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IDENTITY AND COMPOSITION DETERMINATION OF PLANT PROTECTION PRODUCTS IN THEIR QUALITY ASPECTS

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PESTICIDE SPECIFICATIONS

MANUAL ON DEVELOPMENT AND USE OF FAO AND WHO SPECIFICATIONS FOR PESTICIDES

March 2006 revision of the First Edition

WHO, FAO, Rome, 2006

Global standard of product quality → basic quality requirements → proper
manufacture, distribution, use, consumers, animals and environmental
protection



FAO Specifications are an important feature of the authorization Directives



FAO Specifications are a key element of harmonized pesticide registration
and quality control systems



PURPOSE AND USE OF SPECIFICATIONS

Specifications may be used:

- ❑ as a part of a sales contract (a buyer has a product of expected quality),
- ❑ by the competent national authority to check that the quality of a plant protection product on the market is the same as that registered → „post-registration” control

Specifications are „international point of reference”

not intended to replace national and international registration requirements

Important:

analysis and proper understanding of the relation between FAO Specifications and authorization regulations



CATEGORIES OF SPECIFICATION

JMPS – FAO /WHO Joint Meeting on Pesticide Specifications – international expert committee (statutory body of FAO)



recommendation to FAO /WHO on adoption, extension, modification or withdrawal of specifications

old

– to 2002

new

– since 2002 „new procedure” – described in the Manual for Development and use of FAO and WHO Specification for Pesticides – 2002 and rev. 2006

„new” specification consists of two parts:

Part One – The Specification

Part Two – The Evaluation Report – data provided by manufacturer according the Manual requirements

Two types of specifications: full and interim (incomplete validation)



IMPORTANT STATEMENT

**NEW SPECIFICATION DOES NOT APPLY TO SIMILAR PRODUCTS
OF OTHER MANUFACTURER**

nor to those where the active ingredient is produced by other routes of manufacture. FAO (by JMPS) has the possibility to extend the scope of the specifications to similar products but only when JMPS has been satisfied that the additional product is equivalent to that which formed the basis of the reference specification

EVALUATION OF:

- relevance of impurities
- assigning appropriate limits for relevant impurities
- determination of equivalence for technical grade active ingredients produced by different manufacturers or different methods of synthesis

EXAMPLE OF SPECIFICATION

(new)

FAO Specifications and Evaluations for FLUSILAZOLE

Part One:

- Flusilazole information
- Flusilazole technical material – 435/ TC (April 2008)
- Flusilazole Emulsifiable Concentrate
- Flusilazole Emulsion, Oil in water

Part Two:

Evaluations of Flusilazole

- 2007 FAO/WHO Evaluation Report on Flusilazole
- Supporting information
- Annex 1: Hazard summary provided by proposer
- Annex 2: References



ANNEX VI OF DIRECTIVE 91/414

Uniform Principles for evaluation and authorization of plant protection products

A. Introduction

B. Evaluation

C. Decision-making

B.2.6. Analytical methods

B.2.7. Physical and chemical properties

C.2.6. Analytical methods

C.2.7. Physical and chemical properties

B.2.6. Analytical methods – evaluation of the analytical methods for post registration control

Important: description of the nature and quantity of active substance in ppp and any toxicologically, ecotoxicologically or environmentally significant impurities and co-formulants



ANNEX VI OF DIRECTIVE 91/414 (cont'd)

B.2.7. Physical and chemical properties

Evaluation of phys-chem properties of ppp in particular:

- where FAO Specification exists – properties addressed in that Specification
- where no Specification exists – all relevant properties as referred in the Manual ...

C.2.6. Analytical methods

- methods must reflect „state of art” validation
- methods must be able to determine a.i. and significant impurities

C.2.6. Physical and chemical properties

- where Specification exists – that must be met
- where no Specification exists:
 - chemical properties during guarantee period of ppp for a.i. must not exceed values according the table
 - physical properties must comply with the Manual ... for relevant formulation type



TABLE OF TOLERANCES of A.I. (Annex VI of 91/414)

Declared content in g/kg or g/l at 20 C	Tolerance
up to 25	± 15% homogenous formulation
	± 25% non-homogenous formulation
more than 25 up to 100	± 10%
more than 100 up to 250	± 6%
more than 250 up to 500	± 5%
more than 500	± 25 g/kg or ± 25 g/l



TECHNICAL SPECIFICATION

(Annex II and III of 91/414)

- for active ingredient
- for plant protection product

Identity of the active substance and ppp

a.i.

ppp

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·

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- method of manufacture (synthesis)
- specification of purity
- identity of isomers, impurities, additives

- detailed quantitative and qualitative information on the composition of the product (active substances, impurities adjuvants, inert components)



DATA FOR IDENTITY

- ❑ Complete manufacturing process, including all raw materials, reagents and solvents,
- ❑ Complete impurity profile for all impurities present at 1 g/kg or greater
Maximum limits for impurities present at 1 g/kg or greater
- ❑ Five batch analysis of typical manufacturing lots, supporting the impurity limits

(FAO Pesticides Specifications Procedure)



METHODS OF ANALYSIS

European Commission main document: SANCO/3030/99 rev. 4 (11/07/00)

(Working document)

Title: Technical Material and Preparations:

Guidance for generating and reporting methods of analysis in support of pre and post-registration data requirements

To generate Annex II and III data for:

- authorization
- post registration control
- monitoring



robust, accurate, precise analytical methods are required for:

- active substance in technical material
- formulated products



METHODS OF ANALYSIS (cont'd)

- ❑ **problem of validation**
 - **methods must be validated for a.i. determination and for specific formulation**
 - **only for methods where the collaborative study is done validation is not required (CIPAC or AOAC standard methods)**
- ❑ **full method description is required**
- ❑ **confirmation of identification (a.i., impurities) techniques; spectroscopic and highly specific methods as LC-MS, GC-MS, HPLC-UV-DAD**
- ❑ **GLP, Accreditation (ISO 17025) – requirements for laboratories (Guidelines for National Laboratories – Quality control of pesticide products – CIPAC, FAO, 2005)**



EQUIVALENCE

FAO definition: 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

EC Document: Sanco/ 2003 – rev. 0 March 2003

Guidance document on the assessment of the equivalence of technical materials of substances regulated under council Directive 91/414/EEC



EQUIVALENCE (cont'd)

There are several cases for which evaluation of equivalence of technical materials is required:

- 1) During the evaluation process for inclusion of a.s. in Annex I for sources other than those for which a complete dossier has been submitted**
- 2) After Annex I inclusion, when data from large scale production are available and must be compared with the data from a pilot scale production originally evaluated in the context of Annex I inclusion**
- 3) After Annex I inclusion when a change in the manufacturing plant and/or location occurs**
- 4) After Annex I inclusion when a change in the manufacturing process occurs and**
- 5) After Annex I inclusion when new sources, other than those originally evaluated in the context of Annex I inclusion, are applying for registration at MS level**



EQUIVALENCE (cont'd)

Good basis for evaluation of equivalence:

**Manual on development and use FAO and WHO Specifications for pesticides
(2006) – position 3.2. E, F**



detailed description of the procedure

most important: equivalence of a.i. (technical grade)

For formulated products: **formulations are generally considered to be equivalent if a.i. is assessed as equivalent and the formulations comply with the same specification**



CONCLUSIONS

- 1) FAO Specifications and Manual (2005) are key elements of harmonized procedures for pesticide authorization and post-registration control as „international point of reference”.**
- 2) FAO Specifications do not apply to similar products of other manufacturers.**
- 3) Evaluation of relevance of impurities in technical active ingredient and assigning their limits is needed.**
- 4) Determination of equivalence is obligatory.**
- 5) There is a need of proper understanding of the term „identity” of plant protection products.**
- 6) Proper methods of analysis and proper laboratory facilities are required.**
- 7) Detailed determination of identity is required in the cases of parallel import control and analysis of illegal and counterfeit products.**
- 8) It is necessary to exchange information among the countries on the irregularities detected in the process of post-registration control.**

