of the specification and using the analytical method stated therein. The manufacturer's certified reference substances should be made available to the customer so as to avoid any discrepancy in the analytical results, which could otherwise be derived from differences in the purity of the reference substances used by the two parties.

1.1.2 Relations between manufacturer and registration authorities

Each company (not only the inventor company) applying for the registration of a pesticide (new a.i. or formulation) must supply its own certified reference substance, if required by the registration authorities.

1.2 Supply by reference substances producers or suppliers

There are various standards institutions and commercial companies which offer reference substances. They should normally be approached if reference substances are required in situations different from those mentioned above. On request manufacturers may, at their discretion, also supply reference substances in such cases.

2. CERTIFICATION

A certificate of identity and determined content, together with the corresponding measurement uncertainty and a reference to the method(s) of analysis used, must always accompany each sample of a certified reference substance. Descriptions such as “greater than .%” are unacceptable. The recommended storage conditions and an expiry date shall be stated.

Note 1: For more detailed information, see CIPAC Handbook D, pages 186-196.

APPENDIX C

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.
ADI	Acceptable daily intake.
AgroCare	A global association representing the independent post-patent crop protection industry.
AOAC	AOAC International, formerly the Association of Official Analytical Chemists.
Apparent density	see Density.
ARfD	Acute reference dose.
ASTM	American Society for Testing and Materials.
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.

Term	Definition
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 $20 \pm 2^\circ\text{C}$. 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 $50 \mu\text{m}$.
ECCA	European Crop Care Association
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.
EDQM	European Directorate for the Quality of Medicines and HealthCare.
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>

Term	Definition
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 EPS	FAO Experts on Pesticide Specifications.
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.
Friability	The tendency of a solid, such as a granule or tablet, to disintegrate by crumbling. See also Attrition.
GHS	Globally Harmonized System of Classification and Labelling of Chemicals.
GLP	Good Laboratory Practice (OECD Principles).
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.
HDPE	High-density polyethylene.
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.

Term	Definition
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.
IPCS	International Programme on Chemical Safety.
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.
JECFA	Joint FAO/WHO Expert Committee on Food Additives.
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.
LD	Lethal dose.
LOAEL	Lowest observed adverse effect level.
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 microbial or chemical 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

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.
MRL	Maximum residue limit.
MT	Method of testing.
NOAEL	No observed adverse effect level.
NOEL	No observable effect levels.
Non-flammable	Not readily ignitable, with a flash point above 55°C as determined by a closed cup method.
OECD	Organisation for Economic Co-operation and Development.

Term	Definition
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).
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; defoliant; 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>
pH	Potential hydrogen.
Phytotoxic	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.
POP	Persistent organic pollutant.
Proposer	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.
(Q)SAR	Quantitative structure–activity relationship.

Term	Definition
Reference specification	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.
Reference profile	The purity/impurity, toxicological and ecotoxicological profiles upon which the original specification for a technical grade active ingredient is based. 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. Generally, the reference profile of impurities relates to the technical grade active ingredient supported by the most complete toxicological and ecotoxicological profiles.
Release date	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.
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.
RSD	Relative standard deviation.
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.

Term	Definition
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.
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.
UNIDO	United Nations Industrial Development Organization.

Term	Definition
Unintentional ingredients	In contrast to added, chemically characterized active and inert ingredients, that are present in a microbial pesticide product, unintentional ingredients in a MPCA or MPCP are not added on purpose. Examples of such extraneous materials may include: allergens, microbial toxins, and other metabolic products; mutant strains; microbial contaminants with particular reference to potentially infective or antagonistic forms; side products from chemical reactions employed in the manufacturing process, fermentation residues from the growth of bacteria or fungi; extraneous host residues from viruses produced in cell cultures, whole animals, or other living forms; residues of contaminants that remain following the purification or extraction process; and impurities in chemicals used in the manufacturing process (Source: US EPA Microbial Pesticide Test Guidelines, OPPTS 885.1300, Discussion of Formation of Unintentional Ingredients ²¹). The formation, presence and possible consequences of unintentional ingredients must be discussed.
UV	Ultraviolet radiation.
Validation	Process by which the reliability and relevance of a particular approach, method, process, or assessment is established for a defined purpose.
VCP	Vector Control Product Assessment Team (WHO).
WHO	World Health Organization.
WHOPES	WHO Pesticide Evaluation Scheme.
WHO PQT/VCP	WHO Prequalification Unit - Vector Control Product Assessment Team.

²¹ Accessible under <https://nepis.epa.gov/Exe/ZyPDF.cgi/P100IRQS.PDF?Dockey=P100IRQS.PDF>

APPENDIX D

CODING OF ACTIVE INGREDIENTS AND SPECIFICATIONS

ISO common names are used in specifications and methods of analysis, where possible. Each specification or CIPAC method of analysis is assigned a number based on the CIPAC code number for the chemical and its derivatives, forming a cross-reference between the FAO/WHO specification and the method of analysis.

The CIPAC code number system is a simple approach for an unambiguous numerical coding of pesticide active ingredients and their variants (for more details see the document *What are CIPAC Code Numbers?*), <https://www.cipac.org/index.php/code-numbers> (CIPAC, 2021).

The compounds are easily identified and retrieved using these codes. Currently, more than 1 000 pesticides and an extensive lists of variants like esters or salts are covered by the CIPAC coding system. A more detailed description of the background of the coding system and updated alphabetical and numerical lists of pesticides and their codes are provided in the download section under <https://www.cipac.org/index.php/code-numbers> (CIPAC, 2021).

APPENDIX E

CATALOGUE OF PESTICIDE FORMULATION TYPES AND INTERNATIONAL CODING SYSTEM

Courtesy of CropLife International, 2017 – *Technical Monograph No. 2*

Code	Term	Definition
AE	Aerosol dispenser	A container-held formulation which is dispersed generally by a propellant as fine droplets or particles upon the actuation of a valve.
AL	Any other liquid	A liquid not yet designated by a specific code, to be applied undiluted.
AP	Any other powder	A powder not yet designated by a specific code, to be applied undiluted.
BR	Briquette	Solid block designed for controlled release of active ingredient into water.
CB	Bait concentrate	A solid or liquid intended for dilution before use as a bait.
CP	Contact powder	Rodenticidal or insecticidal formulation in powder form for direct application. Formerly known as tracking powder (TP).
CS	Capsule suspension	A stable suspension of capsules in a fluid, normally intended for dilution with water before use.
DC	Dispersible concentrate	A liquid homogeneous formulation to be applied as a solid dispersion after dilution in water. (Note: there are some formulations which have characteristics intermediate between DC and EC).
DP	Dustable powder	A free-flowing powder suitable for dusting.
DS	Powder for dry seed treatment	A powder for application in the dry state directly to the seed.
DT	Tablet for direct application	Formulation in the form of tablets to be applied individually and directly in the field, and/or bodies of water, without preparation of a spraying solution or dispersion
EC	Emulsifiable concentrate	A liquid, homogeneous formulation to be applied as an emulsion after dilution in water.
EG	Emulsifiable granule	A granular formulation, which may contain water-insoluble formulants, to be applied as an oil-in-water emulsion of the active ingredient(s) after disintegration in water.
EO	Emulsion, water in oil	A fluid, heterogeneous formulation consisting of a solution of pesticide in water dispersed as fine globules in a continuous organic liquid phase.
EP	Emulsifiable powder	A powder formulation, which may contain water-insoluble formulants, to be applied as an oil-in-water emulsion of the active ingredient(s) after dispersion in water.
ES	Emulsion for seed treatment	A stable emulsion for application to the seed either directly or after dilution.

Code	Term	Definition
EW	Emulsion, oil in water	A fluid, heterogeneous formulation consisting of a solution of pesticide in an organic liquid dispersed as fine globules in a continuous water phase.
FS	Flowable concentrate for seed treatment	A stable suspension for application to the seed, either directly or after dilution.
FU	Smoke generator	A combustible formulation, generally solid, which upon ignition releases the active ingredient(s) in the form of smoke.
GA	Gas	A gas packed in pressure bottle or pressure tank.
GD	Gel for direct application	A gel-like preparation to be applied undiluted.
GE	Gas generating product	A formulation which generates a gas by chemical reaction.
GL	Emulsifiable gel	A gelatinized formulation to be applied as an emulsion in water.
GR	Granule	A free-flowing solid formulation of a defined granule size range ready for use.
GS	Grease	Very viscous formulation based on oil or fat.
GW	Water soluble gel	A gelatinized formulation to be applied as an aqueous solution.
HN	Hot fogging concentrate	A formulation suitable for application by hot fogging equipment, either directly or after dilution.
KK	Combi-pack solid/liquid	A solid and a liquid formulation, separately contained within one outer pack, intended for simultaneous application in a tank mix.
KL	Combi-pack liquid/liquid	Two liquid formulations, separately contained within one outer pack, intended for simultaneous application in a tank mix.
KN	Cold fogging concentrate	A formulation suitable for application by cold fogging equipment, either directly or after dilution.
LB	Long lasting storage bag	A slow- or controlled-release formulation in the form of a treated bag for storage, providing physical and chemical barriers, e.g. to pests.
LN	Long-lasting insecticidal net	A slow- or controlled-release formulation in the form of netting, providing physical and chemical barriers to insects. LN refers to both bulk netting and ready-to-use products, for example mosquito nets.
LS	Solution for seed treatment	A clear to opalescent liquid to be applied to the seed either directly or as a solution of the active ingredient after dilution in water. The liquid may contain water-insoluble formulants.
MC	Mosquito coil	A coil which burns (smoulders) without producing a flame and releases the active ingredient into the local atmosphere as a vapour or smoke.
ME	Micro-emulsion	A clear to opalescent, oil and water containing liquid, to be applied directly or after dilution in water, when it may form a diluted micro-emulsion or a conventional emulsion.
MR	Matrix release	A slow- or controlled-release formulation in the form of a polymer matrix providing long-lasting effects. It is intended to be applied directly.

Code	Term	Definition
OD	Oil dispersion	A stable suspension of active ingredient(s) in a water- immiscible fluid, which may contain other dissolved active ingredient(s), intended for dilution with water before use.
OF	Oil miscible flowable concentrate (oil miscible suspension)	A stable suspension of active ingredient(s) in a fluid intended for dilution in an organic liquid before use.
OL	Oil miscible liquid	A liquid, homogeneous formulation to be applied as a homogeneous liquid after dilution in an organic liquid.
OP	Oil dispersible powder	A powder formulation to be applied as a suspension after dispersion in an organic liquid.
PA	Paste	Water-based, film-forming composition.
PR	Plant rodlet	A small rodlet, usually a few centimetres in length and a few millimetres in diameter, containing an active ingredient.
RB	Bait (ready for use)	A formulation designed to attract and be eaten by the target pests.
SC	Suspension concentrate (= flowable concentrate)	A stable suspension of active ingredient(s) with water as the fluid, intended for dilution with water before use.
SD	Suspension concentrate for direct application	A stable suspension of active ingredient(s) in a fluid, which may contain other dissolved active ingredient(s), intended for direct application, to rice paddies, for example.
SE	Suspo-emulsion	A fluid, heterogeneous formulation consisting of a stable dispersion of active ingredients in the form of solid particles and of water-non miscible fine globules in a continuous water phase.
SG	Water soluble granule	A formulation consisting of granules to be applied as a true solution of the active ingredient after dissolution in water, but which may contain insoluble inert ingredients.
SL	Soluble concentrate	A clear to opalescent liquid to be applied as a solution of the active ingredient after dilution in water. The liquid may contain water-insoluble formulants.
SO	Spreading oil	Formulation designed to form a surface layer on application to water.
SP	Water soluble powder	A powder formulation to be applied as a true solution of the active ingredient after dissolution in water, but which may contain insoluble inert ingredients.
ST	Water soluble tablet	Formulation in form of tablets to be used individually, to form a solution of the active ingredient after disintegration in water. The formulation may contain water-insoluble formulants.
SU	Ultra-low volume (ULV) suspension	A suspension ready for use through ULV equipment.
TB	Tablet	Pre-formed solids of uniform shape and dimensions, usually circular, with either flat or convex faces, the distance between faces being less than the diameter.
TC	Technical material	A material resulting from a manufacturing process comprising the active ingredient, together with associated impurities. This may contain small amounts of necessary additives.

Code	Term	Definition
TK	Technical concentrate	A material resulting from a manufacturing process comprising the active ingredient, together with associated impurities. This may contain small amounts of necessary additives and appropriate diluents.
UL	Ultra-low volume (ULV) liquid	A homogeneous liquid ready for use through ULV equipment.
VP	Vapour releasing product	A formulation containing one or more volatile active ingredients, the vapours of which are released into the air. Evaporation rate is normally controlled by using suitable formulations and/or dispensers.
WG	Water dispersible granules	A formulation consisting of granules to be applied after disintegration and dispersion in water.
WP	Wettable powder	A powder formulation to be applied as a suspension after dispersion in water.
WS	Water dispersible powder for slurry seed treatment	A powder to be dispersed at high concentration in water before application as a slurry to the seed.
WT	Water dispersible tablet	Formulation in the form of tablets to be used individually, to form a dispersion of the active ingredient after disintegration in water.
XX	Others	Temporary categorization of all other formulations not listed above.
ZC	A mixed formulation of CS and SC	A stable suspension of capsules and active ingredient(s) in fluid, normally intended for dilution with water before use.
ZE	A mixed formulation of CS and SE	A fluid, heterogeneous formulation consisting of a stable dispersion of active ingredient(s) in the form of capsules, solid particles, and fine globules in a continuous water phase, normally intended for dilution with water before use.
ZW	A mixed formulation of CS and EW	A fluid, heterogeneous formulation consisting of a stable dispersion of active ingredient(s) in the form of capsules and fine globules in a continuous water phase, normally intended for dilution with water before use.

For record keeping purposes, the suffix “SB” should be added to the formulation code, if the material is packaged in a sealed water soluble bag (e.g. WP-SB).

FORMULATION CODES WHICH ARE NO LONGER SUPPORTED

Code	Term	Definition
AB	Grain bait	Special form of bait. Refer to RB.
BB	Block bait	Special form of bait. Refer to RB.
CF	Capsule suspension for seed treatment	A stable suspension of capsules in a fluid to be applied to the seed, either directly or after dilution.
CG	Encapsulated granule	A granule with a protective or granule release-controlling coating. Refer to GR.
CL	Contact liquid or gel	Rodenticidal or insecticidal formulation in the form of a liquid/gel for direct application, or after dilution in the case of gels.
ED	Electrochargeable liquid	Special liquid formulation for electrostatic (electrodynamic) spraying.
FD	Smoke tin	Special form of smoke generator. Refer to FU.
FG	Fine granule	A granule in the particle size range from 300 to 2500 µm. Refer to GR.
FK	Smoke candle	Special form of smoke generator. Refer to FU.
FP	Smoke cartridge	Special form of smoke generator. Refer to FU.
FR	Smoke rodlet	Special form of smoke generator. Refer to FU.
FT	Smoke tablet	Special form of smoke generator. Refer to FU.
FW	Smoke pellet	Special form of smoke generator. Refer to FU.
GB	Granular bait	Special form of bait. Refer to RB.
GF	Gel for Seed Treatment	A homogeneous gelatinous formulation to be applied directly to the seed.
GG	Macrogranule	A granule in the particle size range from 2000 to 6000 µm. Refer to GR.
GP	Flo-dust	Very fine dustable powder for pneumatic application in greenhouses.
KP	Combi-pack solid/solid	Two solid formulations, separately contained within one outer pack, intended for simultaneous application in a tank mix.
LA	Lacquer	Solvent-based, film-forming composition.
LV	Liquid vaporizer	A liquid formulation in a cartridge/bottle, designed to fit a suitable heater unit, from which the formulation passes up a heated wick and evaporates into the local atmosphere.
MG	Microgranule	A granule in the particle size range from 100 to 600 µm. Refer to GR.
MV	Vaporizing mats	A mat made from pulp, or other suitable inert materials, and impregnated with an active ingredient. The mat is intended for use in a heating unit designed to produce slow volatilization of the active ingredient.
PB	Plate bait	Special form of bait. Refer to RB.

Code	Term	Definition
PC	Gel or paste concentrate	A solid formulation to be applied as a gel or paste after dilution with water.
PO	Pour-on	Solution for pouring on the skin of animals in a high volume (normally more than 100 ml per animal).
PS	Seed coated with a pesticide	Application form. Not considered a formulation type.
SA	Spot-on	Solution for spot application on the skin of animals in a low volume (normally less than 100 ml per animal).
SB	Scrap bait	Special form of bait. Refer to RB.
SS	Water soluble powder for seed treatment	A powder to be dissolved in water before application to the seed.
TP	Tracking powder	Discontinued term. Refer to CP.

APPENDIX F

DECLARATIONS OF INTERESTS AND CONFIDENTIALITY

DECLARATION OF INTERESTS FOR FAO EXPERTS

Title of meeting or work to be performed, including description of subject-matter, substance (compounds and organisms), technology or process to be considered:

Public health considerations and protection of the environment are of primary importance in all Food and Agriculture Organization of the United Nations (FAO) technical work. Measures need to be taken to ensure that the best possible assessment of scientific evidence is achieved in an independent atmosphere free of either direct or indirect pressures. Thus, to assure the technical integrity and impartiality of FAO's work, it is necessary to avoid situations in which financial or other interests might affect the outcome of that work.

Each expert is therefore asked to declare any interests that could constitute a real, potential or apparent conflict of interest, with respect to his/her involvement in the meeting or work, between (1) commercial entities and the participant personally, and (2) commercial entities and the administrative unit with which the participant has an employment relationship. "Commercial entity" refers to any company, association (e.g., trade association), organization or any other entity of any nature whatsoever, with commercial interests.

What is a conflict of interest?

Conflict of interest means that the expert or his/her partner ("partner" includes a spouse or other person with whom s/he has a similar close personal relationship), or the administrative unit with which the expert has an employment relationship, has a financial or other interest that could unduly influence the expert's position with respect to the subject-matter being considered. An apparent conflict of interest exists when an interest would not necessarily influence the expert but could result in the expert's objectivity being questioned by others. A potential conflict of interest exists with an interest which any reasonable person could be uncertain whether or not should be reported.

Different types of financial or other interests, whether personal or with the administrative unit with which the expert has an employment relationship, can be envisaged and the following list, which is not exhaustive, is provided for your guidance. For example, the following types of situations should be declared:

1. A current proprietary interest in a substance, technology or process (e.g. ownership of a patent), to be considered in - or otherwise related to the subject matter of - the meeting or work.
2. A current financial interest, e.g. shares or bonds, in a commercial entity with an interest in the subject-matter of the meeting or work (except share holdings through general mutual funds or similar arrangements where the expert has no control over the selection of shares).
3. An employment, consultancy, directorship, or other position during the past 4 years, whether or not paid, in any commercial entity which has an interest in the subject-matter

of the meeting/work, or an ongoing negotiation concerning prospective employment or other association with such commercial entity.

4. Performance of any paid work or research during the past 4 years commissioned by a commercial entity with interests in the subject-matter of the meetings or work.
5. Payment or other support covering a period within the past 4 years, or an expectation of support for the future, from a commercial entity with an interest in the subject-matter of the meetings or work, even if it does not convey any benefit to the expert personally but which benefits his/her position or administrative unit, e.g. a grant or fellowship or other payment, e.g. for the purpose of financing a post or consultancy.

With respect to the above, an interest in a competing substance, technology or process, or an interest in or association with, work for or support by a commercial entity having a direct competitive interest must similarly be disclosed.

How to complete this declaration

Please complete this declaration and submit it to the FAO Secretariat. Any financial or other interests that could constitute a real, potential or apparent conflict of interest should be declared (1) with respect to yourself or partner, as well as (2) with respect to the administrative unit with which you have an employment relationship. Only the name of the commercial entity and the nature of the interest is required to be disclosed, no amounts need to be specified (though they may be, if you consider this information to be relevant to assessing the interest). With respect to items 1 and 2 in the list above, the interest should only be declared if it is current. With respect to items 3, 4 and 5, any interest during the past 4 years should be declared. If the interest is no longer current, please state the year when it ceased. With respect to item 5, the interest ceases when a financed post or fellowship is no longer occupied, or when support for an activity ceases.

Assessment and outcome

The information submitted by you will be used to assess whether the declared interests constitute an appreciable real, potential or apparent conflict of interest. Such conflict of interest will, depending on the situation, result in (i) you being asked not to take part in the portion of the discussion or work affecting that interest, (ii) being asked not to take part in the meeting or work altogether, or (iii) if deemed by FAO to be appropriate to the particular circumstances, and with your agreement, you taking part in the meeting or work and your interest being publicly disclosed.

Information disclosed on this Form may be made available to persons outside of FAO only when the objectivity of the meeting or work has been questioned such that the Director-General considers disclosure to be in the best interests of the Organization, and then only after consultation with you.

Declaration

Have you or your partner any financial or other interest in the subject-matter of the meeting or work in which you will be involved, which may be considered as constituting a real, potential or apparent conflict of interest?

Yes: No:

If yes, please give details in the box below.

Type of interest, e.g. patent, shares, employment, association, payment (including details on any compound, work, etc.)	Name of commercial entity	Belongs to you, partner or unit?	Current interest? (or year ceased)

Is there anything else that could affect your objectivity or independence in the meeting or work, or the perception by others of your objectivity and independence?

I hereby declare that the disclosed information is correct and that no other situation of real, potential or apparent conflict of interest is known to me. I undertake to inform FAO of any change in these circumstances, including if an issue arises during the course of the meeting or work itself.

Signature Date

Name Institution

DECLARATION OF INTERESTS FOR WHO EXPERTS

WHO's work on global health issues requires the assistance of external experts who **may have interests related to their expertise**. To ensure the highest integrity and public confidence in its activities, WHO requires that experts serving in an advisory role disclose any circumstances that could give rise to a potential conflict of interest related to the subject of the activity in which they will be involved.

All experts serving in an advisory role must disclose any circumstances that could represent a **potential conflict of interest** (i.e., any interest that may affect, or may reasonably be perceived to affect, the expert's objectivity and independence). You must disclose on this Declaration of Interest (DOI) form any financial, professional or other interest relevant to the subject of the work or meeting in which you have been asked to participate in or contribute towards and any interest that could be affected by the outcome of the meeting or work. You must also declare relevant interests of your immediate family members (see definition below) and, if you are aware of it, relevant interests of other parties with whom you have substantial common interests and which may be perceived as unduly influencing your judgement (e.g. employer, close professional associates, administrative unit or department). Please note that not fully completing and disclosing all relevant information on this form may, depending on the circumstances, lead WHO to decide not to appoint you to WHO advisory bodies / functions in the future.

Please complete this form and submit it to WHO Secretariat if possible at least 4 weeks but no later than 2 weeks before the meeting or work. You must also promptly inform the Secretariat if there is any change in this information prior to, or during the course of, the meeting or work. All experts must complete this form before participation in a WHO activity can be confirmed.

Answering "Yes" to a question on this form does not automatically disqualify you or limit your participation in a WHO activity. Your answers will be reviewed by the Secretariat to determine whether you have a conflict of interest relevant to the subject at hand. One of the outcomes listed in the next paragraph can occur depending on the circumstances (e.g. nature and magnitude of the interest, timeframe and duration of the interest).

The Secretariat may conclude that no potential conflict exists or that the interest is irrelevant or insignificant. If, however, a declared interest is determined to be potentially or clearly significant, one or more of the following three measures for managing the conflict of interest may be applied. The Secretariat (i) allows full participation, with public disclosure of your interest; (ii) mandates partial exclusion (i.e., you will be excluded from that portion of the meeting or work related to the declared interest and from the corresponding decision making process); or (iii) mandates total exclusion (i.e., you will not be able to participate in any part of the meeting or work).

All potentially significant interests will be disclosed to the other participants at the start of the activity and you will be asked if there have been any changes. A summary of all declarations and actions taken to manage any declared interests will be published in resulting reports and work products. Furthermore, if the objectivity of the work or meeting in which you are involved is subsequently questioned, the contents of your DOI form may be made available by the Secretariat to persons outside WHO if the Director-General considers such disclosure to be in the best interest of the Organization, after consulting with you. Completing this DOI form means that you agree to these conditions.

If you are unable or unwilling to disclose the details of an interest that may pose a real or perceived conflict, you must disclose that a conflict of interest may exist and the Secretariat may decide that you be totally recused from the meeting or work concerned, after consulting with you.

Name:
Institution:
Email:

Date and title of meeting or work, including description of subject matter to be considered (if a number of substances or processes are to be evaluated, a list should be attached by the organizer of the activity):

Please answer each of the questions below. If the answer to any of the questions is "yes", briefly describe the circumstances on the last page of the form.

The term "you" refers to yourself and your immediate family members (i.e., spouse (or partner with whom you have a similar close personal relationship) and your children). "Commercial entity" includes any commercial business, an industry association, research institution or other enterprise whose funding is significantly derived from commercial sources with an interest related to the subject of the meeting or work. "Organization" includes a governmental, international or non-profit organization. "Meeting" includes a series or cycle of meetings.

EMPLOYMENT AND CONSULTING

Within the past 4 years, have you received remuneration from a commercial entity or other organization with an interest related to the subject of the meeting or work?

- 1a Employment Yes No
- 1b Consulting, including service as a technical or other advisor Yes No

RESEARCH SUPPORT

Within the past 4 years, have you or has your research unit received support from a commercial entity or other organization with an interest related to the subject of the meeting or work?

- 2a Research support, including grants, collaborations, sponsorships, and other funding Yes No
- 2b Non-monetary support valued at more than US \$1000 overall (include equipment, facilities, research assistants, paid travel to meetings, etc.) Yes No
- Support (including honoraria) for being on a speakers bureau, giving speeches or training for a commercial entity or other organization with an interest related to the subject of the meeting or work?

INVESTMENT INTERESTS

Do you have current investments (valued at more than US \$5 000 overall) in a commercial entity with an interest related to the subject of the meeting or work? Please also include indirect investments such as a trust or holding company. You may exclude mutual funds, pension funds or similar investments that are broadly diversified and on which you exercise no control.

- 3a Stocks, bonds, stock options, other securities (e.g., short sales) Yes No
- 3b Commercial business interests (e.g., proprietorships, partnerships, joint ventures, board memberships, controlling interest in a company) Yes No

INTELLECTUAL PROPERTY

Do you have any intellectual property rights that might be enhanced or diminished by the outcome of the meeting or work?

- 4a Patents, trademarks, or copyrights (including pending applications) Yes No
- 4b Proprietary know-how in a substance, technology or process Yes No

PUBLIC STATEMENTS AND POSITIONS (during the past 3 years)

- 5a As part of a regulatory, legislative or judicial process, have you provided an expert opinion or testimony, related to the subject of the meeting or work, for a commercial entity or other organization? Yes No
- 5b Have you held an office or other position, paid or unpaid, where you represented interests or defended a position related to the subject of the meeting or work? Yes No

ADDITIONAL INFORMATION

- 6a If not already disclosed above, have you worked for the competitor of a product that is the subject of the meeting or work, or will your participation in the meeting or work enable you to obtain access to a competitor's confidential proprietary information, or create for you a personal, professional, financial or business competitive advantage? Yes No
- 6b To your knowledge, would the outcome of the meeting or work benefit or adversely affect interests of others with whom you have substantial common personal, professional, financial or business interests (such as your adult children or siblings, close professional colleagues, administrative unit or department)? Yes No
- 6c Excluding WHO, has any person or entity paid or contributed towards your travel costs in connection with this WHO meeting or work? Yes No

6d Have you received any payments (other than for travel costs) or honoraria for speaking publicly on the subject of this WHO meeting or work? Yes No

6e Is there any other aspect of your background or present circumstances not addressed above that might be perceived as affecting your objectivity or independence? Yes No

7. TOBACCO OR TOBACCO PRODUCTS (answer without regard to relevance to the subject of the meeting or work)

Within the past 4 years, have you had employment or received research support or other funding from, or had any other professional relationship with, an entity directly involved in the production, manufacture, distribution or sale of tobacco or tobacco products or representing the interests of any such entity?

Yes No

EXPLANATION OF "YES" RESPONSES: If the answer to any of the above questions is "yes", check above and briefly describe the circumstances on this page. If you do not describe the nature of an interest or if you do not provide the amount or value involved where relevant, the conflict will be assumed to be significant.

Nos. 1 - 4: Type of interest, question number and category (e.g., Intellectual Property 4.a copyrights) and basic descriptive details.	Name of company, organization, or institution	Belongs to you, a family member, employer, research unit or other?	Amount of income or value of interest (if not disclosed, is assumed to be significant)	Current interest (or year ceased)

Nos. 5-6: Describe the subject, specific circumstances, parties involved, time frame and other relevant details

Empty space for providing details for Nos. 5-6.

CONSENT TO DISCLOSURE. By completing and signing this form, you consent to the disclosure of any relevant conflicts to other meeting participants and in the resulting report or work product.

DECLARATION. I hereby declare on my honour that the disclosed information is true and complete to the best of my knowledge.

Should there be any change to the above information, I will promptly notify the responsible staff of WHO and complete a new declaration of interest form that describes the changes. This includes any change that occurs before or during the meeting or work itself and through the period up to the publication of the final results or completion of the activity concerned.

Date: _____

Signature _____

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS



WORLD HEALTH ORGANIZATION



CONFIDENTIALITY UNDERTAKING

- 1) The Food and Agriculture Organization of the United Nations (“FAO”), acting through its Plant Production and Protection Division, and the World Health Organization (“WHO”), acting through its Department of Regulation and Prequalification, have access to certain information relating to pesticides, including but not limited to pesticide specifications, which information FAO and WHO consider to be proprietary to themselves or to parties collaborating with them, including but not limited to the manufacturers of such pesticides (hereinafter referred to as “*the Information*”).
- 2) The Undersigned, as a [participant in] [temporary adviser to] the FAO/WHO Joint Meeting on Pesticide Specifications (“JMPS”), may have access to the Information in the course of his/her participation in and/or contributions to the meetings of the JMPS.
- 3) FAO and WHO are willing to provide, or to arrange for the provision of, the Information to the Undersigned for the sole purpose of performing his/her responsibilities in connection with the activities of the JMPS, provided that the Undersigned undertakes to treat the Information as confidential and to disclose it only to persons who have a need to know in connection with the activities of the JMPS and are bound by like obligations of confidentiality and non-use as are contained in this Undertaking.
- 4) The Undersigned undertakes to regard the Information as confidential and proprietary to FAO and/or WHO, and/or to parties collaborating with FAO and/or WHO (including but not limited to pesticide manufacturers) and agrees to take all reasonable measures to ensure that the Information is not used, disclosed or copied, in whole or in part, other than as provided in this Undertaking, except that the Undersigned shall not be bound by any such obligations if he/she is clearly able to demonstrate that the Information:
 - a) was known to him/her prior to any disclosure by or on behalf of FAO and/or WHO to the Undersigned; or
 - b) was in the public domain at the time of disclosure by or on behalf of FAO and/or WHO to the Undersigned; or
 - c) becomes part of the public domain through no fault of the Undersigned; or
 - d) becomes available to the Undersigned from a third party not in breach of any legal obligations of confidentiality.
- 5) The Undersigned also undertakes not to communicate the deliberations and decisions of the meetings of the JMPS to persons outside these meetings except as agreed by FAO and WHO.
- 6) The obligations of the Undersigned shall survive the termination of his/her responsibilities in connection with the JMPS.

- 7) The Undersigned agrees to return any and all copies of any Information to FAO and/or WHO (dependent on by whom or on whose behalf the Information was provided to the Undersigned), promptly following the completion of the review thereof by the JMPS.
- 8) Nothing in this Undertaking, or in any document relating thereto, shall be construed as constituting a waiver of privileges and immunities of FAO and/or WHO. [Note: temporary advisers/experts on mission enjoy certain privileges and immunities.]
- 9) Any dispute relating to the interpretation or application of this Undertaking shall, unless amicably settled, be subject to conciliation in accordance with the Conciliation Rules of the United Nations Commission on International Trade Law (UNCITRAL) as at present in force. In the event of failure of the latter, the dispute shall be settled by arbitration. The arbitration shall be conducted in accordance with the Arbitration Rules of UNCITRAL, as at present in force. The parties shall accept the arbitral award as final adjudication of any such dispute.

Name

Signature

Date

APPENDIX G

RECOMMENDED FORMAT OF LETTER OF ACCESS

LETTER OF ACCESS TO CONFIDENTIAL DATA

[Addressed to the evaluator **and** the registration authority]

Within the process of the development of FAO/WHO pesticide specifications, it is necessary to assess whether or not the confidential data on manufacturing process, purity and impurities, provided in support of the technical material for which an FAO/WHO specification is proposed, are similar to those assessed by a competent authority for the purposes of registering the pesticide.

The purpose of this letter of access, provided by [company name and address] in support of the development of pesticide specifications for [name of active ingredient], is to provide the evaluator, [name of evaluator], appointed by [WHO or FAO or both] and the registration authority with the following:

[The company should choose one of the following two options. The option which is most appropriate for the circumstances of the evaluator should be preferred. The option which is not used should be deleted. If the pesticide is registered for both agricultural and public health use, by separate authorities (whether in one country or two), the company should identify both authorities. The letter should state the registration number so as to facilitate access to the national files. The company should ensure that the letter includes the full contact details, including email, and the postal address of the contact person and the national authority.]

- 1) Authorization to access the registration data submitted by [company name] for [name of active ingredient] held by [name of registration authority], in its function as the national registration authority for pesticides in [name of country].; OR
- 2) Authorization to send the data provided by [company name] for [active ingredient] to [contact name and full address of registration authority] for their assessment of the similarity and subsequent communication with the evaluator, [name of evaluator].

This authorization relates only to the above-mentioned substance manufactured by [name of the Company] for the intended purpose as described above.

_____ [signed by company representative]

cc: _____ [Registration authority]

FAO
WHO

APPENDIX H

CALCULATION OF WORST-CASE-POSSIBLE CONTRIBUTION BY AN IMPURITY TO THE TOXIC HAZARDS OF THE ACTIVE INGREDIENT (SEE SECTION 3.1 D.3)

The calculations shown below are normally utilized by WHO/PCS in advising JMPS. They are presented here for the purposes of transparency.

The calculations are based on known concentrations of the active ingredient, and of the impurity in the technical material, and the toxicity (LD₅₀, ADI, BMD, NOAEL, LOAEL, etc.) of the impurity and the technical material (TC), (or technical concentrate (TK)). The calculations apply the dose-additivity model (SCHER 2011) for the active ingredient and the impurities, as: 1) synergistic effects leading to more than additive effect are exceptional at low exposure levels; and 2) IPCS recommendation is that even for response-additive effects, the model of dose additivity be used as the worst case scenario (Meek *et al.*, 2011). They are not used for the assessment of the relevance of impurities that are carcinogenic, mutagenic, sensitizing, toxic to reproduction or development, or irritating to the eye or skin (see Section 3.1, D.3).

The dose-additivity for a mixture of chemicals can be expressed as:

$$\frac{C_{ai} \text{ g/kg}}{TOX_{ai}} + \sum_1^n \frac{C_{imp_i} \text{ g/kg}}{TOX_{imp_i}} = \frac{1000 \text{ g/kg}}{TOX_{TC}} \quad (1)$$

where C_{ai} and C_{imp} are concentrations of the active ingredient and impurities, TOX_{ai}, TOX_{imp} and TOX_{TC} the toxicities of the active ingredient, impurities, and the technical material expressed in figures inversely related to the toxic potency (such as LD₅₀, NOAEL, LOAEL, BMD, BMDL). It should be noted that the TOX_{ai} value is not usually available, and the TOX_{TC} should represent the value for the specific technical material being assessed.

Calculations

(1) Calculate the maximal acceptable concentration of an impurity in the TC.

The maximal acceptable increase in the toxicity of the TC – considered a negligible increase in the hazard is 10%. In the absence of other toxic impurities, it may be deduced from equation (1) that:

$$\frac{C_{impmax}}{TOX_{imp}} = 0.1 * \frac{1000 \text{ g/kg}}{TOX_{TC}} \quad \text{from which} \quad C_{impmax} = \frac{100 * TOX_{imp}}{TOX_{TC}} \text{ g/kg}$$

where C_{impmax} is the maximal acceptable concentration of the impurity, TOX_{imp} = toxicity of the impurity, and TOX_{TC} the toxicity of the TC. If there are more than one impurity which could be relevant, the total of the acceptable impurities will be calculated using the relative toxicities of the different impurities.

(2) Assess the relevance of the impurity.

If the actual highest possible concentration of the impurity (manufacturing QC limit) is less than 10% of the C_{impmax} calculated above, it is usually concluded that the impurity in this TC is

not relevant – but may be relevant in other TC,s with the same active ingredient (See Section 3.1 D.3).

Example 1

The acute oral LD₅₀ of an impurity is 100 mg/kg bw and that of the technical material is 1000 mg/kg bw. The minimum purity of the TC is 920g/kg, and the manufacturing quality control limit of the impurity, supported by the 5-batch analysis, is 2 g/kg.

$$C_{impmax} = \frac{100 * 100}{1000} \frac{g}{kg} = 10 \text{ g/kg}$$

The maximum limit acceptable for the impurity concentration is therefore 10 g/kg. With the minimum purity of the TC of 920 g/kg, concentration of the impurity of 10 g/kg is possible. Furthermore, the manufacturing QC limit 2 g/kg exceeds 10% of the maximal acceptable limit 10 g/kg, and the impurity is thus relevant.

Example 2

A biological pesticide has a minimum purity of 200 g/kg. The acute oral LD₅₀ of an impurity is 2000 mg/kg bw and that of the active ingredient is 1000 mg/kg bw. That is, the impurity is less hazardous than the active ingredient. The manufacturing QC limit for the impurity, supported by the 5-batch analysis, is 20 g/kg.

$$C_{impmax} = \frac{100 * 2000}{1000} \frac{g}{kg} = 200 \text{ g/kg}$$

The maximum limit acceptable for the impurity concentration is therefore 200 g/kg. With the minimum purity of the TC of 200 g/kg, concentration of the impurity of 200 g/kg is possible. The manufacturing QC limit 20 g/kg equals 10% of the maximal acceptable limit, and the impurity is thus relevant.

Example 3

The acute oral LD₅₀ of an impurity is 400 mg/kg bw and that of the technical material is 600 mg/kg bw. The minimum purity of the TC is 980g/kg, and the manufacturing QC limit, supported by the 5-batch analysis, is 5 g/kg.

$$C_{impmax} = \frac{100 * 400}{600} \frac{g}{kg} = 66.7 \text{ g/kg}$$

Rounding to 1 significant figure (or 1.5 significant figures where the difference would be too large), the maximum limit acceptable for the impurity concentration is therefore 70 g/kg. With the minimum purity of the TC of 980 g/kg, concentration of the impurity of 70 g/kg is not possible. Furthermore, the manufacturing QC limit 5 g/kg is less than 10% of the maximal acceptable limit 70 g/kg, and the impurity is thus not relevant.

APPENDIX I

CALCULATION OF EXPANDED TOLERANCES FOR THE ACTIVE INGREDIENT CONTENT OF MIXED SOLID FORMULATIONS (SEE SECTION 4.3.3)

Solid mixtures cannot be blended perfectly but, even if perfection could be achieved, the dispersion of analytical results would remain dependent on the size of test portion analysed. Therefore, the size of test portion to be analysed must be defined in a specification for a blend of solids.

The method of calculating expanded tolerances for such blends is empirical, based on what is routinely achievable in practice with careful mixing of component solids which are well matched in size and density, and by the analysis of appropriately sized test portions. The values for B, in the calculations below, are not intended as tolerances for the addition of a component to a blend, though they inevitably encompass such variations. They provide a simple approach to defining limits which are expected to encompass all sources of manufacturing, sampling and analytical variation.

Calculation

- (i) Calculate the upper and lower limits for each active ingredient present in each formulation component of the blend, referring to the tolerances given in Section 4.3.2.

Active ingredient upper limit in its formulation (E_H) = g/kg declared + tolerance

Active ingredient lower limit in its formulation (E_L) = g/kg declared – tolerance

- (ii) Calculate the upper and lower limits for each component in the blend, applying the tolerances intended for active ingredient content in Section 4.3.2.

Blend component upper limit (F_H) = g/kg declared + tolerance

Blend component lower limit (F_L) = g/kg declared – tolerance

- (iii) Calculate the upper and lower limits for each active ingredient in the blend.

Active ingredient upper limit in the blend = $(E_H \times F_H)/1000$ g/kg

Active ingredient lower limit in the blend = $(E_L \times F_L)/1000$ g/kg

Example

WG formulation A, declared to contain active ingredient X at 20% (200 g/kg), is blended with WG formulation B, declared to contain active ingredient Y at 65% (650 g/kg). The declared ratio of formulations A:B in the blend is 70%:30% and therefore the declared contents of X and Y in the blend are 14% (140 g/kg) and 19.5% (195 g/kg), respectively.

Active ingredient X

- (i) From Section 4.3.2, the tolerance for active ingredient X in formulation A is $\pm 6\%$ (which is equal to ± 12 g/kg) and therefore its upper and lower limits in A are:

$$200 + 12 = 212 \text{ g/kg}$$

$$200 - 12 = 188 \text{ g/kg}$$

- (ii) Applying the values in Section 4.3.2 to the formulation instead of the active ingredient, the tolerance for formulation A in the blend is ± 25 g/kg ($\pm 3.6\%$) and therefore its upper and lower limits in the blend are:

$$700 + 25 = 725 \text{ g/kg}$$

$$700 - 25 = 675 \text{ g/kg}$$

- (iii) The upper and lower limits of active ingredient X in the blend are therefore:

$$(212 \times 725)/1000 = 153.7 \text{ g/kg}$$

$$(188 \times 675)/1000 = 126.9 \text{ g/kg}$$

Note. Without expansion, the tolerance for X at 140 g/kg in the blend would be $\pm 6\%$, implying upper and lower limits of 148.4 g/kg and 131.6 g/kg, respectively. The expanded tolerances do not represent plus and minus exactly the same percentage of the declared value.

Active ingredient Y

- (i) From Section 4.3.2, the tolerance for active ingredient Y in formulation B is ± 25 g/kg and therefore its upper and lower limits in B are:

$$650 + 25 = 675 \text{ g/kg}$$

$$650 - 25 = 625 \text{ g/kg}$$

- (ii) Applying the values in Section 4.3.2 to the formulation instead of the active ingredient, the tolerance for formulation B in the blend is $\pm 5\%$ (which is equal to ± 15 g/kg) and therefore its upper and lower limits in the blend are:

$$300 + 15 = 315 \text{ g/kg}$$

$$300 - 15 = 285 \text{ g/kg}$$

- (iii) The upper and lower limits of active ingredient Y in the blend are therefore:

$$(675 \times 315)/1000 = 212.6 \text{ g/kg}$$

$$(625 \times 285)/1000 = 178.1 \text{ g/kg}$$

Note. Without expansion, the tolerance for Y at 195 g/kg in the blend would be $\pm 6\%$, implying upper and lower limits of 206.7 g/kg and 183.3 g/kg, respectively. The expanded tolerances do not represent plus and minus exactly the same percentage of the declared value.

APPENDIX J

ANALYTICAL BRIDGING STUDIES FOR DETERMINATION OF THE CONTENT OF ACTIVE INGREDIENT IN TC, TK AND FORMULATED PRODUCTS

Introduction

In the context of this manual, the aim of an analytical bridging study is to demonstrate that an in-house analytical method for determination of the content of an active ingredient in technical material and formulated products leads to comparable results as a published, collaboratively validated method, e.g. by CIPAC, AOAC or equivalent. This is done by analyzing the same set of samples of TC, TK and/or formulated products using the collaboratively validated method and the in-house method and by doing statistical evaluation of the results.

This Appendix provides some guidance on analytical bridging studies, yet JMPS expects that a bridging study may lead to delays in evaluating and concluding on a proposer's data package by JMPS.

The data requirements for analytical methods in support of a draft specification or extension of a published specification are detailed in Sections 2.9 and 3.1 C of this manual.

Briefly,

- CIPAC (or AOAC International or equivalent) analytical methods, if available, have to be used and followed as close as possible in studies supporting FAO/WHO specifications because they are fully collaboratively tested or peer-validated.
- CIPAC methods for active ingredient and relevant impurities have to be used also for equivalence. A method validation according to, e.g. EU SANCO/3030 is not sufficient and does not fulfill the requirements of JMPS.
- For non-relevant impurities that are present in a specific TC, TK and/or formulated product a method validation is acceptable.

Parameter	Validation
Active ingredient content	CIPAC full method (provisional also accepted, but not draft)
Relevant impurities content	Peer-validated method e.g. through CIPAC
Non-relevant impurities	e.g. EU SANCO/3030
Physico-chemical properties	CIPAC MT method

If modifications of a CIPAC method were done by a proposer, the reason for deviations have to **be explained and justified** (e.g. use of methanol instead of acetonitrile in the HPLC mobile phase, use of nitrogen instead of helium as gas chromatography carrier gas, different stationary phase in HPLC, different concentrations in calibration solutions, use of another internal standard, etc.).

In case a CIPAC method was not available at the time of carrying out a study, an analytical bridging study is required. This Appendix describes how bridging studies must be carried out and what acceptance criteria are used by JMPS to evaluate the results of such studies.

Bridging studies for relevant impurities are deemed to be not acceptable by JMPS.

Requirements

- As a rule, 5-batch studies must be done using the CIPAC method for determination of the active ingredient content, if available. In case a CIPAC method is (not) yet available, an in-house method can be used.
- Nevertheless, the manufacturer has to apply as soon as possible with CIPAC for a collaborative validation, and after possible adoption, a bridging study is required as soon as the CIPAC method becomes available.
- The bridging study must be done as follows:
 - A minimum of same 3 batches have to be analysed by the CIPAC method and in-house method;
 - Analysis at 2 different days with 2 independent sample weightings, 2 independent calibrations.

Raw data on all weightings, dilutions and details of the method must be provided.

The statistical evaluation by JMPS will include:

- Comparison of RSD of CIPAC method and in-house method;
- Comparison of the r value (repeatability) of the CIPAC method and in-house method.

Based on that evaluation, a bridging study can be accepted or rejected by JMPS.

APPENDIX K

TIMETABLE, CONTENT OF EVALUATION REPORTS, AND COMMUNICATIONS BETWEEN FAO/WHO SECRETARIAT, PROPOSER, EVALUATOR, PEER REVIEWER AND EDITOR

When	Who	What
31 October	Proposer	Sending of the draft specifications and supporting documents to the FAO and/or WHO secretariat depending of the scope of use (agricultural, public health or both).
After 31 October	Evaluator	Evaluation of the data package according to the data requirements and the checklist for submission of application for development of FAO/WHO specifications (Section 3 and Appendix A of the FAO/WHO manual). Consultation with the toxicological experts for any question / clarification on the toxicological aspects.
31 December	Evaluator	Request for additional information if needed, to the secretariat.
28 February	Proposer	Provision of additional information requested.
30 April	Evaluator	Discussion on any open question.
30 April	Evaluator	<p>Sending of draft specifications and evaluation report to the peer reviewer (with copy to FAO/WHO secretariat).</p> <p><u>For new applications (new molecules)</u></p> <ul style="list-style-type: none"> • Specifications for TC/TK and/or formulations according to the appropriate templates with reference to CIPAC or any other reference method for each parameter and appropriate footnotes. • Recommendations: adoption (or not) of the specifications by FAO/WHO or adoption subject to fulfilment of certain conditions. • Appraisal containing the following points, as appropriate: <ul style="list-style-type: none"> – Introduction on the aim of the submission – Brief description of the active ingredient (chemistry, mode of action ...) – Reference to toxicological evaluations (FAO/WHO JMPR, JECFA, WHO IPCS ...), GHS hazard classification – Information on national registrations: certificate of registration or confirmation of comparability of confidential data submitted to FAO/WHO and a national country (letter of access) – Summary of physical-chemical properties of the active ingredient – Summary of non-confidential information from 5-batch analysis data (minimum purity, mass balance, relevant impurities, statistical justification of the manufacturing limits for active ingredients and impurities ...)

When	Who	What
		<ul style="list-style-type: none"> – Reference to CIPAC methods for active ingredient and relevant impurities in the TC/TK, brief information on method validation data in case the CIPAC methods were not used with bridging study with CIPAC methods – Brief summary of analytical methods for non-relevant impurities with information on validation data – Reference to hazard summaries – Reference to test methods for physical-chemical properties of the pure active ingredient – Brief information on the specifications for formulations with explanation for parameters and clauses which differs from the templates of the FAO/WHO Manual – Reference to CIPAC methods for physical-chemical properties of the formulations, as appropriate. • Supporting information: uses, identity of the active ingredient, physical-chemical properties of pure active ingredient, chemical composition and properties of the TC, hazard summary, formulations and co-formulated active ingredients, methods of analysis and testing, containers and packaging, expression of the active ingredient. • Annex 1: hazard summaries provided by the proposer: acute toxicity, irritation and sensitization, repeated administration (subacute to chronic toxicity), mutagenicity profile, ecotoxicology profile. • Annex 2: references (published and unpublished documents). <p><u>For extension to new formulation types</u></p> <ul style="list-style-type: none"> • Specifications for formulations according to the appropriate templates with reference to CIPAC or any other reference method for each parameter and appropriate footnotes. • Recommendations: adoption (or not) of the specifications by FAO/WHO or adoption subject to fulfilment of certain conditions. • Appraisal containing the following points, as appropriate: <ul style="list-style-type: none"> – Introduction on the aim of the submission – Brief summary of the existing FAO/WHO specifications for the active ingredient and other formulation types – Information on national registrations, if any – Reference to CIPAC methods for active ingredient and relevant impurities in the formulations and on method validation data in case the CIPAC methods were not used with bridging study with CIPAC methods, as appropriate – Brief information on the specifications for formulations with explanation for parameters and clauses which differs from the templates of the FAO/WHO Manual – Reference to CIPAC methods for physical-chemical properties of the formulations, as appropriate. • Supporting information: uses, formulations, methods of analysis and testing, containers and packaging, expression of the active ingredient.

When	Who	What
		<ul style="list-style-type: none"> • Annex 1: references (published and unpublished documents). <p><u>For equivalences (molecules and/or formulation types)</u></p> <ul style="list-style-type: none"> • Recommendations: adoption (or not) by FAO/WHO of the equivalence of TC/TK and/or formulations with the reference profile and adoption of the extension (or not) of the reference TC/TK and/or formulations specifications to the products of the second manufacturer, or adoption subject to fulfilment of certain conditions. • Appraisal containing the following points, as appropriate: <ul style="list-style-type: none"> – Introduction on the aim of the submission – Brief reference to the published FAO/WHO specifications for the active ingredient and/or formulations – Reference to any updated toxicological evaluations (FAO/WHO JMPR, JECFA, WHO IPCS ...), GHS hazard classification – Information on national registrations : certificate of registration or confirmation of comparability of confidential data submitted to FAO/WHO and a national country (letter of access) – Summary of non-confidential information from 5-batch analysis data (minimum purity, mass balance, relevant impurities, statistical justification of the manufacturing limits for active ingredients and impurities ...) and comparison with the reference specification (Tier-1) – Brief summary on the comparison of the synthetic process with this of the reference profile, maintaining the confidentiality of information – Brief summary on additional impurities in the new TC/TK evaluated by JMPS and conclusion on the assessment on the relevance or not of these additional impurities, as appropriate, maintaining the confidentiality of information – Reference to CIPAC methods for active ingredient and relevant impurities in the TC/TK, brief information on method validation data in case the CIPAC methods were not used with bridging study with CIPAC methods – Brief summary of analytical methods for non-relevant impurities with information on validation data – Brief summary of the mutagenicity profile (Tier-1) – Brief summary of additional toxicity studies with rationale, as appropriate (Tier-2) – Brief information on the specifications for formulations with explanation for parameters and clauses which comply or differs from those of the reference specifications – Reference to CIPAC methods for physical-chemical properties of the formulations, as appropriate – A brief summary of the updating of the CIPAC methods in the reference specifications.

When	Who	What
		<ul style="list-style-type: none"> Supporting information: chemical composition and properties of the TC, hazard summary (Tier-1 or Tier-2), formulations and co-formulated active ingredients, methods of analysis and testing, containers and packaging, expression of the active ingredient. Annex 1: hazard summaries provided by the proposer: mutagenicity profile (Tier-1), additional toxicity studies (Tier-2). Annex 2: references (published and unpublished documents). Equivalence assessment report: specification, manufacturing process, purity/impurity profile, 5-batch analysis data, mutagenicity profile (Tier-1), equivalence evaluation table, assessment of the proposed material by a competent registration authority, conclusion on Tier 1, additional toxicity studies, conclusion on Tier-2.
15 May	Peer reviewer	Sending of comments to the evaluator (with copy to FAO/WHO secretariat).
20 May	Evaluator	Sending of the updated draft specifications, evaluation report and equivalence assessment report, as appropriate, to the FAO/WHO secretariat, JMPS chair and co-chair including comments from the peer reviewer.
20 May	FAO/WHO secretariat	Sending of the updated draft specifications, evaluation report and equivalence assessment report, as appropriate, to the JMPS panel members.
1st week of June	JMPS	Discussion and decision on the draft specifications, evaluation report and equivalence assessment report, as appropriate, identification of eventual request of further information from the proposer (data requirements) and of clarifications needed by the evaluator (open points).
30 June	Rapporteurs	Sending of the draft Minutes of the JMPS Closed Meeting to FAO/WHO secretariat, chair, co-chair and all other panel members.
10 July	FAO/WHO secretariat and all panel members	Sending of the comments to the draft Minutes of the JMPS Closed Meeting to rapporteurs.
20 July	Rapporteurs	Finalisation of the Minutes of the JMPS Closed Meeting and sending to FAO/WHO secretariat, chair and co-chair.
30 July	FAO/WHO secretariat	Sending of the relevant part of the Minutes (summary of the JMPS discussions, data requirements, open points, recommendations) of the JMPS Closed Meeting to each individual proposer.
As soon as possible	Evaluator	Once all the data requirements and open points are fulfilled, sending of updated draft specifications and/or evaluation report (with supporting information and references) to the FAO/WHO secretariat and FAO/WHO editor (D0). The specifications should be completely finalized including footnotes. The evaluation report (recommendations, appraisal) should be as complete as possible and written in

When	Who	What
		good English in such a way that any reader can easily understand it without leading to any misinterpretation. The supporting information, hazard summaries and references have to be correctly written and formatted in order to avoid any loss of time by the FAO/WHO editor.
D0 + 1 month	FAO/WHO editor	Editing of the specification and evaluation report and sending to the FAO/WHO secretariat.
D0 + 1.5 month	FAO/WHO secretariat	Sending of the edited specification and evaluation report to the proposer for factual comments, omissions and errors (with copy to the FAO/WHO editor).
D0 + 2 months	Proposer	Sending of the comments to the FAO/WHO secretariat.
D0 + 2.5 months	FAO/WHO editor	Finalisation of the specifications and evaluation report.
D0 + 3 months	FAO/WHO secretariat	Publication of the final specifications and evaluation report on the FAO/WHO website.

APPENDIX L

EXAMPLES OF "IF REQUIRED" CLAUSES IN CERTAIN MODEL SPECIFICATIONS AND JUSTIFICATIONS FOR BEING ACTUALLY REQUIRED IN PARTICULAR PUBLISHED SPECIFICATIONS

Clause	Compound and Specification	Justification
Isomeric composition	Cyfluthrin TC	The ISO common name cyfluthrin does not provide a definition of the composition of diastereomers in cyfluthrin technical material, therefore the any other relevant clause "if required" applies.
Relevant impurities	Malathion TC, DP, EC, EW and UL	Relevant impurities are identified in certain technical materials only. There are 4 relevant impurities identified in malathion TC and formulated products. Therefore, the clause of by-products of manufacture or storage "if required" applies.
Description - stabilizer	Pirimiphos-methyl TC and formulated products	Pirimiphos-methyl technical material has limited stability against hydrolysis and oxidation. A stabilizer is added to minimize degradation of the TC and formulated products in storage. Therefore, the information provided in the description clause for a stabilizer "if required" applies.
Acidity	Pirimiphos-methyl TC	As detailed above, excess acidity carried over from the manufacturing process may adversely affect the stability of the TC. Therefore, the acidity clause "if required" in the TC applies.
Accelerated storage - relevant impurities, e.g. CS	Pirimiphos-methyl CS	The relevant impurities may increase in accelerated storage, as they are formed by degradation from the active ingredient. Therefore, a sub-clause in the accelerated storage is required to ensure that the limits set under clause 3 are still compliant.
Suspensibility	Thiamethoxam FS	The suspensibility clause is not required as the FS is just little diluted before use and the application concentration exceeds the upper limit of CIPAC MT 184.1 (approx. 10 % w/v).
Persistent foam	Thiamethoxam FS	The persistent foam clause is not required as the FS is just little diluted before use and the application concentration exceeds the upper limit of CIPAC MT 47.3.
Synergist content	Deltamethrin + piperonyl butoxide LN	Piperonyl butoxide is included in the LN as a synergist. Therefore, the clauses of synergist content "if required" applies.

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In 2001, the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) agreed to develop specifications for pesticides jointly, thus providing unique, robust and universally applicable standards for pesticide quality. This joint programme is based on a Memorandum of Understanding between the two Organizations. This 2021 second edition of the *Manual on development and use of FAO and WHO specifications for pesticides*, which is only available online, supersedes the March 2020 third revision of the first edition and previous manuals and guidance documents published by either FAO or WHO on this subject.

This Manual provides the standard process, unified requirements and procedures, harmonized definitions and nomenclature, technical guidelines and standards applicable to pesticides for use in agriculture and public health. FAO and WHO specifications for pesticides based on this manual are developed through the FAO/WHO Joint Meeting on Pesticide Specifications (JMPS) and published on the web sites of the two Organizations.

www.fao.org/pest-and-pesticide-management/guidelines-standards/faowho-joint-meeting-on-pesticide-specifications-jmps/en

and

<https://extranet.who.int/pqweb/vector-control-products/who-specifications-pesticides>

FAO/WHO specifications apply only to the products of manufacturers whose technical materials have been evaluated. The specifications may be used to provide an international point of reference against which the quality of products can be judged, either for regulatory purposes or in commercial dealings, thereby helping to prevent the trade, sale and use of inferior quality pesticide products. Thus, the specifications will enhance confidence in the purchase and use of pesticides, and at the same time contribute towards better pest control, sound agricultural production, effective vector control measures and improved user, public and environmental safety throughout the world, especially in developing countries.

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