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EVALUATION OF CERTAIN FOOD ADDITIVES AND CONTAMINANTS

Sixty-first report of the
Joint FAO/WHO Expert Committee on
Food Additives

World Health Organization
Geneva

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the World Health Organization or of the Food and Agriculture Organization of the United Nations

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Rome, 10–19 June 2003

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Monographs containing summaries of relevant data and toxicological evaluations are available from WHO under the title:

Safety evaluation of certain food additives and contaminants. WHO Food Additive Series, No. 52, in press.

Specifications are issued separately by FAO under the title:

Compendium of food additive specifications, Addendum 11. FAO Food and Nutrition Paper, No. 52, Add. 11, 2003.

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

The preparatory work for toxicological evaluations of food additives and contaminants by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) is actively supported by certain of the Member States that contribute to the work of the International Programme On Chemical Safety (IPCS).

The IPCS is a joint venture of the United Nations Environment Programme, the International Labour Organization and the World Health Organization. One of the main objectives of the IPCS is to carry out and disseminate evaluations of the effects of chemicals on human health and the quality of the environment.

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1. Introduction

The Joint FAO/WHO Expert Committee on Food Additives met in Rome from 10 to 19 June 2003. The meeting was opened by Mr H. de Haen, Assistant Director-General, FAO, on behalf of the Directors-General of the Food and Agriculture Organization of the United Nations and the World Health Organization. Mr de Haen made reference to the recently completed evaluation of the work of the Joint FAO/WHO Food Standards Programme (Codex Alimentarius Commission) and of this Committee and other joint FAO/WHO activities in providing scientific advice to Member countries. He noted that at the forthcoming twenty-sixth session of the Codex Alimentarius Commission, FAO and WHO would report on steps underway to improve the work of the scientific expert committees and ad hoc consultations that provide scientific advice to Codex committees and to FAO/WHO Member countries. FAO and WHO were committed to increasing efforts and resources to improve the provision of this advice; within FAO, a significant increase of staff and non-staff resources was being negociated for the forthcoming years.

2. General considerations

As a result of the recommendations of the first Joint FAO/WHO Conference on Food Additives, held in September 1955 *(1)*, there have been sixty previous meetings of the Expert Committee (Annex 1). The present meeting was convened on the basis of the recommendation made at the fifty-ninth meeting (Annex 1, reference *160*).

The tasks before the Committee were:

— to elaborate further principles for evaluating the safety of food additives and contaminants (section 2);
— to undertake toxicological evaluations of certain food additives, flavouring agents and contaminants (sections 3, 4 and 7, and Annex 2);
— to review and prepare specifications for selected food additives and flavouring agents (sections 3 and 4, and Annex 2);
— to undertake a toxicological evaluation of a nutritional source of iron (section 5); and
— to undertake a toxicological evaluation of a disinfectant for drinking-water (section 6).

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2.1 Modification of the agenda

Flavouring agents Nos 909, 919 and 925 were removed from the agenda because the data necessary to establish full specifications were not available.

2.2 Principles governing the toxicological evaluation of compounds on the agenda

In making recommendations on the safety of food additives and contaminants, the Committee took into consideration the principles established and contained in Environmental Health Criteria, No. 70 (EHC 70), Principles for the safety assessment of food additives and contaminants in food (Annex 1, reference *76*), as well as the principles elaborated subsequently at a number of its meetings (Annex 1, references *77*, *83*, *88*, *94*, *101*, *107*, *116*, *122*, *131*, *137*, *143*, *149*, *152* and *154*), including the present one. Environmental Health Criteria, No. 70, contains the most important observations, comments and recommendations made, up to the time of its publication, by the Committee and associated bodies in their reports on the safety assessment of food additives and contaminants.

2.2.1 *Chemical and technical assessments of food additives*

At previous meetings, the Committee had access to documents called *Technical Data Sheets*, which were prepared for new or existing food additives and which were not published because the detailed information on manufacturing processes described therein could be commercially sensitive. These documents, however, also contain valuable information, which was not made public, on chemical and technological aspects of the compounds under discussion. At the fifty-ninth meeting (Annex 1, reference *160*), the Committee recommended that these documents should include comprehensive information on technological use levels for foods, which should also form the basis for intake assessment. Furthermore, the importance of specifications as an integral part of the risk assessment of food additives was stressed.

Taking these recommendations into consideration, the Secretariat has adapted the format and structure of the *Technical Data Sheet* and renamed it the *Chemical and Technical Assessment* (CTA), with the intention of making this document publicly available. The CTA reflects and emphasizes the role that chemical characterization plays in the risk assessment of food additives. The document is prepared by an expert assigned before the meeting and is intended to provide to the Committee the basic information regarding the identity, purity and use of the food additive, as related to its risk assessment.

The drafting expert responsible for preparing a CTA is asked to identify those sections of a confidential nature and the Secretariat will ensure that they are removed before publication. The CTAs will be available via the FAO JECFA website; it is not anticipated that they will be published in printed form.

At its present meeting, the Committee reviewed the first set of CTA for certain food additives and provided feedback to the Secretariat on the *FAO guidelines on the structure and content of the document called "Chemical and Technical Assessment (CTA)*[1]".

2.2.2 *Safety evaluation of flavouring agents*

Working definition of "flavouring agent"

At its fifty-ninth meeting, the Committee recognized the need for a working definition of the term "flavouring agent" and recommended that such a definition be agreed at a future meeting. At its present meeting, the Committee noted that a range of regulatory definitions of "flavouring" and similar terms exist in different countries and concluded that any definition would need to be elaborated in an international forum, such as the Codex Alimentarius Commission.

The Committee re-iterated the criteria that need to be met for an individual flavouring agent to be evaluated by the existing Procedure for the Safety Evaluation of Flavouring Agents:

- The substance should be chemically defined, such that at least 95% of the commercially used material consists either of the named chemical, or of the named chemical and identified secondary constituents.
- The substance is added to food for flavouring purposes, including the generation of active flavouring substances during storage or processing of the food.
- There is a valid estimate of current exposure to the named substance and, if appropriate, its breakdown or reaction products.

Some substances that have a use as flavouring agents may have been evaluated previously by the Committee in relation to other food additive functions. The use of such a substance, or its breakdown or reaction products, as a flavouring agent is included in the relevant, previously-established ADI.

[1] FAO guidelines on the structure and content of the document called "Chemical and Technical Assessment (CTA)": http://www.fao.org/es/ESN/jecfa/guidelines1_en.stm

Consideration of flavouring agents with high intakes, evaluated by the "B-side" of the Procedure for the Safety Evaluation of Flavouring Agents

At the present meeting, two flavouring agents, dihydrocoumarin (No. 1171) and 6-methylcoumarin (No. 1172) that were evaluated by the Procedure for the Safety Evaluation of Flavouring Agents could not be predicted to be metabolized to innocuous end products (step B2) and their intake exceeded the human intake threshold for their structural class (step B3). In application of the Procedure, more extensive data on the toxicity of these substances are required in order to complete their evaluation. In considering such substances, the Committee noted that the data required would include studies of metabolism and toxicity of the substance, and that refined estimates of intake might additionally be needed. Data on structurally related substances could also be used to support the evaluation. These studies would need to be of sufficient quality and duration to enable the flavouring agent to be evaluated at its specified intake.

The Committee noted that flavouring agents for which more extensive data were required should be clearly identified in the report of the meeting and that a complete description of the evaluation of such flavouring agents should be provided in the report item and the monograph. The Committee recommended that the guidelines for the preparation of monographs for flavouring agents be revised to ensure that a consistent approach is applied to the evaluation of such substances.

Safety evaluation of natural flavouring complexes

At its present meeting, the Committee considered a working paper outlining a revision to the safety evaluation of flavouring agents to accommodate the safety evaluation of natural flavourings that are complex mixtures (natural flavouring complexes). These flavourings are obtained from a single source material by physical processes such as distillation, or extraction with water or organic solvents. Many natural flavouring complexes consist of mixtures of individual flavouring agents, several of which have been evaluated previously by the Committee. The revised Procedure builds on the Procedure for the Safety Evaluation of Flavouring Agents (Annex 1, reference *131*), organizing the components of a natural flavouring complex into congeneric groups, which become the focus of the safety evaluation. The steps in the existing Procedure have been modified to accommodate the evaluation of congeneric groups and provide for an overall evaluation of the natural flavouring complex.

In considering the revised Procedure, the Committee noted that several hundred natural flavouring complexes are currently in commercial use. These include essential oils, which are relatively well characterized in terms of their chemical composition, as well as extracts and oleoresins, some of which are currently less well characterized. Since compositional data are required to complete a safety evaluation by the revised Procedure, the Committee noted that further modification of the Procedure could be required for natural flavouring complexes that cannot be well characterized in terms of their composition.

The Committee concluded that the revised Procedure provides a potentially efficient way of evaluating natural flavouring complexes that are well characterized, such as essential oils. To determine the applicability of the revisions, the Committee recommended that a small number of natural flavouring complexes be evaluated by the revised Procedure at a future meeting.

The Committee noted that numerous products from different geographical regions are used as flavouring complexes, and the importance of ensuring that an inventory of commercial products be compiled was stressed. The Committee considered that it was necessary to take account of the range of composition of natural flavouring complexes across all regions.

The Committee was aware that different organizations have different approaches to the establishment of specifications for natural flavouring complexes. The Committee also noted that criteria would need to be developed to elaborate specifications for natural flavouring complexes.

Intake data on flavouring agents

The Committee discussed the data requirements for substances to be evaluated by the Procedure for the Safety Evaluation of Flavouring Agents. For those substances with current usage in food, poundages used for intake assessments should be reported using no more than two significant figures. Flavouring agents without reported poundage data will not be evaluated by the Committee.

2.3 Joint FAO/WHO Project to Update the Principles and Methods for the Risk Assessment of Chemicals in Food

The Committee was informed about the progress of this Project and recognized its importance. The Committee noted that several issues being considered by this Project were of particular relevance to some of their present evaluations:

— dose–response modelling of endpoints, both carcinogenic and non-carcinogenic, which cannot be assigned a threshold;
— probabilistic modelling for estimation of intake;
— biomarkers of effect and their relationships to disease outcome;
— relevance of reversible, non-progressive, treatment-related effects;
— longer tolerable intake periods, e.g. provisional tolerable monthly intake (PTMI), for contaminants with longer biological half-lives;
— revision of the approach to the safety evaluation of flavouring agents, in order to accommodate natural flavours;
— approaches for the development of specifications for complex mixtures, particularly those of natural origin.

2.4 Provision of scientific advice by FAO and WHO

The Committee was informed about a consultative process initiated by FAO and WHO, which would consider the provision of scientific advice by both organizations to the Codex Alimentarius Commission and to Member countries.

Such advice may be elaborated by committees, such as JECFA, ad hoc consultations or consultants. This consultative process is designed to improve the scientific advice provided with regard to quality, independence, integrity, transparency, timeliness, efficiency and sustainability. The outcome of the process would be a set of recommendations, addressed to the Directors-General of FAO and WHO, for the development of a consistent, harmonized and flexible overarching framework (an "umbrella"), which is realistic, feasible and acceptable to all stakeholders.

The Committee noted that this exercise would take into consideration and build upon the experience of and the improvements already being implemented by the Secretariat of this Committee.

The Committee was informed that Maria Lourdes Costarrica (FAO) and Wim van Eck (WHO) were responsible for the coordination of this consultative process.

2.5 Food additive specifications

2.5.1 Compendium of Food Additive Specifications *and* Guide to Specifications

At its forty-sixth and fifty-fifth meetings, the Committee had recommended the revision of the *Compendium of Food Additive Specifications* (Annex 1, reference *96*) and the *Guide to Specifications* (Annex 1, reference *100*). At the present meeting, the Secretariat presented a project that had been proposed recently to FAO, with the following objectives:

- The current edition of the *Guide to Specifications* will be updated and published together with a consolidated edition of the *Compendium of Food Additive Specifications* as one document in two volumes.
- The update shall reflect state-of-the-art analytical methodologies and practice by regulators and industry. These methods should also respect the fact that they are applied by laboratories in developing and developed countries with varying levels of equipment and expertise.
- The update shall consider the general guidelines laid out by this Committee and the Joint FAO/WHO Conference on Food Additives (summarized in EHC 70) and the work of other relevant standard-setting bodies
- The update shall be available in print and electronically.

Depending on the availability of funds, the project will start during 2003 and will terminate in 2005.

2.5.2 *Residual solvents*

Several of the specifications for food additives under review at the present meeting include limits for residual solvents. In some cases, the methods of analysis to be used are included in the specifications and in others reference is made to the General Method included in the *Guide to Specifications*, FNP 5 (Annex 1, reference *100*). The Committee noted that the General Method described in FNP 5 refers to obsolete gas chromatographs with packed columns, and that it may be difficult to obtain such chromatographs, since injectors for packed columns are no longer available.

It was also noted that a variety of gas chromatographic methods for the determination of residual solvents were included in the specifications. The Committee concluded that specifications containing limits for residual solvents should refer to the same General Method in FNP 5 wherever possible. The Committee recommended that FNP 5 be revised to include modern methodology.

At its present meeting, the Committee formulated a general method of analysis for residual solvents, using head-space gas chromatography with flame ionization detection (FID). This method is to be published in Section E of FNP 52, Add 11.

2.5.3 *Specifications of purity for flavouring agents*

The Committee agreed to replace the now outdated Council of Europe numbers with the recently introduced European Commission "FLAVIS database" numbers.

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