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EVALUATION OF CERTAIN FOOD ADDITIVES

**Some Food Colours, Thickening Agents,
Smoke Condensates, and Certain Other Substances**

**Nineteenth Report
of the Joint FAO/WHO Expert Committee
on Food Additives**



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Toxicological evaluation of some food colours, thickening agents, and certain other substances

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WHO Food Additives Series No. 8

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CONTENTS

	Page
1. Introduction	5
2. General considerations	6
2.1 The importance of food additives	6
2.2 General principles for establishing acceptable daily intakes (ADI)	6
2.3 General considerations for establishing and revising specifications	7
2.4 Impurities or transformation products of intentional and unintentional food additives	10
2.5 Smoke, smoke condensates, and liquid smoke	11
3. Revision of certain specifications	12
4. Comments on particular substances	13
4.1 Food colours	13
4.2 Thickening agents	14
4.3 Smoke condensates and liquid smoke	15
4.4 Miscellaneous	15
5. Future work	16
6. Recommendations to FAO and WHO	17
Annex 1. Reports and other documents resulting from previous meetings of the Joint FAO/WHO Expert Committee on Food Additives	18
Annex 2. Acceptable daily intakes and information on specifications	21
Annex 3. Further toxicological studies and information required	23

JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

Geneva, 14-23 April 1975

Members invited by FAO

- Mr D. F. Dodgen, Director, Food Chemicals Codex, National Academy of Sciences, Washington, DC, USA
- Mr A. W. Hubbard, Head, Food Science Division, Ministry of Agriculture, Fisheries and Food, London, England (*Vice-Chairman*)
- Dr K. Kojima, Director, Laboratory for Medicinal Plants, National Institute of Hygienic Sciences, Tokyo, Japan
- Mr A. J. Schmitz, Jr., Director, Quality Control and Assurance, Pfizer, Inc., New York, NY, USA
- Dr P. L. Schuller, Head, Laboratory for Chemical Analysis of Foodstuffs, National Institute of Public Health, Bilthoven, Netherlands

Members invited by WHO

- Dr F. Berglund, Aktiebolaget KABI, Stockholm, Sweden (*Rapporteur*)
- Professor I. A. Karpljuk, Head, Department of Hygiene of Nutrition, Central Institute of Postgraduate Training, Moscow, USSR
- Dr P. Shubik, Director, Eppley Institute for Research in Cancer, University of Nebraska Medical Center, Omaha, NE, USA (*Chairman*)
- Professor R. Truhaut, Director, Toxicological Research Centre, Department of Pharmaceutical and Biological Sciences, René Descartes University, Paris, France
- Dr A. Wolf, Research Centre for Food Hygiene and Human Nutrition, Institute of Hygiene, Prague, Czechoslovakia
- Professor G. Zbinden, Institute of Pathological Anatomy, University of Zurich, Zurich, Switzerland

Observers (invited by FAO)

- Dr R. Marcuse, Chairman, Food Section, IUPAC, Swedish Institute for Food Preservation Research, Göteborg, Sweden
- Dr G. F. Wilmink, Chairman, Codex Committee on Food Additives, Ministry of Agriculture and Fisheries, The Hague, Netherlands

Secretariat

- Dr H. Blumenthal, Acting Director, Division of Toxicology, Bureau of Foods, Food and Drug Administration, Washington DC, USA (*Temporary Adviser*)
- Miss S. Edstam, Food Standards and Food Science Service, Food Policy and Nutrition Division, FAO, Rome, Italy
- Dr P. S. Elias, Principal Medical Officer, Department of Health and Social Security, London, England (*Temporary Adviser*)
- Dr K. O. Herz, Nutrition Officer, Food Standards and Food Science Service, Food Policy and Nutrition Division, FAO, Rome, Italy (*Joint Secretary*)
- Dr F. C. Lu, Chief, Food Additives, WHO, Geneva, Switzerland (*Joint Secretary*)
- Dr G. Vettorazzi, Scientist, Food Additives, WHO, Geneva, Switzerland

EVALUATION OF CERTAIN FOOD ADDITIVES

Nineteenth Report of the Joint FAO/WHO Expert Committee on Food Additives

The Joint FAO/WHO Expert Committee on Food Additives met in Geneva from 14 to 23 April 1975. The meeting was opened by Dr A. S. Pavlov, Assistant Director-General, WHO, on behalf of the Directors-General of the Food and Agriculture Organization of the United Nations and of the World Health Organization. Dr Pavlov, in his opening remarks, stressed the increasing need for food, especially processed food, in the world. Processed food can be transported and distributed for consumption by the ever-growing urban populations as well as in those parts of the world where nutritional deficiencies exist. In addition, the consumer desires food that is palatable, attractive, and convenient to serve. To fulfil these various requirements, different classes of food additives have been developed and utilized by the industry.

Aware of the trend, the consumer demands more assurance that these additives be properly and adequately tested for safety. A wide variety of testing procedures are therefore generally employed. To evaluate these diverse types of findings, collected throughout the world, an international multidisciplinary team such as the Joint FAO/WHO Expert Committee on Food Additives is essential. In addition, for technological and public health considerations, it is also necessary to ensure the identity and purity of these additives. The previous reports of the Committee have been important guides for health and food authorities as well as for industry.

1. INTRODUCTION

As a result of the recommendation of the first Joint FAO/WHO Conference on Food Additives held in September 1955^a there have been 18 previous meetings of the Joint FAO/WHO Expert Committee on Food Additives (see Annex 1). The present meeting was convened on the recommendation made in the eighteenth report^b. Its terms of reference were :

^a FAO Nutrition Meetings Report Series, No. 11, 1956 ; WHO Technical Report Series, No. 107, 1956.

^b See Annex 1, ref. 34.

(1) to prepare specifications and carry out the toxicological evaluation of certain food additives; (2) to review and adopt general principles and methods for specifications; (3) to revise the specifications for certain food additives; and (4) to undertake the toxicological re-evaluation of certain food additives.

2. GENERAL CONSIDERATIONS

2.1 The importance of food additives

The Committee concurred with the opening statement made by the Assistant Director-General of WHO concerning the need for processed foods and for food additives in the handling, preservation, and distribution of foods in the world. The continuing increase in the world population without a comparable increase in the available amount of conventional foodstuffs must stimulate further efforts to develop new sources of food. In addition to ensuring the safety of these new foods, there is also a need to ensure their palatability and acceptability to consumers and food additives will thus be required for the purposes of preserving, texturizing, flavouring, and colouring them. Therefore, the work of this Committee can be looked upon as a means of ensuring wholesome nutritious foods for the present and future generations.

The Committee was aware of the increasing interest of the consumer in the safety and wholesomeness of foods and, consequently, in the work of the Committee. There is therefore a need for wider distribution of information to the public on the nature, benefits, and safety evaluation of food additives.

2.2 General principles for establishing acceptable daily intakes (ADI)

The Committee reiterated its practice of following the principles stated in its previous reports (see Annex 1) and in the reports of a WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives^a and a WHO Scientific Group on the Assessment of the Carcinogenicity and Mutagenicity of Chemicals.^b In addition, it reaffirmed the need to take advantage of recent developments in toxicological techniques, as expressed in the seventeenth report of the Committee.^c

Since toxicology is an evolving multidisciplinary science, the Committee felt it important to repeat at this time that toxicologists should be aware of new developments in the relevant disciplines and endeavour to employ these

^a WHO Technical Report Series, No. 348, 1967.

^b WHO Technical Report Series, No. 546, 1974.

^c See Annex 1, ref. 32.

to provide for a better assessment of safety. Substances with established ADIs must therefore be re-evaluated as new information relevant to the safety of additives becomes available.

For several substances the Committee established a "temporary ADI". In doing so, it specified the further work required to be completed by a specified date. The conditions relating to a temporary ADI, as expressed in the seventeenth report,^a are quoted as follows :

An ADI may be allocated temporarily, pending the provision of additional data within a stated period of time. This measure implies that the toxicological data are adequate to ensure the safety in use of the additive during the time for which the temporary ADI applies. If the additional data requested do not become available within the stated period, the temporary ADI may be withdrawn at a future meeting of the Committee.

2.3 General considerations for establishing and revising specifications

2.3.1 General principles

A summary of the general principles governing the establishment of specifications for food additives was published in the tenth report.^b Subsequent reports have reaffirmed the essential validity of these principles, but recommendations were made in the seventeenth^a and eighteenth^c reports for their review, updating, and presentation in a uniform manner.

A working document entitled "General principles applying to tests, assays, and specifications" was prepared and considered by the Committee. The document is designed to provide (a) guidance on the application of uniform scientific criteria for standardizing the format in the establishment of specifications, and (b) basic guidelines for the use of the specifications, including the application and interpretation of assays, identification tests, and purity tests. The Committee recommends that this document appear in a single publication that will include details of the general methods of analysis adopted by the Committee (see section 2.3.2) and an index of the specifications to which they apply.

The Committee reaffirmed that specifications for identity and purity are established primarily for the use of toxicologists and others concerned with the safety and quality of food additives. Specifications should therefore refer to substances as (a) tested and evaluated toxicologically ; (b) available in commerce ; (c) produced in accordance with good manufacturing practice ; and (d) required to produce the intended technological effects.

^a See Annex 1, ref. 32.

^b See Annex 1, ref. 12.

^c See Annex 1, ref. 34.

The seventeenth and eighteenth reports drew attention to the fact that specifications prepared at earlier meetings could be improved as a result of advances in methods of assay and of methods of analysis of impurities or contaminants that may be of toxicological importance.

The Committee recognized that periodic review of specifications of food additives is called for on the grounds of changes in patterns of use, of raw materials, and because of the introduction of new processes that differ significantly from those existing when the specifications were established or last revised. Also additional information may become available as a result of work by national and international standardization organizations. Periodic reviews of specifications are therefore indispensable and may also serve to suggest where a toxicological re-evaluation may be needed. The Committee recommends that periodic revision of specifications for general classes of compounds be continued and notes that such revisions have recently been made for antimicrobials and preservatives, anticaking agents, antioxidants and synergists, emulsifiers and stabilizers, flavour enhancers, and thickening agents. Classes that remain to be reviewed include flavouring substances, some colours, extraction and carrier solvents, and a class of miscellaneous substances, including processing aids and flour treatment agents.

The Committee also discussed (a) the applicability of specifications in relation to food additives stored for some period before their use ; (b) the case of substances of exceptionally high purity, and (c) the influence of the presence of minor quantities of certain other substances in a food additive product.

(a) When a specification is established or revised, limits are set for those decomposition products that may form during storage and may have special significance. Manufacturers and users of food additives should ensure good packaging and storage conditions and use good handling practices to minimize deleterious changes in quality or purity. The Committee considered it would be useful to have information on changes that occur during storage or handling that should be taken into account when establishing tests for purity or for identity in the specifications.

(b) The specifications for food-grade additives contain the minimum requirements as regards composition and quality to allow for acceptable variations in their production. The specifications do not exclude the use as additives of substances of higher quality (e.g., analytical grade reagents)—such substances may deviate somewhat from certain identification criteria, such as melting range, pH, and specific rotation—provided that the substances meet the stated requirements under the specified purity tests and are otherwise suitable for use as food additives.

(c) The Committee wished to draw attention to the influence of intentionally added substances on analytical results. Commercially available food additives may contain small amounts of anticaking agents, antioxidants, stabilizers, etc., added primarily to enhance usefulness or shelf-life. Manufacturers of food additives should indicate the presence of such minor acceptable constituents that can influence the results of tests given in specifications established to characterize only the food additive proper.

2.3.2 *Review of methods of analysis*

The review and updating of the general methods of analysis was initiated by the seventeenth meeting. These methods were finalized at the present meeting of the Committee and the Committee recommends that they should be published together with the "General principles . . ." (see section 2.3.1) and an index of the specifications to which they apply.

The Committee also reviewed and finalized a number of methods of analysis referred to in specifications for anticaking agents, emulsifiers, and thickening agents.

2.3.3 *Other considerations*

The seventeenth report referred to the necessity of establishing microbiological criteria and limits for certain classes of food additives. Such criteria are needed especially for products obtained by using microorganisms, derived from natural materials, or liable to be contaminated during manufacture, handling, or storage. The Committee was informed that a group of experts had recently selected referee methods suitable for establishing compliance with microbiological provisions that are or might be included in food standards proposed for adoption by the Codex Alimentarius Commission.

The Committee experienced some difficulty in defining the functional uses in connexion with several specifications under review. It noted the achievement of some consistency and of harmony with descriptions employed by the committees of the Codex Alimentarius Commission. The Committee understood that the Codex Committee on Food Additives might look into the possibility of compiling—in cooperation with Codex Commodity Committees—a list of functional uses of food additives and a matching glossary. The Committee was aware of the preparatory work already done by the Codex Secretariat towards the publication and updating of a "List of additives evaluated for their safety of use in food."

Occasionally specifications indicate that an analytical reference compound is required for carrying out the assay or purity test. As suggested in the seventeenth report, when an analytical standard of comparison is called

for, a reliable source should be given. The Committee also recognized the need to have commercial food additive material typical of that used for establishment of the specifications and the ADI available for reference purposes.

2.4 Impurities or transformation products of intentional and unintentional food additives

In a number of instances the Committee has been faced with the task of evaluating compounds that contain unique impurities or that give rise to transformation products of possible toxicological significance. Four categories may be distinguished on the basis of different modes of formation :

(1) Unique impurities present by virtue of the manufacturing process, e.g., 5-benzyl-3,6-dioxo-2-piperazine, (diketopiperazine, DKP) in aspartame, ortho-toluenesulfonamide in saccharin, cyclohexylamine in cyclamate, 4-methylimidazole in caramel produced by the ammonia process.

(2) Transformation of the additive in food processing or storage, e.g., formation of DKP from aspartame, and fluorescein from erythrosine.

(3) Reaction products with food constituents, e.g., formation of ethylurethane from diethyl pyrocarbonate, dichlorovinylcysteine from trichloroethylene, methionine sulfoximine from nitrogen trichloride, ethylene chlorhydrin from ethylene oxide, nitroso compounds from nitrites, tin compounds in certain canned products.

(4) Metabolic transformation products, e.g., formation of cyclohexylamine from cyclamates, free aromatic amines from azo dyes, nitrites from nitrates.

It will be noted that certain food additives may contain impurities or give rise to transformation products as a result of more than one of the above mechanisms.

At previous meetings of the Committee attention has been drawn to the need for studies of metabolism, including that of metabolism involving the intestinal flora, in toxicological evaluation.^a

The Committee recognizes that at an early stage in toxicological testing of food additives there is a need to consult with food technologists and chemists so as to be alerted to the possible occurrence of impurities or transformation products. Under certain circumstances an impurity or transformation product may have to be tested separately.

Three of the compounds considered at this meeting were associated with impurities or transformation products of toxicological importance. Ama-

^a See Annex 1, ref. 22.

ranth has not been uniformly specified as to its content of impurities in different countries and this may account for the conflicting results reported in biological tests (see section 4.1). Aspartame contains about 0.5% of DKP as a manufacturing impurity. The amount of DKP may further increase through cyclization of aspartame on storage or when aspartame is added to liquid food of an acid pH (see section 4.4). The high levels of tin that may occur in citrus juices and other acid foods when stored over a long period in certain cans have been associated with acute gastrointestinal disturbances (see section 4.4).

Other impurities or transformation products that are more toxic than the parent food additive have been dealt with at previous meetings, as illustrated by the following examples. The presence of up to 6 g of ortho-toluenesulfonamide per kilogram of saccharin has been reported and may have been the cause of the magnesium ammonium phosphate calculi that occurred in rats fed very high doses of saccharin.^a Ethylurethane is formed in amounts of the order of 0.01–0.04 mg/litre in beverages treated with diethylpyrocarbonate, depending on the pH and ammonium content.^b

The transformation of nitrates to nitrites in food or water or in the gastrointestinal tract of young infants, as well as the possibility of the formation of nitroso compounds, largely by interaction with secondary and tertiary amines, was especially dealt with in the seventeenth report.^c

Cyclohexylamine may occur as a manufacturing impurity in cyclamate, but much larger amounts of cyclohexylamine may be formed by the action on cyclamate of anaerobic bacteria in the gut.

2.5 Smoke, smoke condensates, and liquid smoke

The preservation and flavouring of food by smoking procedures was dealt with by the Committee. The preservation of food by smoking is of ancient origin. The process preserves foodstuffs such as meat and fish and imparts to these products colour and flavour that have proved attractive to the consumer. The preservative action is exerted, *inter alia*, by diminution of the number of surface bacteria and by dehydration. Modern methods of food preservation such as refrigeration have reduced the need for smoking as a method of preservation, but the demand persists for the traditional flavour and colour obtained by smoking.

When traditional smoking processes are used, certain elementary precautions should be observed, e.g., tarred or chemically treated wood

^a See Annex 1, ref. 34.

^b Fischer, E. *Z. Lebensm. -Unters. -Forsch.*, **148** : 221–222 (1972).

^c See Annex 1, ref. 32.

should not be used. There are several disadvantages in the traditional process. Smoking is difficult to standardize and control, and some of the constituents of smoke absorbed by the products may be hazardous to health.

The presence of polycyclic aromatic hydrocarbons in traditionally smoked foods has led to changes in technological processing with a view to excluding direct contact of the food with smoke. A range of purified smoke condensates and liquid smokes are now commonly employed. Their use reduces contamination by carcinogenic polycyclic aromatic hydrocarbons and enables the intensity of the flavour of the final product to be accurately controlled. With the exception of one wholly synthetic product, all originate from the dry distillation of various woods at temperatures usually between 100–1000°C. All or part of the resultant smoke is trapped by either solution in water or condensation. The solution or condensate is further treated to remove unwanted compounds.

These smoke condensates are food additives and should be evaluated as such. Therefore, more detailed information is required on the raw materials, the process, the composition of the smokes, and the end-products obtained. More information is needed about the smoke compounds required to impart flavour and colour to the products, and about the effects of different conditions of combustion on the composition of smoke, including the formation of impurities such as methanol and polycyclic aromatic hydrocarbons. A generally accepted analytical procedure for the determination of polycyclic aromatic hydrocarbons in smoke condensates is also required.

The use of suitably "purified" smoke condensates or liquid smoke can provide traditional colour and flavour while effectively reducing the level of carcinogenic polycyclic aromatic hydrocarbons. However, since such use would not adequately preserve the treated food, additional measures must be taken to secure the desired shelf-life.

3. REVISION OF CERTAIN SPECIFICATIONS

At the eighteenth meeting of the Committee, revision of the specifications of miscellaneous substances was postponed. The present Committee revised the specifications for 31 substances, including certain acids, bases, and salts, as well as azodicarbonamide, benzoyl peroxide, calcium oxide, oxystearin, and sodium carboxymethylcellulose (see annex 2).

The revision of specifications for eight substances on the agenda was not possible. For *chlorine dioxide* the present specification was judged inadequate but revised specifications could not be prepared on the basis of the available information.

Dipotassium hydrogen phosphate specifications were to be prepared as part of the revision of a group of phosphates. The Committee was not aware of a food additive use or of a manufacturer of this substance. No further action was taken.

The Committee could not prepare a specification for *polyvinyl pyrrolidone* because of insufficient information (see section 5).

The Committee decided to defer revision of the existing specifications for *propylene glycol* pending receipt of additional information.

Further information is also required to complete specifications for *pentasodium triphosphate*.

The seventeenth report indicates the desirability of a limit for the content of cyclic polyphosphates in *sodium polyphosphate*. The Committee did not have the details of a suitable method and suggested that revised specifications be prepared as soon as this information and data on the contents of higher polyphosphates have been obtained.

The Committee had no new information on which to base a revision of the existing specifications for *sorbitol*. It considered that separate specifications should be available for sorbitol solutions. Further information required includes the contents of other polyols and of saccharides, and methods useful for their determination.

Stearyl tartrate was reported to have minimal current technical use. No revised specification was prepared.

4. COMMENTS ON PARTICULAR SUBSTANCES

The Committee evaluated a number of food additives for the first time and also re-evaluated some substances that had been considered at previous meetings. Points of interest arising from these evaluations are set out below. The acceptable daily intakes and information on specifications are summarized in Annex 2. Additional information about the substances is given in the monographs to be published separately.^a

4.1 Food colours

Amaranth

Previous difficulties with amaranth concerning potential carcinogenicity and teratogenicity have been evaluated in the light of new data. The problem appears to have arisen from the use, in some of the tests, of

^a FAO Nutrition Meetings Report Series No. 55A; WHO Food Additives Series No. 8.

samples of amaranth with specifications different from those established by this Committee. The existing specification^a is considered adequate. Toxicological evidence indicates that this product, when it complies with this specification, justifies the maintenance of the temporary ADI of 0-0.75 mg/kg body weight. The Committee hopes that international cooperative studies with standard samples may be undertaken to elucidate the reason for the reported discrepancies.

Ferrous gluconate

This compound was evaluated by the Committee not in relation to its use as a nutritional supplement but as a colouring adjunct. It was given an "ADI not specified", with the proviso that the contribution from ferrous gluconate to the total dietary gluconic acid intake from all sources should be included in the ADI for gluconic acid. Specifications were prepared at the eighteenth meeting of the Committee.

Quinoline Yellow

There are two commercial preparations of this food colour, one of which contains about 30% of the methylated colour, while the other contains only the nonmethylated colour. The specification prepared at the eighteenth meeting adequately covers both types of commercial products.

In the manufacture of these colours the impurities are qualitatively the same. Therefore, toxicological data obtained on the colour containing the methylated derivative could be used as collateral evidence to ensure also the safety of the nonmethylated preparation. Thus the Committee retained the temporary ADI of 0-0.5 mg/kg body weight established at the eighteenth meeting.

4.2 Thickening agents

Specifications were available to the Committee for all substances being re-evaluated. The specification prepared at the eighteenth meeting for pectin also covers amidated pectin.

Guar gum, carob (locust) bean gum, and tara gum were reconsidered by the Committee. A temporary "ADI not specified" was established for carob bean gum and tara gum, subject to the completion of further work by 1978. In the case of guar gum the evaluation of "ADI not specified" was confirmed.

^a See Annex 1, ref. 10.

Microcrystalline cellulose was re-evaluated by the Committee and the question of the demonstrated persorption was considered as part of the total toxicological evaluation of this and other celluloses. The previously established "ADI not specified" was confirmed.

Amidated pectin was reconsidered by the Committee. Part of the additional information requested by the Committee was received. This was not found adequate to change the previously established temporary ADI of 0-25 mg/kg body weight. Additional long-term studies are now requested to be completed by 1980.

4.3 Smoke condensates and liquid smoke ^a

A complete toxicological evaluation was not possible in the absence of additional information. The establishment of specifications that include a method for detecting the presence of carcinogenic polycyclic aromatic hydrocarbons is required. No monograph or specification was prepared.

4.4 Miscellaneous

Aspartame was evaluated by the Committee. A special problem was posed by the presence of an impurity, 5-benzyl-3,6-dioxo-2-piperazine, (diketopiperazine, DKP). Lesions seen in long-term feeding studies with DKP in rats were described as uterine polyps. This description was an inadequate basis for a decision by the Committee.

At the request of the Committee, the International Agency for Research on Cancer (IARC) assembled a group of pathologists to review during the meeting of the Committee all the histological sections of the uterine lesions that were made available to them. The IARC pathologists submitted a report stating that they could not give a final judgement on the basis of the limited histological material available (report submitted to WHO). The Committee was therefore unable to arrive at an evaluation of this compound. Neither a monograph nor a specification was prepared.

New specifications were prepared for *calcium hydrogen phosphate* as part of the revision of specifications for a group of phosphates.

Dichlorodifluoromethane was evaluated by the Committee and specifications were prepared. An ADI of 0-1.5 mg/kg body weight was established. Owing to the volatility of this compound, gavage was employed as the route of administration in the toxicological studies reported.

Sucrose acetate isobutyrate was evaluated by the Committee. The data reporting reversible lesions of the liver in dogs were not adequate for evalua-

^a Excluding synthetic smoke preparations.

tion. Additional studies of these lesions, as well as additional metabolism, reproduction, and long-term studies are requested. No ADI could be established. Neither specifications nor a monograph were prepared.

L(+)-*Tartaric acid* was re-evaluated. Specifications were available to the Committee. Since only interim additional data were available, no further action was taken.

Tertiary butylhydroquinone (TBHQ) was evaluated by the Committee and a temporary ADI of 0-0.75 mg/kg body weight was established. The Committee noted the structural similarity of this compound to butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) and therefore requested, as for the latter compounds, reproduction studies with TBHQ in mixtures with propylgallate. Tentative specifications were prepared.

Tin compounds as contaminants and *stannous chloride* as a food additive could not be re-evaluated because the available data were insufficient. The Committee noted the reported association between levels of tin in certain canned products and acute gastrointestinal disturbances and the lack of knowledge about a compound that might cause these disturbances. No monograph was prepared.

Triacetin was evaluated by the Committee and an "ADI not specified" established. Specifications were available to the Committee.

5. FUTURE WORK

The broad areas of future work are described in the seventeenth report.^a This Committee wished to endorse them and to point out the need to consider the following specific additives :

(1) The Committee was informed of new findings and the consequent need for re-interpretation of the results of studies on some modified starches considered in the seventeenth and eighteenth reports of the Committee. It was suggested that these substances be placed on the agenda of a future meeting.

(2) At present there is no ADI for polyvinyl pyrrolidone (PVP) as the conditional ADI was withdrawn at the seventeenth meeting because of a general concern over body storage of macromolecules. The need for further work was indicated at the same time. In order to prepare a specification, information will be required on the molecular weight ranges of the PVP employed in the toxicological studies.

^a See Annex 1, ref. 32.

(3) It was brought to the attention of the Committee that the present use levels of DL-menthol and L-menthol may exceed the ADI. The Committee considered it appropriate to request any new data that might be available.

(4) For certain kinds of food additives microbiological specifications are required (see section 2.3.3).

6. RECOMMENDATIONS TO FAO AND WHO

1. The procedures for the testing of food additives should be comprehensively reviewed and brought into line with advances in food science, toxicology, and related disciplines by convening an appropriate meeting (see section 2.2).

2. The Committee recognizes the benefits of food additives although the assessment of these is outside its terms of reference (see section 2.1). The Committee recommends that FAO and WHO convene a meeting of appropriate experts to discuss this problem.

3. There is a need for international cooperation in toxicological testing. WHO and FAO should act as focal points for establishing agreed protocols, and if necessary, providing reference samples (see section 4.1).

4. Recognizing the need for analytical standards, the Committee considers that a list of the sources of analytical standards and of comparison compounds should be compiled with the assistance of other authoritative bodies (see section 2.3.3).

5. The general principles governing the establishment of specifications should be published in a separate volume that can be kept up-to-date, together with details of the general methods of analysis and an index of the current specifications (see sections 2.3.1 and 2.3.2).

6. FAO and WHO should develop procedures for disseminating the essence of the reports of this Committee in a form comprehensible to the public at large (see section 2.1).

7. In view of the large number of food additives and contaminants requiring evaluation or re-evaluation, meetings of the Joint FAO/WHO Expert Committee on Food Additives should continue to be held annually.

8. There is a need for the establishment of microbiological criteria and their application in appropriate specifications prepared by the Committee. A meeting of appropriate experts should be convened to meet this need.

**REPORTS AND OTHER DOCUMENTS RESULTING
FROM PREVIOUS MEETINGS OF THE JOINT FAO/WHO
EXPERT COMMITTEE ON FOOD ADDITIVES**

1. General Principles Governing the Use of Food Additives. First Report. FAO Nutrition Meetings Report Series, No. 15, 1957 ; WHO Technical Report Series, No. 129, 1957 (out of print).
2. Procedures for the Testing of Intentional Food Additives to Establish their Safety for Use. Second Report. FAO Nutrition Meetings Report Series, No. 17, 1958 ; WHO Technical Report Series, No. 144, 1958 (out of print).
3. Specifications for Identity and Purity of Food Additives (Antimicrobial Preservatives and Antioxidants). Third Report. These specifications were subsequently revised and published as *Specifications for Identity and Purity of Food Additives*, vol. I. *Antimicrobial Preservatives and Antioxidants*, Rome, Food and Agriculture Organization of the United Nations, 1962 (out of print).
4. Specifications for Identity and Purity of Food Additives (Food Colours). Fourth Report. These specifications were subsequently revised and published as *Specifications for Identity and Purity of Food Additives*, vol. II. *Food Colours*, Rome, Food and Agriculture Organization of the United Nations, 1963 (out of print).
5. Evaluation of the Carcinogenic Hazards of Food Additives. Fifth Report. FAO Nutrition Meetings Report Series, No. 29, 1961 ; WHO Technical Report Series, No. 220, 1961 (out of print).
6. Evaluation of the Toxicity of a Number of Antimicrobials and Antioxidants. Sixth Report. FAO Nutrition Meetings Report Series, No. 31, 1962 ; WHO Technical Report Series, No. 228, 1962.
7. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Emulsifiers, Stabilizers, Bleaching and Maturing Agents. Seventh Report. FAO Nutrition Meetings Report Series, No. 35, 1964 ; WHO Technical Report Series, No. 281, 1964 (out of print).
8. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Food Colours and Some Antimicrobials and Antioxidants. Eighth Report. FAO Nutrition Meetings Report Series, No. 38, 1965 ; WHO Technical Report Series, No. 309, 1965 (out of print).
- *9. Specifications for Identity and Purity and Toxicological Evaluation of Some Antimicrobials and Antioxidants. FAO Nutrition Meetings Report Series, No. 38A, 1965 ; WHO/Food Add/24.65.
- *10. Specifications for Identity and Purity and Toxicological Evaluation of Food Colours. FAO Nutrition Meetings Report Series, No. 38B, 1966 ; WHO/Food Add/66.25.

* These documents can be obtained on request from : Food Additives, World Health Organization, 1211 Geneva 27, Switzerland, or Food Standards and Food Science Service, Food and Agriculture Organization of the United Nations, 00100 Rome, Italy.

11. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Some Antimicrobials, Antioxidants, Emulsifiers, Stabilizers, Flour-Treatment Agents, Acids and Bases. Ninth Report. FAO Nutrition Meetings Report Series, No. 40, 1966 ; WHO Technical Report Series, No. 339, 1966.
12. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Some Emulsifiers and Stabilizers and Certain Other Substances. Tenth Report. FAO Nutrition Meetings Report Series, No. 43, 1967 ; WHO Technical Report Series, No. 373, 1967.
- *13 Toxicological Evaluation of Some Antimicrobials, Antioxidants, Emulsifiers, Stabilizers, Flour-treatment Agents, Acids and Bases. FAO Nutrition Meetings Report Series, No. 40A, B, C ; WHO/Food Add/67.29.
14. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Some Flavouring Substances and Non-Nutritive Sweetening Agents, Eleventh Report. FAO Nutrition Meetings Report Series, No. 44, 1968 ; WHO Technical Report Series, No. 383, 1968.
- *15. Toxicological Evaluation of Some Flavouring Substances and Non-Nutritive Sweetening Agents. FAO Nutrition Meetings Report Series, No. 44A, 1968 ; WHO/Add/68.33.
- *16. Specifications and Criteria for Identity and Purity of Some Flavouring Substances and Non-Nutritive Sweetening Agents. FAO Nutrition Meetings Report Series, No. 44B, 1969 ; WHO/Food Add/69.31.
17. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Some Antibiotics. Twelfth Report. FAO Nutrition Meetings Report Series, No. 45, 1969 ; WHO Technical Report Series, No. 430, 1969.
- *18. Specifications for the Identity and Purity of Some Antibiotics. FAO Nutrition Meetings Report Series, No. 43A, 1969 ; WHO/Food Add/69.34.
19. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Some Food Colours, Emulsifiers, Stabilizers, Anticaking Agents, and Certain Other Substances. Thirteenth Report. FAO Nutrition Meetings Report Series, No. 46, 1970 ; WHO Technical Report Series, No. 445, 1970.
- *20. Toxicological Evaluation of Some Food Colours, Emulsifiers, Stabilizers, Anticaking Agents and Certain Other Substances. FAO Nutrition Meetings Report Series, No. 46A ; WHO/Food Add/70.36.
- *21. Specifications for the Identity and Purity of Some Food Colours, Emulsifiers, Stabilizers, Anticaking Agents and Certain Other Food Additives. FAO Nutrition Meetings Report Series, No. 46B ; WHO/Food Add/70.37.
22. Evaluation of Food Additives. Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Some Extraction Solvents and Certain Other Substances ; and a Review of the Technological Efficacy of Some Antimicrobial Agents. Fourteenth Report. FAO Nutrition Meetings Report Series, No. 48, 1971 ; WHO Technical Report Series, No. 462, 1971.
- *23. Toxicological Evaluation of Some Extraction Solvents and Certain Other Substances. FAO Nutrition Meetings Report Series, No. 48A, 1971 ; WHO/Food Add/70.39.
- *24. Specifications for the Identity and Purity of Some Extraction Solvents and Certain Other Substances. FAO Nutrition Meetings Report Series, No. 48B, 1971 ; WHO/Food Add/70.40.

- *25. A Review of the Technological Efficacy of some Antimicrobial Agents. FAO Nutrition Meetings Report Series, No. 48C, 1971 ; WHO/Food Add/70.41.
26. Evaluation of Food Additives. Some Enzymes, Modified Starches, and Certain Other Substances : Toxicological Evaluations and Specifications and a Review of the Technological Efficacy of Some Antioxidants. Fifteenth Report. FAO Nutrition Meetings Report Series, No. 50, 1972 ; WHO Technical Report Series, No. 488, 1972.
27. Toxicological Evaluation of Some Enzymes, Modified Starches and Certain Other Substances. FAO Nutrition Meetings Report Series, No. 50A, 1972 ; WHO Food Additives Series, No. 1, 1972.
28. Specifications for the Identity and Purity of Some Enzymes and Certain Other Substances. FAO Nutrition Meetings Report Series, No. 50B, 1972 ; WHO Food Additives Series, No. 2, 1972.
29. A Review of the Technological Efficacy of Some Antioxidants and Synergists. FAO Nutrition Meetings Report Series, No. 50C, 1972 ; WHO Food Additives Series, No. 3, 1972.
30. Evaluation of Certain Food Additives and the Contaminants Mercury, Lead and Cadmium. Sixteenth Report. FAO Nutrition Meetings Report Series, No. 51, 1972 ; WHO Technical Report Series, No. 505, 1972, and Corrigendum.
31. Evaluation of Mercury, Lead, Cadmium and the Food Additives Amaranth, Diethylpyrocarbonate and Octyl Gallate. FAO Nutrition Meetings Report Series, No. 51A, 1972 ; WHO Food Additives Series, No. 4, 1972.
32. Toxicological evaluation of certain food additives with a review of general principles and of specifications. Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, FAO Nutrition Meetings Report Series, No. 53, 1974 ; WHO Technical Report Series, No. 539, 1974, and Corrigendum.
33. Toxicological evaluation of certain food additives including anticaking agents, antimicrobials, antioxidants, emulsifiers, and thickening agents. FAO Nutrition Meetings Report Series, No. 53A ; WHO Food Additives Series, No. 5, 1974.
34. Evaluation of Certain Food Additives. Eighteenth Report of the Joint FAO/WHO Expert Committee on Food Additives. FAO Nutrition Meetings Report Series, No. 54, 1974 ; WHO Technical Report Series, No. 557, 1974, and Corrigendum.
35. Toxicological evaluation of some food colours, enzymes, flavour enhancers, thickening agents, and certain other food additives. FAO Nutrition Meetings Report Series, No. 54A, 1975 ; WHO Food Additives Series, No. 6, 1975.
36. Specifications for the identity and purity of some food colours, flavour enhancers, thickening agents and certain food additives. FAO Nutrition Meetings Report Series, No. 54B, 1975 ; WHO Food Additives Series, No. 7, 1975.

Annex 2

ACCEPTABLE DAILY INTAKES AND INFORMATION
ON SPECIFICATIONS ^a

<i>Substance</i>	<i>Specification</i> ^b	<i>ADI</i> (mg/kg body weight)
amaranth	S	0-0.75 ^c
aspartame	O	No ADI allocated
dichlorodifluoromethane	N	0-1.5
ferrous gluconate	S	Not specified ^{a, e}
gum, carob (locust) bean	S	Not specified ^{c, d}
gum, guar	S	Not specified ^d
gum, tara	T	Not specified ^{c, d}
microcrystalline cellulose	S	Not specified ^d
pectin, amidated	S	0-25 ^c
Quinoline Yellow	RT	0-0.5 ^c
stannous chloride	S	No ADI allocated
sucrose acetate isobutyrate	O	No ADI allocated
tertiary butyl hydroquinone	T	0-0.75 ^c
tin compounds	O	No ADI allocated
triacetin	N	Not specified ^d

^a The Committee draws attention to the issue of a corrigendum to the seventeenth report of the Joint FAO/WHO Expert Committee on Food Additives in which substantive corrections are made in connexion with the ADIs for alginic acid and its ammonium, calcium, sodium, and potassium salts; calcium gluconate; and 1,2-propylene glycol.

^b O, Specification not prepared; N, new specification prepared; R, existing specification revised; S, a specification exists, revision not considered; T, the new specification (NT) or revised specification (RT) is tentative and comments are invited.

^c Temporary.

^d The statement "not specified" means that, on the basis of available data (chemical, biochemical, and toxicological), the total daily intake of the substance arising from its use or uses at levels necessary to achieve the desired effect and from its acceptable background in food, does not, in the opinion of the Committee, represent a hazard to health. For this reason, and for reasons stated in the individual evaluations, the establishment of an acceptable daily intake (ADI) expressed in mg per kg of body weight is not deemed necessary.

^e However, the contribution from ferrous gluconate to the total dietary gluconic acid intake from all sources should be included in the ADI for gluconic acid (0-50 mg/kg body weight).

Specifications only

<i>Substance</i>	<i>Specification</i>
acetic acid, glacial	R
adipic acid	R
ammonium carbonate	R
ammonium hydrogen carbonate	R
azodicarbonamide	R
benzoyl peroxide	R
calcium chloride	R
calcium hydrogen phosphate	N
calcium hydroxide	R
calcium oxide	R
calcium citrate	R
calcium sulfate	R
dipotassium hydrogen phosphate	R
disodium hydrogen phosphate	R
hydrochloric acid	R
magnesium hydroxide	R
DL-malic acid	R
oxystearin	R
potassium bromate	R
potassium carbonate	R
potassium dihydrogen phosphate	R
potassium hydrogen carbonate	R
potassium hydroxide	R
potassium phosphate	R
sodium carbonate	R
sodium carboxymethylcellulose	R
sodium hydrogen carbonate	R
sodium hydroxide	R
sodium phosphate	R
tripotassium citrate	R
trisodium citrate	R

**FURTHER TOXICOLOGICAL STUDIES AND
INFORMATION REQUIRED**

Amaranth^a

The result of long-term feeding study on the progeny of rats that were fed amaranth during the gestation and lactation period.

Gum, carob (locust) bean^b

- (1) An adequate long-term study in a rodent species.
- (2) Reproduction studies.

Gum, tara^b

- (1) Adequate long-term studies in a rodent species.
- (2) Reproduction and embryotoxicity (including teratogenicity) studies.

Pectin (amidated)^b

- (1) Adequate reproduction and embryotoxicity studies including teratology studies in rats.
- (2) Adequate long-term study in a rodent species.

Quinoline Yellow^a

- (1) Metabolic studies in several species, preferably including man.
- (2) Adequate long-term studies in another species.
- (3) Results of multi-generation study in progress.

Tertiary butyl hydroquinone^a

Appropriate studies on reproduction using monotertiary butyl hydroquinone in mixtures with propylgallates.

^a Required by 1978.

^b Required by 1980.

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