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**SPECIFICATIONS FOR THE IDENTITY AND
PURITY OF FOOD ADDITIVES AND THEIR
TOXICOLOGICAL EVALUATION :
SOME EMULSIFIERS AND STABILIZERS
AND CERTAIN OTHER SUBSTANCES**

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

Geneva, 11-18 October 1966



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JOINT FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES

Geneva, 11-18 October 1966

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CONTENTS

	Page
Introduction	5
1. General considerations	6
2. Modification of agenda	7
3. Comments on monographs—specifications	9
3.1 Revised approach to specifications	10
3.2 Specifications for arsenic, lead and “heavy metals” in food additives	10
3.3 Review of specifications	11
3.4 Revised specifications for carboxymethylcellulose and methylcellulose	11
4. Comments on monographs—biological data	11
4.1 Possible substitution of biochemical and metabolic studies for formal toxicity studies	12
4.2 Grouping of related food additives	13
4.3 References	14
5. Some trace elements	14
5.1 Arsenic	14
5.2 Copper	15
5.3 Lead	15
5.4 Mercury	16
5.5 Tin	16
5.6 Zinc	17
6. Emulsifiers and stabilizers	17
6.1 Stabilizers made by modifying natural materials	17
6.2 Fatty emulsifiers	18
6.3 Natural stabilizers	19
6.4 Steroid emulsifiers	19
6.5 Miscellaneous emulsifiers	19
7. Miscellaneous food additives	20
8. Substances postponed from previous meetings	20
9. Re-evaluation	21
10. Monographs	23
11. Tolerances of a food additive in relation to its daily intake	23
12. Recommendations	24
Annex 1. Acceptable daily intakes for man of some emulsifiers and stabilizers	26
Annex 2. Acceptable daily intakes for man of some miscellaneous food additives	27
Annex 3. Acceptable daily intakes for man and classification of some food colours	27
Annex 4. Explanatory notes on the activities of the Joint FAO/WHO Expert Committee on Food Additives	28
Annex 5. Proposed modification of the procedure for establishing acceptable daily intakes	47

Monographs containing biological data and toxicological evaluation will be issued by FAO and WHO in a separate document entitled :

Toxicological Evaluation of Some Antimicrobials, Antioxidants, Emulsifiers, Stabilizers, Flour-Treatment Agents, Acids and Bases.

FAO Nutrition Meetings Report Series, 1967, No. 40 A, B, C ;
WHO/Food Add./67.29.

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on Food Additives**

INTRODUCTION

A Joint FAO/WHO Expert Committee on Food Additives met in Geneva from 11-18 October 1966. The meeting was opened by Dr J. Karefa-Smart, 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 O. G. Fitzhugh was unanimously elected Chairman and Professor J. F. Reith, Vice-Chairman. Professor R. Truhaut and Dr W. A. Mannell agreed to serve as Rapporteurs.

As a result of the recommendations of the Joint FAO/WHO Conference on Food Additives held in September 1955¹ nine Joint FAO/WHO Expert Committees on Food Additives have met and issued the following reports : " General Principles Governing the Use of Food Additives : First Report ",² " Procedures for the Testing of Intentional Food Additives to Establish their Safety for Use : Second Report ",³ " Specifications for Identity and Purity of Food Additives (Antimicrobial Preservatives and Antioxidants) : Third Report ",⁴ " Specifications for Identity and

¹ *FAO Nutrition Meetings Report Series*, 1956, No. 11 ; *Wld Hlth Org. techn. Rep. Ser.*, 1956, **107**.

² *FAO Nutrition Meetings Report Series*, 1957, No. 15 ; *Wld Hlth Org. techn. Rep. Ser.*, 1957, **129**.

³ *FAO Nutrition Meetings Report Series*, 1958, No. 17 ; *Wld Hlth Org. techn. Rep. Ser.*, 1958, **144**.

⁴ 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.

Purity of Food Additives (Food Colours) : Fourth Report ”,¹ “ Evaluation of the Carcinogenic Hazards of Food Additives : Fifth Report ”,² “ Evaluation of the Toxicity of a Number of Antimicrobials and Antioxidants : Sixth Report ”,³ “ Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Emulsifiers, Stabilizers, Bleaching and Maturing Agents : Seventh Report ”,⁴ “ Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Food Colours and Some Antimicrobials and Antioxidants : Eighth Report ”,⁵ “ 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 ”.⁶

The present meeting was convened on recommendations made in the previous reports of the Joint FAO/WHO Expert Committee on Food Additives. Its terms of reference were to draw up specifications for and to make a toxicological evaluation of some emulsifiers and stabilizers not considered at earlier meetings. The Committee was also asked to re-evaluate some food additives already considered and to review their specifications or toxicological evaluation in the light of new biological and chemical data.

Some trace elements that are usually present in food and certain other items were also considered at this meeting at the request of the FAO/WHO Codex Committee on Food Additives.

The Expert Committee wishes to draw attention to the continuing nature of its work.

1. GENERAL CONSIDERATIONS

1.1 Principles

The Committee agreed to base its considerations on the general principles set out in the first, second, fifth, sixth and ninth reports of the Joint

¹ These specifications were subsequently revised and published as *Specifications for Identity and Purity of Food Additives. Vol. II. Food Colors*, Rome, Food and Agriculture Organization of the United Nations, 1963.

² *FAO Nutrition Meetings Report Series*, 1961, No. 29 ; *Wld Hlth Org. techn. Rep. Ser.*, 1961, 220.

³ *FAO Nutrition Meetings Report Series*, 1962, No. 31 ; *Wld Hlth Org. techn. Rep. Ser.*, 1962, 228.

⁴ *FAO Nutrition Meetings Report Series*, 1964, No. 35 ; *Wld Hlth Org. techn. Rep. Ser.*, 1964, 281.

⁵ *FAO Nutrition Meetings Report Series*, 1965, No. 38 ; *Wld Hlth Org. techn. Rep. Ser.*, 1965, 309.

⁶ *FAO Nutrition Meetings Report Series*, 1966, No. 40 ; *Wld Hlth Org. techn. Rep. Ser.*, 1966, 339.

FAO/WHO Expert Committee on Food Additives. The Committee also agreed to support in principle the recommendations made by the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives.¹

1.2 Publication of experimental results

The Committee wished to re-emphasize the importance of publishing experimental results. It also reaffirmed its policy with respect to the supply of information to FAO and WHO as outlined in the ninth report.²

1.3 Evidence submitted for re-evaluation

The Committee drew the attention of manufacturers and other interested parties to the requests for further biological evidence. Reconsideration of a substance cannot proceed until the further information requested has been provided. If no further information is forthcoming it may be assumed that there is no further need for that food additive and the Committee may therefore decide to delete it from the list of acceptable food additives.

2. MODIFICATION OF AGENDA

2.1 Removal of items from the agenda

The Committee considered that it would be more appropriate if diphenyl, *o*-phenylphenol and sodium *o*-phenylphenol could be considered at a forthcoming Joint Meeting of the FAO Working Party on Pesticide Residues and the WHO Expert Committee on Pesticide Residues. Sodium sorbate and the sodium salts of esters of *p*-hydroxybenzoic acid were known to be unsuitable for use as food additives and were not, therefore, considered further.

2.2 Postponement of consideration

Evidence of significant use of the following substances as food additives had not been obtained and these were not further considered: taurocholic acid, glycocholic acid, oat gum, potassium propionate, hydroxyethylcellulose and carboxymethylgalactomannan.

The Food Additives Committee of the FAO/WHO Codex Alimentarius Commission had suggested that hexane be evaluated by the FAO/WHO Joint Expert Committee on Food Additives in view of its common use

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1967, 348.

² *FAO Nutrition Meetings Report Series*, 1966, No. 40; *Wld Hlth Org. techn. Rep. Ser.*, 1966, 339.

as a solvent in food technology. The Expert Committee agreed that the question of the use of solvents in food technology was an important matter calling for establishment of specifications and for toxicological evaluation. The Committee considered that there need be no serious concern about traces of hexane in food but that impurities in the solvent might be of greater toxicological significance. Since a wide range of solvents were used, it seemed undesirable to deal with hexane alone. The Committee therefore recommended that the organic solvents in food technology should be studied from the point of view of specification and possible toxic effect at a further meeting of the Joint FAO/WHO Expert Committee on Food Additives. The Committee also recommended that the International Union of Pure and Applied Chemistry should be asked to assist in the compilation of information on these solvents. Hexane was, therefore, not considered further. Similarly, the Committee felt it would be unwise to single out the antibiotic pimaricin from other antibiotics for evaluation. It was recommended that the use of antibiotics as food additives should be examined as a whole by a future Joint Expert Committee.

2.3 Tentative specifications

Tentative specifications were drawn up for a number of compounds on the agenda which could not be treated fully from a toxicological point of view. Since monographs on these substances will not be published for the time being, the following individual tentative specifications will be made available on request to those interested :

- Brominated vegetable oil
- Carrageen
- Gums (arabic, guar, karaya, tragacanth and carob bean)
- Furcellaran
- Hydroxylated lecithin
- Pimaricin
- Propylene glycol alginate
- Stearyl citrate
- Sucrose esters of fatty acids
- Sulfoacetic acid and fatty acid esters of glycerol and their sodium salts

2.4 Preliminary evaluation

The Codex Committee on Food Additives had requested guidance on the maximum acceptable loads of arsenic, lead, copper, mercury, tin and zinc in the diet. The Expert Committee considered that contamination with these substances could be properly evaluated only when more data

became available. Nevertheless, the Expert Committee was anxious to assist the Codex Committee so far as this was possible. It consequently agreed to study the toxicological evidence available on these six trace elements.

2.5 Items postponed from last meeting

The evaluation of certain food additives had been postponed at the last meeting because it was hoped that further biological information would be available by the time the present meeting was held. No such additional information had been received for brominated vegetable oil, propylene glycol alginate and butyl *p*-hydroxybenzoate and these substances were not further considered. In the case of hexamethylenetetramine the additional information provided was still incomplete and re-evaluation was again postponed.

2.6 Re-evaluation

The compounds re-evaluated were: the nitrates and nitrites, ascorbic acid, citric acid, monoisopropyl citrate, DL-lactic acid, DL-malic acid and the gallates.

The following food colours were also considered: riboflavin, beta-carotene, beta-apo-8'-carotenal, methyl and ethyl esters of beta-apo-8'-carotenic acid, canthaxanthine, quinoline yellow, indanthrene blue RS and Black 7984.

2.7 Others

Other matters discussed by the Committee included the revised approach to specifications suggested by the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives, the possible substitution of biochemical and metabolic studies for formal toxicity studies, and suggestions for a slight modification of the procedure for establishing acceptable daily intakes.

3. COMMENTS ON MONOGRAPHS—SPECIFICATIONS

The Committee stressed again the need for a more effective liaison with the chemical and food industries in order to obtain information as complete as possible on methods of manufacture of and specifications for the substances under consideration and on their uses. It is recommended that the International Union of Pure and Applied Chemistry should be asked to assist in facilitating this exchange of information.

3.1 Revised approach to specifications

The following approach suggested by the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives¹ was adopted in the development of specifications.

“Adequate specifications for identity and purity should be available before toxicological work is initiated. Toxicologists and regulatory bodies need assurance that the material to be tested corresponds to that to be used in practice. Ideally, the specifications should be such as to define a material that will give reproducible biological results.

“Specifications for food additives produced commercially should be broad enough to include all the variations in the composition of these additives that, according to current knowledge, do not significantly affect their biological properties. As an example, mono- and di-glycerides of edible fatty acids² were considered as coming under one specification for the purpose of the toxicological evaluation. In any case, each such group of additives will have to be judged individually with respect to the limits of composition set out in the specifications.”

3.2 Specifications for arsenic, lead and “heavy metals” in food additives

It was the general opinion that a test for selenium should be inserted in specifications for food additives composed of sulfates, sulfites and persulfates as selenium often accompanies sulfur. For a similar reason, a test for fluorine should be included in specifications for phosphates and a test for barium in specifications for additives containing calcium that are used at high levels in food.

Such guiding rules are not available for arsenic, lead and “heavy metals”, i.e., substances giving dark precipitates with hydrogen sulfide under acid conditions. It can at best be said that the raw materials for iron and aluminium salts may have a rather high arsenic or lead content and natural phosphates may contain relatively large quantities of arsenic. Historically, tests for the latter elements were first applied in the control of food additives; in former times the danger of the presence of arsenic, lead and “heavy metals” in food additives was very real. Since then, much has changed. The chances that a toxic level of arsenic or lead may be present in a food additive are nowadays extremely small. Giving specifications for arsenic, lead and “heavy metals” may, however, be justified primarily as a means to encourage industry to select raw materials of good quality and to use adequate equipment.

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1967, **348**, 8.

² *FAO Nutrition Meetings Report Series*, 1964, No. 35; *Wld Hlth Org. techn. Rep. Ser.*, 1964, **281**.

Moreover, even if it is true that the tests show that the limits for arsenic, lead and "heavy metals" are seldom exceeded in certain highly developed countries, it has to be remembered that the raw materials and the equipment may not be of the same favourable quality in other countries.

The following recommendations for food additives were accepted :

- (1) The arsenic content to be generally at a maximum of 3 mg/kg.
- (2) A "heavy metals" content to be generally at a maximum of 40 mg/kg (for certain food additives a lower maximum should be set).
- (3) The lead content to be generally at a maximum of 10 mg/kg in those cases where the daily intake of the food additive may exceed 1 g. This requirement is not necessary if the maximum set for the heavy metal content is 10 mg/kg or less.

3.3 Review of specifications

The Committee agreed that a systematic review of all specifications is necessary for the following reasons :

- (a) There is a need for certain new types of criteria in the specifications, whereas other criteria have become obsolete.
- (b) Owing to the rapid progress in methods of analysis, it is essential to select reliable methods that do not require expensive equipment. However, if such methods are necessary to obtain reliability or precision, they should be used. Recently developed methods, if shown to be more reliable and accurate, should be regarded as suitable alternatives.
- (c) New information on the production, use, composition and purity of food additives is being obtained from industrial and other sources and such advances should be incorporated into the specifications.

3.4 Revised specifications for carboxymethylcellulose and methylcellulose

In the light of practical experience with the original specifications, it has been found expedient to devise an improved version incorporating a new method for estimating free glycolate.

4. COMMENTS ON MONOGRAPHS—BIOLOGICAL DATA

The Committee agreed that monographs dealing with the evaluation of the biological data should be drafted along the lines adopted in the previous reports, taking into account the recommendations of the WHO

Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives.¹

4.1 Possible substitution of biochemical and metabolic studies for formal toxicity studies

The Committee emphasized again the importance of metabolic and biochemical studies in the investigation of the biological effects of a food additive.

It was suggested that any food additive that is completely broken down in the food or in the gastro-intestinal tract to substances that are common dietary or body constituents might be satisfactorily evaluated with respect to safety-in-use on the basis of appropriate biochemical and metabolic studies alone, without the necessity for the usual toxicological investigations. It was considered that the carrying out of extensive toxicological investigation of small amounts of common food constituents with the object of establishing the safety of their use as food additives was an unwarranted waste of scientific effort.

Provision of adequate specifications is just as important for biochemical as for toxicological evaluation of a substance. The specification should ensure that only acceptable food constituents are present in significant amounts in a food additive that is to be assessed on biochemical grounds alone.

4.1.1 Evidence required

In order that the biochemical and metabolic studies may suffice for the establishment of an acceptable daily intake for a food additive they should cover at least the following points :

(a) Evidence that the substance is readily broken down in the food or in the gastro-intestinal tract to common food constituents under the conditions of use.

(b) Evidence to indicate the main factors concerned in this breakdown, e.g., pH and enzymes. Special problems may arise in individuals with defective enzymes.

(c) Evidence, preferably including studies in human subjects, that the material, when given in moderate amounts and under conditions similar to those that will prevail if used as a food additive, is absorbed to the same extent as the food materials to which it gives rise, and does not interfere with the absorption of other nutrients.

(d) Evidence that unhydrolysed or partly hydrolysed material does not occur in significant amounts in the stools, and that it does not cumulate in body tissues.

¹ *Wld Hlth Org. techn. Rep. Ser.*, 1967, 348.

(e) Evidence that the most important food components in the additive are metabolized and utilized as effectively when administered in composite form as the food additive as when given separately, and that overloading does not occur.

If adequate evidence along these lines is presented, it might be concluded that the food additive is handled in the body in a way that is not significantly different from that required for the component food materials. If so, no toxicological studies need be demanded, since the problem now becomes one involving the toxicology of foods themselves rather than the toxicology of a food additive. However, if knowledge of the technological processes in which the food additive participates suggests the possible production of a toxic component, appropriate short-term studies might be necessary to exclude unforeseen effects.

4.1.2 *Evaluation of biochemical and metabolic data to establish an acceptable daily intake*

In the case of a food additive that is completely broken down to normal food components prior to absorption there is no necessity on grounds of safety to impose limits of daily intake, since it is a general principle¹ that a food additive should not be used at a higher level than that needed to achieve the required technological effect. However, for administrative purposes an acceptable daily intake (ADI) has been allocated to such substances. This figure was calculated on the basis that the food additive would not increase the food component into which it is converted by more than about 5% of the quantity in an average diet. If any substance is liberated for which an ADI already exists or for which the Committee considers that an ADI is desirable, the level of this substance will automatically become the controlling factor. In appropriate cases, the Committee may also require substances liberated to be included in the overall acceptable dietary level of a specified chemical family.

4.2 **Grouping of related food additives**

The Committee has continued the system adopted in previous reports, whereby chemically and biologically related food additives are grouped together and an acceptable daily intake is established that covers all the specified members of the group that may be included in the diet. In cases where a given food additive is related to several groups, the level in the diet should not exceed the maximum acceptable load for any of the groups.

¹ *FAO Nutrition Meetings Report Series, 1957, No. 15; Wld Hlth Org. techn. Rep. Ser., 1957, 129.*

4.3 References

In the interest of brevity, only a restricted list of references has been provided in the bibliographies accompanying the monographs. Nevertheless, the Committee wished to stress that all available information has been carefully studied.

5. SOME TRACE ELEMENTS

The toxicological evidence available was inadequate for satisfactory evaluation of acceptable loads of trace elements, since for this purpose it would be necessary to take into account not merely the normal dietary variations and existing administrative limits in various countries, but also the following: the differential toxic potentialities of the various elements; the epidemiological, environmental and experimental observations on variations in the occurrence of trace elements in foods and tissues; dose-effect relationships in man and animals; and possible interactions of trace elements.

Since such elaborate studies are not possible at present, the Committee was able to provide for the provisional guidance of the Codex Committee only a very approximate assessment of the maximum acceptable daily load where necessary. The figures presented are *not* to be regarded as in any way equivalent to an acceptable daily intake, for the establishment of which detailed study of all the relevant toxicological information is essential.

5.1 Arsenic

Arsenic occurs naturally in foods and beverages and is normally present in relatively high concentrations in Crustacea and other shellfish. The levels of arsenic in foods can be increased as a result of industrial contamination and by contamination from the use of arsenicals as insecticides and as additives to animal feeds. Arsenic is not known to be an essential element, although its inclusion within prescribed limits in animal feeds in various forms improves the growth, health, and feed efficiency of livestock, especially pigs and poultry. The problem of potential carcinogenicity of inorganic arsenical compounds has been discussed in the fifth report of this Committee.

Inorganic compounds of arsenic are highly toxic when ingested in large quantities and chronic arsenic poisoning in man, with harmful accumulation of the element in the tissues, occurs as a result of occupational exposure to the element and of excessive industrial contamination of foods and beverages. For this reason, maximum limits of arsenic in foods and liquids have been legally imposed in many countries. These are very similar in

different countries. Calculations of possible total average arsenic loads in which all the dietary components contain the acceptable limits, indicate closely similar levels in Canada, the United Kingdom, the USA and France, ranging from 0.025 to 0.033 mg per kg body-weight. The estimated actual intakes from normal diets by persons not exposed to special occupational hazards range from 0.007 to 0.06 mg per kg body-weight. It is probable that most normal diets supply 1.5-2.0 mg arsenic per day, which corresponds closely to the calculated intakes if all foods and beverages were to contain the maximum permissible limits.

Since there is no evidence that arsenic intakes of this magnitude result in toxic accumulations in the tissues or impose any human health hazards, it appears that the present legal tolerances provide adequate safeguards and do not require revision on the basis of present knowledge. Until further data are obtained, the maximum acceptable load of arsenic can tentatively be placed at 0.05 mg per kg body-weight per day.

5.2 Copper

Copper is an essential constituent of the human diet, which supplies 0.033-0.05 mg per kg body-weight per day. At these levels of intake there is no demonstrable accumulation of copper in normal persons. Very high intakes of copper can cause symptoms of acute toxicity, but copper does not appear to constitute a cumulative toxic or carcinogenic hazard to man. A very considerable margin appears to exist between normal intakes and those that could lead to chronic copper poisoning in man.

The palatability and nutritive value of most foods are adversely affected by copper contents beyond certain levels. The statutory limits set for the copper content of these foods in some countries are necessary and are lower than the levels known to cause possible copper poisoning.

A maximum acceptable load of 0.5 mg of copper per kg body-weight per day is tentatively proposed. This figure is suggested on the understanding that the dietary levels of those constituents such as molybdenum and zinc, which are known to affect copper metabolism, lie within normal limits.

5.3 Lead

Lead is a non-essential element that occurs naturally in foods and beverages and as a contaminant from the use of lead arsenate sprays and from contact with processing equipment and containers. There is evidence that these sources of contamination are decreasing. On the other hand, inhalation of lead from air pollution, such as exhaust fumes and industrial smoke, appears to be increasing; tobacco smoking may also contribute to lead intake.

Average daily intakes of lead from normal food and beverages probably lie between 0.0033 and 0.005 mg per kg body-weight, with approximately a further 0.0013 mg per kg body-weight per day from the atmosphere in urban environment. Total intakes of lead of this magnitude are known to cause accumulation of lead in the tissues with age, but there is no direct evidence that tissue accumulations at existing levels are harmful or potentially harmful to healthy man. However, extrapolation from the results of animal experiments suggests that present environmental exposures to lead may be harmful and points to the need to consider means of reducing the lead burden to which modern man is exposed.

The maximum acceptable load of lead from food can tentatively be placed at 0.005 mg per kg body-weight per day.

5.4 Mercury

Mercury occurs naturally in minute amounts in foods and beverages and as a contaminant from the use of mercury compounds as fungicides and in industry. Mercury is a particularly cumulative poison and not known to serve any essential function in man or animals. However, there is evidence that contamination of the environment with mercury is increasing.

Average intakes of mercury from the diet were estimated some years ago to range from 0.001 to 0.0003 mg per kg body-weight per day, with little tissue accumulation at these levels of intake. Modern studies of the distribution of mercury in human foods and beverages and in human tissues in different environments and at different ages are urgently required. Until the results of such studies are available it is not possible to set meaningful maximum permissible limits to dietary intakes of this element. Every effort should therefore be made to control and reduce this form of contamination of the environment and consequently of food.

5.5 Tin

Tin is a normal constituent of the diet with no known physiological function but with a low toxicity. A high proportion of the normal intake of tin comes from canned foods and beverages. A typical North American diet, with its usual proportion of canned foods, supplies about 4 mg of tin per person per day, whereas a typical European diet supplies only about 2 mg per person per day. At these levels of intake there is virtually no accumulation of tin in the tissues and no evidence of long-term harmful effects on man. Moreover, there is evidence that, with modern methods of canning and processing, contamination of foods and beverages with tin is decreasing.

The maximum safe dietary level of tin is unknown, but it is probably much higher than the present-day level of exposure. The usual amounts present in food do not appear to pose any toxicological problem.

5.6 Zinc

Zinc is a natural constituent of human foods and it is an essential element for living organisms. A typical human diet supplies 0.17-0.25 mg per kg body-weight per day. The advent of modern processing plants has decreased the risks of contamination of foods with zinc. All animal species possess a high tolerance to zinc and its toxicity is reduced by high dietary levels of copper and iron and possibly also by interaction with other elements. There appears to be a very wide margin of safety between the levels of zinc in ordinary diets and those that could induce cumulative toxic effects.

6. EMULSIFIERS AND STABILIZERS

The monographs on these food additives will appear in a publication to be entitled "Toxicological Evaluation of Some Antimicrobials, Emulsifiers, Stabilizers, Flour-Treatment Agents, Acids and Bases";¹ the recommended acceptable daily intakes are summarized in Annex 1.

6.1 Stabilizers made by modifying natural materials

Since all the members of the group of cellulose derivatives are similar in their metabolic behaviour and their lack of absorption from the gastrointestinal tract, it was possible to establish an acceptable daily intake for this group in terms of total cellulose ethers. Consideration of hydroxypropyl methylcellulose had had to be postponed at the last meeting because of doubtful correlation of the specifications for the different available forms. This problem has now been solved and a specification has been prepared. A monograph on this substance has been drawn up. The monograph on sodium carboxymethylcellulose, the evaluation of which is given in the seventh report, was amended to include a revised specification and additional biological data made available to the Committee.

The information on hydroxyethylcellulose was not sufficient to allow elaboration of a specification; furthermore, there was uncertainty about its use as a food additive. No information was received on carboxymethyl-gallactomannan and this substance was therefore not considered. There was insufficient information on propylene glycol alginate, especially on

¹ *FAO Nutrition Meetings Report Series*, 1967, No. 40 A, B, C; WHO/Food Add./67.29.

the biochemical aspect, to allow an estimate of an acceptable daily intake to be made. However, tentative specifications were prepared as stated in section 2.3.

6.2 Fatty emulsifiers

The Committee found it convenient to consider the acetic acid and fatty acid esters of glycerol, and the corresponding additives with citric acid, lactic acid, tartaric acid and mixed tartaric and acetic acids in place of acetic acid, as a group of related compounds because of their complete hydrolysis during manufacture and/or digestion into acceptable constituents of the diet. Bearing in mind the established principle that no food additive should be used at a higher level than that needed to achieve the technological effect required, the Committee agreed on an acceptable daily intake for the whole group in terms of total fatty acids esters of glycerol, with the following proviso: any contribution made by liberated lactic or tartaric acid to the total dietary intake of these two acids must not exceed their respective acceptable daily intakes, set forth in the eighth and ninth reports of this Committee. No such limitation need be imposed in the case of citric acid because of the revised evaluation mentioned in a later section in this report. A new member, mixed acetic and tartaric and fatty acid esters of glycerol, was considered and included in the group evaluation. In the interest of simplicity the Committee renamed the individual members of this group as follows: acetic (or citric, lactic, tartaric, etc.) acid and fatty acid esters of glycerol.

Evaluation of diacetyltartaric acid and fatty acid esters of glycerol had been postponed at the last meeting because of the absence of suitable specifications. These have now been provided and an acceptable daily intake agreed which is, however, independent of that established for the group of glyceride esters mentioned above, the reason being that diacetyltartaric acid is not found naturally in the diet. The evaluation of sulfoacetic acid and fatty acids esters of glycerol and their sodium salts was postponed because of insufficient biological data. Moreover, the hydrolysis of these esters gives rise to components that are not acceptable dietary constituents, and this necessitates separate evaluation.

The group of polyglycerol esters of fatty acids was evaluated on the basis of extensive toxicological data provided for a typical member and a specification was prepared. Because of the similarity in their biochemical behaviour, all compounds complying with the agreed specification are covered by the evaluation, but related compounds, not complying with the specification, will require individual biochemical studies to exclude unforeseen toxicological effects.

The sucrose esters and sucroglycerides could not be evaluated because of inadequacy of available biochemical information and lack of proper

toxicological data on dimethyl formamide present as a contaminant in these compounds ; such data might have enabled the Committee to set a limit for this unavoidable contaminant.

6.3 Natural stabilizers

Furcellaran and its salts could not be evaluated because of lack of relevant toxicological information but a tentative specification was prepared and is available. Carrageen and its salts are at present being used as food additives and for pharmaceutical purposes. The available toxicological data are, however, inadequate for the establishment of an acceptable daily intake. The Committee recommends that suitable information, particularly from the use of carrageen in man, should be provided within the next four years to allow a decision to be taken on permission to continue the use of this substance.

Notwithstanding the fact that gum arabic, karaya, tragacanth, carob bean gum and oat gum have been employed in and as food over many years in various countries, the Committee felt that the available toxicological information on these substances was insufficient for the establishment of acceptable daily intakes. However, tentative specifications have been prepared for all these substances except oat gum, and it was considered desirable that further studies with emphasis on absorption and fate in the human body should be carried out.

6.4 Steroid emulsifiers

Specifications could be established only for cholic and deoxycholic acids and their salts. These bile acids are physiological substances and were found to be limited in their use because of their bitter taste. An acceptable daily intake was established on the basis that a 5% variation in the daily output of bile salts is of normal physiological occurrence, so that an intake of corresponding magnitude would not contribute significantly to the normal body load.

6.5 Miscellaneous emulsifiers

No evaluation was possible for hydroxylated lecithin on the basis of the information available to the Committee. It was noted that bleached lecithin was included in the specification and evaluation given for lecithin in the seventh report of the Joint FAO/WHO Expert Committee on Food Additives.¹

¹ *FAO Nutrition Meetings Report Series*, 1964, No. 35 ; *Wld Hlth Org. techn. Rep. Ser.*, 1964, 281.

7. MISCELLANEOUS FOOD ADDITIVES

When evaluating pimaricin it was noted that only few data on its metabolism were available. Furthermore, because this substance is an antibiotic, the Committee thought it advisable to recommend that pimaricin should not be singled out from other antibiotics for consideration.

The incompleteness of the toxicological data supplied for glucono-delta-lactone was compensated by the available knowledge on the metabolic fate of this compound and its role as an intermediary in glucose metabolism. A specification was elaborated and an acceptable daily intake established.

With regard to D-mannitol, it was appreciated that this substance is not easily metabolized and that it is poorly absorbed from the human gastro-intestinal tract. Furthermore, the use is self-limiting because of the known laxative effect. The Committee established an acceptable daily intake for food additive purposes based on a clinically supported no-effect level in man.

Although polyvinylpyrrolidone is known to be metabolically inert and has been widely used clinically, it was given only a conditional acceptable daily intake because of the possible cumulation of this compound in the mesenteric lymph nodes. Further feeding studies will be required within the next two years in order to clarify this problem. The decisions on this substance and on D-mannitol are given in Annex 2.

8. SUBSTANCES POSTPONED FROM PREVIOUS MEETINGS

The Committee was asked to reconsider the newly available evidence on a number of substances that had not been evaluated at previous meetings because of the lack of relevant information. Evaluation of brominated vegetable oils had been postponed from the ninth meeting because of inadequacy of evidence from appropriate long-term studies with special reference to possible cumulative effects. No results of such further studies were submitted in time for consideration by this Committee and a decision on permission to continue the use of brominated oils as a food additive was postponed for consideration at a future meeting of the Committee. A specification was elaborated for the additive "propylene glycol esters of fatty acids" which had been considered at the ninth meeting and a monograph has been prepared for inclusion with those on other emulsifiers and stabilizers. The decisions on diacetyltartaric acid and fatty acid esters of glycerol and on propylene glycol alginate and hydroxypropylmethylcellulose are mentioned in the respective sub-sections on emulsifiers and stabilizers.

There was doubt whether stearyl citrate, an antioxidant synergist, which was considered at the ninth meeting, is presently used as a food additive.

The biological data on butyl *p*-hydroxybenzoate were considered to be insufficient to allow an evaluation to be made when this substance was studied at the ninth meeting. As no further information has been received since then it was not possible to proceed further with the evaluation.

Since potassium propionate and sodium sorbate are not used in food technology no further consideration was given to these substances.

9. RE-EVALUATION

The Committee was asked to re-evaluate a number of substances. The decisions are given in Annexes 2 and 3.

Hexamethylenetetramine was evaluated in the sixth report of the Committee,¹ but re-evaluation has been postponed because of the considerable amount of further work since reported to be in progress. Much of this work has been completed and the results were made available to the present Committee. These removed previous doubts with respect to carcinogenicity in rodents, but the Committee recommended postponement of consideration of this food additive until further reproduction studies in dogs have been conducted and more information has been obtained on the metabolic fate in man from studies based on the therapeutic use of this substance. Hexamethylenetetramine should not be put forward for re-evaluation until the further work required has been completed and the results made available. A specification for this substance is available.

When discussing nitrates and nitrites, reference was made to the fact that methaemoglobinaemia has been reported in infants who have consumed spinach and water containing these substances. On the other hand, the possible presence of nitrosamines in some food needs investigation, and reference is again made to the statement in the ninth report of the Committee relating to the urgent need for investigating the problem in connexion with the treatment of flour by nitrogen oxides. It is strongly recommended that a future meeting of the Committee should consider this problem.

The acceptable daily intake for citric acid was reviewed as requested in the Committee's seventh report and, in line with the assessment for citrates given there, it was decided not to set a limit for daily intake of this substance. The acceptable daily intake for ascorbic acid was left unaltered because the Committee had no new information before it justifying any change in the evaluation.

¹ *FAO Nutrition Meetings Report Series*, 1962, No. 31; *Wld Hlth Org. techn. Rep. Ser.*, 1962, 228.

In accordance with the principle of grouping chemically and biologically related compounds, the Committee agreed to place propyl, octyl and dodecyl gallates in one group, as shown in Annex 2. A specification has now been elaborated and is available on request from the joint FAO/WHO Food Standards Branch (Codex Alimentarius), FAO, Rome.

Further clinical information was supplied to the Committee on DL-lactic acid confirming the difficulties encountered by premature and young infants in metabolizing the D(-)isomer and coping with excess L(-)isomer. It is highly probable that the same difficulty occurs with DL-malic acid, although no published observations are available. Consequently the evaluation made in the ninth report was left unchanged.

At the request of the Food Additives Committee of the Codex Alimentarius Commission a number of food colours were re-evaluated.

Riboflavin was submitted as a food colour but the Committee considered it technologically unsuitable for this purpose and recommended that its use in food should be based upon its properties as a vitamin.

The four carotenoids beta-carotene, beta-apo-8'-carotenal and the methyl and ethyl esters of beta-apo-8'-carotenoic acid were evaluated as a group on the basis of satisfactory biochemical and toxicological information in animals and man and their activity as provitamin A. It was considered unlikely that any of these carotenoids would present a risk of hypervitaminosis A in man because of their poor absorption from the gastro-intestinal tract. Specifications are available and the establishment of ADIs for these four compounds permits their transfer to Category A of food colours in accordance with the principles of classification of food colours laid down in the eighth report. Although the methyl ester of beta-apo-8'-carotenoic acid had not been classified previously it is now included in Category A. The carotenoid canthaxanthine was evaluated separately because of its lack of activity as provitamin A, and an acceptable daily intake was established from the available toxicological data.

A number of colours at present classified as CII were re-evaluated in the light of new information available. Only for indanthrene blue RS and Quinoline Yellow did the results of long-term studies provide justification for recommending inclusion in group CI. The biological information available on Black 7984 was such as to necessitate postponement of consideration until it could be presented in a more detailed manner.

The monographs on these food colours will be published along with those on the other food colours considered earlier.¹

¹ *Specifications for Identity and Purity and Toxicological Evaluation of Food Colours. FAO Nutrition Meetings Report Series, 1967, No. 38 B, WHO/Food Add./66.25.*

10. MONOGRAPHS

The specifications, biological data and toxicological evaluations relating to the compounds considered at this and earlier meetings will be found in the monographs in a series of documents. Annex 4 indicates in which documents the desired information on individual compounds may be found and provides some general remarks on these monographs.

11. TOLERANCES OF A FOOD ADDITIVE IN RELATION TO ITS DAILY INTAKE

At the request of the Codex Committee on Food Additives, the Expert Committee examined a recently published paper¹ describing a mathematical approach for converting the ADI into upper limits of levels of use of a food additive. The members of the Expert Committee were impressed with the amount of thought, ingenuity and work that had been put into the development of this method. It was apparent to the Committee, however, that no single formula could, or indeed was ever likely to, encompass the whole of the complex field involved in the use of an additive in several different foods, which might be consumed in varying amounts by different population groups in many different communities.

The Committee reaffirmed the validity of the method, described in its second² and sixth reports,³ of calculating the daily intake of a food additive based on the levels arising from good technological practice, average consumption of foods containing the additive, and average body-weight. The use of various types of consumption data, high as well as average, was considered by the Committee and the implications analysed for subsequent calculation of the daily intakes and the likely protection thereby afforded to persons with different levels of consumption.

The Committee noted that, whilst data on average food consumption were available from many countries, high consumption data were available from only two countries. Data were presented showing the variation in the consumption of classes and items of food between countries and regions. With classes of food the variations in consumption higher than the average were small, but with some individual food items the variation was relatively

¹ Hansen, S. C. (1966) *Food and cosmet. Toxicol.*, **4**, 427.

² *FAO Nutrition Meetings Rep. Ser.*, 1958, No. 17; *Wld Hlth Org. techn. Rep. Ser.*, 1958, **144**.

³ *FAO Nutrition Meetings Rep. Ser.*, 1962, No. 31; *Wld Hlth Org. techn. Rep. Ser.*, 1962, **228**.

great. Such instances were, however, considered to represent mainly a local problem.

Since it is necessary to determine how much of a food additive is likely to be consumed by various sections of a wide range of communities throughout the world, especially those groups that have a high level of consumption, the Committee strongly recommended that every effort should be made to obtain such information on food consumption. It is important that the needs of the Codex Committee be made known to those concerned with food surveys to ensure that the type of information required by the Codex Committee is obtained. In the absence of comprehensive actual food consumption data, it might well be necessary for the Codex Committee to make temporary use of alternative methods of obtaining these data, such as by appropriate extrapolation from relevant information.

In an attempt to facilitate the work of the Codex Committee on Food Additives, the Expert Committee agreed on a new procedure concerning the establishment of acceptable daily intakes. Details of this procedure may be found in Annex 5.

12. RECOMMENDATIONS

1. The Second Joint FAO/WHO Conference on Food Additives recommended that the Joint FAO/WHO Expert Committee on Food Additives should serve as the advisory body to the Joint FAO/WHO Codex Alimentarius Commission on matters relating to specifications and toxicological evaluation of food additives. It is essential that the Committee continue to meet annually in order that it may keep up with the progress made, through the said Commission, in the Food Standards Programme.

2. Further meetings of the Joint FAO/WHO Expert Committee on Food Additives should be convened to draw up specifications for flavouring substances, non-nutritive sweeteners, solvents and antibiotics used as food additives, and to evaluate the toxic hazards involved in their use.

3. The Joint FAO/WHO Expert Committee on Food Additives should be convened to consider the toxic hazards associated with trace elements in foods, as soon as the information required (see page 14) becomes available.

4. A special sub-committee of the Joint FAO/WHO Expert Committee on Food Additives should be set up, including among its members, pediatricians, to study the special problems arising from exposure of infants and young children to food additives.

5. Data on the average consumption and high consumption of certain groups or individual items of food should be collected at national and

regional levels to facilitate proper establishment of limits of use of food additives.

6. It is suggested that if the Joint FAO/WHO Codex Alimentarius Commission should consider any substances in food that, in their opinion, have toxicological significance, then relevant biological data be sent to WHO, and information on chemical properties to FAO, for transmission to the Joint FAO/WHO Expert Committee on Food Additives for evaluation.

Annex 1

ACCEPTABLE DAILY INTAKES FOR MAN
OF SOME EMULSIFIERS AND STABILIZERS

Compounds considered	Specifications available	Overall daily intake zone ^a (mg/kg body-weight)	
		Unconditional	Conditional
Sodium carboxymethylcellulose	Yes	0-30 ^b	Higher levels for dietetic or calorie control purposes
Hydroxypropylmethylcellulose	Yes		
Methylcellulose	Yes		
Methylethylcellulose	Yes		
Acetic acid and fatty acid esters of glycerol	Yes	0-100 ^c	
Citric acid and fatty acid esters of glycerol	Yes		
Lactic acid and fatty acid esters of glycerol ^d	Yes		
Mixed tartaric and acetic and fatty acid esters of glycerol ^e	Yes		
Diacetyltartaric acid and fatty acid esters of glycerol	Yes	0-25	25-50
Polyglycerol esters of fatty acids	Yes	0-12.5	12.5-25
Propylene glycol esters of fatty acids	Yes	0-20 ^f	20-60 ^f
Cholic and deoxycholic acids and their salts	Yes	0-1.25	

^a The first part of the overall acceptable daily intake zone is termed unconditional and this represents levels that can be safely employed without further expert advice. The second part of the zone is termed conditional and represents levels that can be employed safely but at which it is thought desirable that some degree of expert supervision and advice should be readily available.

^b As the sum of these cellulose derivatives.

^c As the sum of these fatty emulsifiers.

^d The conditional zone of acceptability for the total intake of D(—)-lactic acid is 0-100 mg/kg.

^e The zone of acceptability for the total food additive intake of tartaric acid is 0-6 mg/kg (unconditional) and 6-20 mg/kg (conditional).

^f As propylene glycol.

Annex 2

ACCEPTABLE DAILY INTAKES FOR MAN
OF SOME MISCELLANEOUS FOOD ADDITIVES

Compounds considered	Specifications available	Overall daily intake zone ^a (mg/kg body-weight)	
		Unconditional	Conditional
Ascorbic acid	Yes	0-2.5	2.5-7.5
Citric acid	Yes	Not limited	
Propyl gallate	Yes	0-0.2 ^b	0.2-0.5 ^b
Octyl gallate	Yes		
Dodecyl gallate	Yes		
Glucono-delta-lactone	Yes	0-15	15-50
Hexamethylenetetramine	Yes	Decision	postponed
Isopropyl citrate mixture	Yes	0-7	7-20
DL-Lactic acid	Yes		0-100 ^c
DL-Malic acid	Yes		0-100 ^d
D-Mannitol	Yes	0-50	50-150
Polyvinylpyrrolidone	Yes		0-1

^a The first part of the overall acceptable daily intake zone is termed unconditional, and this represents levels that can be safely employed without further expert advice. The second part of the zone is termed conditional and represents levels that can be employed safely but at which it is thought desirable that some degree of expert supervision and advice should be readily available.

^b As the sum of these gallates (calculated as gallic acid).

^c Refers to content of D(-)-lactic acid.

^d Refers to content of D(-)-malic acid. The maleic acid content of malic acid should not exceed 0.05%.

Annex 3

ACCEPTABLE DAILY INTAKES FOR MAN
AND CLASSIFICATION OF SOME FOOD COLOURS ^a

Compounds considered	Specifications available	Toxicological classification	Overall daily intake zone ^b (mg/kg body-weight)	
			Unconditional	Conditional
Beta-carotene	Yes	A	0-2.5 ^c	2.5-5.0 ^c
Beta-apo-8'-carotenal	Yes	A		
Methyl and ethyl esters of beta-apo-8'-carotenoic acid (C ₃₀)	Yes	A		
Canthaxanthine	Yes	A	0-12.5	12.5-2.5
Black 7984	Yes	CII		
Indanthrene Blue RS	Yes	CI		
Quinoline Yellow	Yes	CI		

^a See the eighth report of the Joint FAO/WHO Expert Committee on Food Additives (1965), page 14.

^b The first part of the overall acceptable daily intake zone is termed unconditional, and this represents levels that can be safely employed without further expert advice. The second part of the zone is termed conditional and represents levels that can be employed safely but at which it is thought desirable that some degree of expert supervision and advice should be readily available.

^c As the sum of all these carotenoids.

Annex 4**EXPLANATORY NOTES ON THE ACTIVITIES
OF THE JOINT FAO/WHO EXPERT COMMITTEE
ON FOOD ADDITIVES****A. General Remarks**

Satisfactory control of the use of food additives presents considerable problems. In many countries, special agencies are responsible for such control and some of them have supporting scientific facilities at their disposal. In other countries, however, there is a lack of adequate machinery to handle these problems. A joint FAO/WHO programme was therefore initiated with the object of making systematic evaluations of food additives and providing advice to Member States of FAO and WHO on the control of these chemicals and on related health aspects. It is hoped that this advice will also help to render the legislation of countries more uniform with regard to the control of food additives and thus facilitate international trade.

The two bodies responsible for implementing the programme are the Joint FAO/WHO Expert Committee on Food Additives and the Committee on Food Additives of the Joint FAO/WHO Codex Alimentarius Commission. The respective functions of these two bodies are indicated below.

The Expert Committee

Several meetings of the Joint FAO/WHO Expert Committee on Food Additives have been held in the past few years. The members attending these meetings are invited by FAO and WHO and serve in their individual capacity as scientists and not as representatives of their governments. The main terms of reference of the Expert Committee are to establish specifications for identity and purity for food additives and to evaluate the toxicological data and recommend, where possible, acceptable daily intakes for man.

The Codex Committee

The Expert Committee also acts in an advisory capacity to the Codex Committee on Food Additives. The Codex Committee is attended by representatives of member governments. Through the Codex Alimentarius

Commission it proposes to governments for international acceptance tolerances for additives in various foods. The relation of the Expert Committee to the Codex Committee, the Codex Alimentarius Commission and the governments is shown in the Appendix 1.

Substances selected for consideration

The substances to be considered at a meeting of the Expert Committee are selected by the Codex Committee. In making this selection priorities are given to those substances used extensively on food entering international trade in substantial amounts. However, substances used extensively in domestic food in individual countries are also considered by the Expert Committee upon request from governmental authorities. *The fact that a substance has not yet been considered by the Expert Committee does not necessarily imply any doubt about its technical usefulness or safety in use.*

The data on which the evaluation is based

Before each meeting every effort is made to collect as many relevant published and unpublished data as possible. The Expert Committee has repeatedly emphasized the great value of publishing experimental results. Findings published in the scientific literature are subject to examination, criticism and refutation or confirmation by other scientists. Unpublished reports are not necessarily subjected to this scrutiny. For this reason, when considering scientific information greater weight is usually given to published than unpublished work. Under no circumstances does the Expert Committee consider confidential documents.

Research workers are invited to send reports of investigations relating to food additives to the following addresses :

- (1) Toxicological data (in duplicate) : Food Additives, WHO, Geneva, Switzerland.
- (2) Data on specifications for identity and purity : Food Science and Technology Branch, FAO, Rome, Italy.
- (3) Data on use and tolerances : Chairman of the Codex Committee on Food Additives, Ministry of Agriculture and Fisheries, The Hague, Netherlands.

Research workers who submit such data but find subsequently that their work is not mentioned in the monograph may rest assured that their results have been taken into account ; in the interests of brevity, however, the bibliographies in the monographs are limited to strictly relevant and more recent investigations.

The report of the Expert Committee

The report contains a description of the general principles used in the evaluation as well as a brief summary of the deliberations on the substances listed on the agenda.

Decisions on the use of a chemical should be taken only after consulting the detailed monographs.

The Monographs

Following each meeting, one or more documents are published in addition to the report mentioned above. Each document contains a number of monographs, the general content of which is given in the next section.

If the Expert Committee finds it necessary to re-evaluate a food additive, even though no fresh toxicological data are available, a new monograph is published giving only the new evaluation. If a limited amount of fresh information is available, this is included in the new monograph, whether or not it alters the evaluation; the information given in the original monograph is not repeated. The documents containing the relevant information on the various additives so far examined by the Expert Committee may be found by reference to the tables in Appendix 2.

B. Specifications

1. General principles governing the establishment of specifications

The specifications needed for each food additive have been compiled with three main objects in mind:

- (a) to identify the substance that has been subjected to biological testing;
- (b) to ensure that the substance is of the quality required for safe use in food;
- (c) to reflect and encourage good manufacturing practice.

Identification of the substance

Adequate specifications of identity and purity should be available before toxicological work is initiated. Toxicologists and regulatory bodies need assurance that the material to be tested corresponds to that to be used in practice. Ideally, the specifications should be such as to define a material that will give reproducible biological results.

It is essential to know the identity and concentration of the major component or components of a food additive before carrying out an effective toxicological investigation of its properties. Even small differences

in composition of a compound may materially alter the results of toxicity tests. The investigator must also know the nature and quantity of the important impurities. Toxicologists have frequently emphasized that impurities or minor constituents may have a significant importance far greater than their amounts might indicate.

In many animal tests, particularly with some of the relatively inert food additives, large amounts of the chemical are required and therefore the investigator must be certain that he has sufficient material of a uniform nature or a reliable source of the material of the same composition. In certain instances, years of animal studies have been wasted because the various batches of the food additive differed in composition. Furthermore, even if tests demonstrate beyond any reasonable doubt that a particular substance is safe for use, their value is impaired when the food additive used commercially differs significantly from the material tested.

The results of a single investigation are not likely to answer for all time the question of the safety for use of a particular material. The Joint FAO/WHO Expert Committee on Food Additives stated in its first report that permitted additives should be subjected to continuing observation for possible deleterious effects under changing conditions of use and should be reappraised whenever indicated by advances in knowledge. Specifications based on the material used in previous tests would therefore be of great value in making certain that a comparable product was employed in such reappraisals. The divergent results that are occasionally encountered in the toxicological investigation of the same product may conceivably be due to variations in the composition of batches of the material under test.

Quality control

Whereas a natural food may vary in composition, sometimes to a considerable degree or in undefined ways, considerations of public health dictate that, as a matter of principle, additives to food should be of known composition and purity. In fact, modern methods make it possible to produce synthetic chemicals of greater purity and uniformity than is usually achieved in the production of substances of natural origin. The adoption of official specifications for food additives would give assurance to the consuming public that substances meeting established standards of quality are available for use in food.

Specifications for food additives produced commercially should be broad enough to include all the variations in the composition of these additives that, according to current knowledge, do not significantly affect their biological properties. As an example, mono- and di-glycerides of edible fatty acids are considered as coming under one specification for the purpose of the toxicological evaluation. In any case, each such group

of additives will have to be judged individually with respect to the limits of composition set out in the specifications.

At the present time most food legislation merely indicates by name the substances that may be used in a particular food. It is well known that chemicals are produced in a variety of technical and refined grades. Toxicological evaluation, which is a costly and time-consuming procedure, must be related to the particular grade or quality of chemical intended for use in food. The adoption of specifications for purity of food additives would provide a means of accurate identification of the additive for regulatory purposes and would limit the known undesirable ingredients or contaminants to acceptable tolerance levels.

Good manufacturing practice

The existence of specifications, agreed upon by qualified specialists, serves to ensure a degree of reproducibility and of conformity to criteria of quality which are acceptable to both chemical manufacturers and food processors. Furthermore, established specifications might well act as a guide in the development of new chemicals of a quality suitable for food use. Specifications for identity and quality of food additives, however, need not be more stringent than necessary to accomplish their purpose and should be reasonably attainable by the producing industries.

Tests for impurities such as lead, arsenic and heavy metals as a measure of good manufacturing practice should be maintained, unless and until there is a better alternative.

2. Source and nature of impurities

The purity of a food additive, as the term is here employed, refers to its freedom from substances other than those named in specifications. "Foreign substances" or "impurities" not included in the specifications may be, for example, simple inorganic salts or other substances not necessarily deleterious from the technological or safety standpoint.

Impurities may arise from the raw materials used in the manufacture of chemicals (especially when they are complex natural substances), from substances used in processing, from solvents used in extraction or crystallization and from equipment. They may also be unreacted intermediates or by-products formed in the course of processing, such as incompletely esterified acids or isomeric derivatives. Products of decomposition during storage, such as may result from oxidation, hydrolysis or polymerization, are likewise regarded as impurities. However, the constituents of polymeric or other mixtures of reproducible composition are not regarded as impurities if they contribute to the functional properties of the substance as a whole and are not deleterious. Obviously contaminants like dirt,

soot, rust, lubricants and insect fragments must be avoided in manufacture, packing and storage of food additives.

The levels of impurities that, according to current knowledge, are considered to be toxicologically significant and the methods for determining them must appear in the specifications.

3. Details of specifications

Nomenclature

The title of each monograph contains the name by which the substance is most commonly known in food manufacture. Where other recognized names exist, they are listed as synonyms. For the chemical names, the recommendations of the International Union of Pure and Applied Chemistry (IUPAC) and, when this was not possible, the usages of the various national chemical societies have been taken into consideration. Where the structure or composition of a food additive has not been clearly elucidated, a description of its chemical nature is given instead of the chemical name.

Formulas

An empirical formula is given for each inorganic and organic substance and structural formulas are shown, where known, for organic substances. All formulas represent the pure compounds and serve only a descriptive purpose.

Molecular weight

For purposes of information and description, the molecular weights of the compounds are given where known. These have been calculated from the table of atomic weights approved by the Commission on Atomic Weights of the International Union of Pure and Applied Chemistry.

Definition. The amount of the main substance that should be present is given as the percentage of the material having a stated formula. A short description indicating the starting materials used and the processes of synthesis or the origin of the material as well as materials used in the purification is included, if relevant.

Description. The properties of the compound that may be perceived by the senses are given. These include colour, odour, texture, general appearance and taste.

The specifications refer only to the main ingredient as a pure substance. A food additive, however, may be marketed as a formulated preparation consisting of the main ingredient, a vehicle and possibly other substances.

Cautions. A cautionary note is added where a material is dangerous to handle.

Identification tests. In this section, specific and non-specific tests are included that should, either singly or collectively, enable the material to be identified.

Purity tests. These include limits for loss on drying, sulfated ash, physical constants such as the pH of a 10% solution, and arsenic, lead, heavy metals and certain other elements. It is assumed that all food additives should be products of high-grade chemical manufacture and that they should be free from dirt or other foreign matter. The nature of impurities that might be present in a food additive has been discussed above. In the case of arsenic and lead, limits of 3 mg/kg and 10 mg/kg, respectively, may be considered acceptable unless otherwise stated. Mercury, cadmium, selenium and fluorine may occur in food additives in rare cases; the limits fixed apply only when these elements may be introduced through raw materials or conditions of manufacture. For heavy metals collectively a limit of 40 mg/kg is proposed, except where otherwise stated. It is stressed that these limits are established to ensure good manufacturing practice; in most cases, there is no toxicological risk involved at these tolerance levels in food additives. The methods to be used for the determinations required, if not given in the monographs, are published in a separate document.

Assays. The assay methods described for the compounds are those that are considered to be the most suitable. A second method is included if the preferred procedure requires instrumentation not widely available.

The percentage composition determined by the assay should not exceed 100.5%, unless otherwise stated in the definition. It should not be less than the minimum content given in the definition, within the limits indicated by the last significant figure of the stated value. Thus, an assay of 98.8% is acceptable if the requirement is "not less than 99%", but it is not acceptable if the requirement is "not less than 99.0%".

Temperature. All temperatures are given in degrees centigrade.

Solubility. The solubilities of the substances contained in the monographs are given without reference to possible chemical changes. Unless otherwise stated, the solubility at room temperature is given.

Solvents. Unless otherwise stated, reference to water in the monographs presumes distilled water. The term "ethanol" is used as referring to 95% v/v ethyl alcohol, and the term "absolute ethanol" for solvent containing not less than 98.8% v/v ethyl alcohol. Other v/v concentrations of ethanol may be specified in individual cases.

Test solutions. All reagents referred to in the identification and purity tests and in the assays are assumed to be analytical grade, unless otherwise specified.

Test solutions (TS) are given in alphabetical order in a separate publication; the indication (PbT) means that the test solution used must be free of lead.

In general, solutions are brought to approximate normality or to a simple multiple or fraction of normality. When the normality or percentage composition of acids is not indicated, the concentrated commercial form should be used.

Where the use of a test solution as indicator is specified in a test or assay, 3 drops of the solution should be added.

C. Biological Data and Toxicological Evaluation

1. Biochemical studies

Under this heading is recorded information as to whether a substance is absorbed, what factors may affect its absorption, how the substance is distributed in the body, how it is metabolized and the route by which it is eliminated. In addition, there may be studies on the metabolic pathway that a substance follows in the body and whether the change in structure that takes place during metabolism results in any significant change in its biological effect. Such biochemical changes as alterations in enzyme activities induced by the substance under study are also given under this heading.

2. Acute toxicity

Since this information is of limited use in the evaluation of the chronic toxicity it is presented only in tabulated form. The LD_{50} gives some indication of the general toxicity class, and the differences in toxicity following different routes of administration may be of interest. The studies are usually performed on several species and this may give some indication of the relative sensitivity of these species. The LD_{50} 's listed should only be considered as examples because no attempt has been made to include all the work on acute toxicity.

3. Short-term studies

These include all investigations the duration of which does not exceed 50% of the animal's lifespan. As a rule, a number of different species are used. It is probable that most of the toxic effects can be demonstrated in such studies.

4. Long-term studies

In this category are those tests that have been carried out over the greater part of the animal's lifespan. Such tests are essential for assessing

the carcinogenic risk. They are, generally speaking, the most important studies for the evaluation of the acceptable daily intakes of food additives, since these substances may be consumed by man for the whole lifespan. For the purpose of recording the data, a study is considered long-term if it has been carried out over 1 year in mice and rats or over 5 years in dogs.

5. Comments

In each monograph the presentation of the relevant biological data is followed by the comments of the Expert Committee, which constitute a brief appraisal of the main evidence.

Under this heading the reader will also find comments on further work considered desirable. As the methodology for testing chemicals for their safety in use advances constantly, the Expert Committee in certain cases considers it desirable to indicate some further test which should be performed.

6. Evaluation

6.1 *Level causing no toxicological effect in animals*

The evaluation is, in most cases, based essentially on the long-term studies. The highest dose level that causes no toxicological effect is usually the most useful quantitative index. In some cases, a particular dose level has been found to have only one effect, the significance of which from the toxicological viewpoint might be doubtful. In general, it is considered advisable to regard such doubtful effects as significant, even though they may later be found to be toxicologically unimportant. Interference with weight gain is regarded as of no significance only if it has been demonstrated that there was a corresponding reduction in food intake due to interference with palatability. The dose level at which no significant toxicological effect was observed is expressed as milligrams per kilogram of body-weight per day for a stated animal species.

6.2 *Acceptable daily intakes for man*

The acceptable daily intake is the daily dose of a chemical that appears to be without appreciable risk on the basis of all the facts known at the time. "Without appreciable risk" is taken to mean the practical certainty that injury will not result even after a lifetime of exposure.

Many factors have to be considered in deriving from the dose level that causes no toxicological effect in an experimental animal an estimate of the acceptable intake in man. It is necessary to take into account species differences, individual variations, incompleteness of available data, and a number of other matters. It must be remembered that food additives may be consumed by people of all ages throughout the whole lifespan, that

they are eaten by the sick as well as the healthy, and that there are wide variations in individual dietary patterns. Each case must be judged on its merits.

It will be observed from the above that the acceptable daily intake is only an estimate and depends upon a great number of factors, all of which should be taken into consideration. Therefore an exact maximum acceptable daily intake cannot be calculated. This is one of the reasons why, in some cases, the zone of acceptability is divided into two parts—"conditional" and "unconditional". Although the whole zone of acceptability may be safely used, obviously the smaller the amount of a given chemical consumed, the smaller the risk. However, there are circumstances where one has to weigh one risk against another. For a food colour, for instance, one would be inclined to make the acceptable risk smaller than for an antimicrobial used to preserve food that is scarce in many parts of the world. The conditional zone is one that can be safely used under certain conditions, which are specified where appropriate. Thus, in some cases, the use of the chemical might also be permitted for a limited length of time in order to obtain information from further work. In cases where the conditions are not specified, a final decision on whether intakes that fall within the range of conditional acceptance may be considered acceptable in particular circumstances should be taken by a group of scientists, including a toxicologist, experienced in this field.

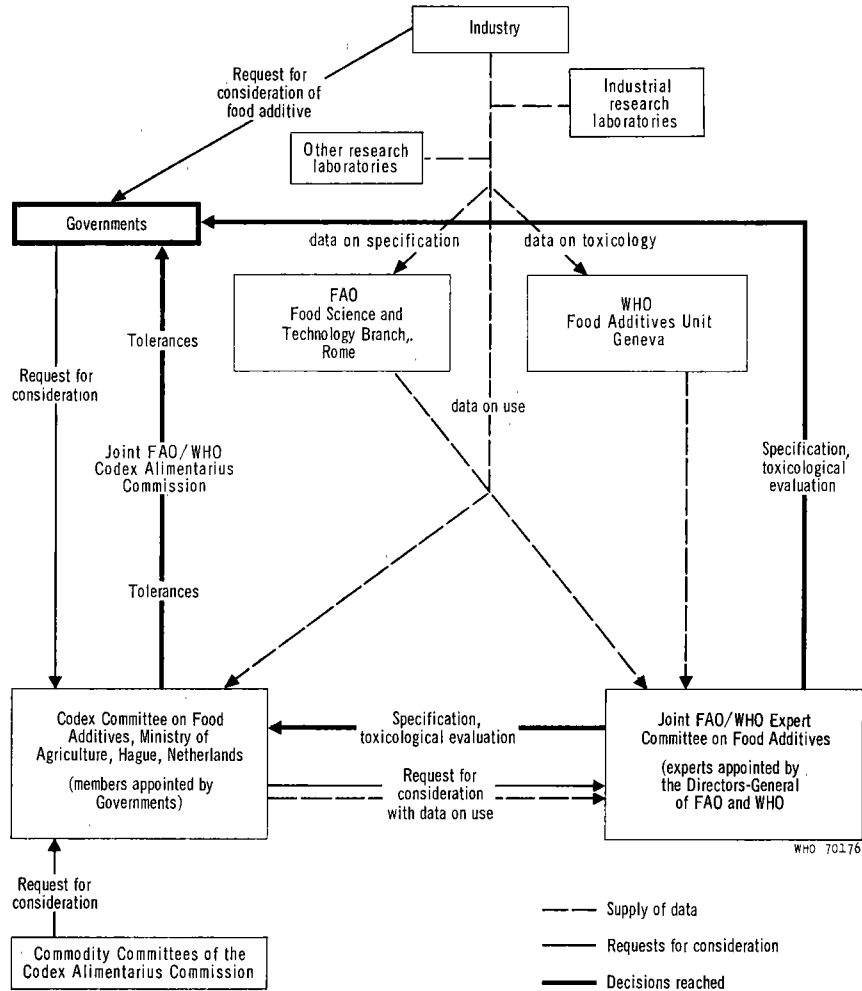
7. Further work required

Under this heading is listed all the work that the Expert Committee considers desirable before an unconditional acceptable daily intake can be established.

It must be emphasized that these recommendations are only a guideline and that the investigator should carry out any additional studies that he deems necessary to ensure the safe use of a particular substance.

Appendix 1

FLOW DIAGRAM FOR INTERNATIONAL ACCEPTANCE OF FOOD ADDITIVES *



* Reproduced with slight modifications from the ninth report of the Joint FAO/WHO Expert Committee on Food Additives (FAO Nutrition Meetings Report Series, 1966, No. 40; Wld Hlth Org. techn. Rep. Ser., 1966, 339).

Appendix 2**FOOD ADDITIVES EXAMINED BY THE JOINT
FAO/WHO EXPERT COMMITTEE ON FOOD ADDITIVES :
INDEX TO PUBLICATIONS****General Remarks****1. Grouping**

The substances are grouped according to technological use, with cross-references for those substances that have more than one application. The principal groups are in some cases subdivided, taking into account common technological or toxicological characteristics.

2. Name

The name used in the tables is the one appearing at the head of the monographs. As a rule this is the name by which the substance is most commonly known in food manufacture. The components of the names have sometimes been rearranged in order that chemically similar substances may be grouped together alphabetically.

3. Compounds that have been omitted from the tables

The following substances mentioned in reports of the Expert Committee do not appear in the tables because they have not been fully studied. The reasons for not examining them further are indicated in parentheses.

Benzoate, calcium (evidence that it is no longer used extensively in food industry).

Benzoates, *p*-hydroxy-, alkyl, sodium salts (probably a mixture of two additives already considered, namely, sodium hydroxide and the corresponding *p*-hydroxybenzoate ester).

Carboxymethylgalactomannan (evidence of its significance in the food industries not available).

Dithionite, sodium (no evidence of its present use in food industry).

Ethylene oxide (this compound is a fumigant and was referred to the Joint Expert Committee on Pesticide Residues).

Glycocholic and taurocholic acids (no evidence of significant use as food additives).

Hydroxyethylcellulose (no evidence of significant use as a food additive).

Nitrofurazone (withdrawn from consideration on toxicological and other grounds, see ninth report ⁶).

Nitrosyl chloride (no evidence of its present use as a food additive).

Propionate, potassium (no evidence of its significant use as a food additive).

Propylene oxide (see ethylene oxide).

Sorbate, sodium (not of significant use as a food additive for technological reasons).

Tannic acids (insufficient chemical data for establishment of specifications).

Thiodipropionate, distearyl (toxicological evaluation given in the sixth report,³ but stated in eighth report⁵ not to be on any of the permitted lists and withdrawn from consideration).

2,4,5-Trihydroxybutyphenone (no longer marketed as a food additive).

I. ACIDS AND BASES

<i>Name</i>	<i>Specification</i>	<i>Document</i>
		<i>Toxicological Evaluation</i>
<i>Acids</i>		
Acetic Acid	11	6, 10
Adipic Acid	11	6, 10
Citric Acid	1	3, 7
Fumaric Acid	11	6, 10
Gluconic Acid (see Glucono-delta-Lactone)		
Glucono-delta-Lactone (Gluconic Acid)	11	7, 10
Hydrochloric Acid	11	6, 10
DL-Lactic Acid	11	6, 10, 7
DL-Malic Acid	11	6, 10, 7
Monocalcium Phosphates	11	6, 10
Phosphoric Acid	1	3, 5, 8
Tartaric Acid	1	3, 5, 8
<i>Bases</i>		
Ammonium Carbonate	11	6, 10
Ammonium Hydrogen Carbonate	11	6, 10
Ammonium Hydroxide	11	6, 10
Calcium Carbonate	11	6, 10
Calcium Hydroxide	11	6, 10
Calcium Oxide	11	6, 10
Magnesium Carbonate	11	6, 10
Magnesium Hydroxide	11	6, 10
Magnesium Oxide	11	6, 10
Potassium Carbonate	11	6, 10
Potassium Hydrogen Carbonate	11	6, 10
Potassium Hydroxide	11	6, 10
Sodium Carbonate	11	6, 10
Sodium Hydrogen Carbonate	11	6, 10
Sodium Hydroxide	11	6, 10

II. ANTIMICROBIAL PRESERVATIVES

Name	Document	
	Specification	Toxicological Evaluation
Benzoic Acid	1	3, 6, 10
Benzoate, Potassium	11	6, 10
Benzoate, Sodium	1	3, 6, 10
Benzoate, <i>p</i> -Hydroxy-, Butyl	11	7, 10
Benzoate, <i>p</i> -Hydroxy-, Ethyl	1	3, 6, 10
Benzoate, <i>p</i> -Hydroxy-, Methyl	1	3, 6, 10
Benzoate, <i>p</i> -Hydroxy-, Propyl	1	3, 6, 10
Boric Acid	3	3
Borax	3	3
Diethyl Pyrocarbonate	11	6, 10
Diphenyl	8	3, 5, 8, 7, ^a
Formic Acid	8	3, 5, 8
Hexamethylenetetramine	11	6 (p. 17), 7
Hydrogen Peroxide	11	6, 10
Nitrate, Potassium	8	3, 5, 8, 7
Nitrate, Sodium	8	3, 5, 8, 7
Nitrite, Potassium	8	3, 5, 8, 7
Nitrite, Sodium	8	3, 5, 8, 7
<i>o</i> -Phenylphenol	8	3, 5, 8, 7, ^a
<i>o</i> -Phenylphenolate, Sodium	8	3, 5, 8, 7, ^a
Propionic Acid	11	6, 10
Propionate, Calcium	1	3, 10, 6
Propionate, Potassium	none	3, 6
Propionate, Sodium	1	3, 10, 6
Salicylic Acid	none	3
Sodium Diacetate	1	3
Sorbic Acid	1	3, 6, 10
Sorbate, Calcium	11	6, 10
Sorbate, Potassium	11	6, 10
Sulfur Dioxide	1	3, 8, 6, 10
<i>Other sources of sulfur dioxide</i>		
Potassium Metabisulfite	11	6, 10
Sodium Hydrogen Sulfite	1	3, 8, 6, 10
Sodium Metabisulfite	1	3, 8, 6, 10
Sodium Sulfite	1	3, 8, 6, 10
Thiodipropionic Acid	8	3, 5, 8
Thiodipropionate, Dilauryl	8	3, 5, 8

III. ANTIOXIDANTS AND ANTIOXIDANT SYNERGISTS

Ascorbic Acid	1	3, 7
Ascorbate, Sodium	1	3
Ascorbic Acid, Iso-	1	3
Ascorbate, Iso-	1	3

^a Pesticides referred to the Joint Meeting of the FAO Working Party and the WHO Expert Committee on Pesticide Residues.

Name	Specification	Document
		Toxicological Evaluation
Ascorbyl Palmitate	1	3
Butylated Hydroxyanisole (BHA)	1	3, 6
Butylated Hydroxytoluene (BHT)	1	5, 8, 6, 10
Citric Acid	1	3, 7
Citrate, Stearyl	— ^a	—
Ethylenediaminetetraacetate, Calcium Disodium	11	6, 10
Ethylenediaminetetraacetate, Disodium	11	6, 10
Gallate, Dodecyl	1	3, 8, 7
Gallate, Octyl	1	3, 8, 7
Gallate, Propyl	1	3, 8, 7
Guaiac, Gum	3	3
Isopropyl Citrate Mixture	11	3, 10, 7
Monoisopropyl Citrate (see Isopropyl Citrate Mixture)		
Nordihydroguaiaretic Acid (NDGA)	1	5, 8
Phosphoric Acid	1	5, 8
Tartaric Acid	1	5, 8
Tocopherol, Alpha	1	3
Tocopherols, Mixed concentrate	1	3

IV. EMULSIFIERS AND STABILIZERS

Natural Stabilizers

Agar	4	4
Alginic Acid	4	4
Alginate, Ammonium	4	4
Alginate, Calcium	4	4
Alginate, Potassium	4	4
Alginate, Sodium	4	4
Carrageen	— ^a	7
Furcellaran	— ^a	7
Gum, Arabic	— ^a	7
Gum, Carob bean	— ^a	7
Gum, Guar	— ^a	7
Gum, Karaya	— ^a	7
Gum, Oat	— ^a	7
Gum, Tragacanth	— ^a	7

Stabilizers made by modifying natural materials

Alginate, Propylene glycol	— ^a	7
Cellulose, Hydroxypropylmethyl-	11	7, 10
Cellulose, Methyl-	4, 11	4, 11
Cellulose, Methylethyl-	11	7, 10 ¹
Cellulose, Carboxymethyl-, Sodium	4, 11	4, 7, 10

Fatty Emulsifiers

Glycerides, Mono- and Di-	4	4
Acetic Acid and Fatty Acid Esters of Glycerol	11	7, 10

^a Tentative specification is available on request.

<i>Name</i>	<i>Document</i>	
	<i>Specification</i>	<i>Toxicological Evaluation</i>
Citric Acid and Fatty Acid Esters of Glycerol	11	7, 10
Diacetyltartaric Acid and Fatty Acid Esters of Glycerol	11	7, 10
Lactic Acid and Fatty Acid Esters of Glycerol	11	7, 10
Mixed Tartaric and Acetic Acid and Fatty Acid Esters of Glycerol	11	7, 10
Sulfoacetic Acid and Fatty Acid Esters of Glycerol (Sodium Salt)	— ^a	7
Polyglycerol Esters of Fatty Acids	11	7, 10
Polyoxyethylene (20) Sorbitan Monolaurate	4	4
Polyoxyethylene (20) Sorbitan Monooleate	4	4
Polyoxyethylene (20) Sorbitan Monopalmitate	4	4
Polyoxyethylene (20) Sorbitan Monostearate	4	4
Polyoxyethylene (20) Sorbitan Tristearate	4	4
Polyoxyethylene (8) Stearate	4	4
Polyoxyethylene (40) Stearate	4	4
Propylene Glycol Esters of Fatty Acids	11	7, 10
Propylene Glycol Monopalmitate	11	7, 10
Propylene Glycol Monostearate	11	7, 10
Sorbitan Monopalmitate	4	4
Sorbitan Monostearate	4	4
Sorbitan Tristearate	4	4
Sucrose Esters of Fatty Acids	— ^a	7
<i>Steroid Emulsifiers</i>		
Cholic Acid (and Sodium Salt)	11	7, 10
Cholic Acid, Deoxy- (and Sodium Salt)	11	7, 10
<i>Miscellaneous Emulsifiers</i>		
Lecithin	4	4
Lecithin, Hydroxylated	— ^a	7
<i>Salts</i>		
Acetate, Calcium	4	4
Chloride, Calcium	4	4
Citrate, Calcium	4	4
Citrate, Potassium	4	4
Citrate, Sodium	4	4
Phosphate, Monosodium	4	4
Phosphate, Disodium	4	4
Phosphate, Trisodium	4	4
Phosphate, Monopotassium	4	4
Phosphate, Dipotassium	4	4
Phosphate, Tripotassium	4	4
Phosphate, Di-		
Disodium	4	4
Tetrasodium	4	4

^a Tentative specification is available on request.

Name	Specification	Document
		Toxicological Evaluation
Phosphate, Tri-, Pentasodium	4	4
Phosphate, Poly-, Sodium	4	4
Tartrate, Sodium	4	4
Tartrate, Potassium Sodium	4	4

V. FLOUR TREATMENT AGENTS

Azodicarbonamide	11	6, 10
Bromate, Potassium	4	4
Chlorine	none	6, 10
Chlorine Dioxide	4	4
Iodate, Calcium	11 ^a	6, 10
Iodate, Potassium	11 ^a	6, 10
Monocalcium Phosphates	11	6, 10
Nitrogen, Oxides of	— ^b	6, 10
Peroxides, Acetone	11	6, 10
Peroxide, Benzoyl	4	4
Peroxide, Calcium	11	6, 10
Persulfate, Ammonium	11	6, 10
Persulfate, Potassium	11	6, 10
Stearyl-2-Lactylate, Calcium	11	6
Stearyl Tartrate	11	6, 10

VI. FOOD COLOURS *

Colours in toxicological categories A, B, and CI

Amaranth	9	5, 9
Brilliant Blue FCF	9	5, 9
Canthaxanthine	9	5, 9, 7
Beta-Apo-8'-Carotenal	9	5, 9, 7
Beta-Carotene	9	5, 9, 7
Beta-Apo-8'-Carotenoic Acid, Methyl or Ethyl Ester	9	5, 9, 7
Citrus Red No. 2	9	5, 9
Erythrosine	9	5, 9
Fast Green FCF	9	5, 9
Idanthrene Blue RS	9	5, 9, 7
Indigotine	9	5, 9
Orange I	9	5, 9
Patent Blue V	9	5, 9
Ponceau 4R	9	5, 9

^a Identification tests only.

^b According to ninth report,⁸ no satisfactory specification available, but use for treatment of flour has greatly declined.

* A number of other food colours were considered by the Joint FAO/WHO Expert Committee on Food Additives in 1964. A table showing the status of the specifications and the classification according to toxicological evaluation is given in the eighth report of this Committee.⁵

Name	Document	
	Specification	Toxicological Evaluation
Quercetin and Quercitron	9	5, 9
Quinoline Yellow	9	5, 9, 7
Sunset Yellow FCF	9	5, 9
Tartrazine	9	5, 9
Titanium Dioxide	9	5, 9
Wool Green BS	9	5, 9

*Colours in toxicological categories CII^a, CIII^a,
which are used in some countries*

Acid Fuchsin FB	9	5, 9
Azo Rubine	9	5, 9
Benzyl Violet 4B	9	5, 9
Black 7984	9	5, 7, 9
Blue VRS	9	5, 9
Brilliant Black BN " Specially Pure "	9	5, 9
Brown FK	9	5, 9
Chocolate Brown HT	9	5, 9
Chrysoine	9	5, 9
Eosine	9	5, 9
Fast Red E	9	5, 9
Fast Yellow AB	9	5, 9
Light Green SF Yellowish	9	5, 9
Methyl Violet	9	5, 9
Naphthol Yellow S	9	5, 9
Orange G	9	5, 9
Orange GGN	9	5, 9
Ponceau 2R	9	5, 9
Ponceau 6R	9	5, 9
Red 10B	9	5, 9
Red 2G	9	5, 9
Rhodamine B	9	5, 9
Scarlet GN " Specially Pure "	9	5, 9
Sudan G	9	5, 9
Sudan Red G	9	5, 9
Violet 5 BN	9	5, 9
Yellow 27 175N " Specially Pure "	9	5, 9

VII. OTHERS

Brominated vegetable oils	— ^a	6
Mannitol	11	10, 7
Polyvinylpyrrolidone	11	10, 7
Propylene Glycol	4	4
Sorbitol	4	4, 6, 10

^a Identification tests only.

References

- ¹ *Specifications for Identity and Purity of Food Additives. Vol. I. Antimicrobial Preservatives and Antioxidants*, Rome, FAO, 1962
- ² *Specifications for Identity and Purity of Food Additives. Vol. II. Food Colors*, Rome, FAO, 1963
- ³ *Evaluation of the Toxicity of a Number of Antimicrobials and Antioxidants*, FAO Nutrition Meetings Report Series, 1962, No. 31; *Wld Hlth Org. techn. Rep. Ser.*, 1962, 228 (Sixth Report)
- ⁴ *Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation: Emulsifiers, Stabilizers, Bleaching and Maturing Agents*, FAO Nutrition Meetings Report Series, 1964, No. 35; *Wld Hlth Org. techn. Rep. Ser.*, 1964, 281 (Seventh Report)
- ⁵ *Specifications for Identity and Purity of Food Additives and their Toxicological Evaluation: Food Colours and some Antimicrobials and Antioxidants*, FAO Nutrition Meetings Report Series, 1965, No. 38; *Wld Hlth Org. techn. Rep. Ser.*, 1965, 309 (Eighth Report)
- ⁶ *Specifications for Identity and Purity of Food Additives and their Toxicological Evaluation: Some Antimicrobials, Antioxidants, Emulsifiers, Stabilizers, Flour-Treatment Agents, Acids and Bases*, FAO Nutrition Meetings Report Series, 1966, No. 40; *Wld Hlth Org. techn. Rep. Ser.*, 1966, 339 (Ninth Report)
- ⁷ *Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation: Some Emulsifiers, Stabilizers and Certain Other Substances*, FAO Nutrition Meetings Report Series, 1967, No. 43; *Wld Hlth Org. techn. Rep. Ser.*, 1967, 373 (Tenth Report)
- ⁸ *Specifications for Identity and Purity and Toxicological Evaluation of some Antimicrobials and Antioxidants*, FAO Nutrition Meetings Report Series, 1965, No. 38A; WHO/Food Add/24.65
- ⁹ *Specifications for Identity and Purity and Toxicological Evaluation of Food Colours*, FAO Nutrition Meetings Report Series, 1965, No. 38B; WHO/Food Add/66.25
- ¹⁰ *Toxicological Evaluation of Some Antimicrobials, Antioxidants, Emulsifiers, Stabilizers, Flour-Treatment Agents, Acids and Bases*, FAO Nutrition Meetings Report Series, 40 A,B,C; WHO/Food Add/67.29
- ¹¹ Specification for these food additives will be submitted to the Fourth Meeting of the Codex Committee on Food Additives, September 1967, and will be available on request from the Joint FAO/WHO Food Standards Branch (Codex Alimentarius) FAO, Rome.

Annex 5

**PROPOSED MODIFICATION OF THE PROCEDURE
FOR ESTABLISHING ACCEPTABLE DAILY INTAKES**

Problems have been encountered by the Committee on Food Additives of the FAO/WHO Codex Alimentarius Commission in the estimation of the daily intake of food additives for which tolerances have been established and in the confinement of these intakes within the limits of the zones of acceptability. For this reason, the Joint FAO/WHO Expert Committee on Food Additives proposes in future to establish only unconditional zones of acceptability, which will then be transmitted to the Codex Committee on Food Additives. When the latter Committee has examined all the aspects involved, any problem that arises will be referred to the Expert Committee together with the following items of information :

1. A list of commodities in which the food additive may be used.
2. Residue data where applicable and the proposed tolerances.
3. The daily intake of the additive based on 1 and 2 and food consumption data.

When the information listed in 1, 2 and 3 has been reviewed by the Expert Committee one of the following actions will be taken :

1. The unconditional zone of acceptability will be restated without the Expert Committee being able to allocate a conditional zone¹ of acceptability.
2. A conditional zone¹ of acceptability in addition to the unconditional zone may be established based on further information supplied by the Codex Committee.

This re-evaluation will then be referred back to the Codex Committee. If it resolves the problem, the Codex Committee will so inform the Expert Committee. It is emphasized that the safety of the consumer should be considered to be of paramount importance in all decisions of the Expert Committee.

¹ This conditional zone of acceptability is not to be confused with the conditional (temporary) ADI, which is established on toxicological information not fully adequate by current standards and to which a safety margin greater than usual is applied.

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370	(1967) Pesticide Residues in Food Joint report of the FAO Working Party on Pesticide Residues and the WHO Expert Committee on Pesticide Residues (19 pages)	3/6	0.60	2.—
371	(1967) Research in Psychopharmacology Report of a WHO Scientific Group (39 pages)	5/-	1.00	3.—
372	(1967) Epidemiology and Control of Schistosomiasis Report of a WHO Expert Committee (35 pages)	5/-	1.00	3.—
373	(1967) Specifications for the Identity and Purity of Food Additives and their Toxicological Evaluation : Some Emulsifiers and Stabilizers and Certain Other Substances Tenth report of the Joint FAO/WHO Expert Committee on Food Additives (47 pages)	5/-	1.00	3.—