CHAPTER 8

USE OF JMPR RECOMMENDATIONS BY REGULATORY AUTHORITIES

CONTENTS

8.1 INTRODUCTION

The evaluations and appraisals of the compounds are, in most cases, based on unpublished proprietary data submitted for the purpose of the JMPR assessment. In this context the JMPR documents are a unique source of information. Regulatory authorities and other interested specialists are encouraged to make use of the critical evaluations of the JMPR.

8.2 SAFETY ASSESSMENT OF PESTICIDES

The JMPR monographs and reports should be of help to FAO and WHO Member States in the safety assessment of pesticides and their residues. However, two major problems can be encountered when a Member State attempts to use these assessments: (1) the JMPR assesses the toxicology of active ingredients and not formulations, which are controlled at the national level, and (2) relationships between the purity and specifications of the active ingredients involved in the tests evaluated by the JMPR and the technical materials of commerce are often unknown.

The purity of technical active ingredient depends on, among others, the route and conditions of synthesis, the purity of raw materials used for the manufacture, and the packing and storage conditions. The toxicity of certain impurities can be several magnitudes higher than that of the active ingredient, and therefore their presence even in very small concentrations may substantially affect the toxicity of the pesticide product.

The Joint Meeting evaluates toxicological studies on test materials that in most cases correspond to active ingredients that are sold by the companies which provided the data. The purity and specifications of active ingredients that national regulatory authorities are asked to approve may or may not correspond to those that were tested and summarized in the JMPR monographs. For this reason, national registration authorities should carefully consider the extent of similarity between any active ingredient being considered for registration and the technical material assessed by the Joint Meeting. To be able to make this determination, registration authorities should seek information on manufacturing impurities in pesticide products, as emphasised in the *FAO International Code of Conduct on the Distribution and Use of Pesticides* (Sections 6.2.2 and 6.2.3)[63]. The safety of other components of formulations should also be considered when registering pesticides. For these reasons the JMPR does not

[63] FAO International Code of Conduct on the Distribution and Use of Pesticides http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/code/en/

recommend use of JMPR Evaluations as the sole basis for safety assessment for national registrations.

If the evaluations are used for registration purposes, authorities should use documentation provided by manufacturers in accordance with national laws relating to the submission and use of unpublished proprietary data to ensure that the JMPR evaluations are of pesticides manufactured by the same routes, of comparable purity and with similar impurities to the pesticides that are being registered.

8.2.1 Relevance of pesticide specifications for JMPR evaluations

The 2006 edition of the FAO Manual on the development and use of FAO specifications for plant protection products[64] provide an outline of the current procedure for data evaluation. Under this new procedure the data requirements were expanded dramatically. FAO in co-operation with WHO now evaluates, in confidence, the physico-chemical properties, the impurity, toxicological and ecotoxicological profiles of technical materials. The evaluations ensure that specifications include all relevant impurities. These impurities, following the definition in the FAO-Manual on specifications, are those by-products of the manufacture or storage of a pesticide which, compared with the active ingredient, are toxicologically significant to health or the environment, are phytotoxic to treated plants, cause taint in food crops, affect the stability of the pesticide, or cause any other adverse effect. Besides the assessment of the toxicological, ecotoxicological and impurity profile data by WHO, the FAO also seeks access to registration data from competent authorities to assess whether:

(i) the technical material, for which an FAO specification is proposed, is equivalent to that registered by the authority, as assessed by a comparison between the data submitted to FAO and those submitted for registration; or

(ii) their decision that technical materials from different manufacturers are equivalent was based on data similar to those provided to FAO.

FAO specifications apply now only to products for which the technical materials produced by each manufacturer have been evaluated by these organisations. This is a radical change because, under the previous procedure, the FAO specification could be taken to apply to any notionally similar product. To take account of this change, the new procedure also defines the process for the determination of equivalence (similarity) of technical pesticides, so that an FAO specification can be extended to truly equivalent products.

The new procedure, including the definition of equivalence, was developed to enhance product quality, to improve pesticide user and consumer protection as well as to reduce unwanted effects on the environment. This procedure is now widely accepted by both research companies and manufacturers of generic compounds.

The data submissions to the Joint FAO/WHO Meeting on Pesticide Specifications (JMPS) are coordinated with JMPR evaluations, however it should be noted that JMPS itself does not serve Codex directly.

[64] Manual on development and use of FAO and WHO specifications for pesticides. February 2006 Revision of First Edition. FAO Plant Production and Protection Paper. Revised. www.fao.org/ag/AGP/AGPP/Pesticid/Default.htm

8.3 RESIDUE STUDIES AND RECOMMENDED MRLs

The information relating to pesticide residues, e.g., results of supervised trials, metabolism, animal transfer and processing studies, can be used more generally than the safety assessments of pesticides.

The comparability of the trial conditions discussed in detail in Chapters 5 and 6 should be assessed for deciding on the applicability of JMPR conclusions and recommendations for the particular national use conditions.

Codex MRLs are intended to be used primarily to enforce and control compliance with nationally authorized uses of pesticides on commodities moving in international trade. The applicability of Codex MRLs for national use, depends on the relation of GAP on which the maximum residue level estimates were based to the national GAP. In making decisions on comparability of national use conditions to the trial conditions described in the monographs, the results of a few supervised trials carried out under typical growing conditions of the country can be of great value.

In accordance with the principles of *FAO International Code of Conduct on the Distribution and Use of Pesticides*, governments "should promote the use of safe, efficient and cost effective application methods" in order to reduce the exposure of consumers and the environment resulting from the use of pesticides. When the national use conditions lead to substantially lower residues than the Codex MRL, the establishment of lower national MRLs may be considered for enforcing domestic uses since higher MRLs would encourage unauthorized use of the pesticide, which is against the principle of GAP. However, for imported commodities the national authorities have an obligation to accept higher Codex MRLs which afford an acceptable level of consumer protection, in accordance with the provisions laid down in the Sanitary and Phytosanitary (SPS) agreement of the Uruguay Round of GATT (General Agreements on Tariffs and Trade).

8.4 INTERPRETATION OF RESIDUE ANALYTICAL RESULTS IN COMPARISON WITH MRLs

A question frequently asked is whether the Codex MRLs, which are based on the limits recommended by the JMPR, should be considered either as strict limits or with the allowance of a further margin when considering the analysis of samples for enforcement purposes.

By definition an MRL is a limit not to be exceeded. The burden of proof is on the monitoring authority to establish, with a high degree of assurance, whether the residue in the lot being examined exceeds the MRL, in order to take any regulatory actions.

The uncertainty of the analytical results (S_R) deriving from the random variation of the consecutive procedures comprises the uncertainties of sampling (S_S), sample preparation (S_{Sp}) and analysis (S_A).

$$(S_R) = \sqrt{[(S_S)^2 + (S_{Sp})^2 + (S_A)^2]}$$

Since the average residue is the same the equation can be written as:

$$(CV_R) = \sqrt{[(CV_S)^2 + (CV_{Sp})^2 + (CV_A)^2]}$$

The uncertainty of the final analytical result (CV_R) cannot be smaller than that of any step of its measurement.

Based on the evaluation of large number of residue data, the average sampling uncertainty following the Codex sampling procedure was estimated[65] to be:

- small and medium size crops (unit mass ≤ 250g, minimum sample size =10): 25%
- large crops (unit mass > 250 g, minimum sample size = 5): 33%
- Brassica leafy vegetables (unit mass > 250 g, minimum sample size = 5): 20%.

The Codex Committee on Pesticide Residues[66] is currently working on a revision of the Guidelines on the estimation of uncertainty of results for the determination of pesticide residues (CAC/GL 59-2006), taking into account the general Codex criteria for acceptable precision and trueness of the residue data. Both parameters should be considered when the measurement results are interpreted.

International collaborative studies revealed that, in the comparison of an analytical result with the MRL, trueness (influenced by mainly systematic errors) is more important than precision, i.e., random errors.

In order to obtain reliable results, the laboratories performing regulatory enforcement analysis are encouraged to:

- establish internal quality control measures which enable them to assess the within laboratory variation of results
- participate in international sample check programmes to assess the accuracy of their analysis
- pay attention to information on storage stability of residues and the definition of residues
- strictly adhere to Codex guidelines for preparing the portion of commodity for analysis
- validate the sampling procedures used for obtaining samples, and ensure proper training of sampling officers.

The same precautions should be applied in performing supervised trials or selective surveys to provide data for estimating maximum residue levels.

[65] Ambrus, A. & Soboleva, E. (2004) JAOAC International. 87, 1368-1379

[66] Report of the Forty-first Session of the Codex Committee on Pesticide Residues, B*eijing, China, 20 – 25 April 2009, http://www.codexalimentarius.net/download/standards*