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TECHNICAL REPORT SERIES**

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No. 46

**SPECIFICATIONS FOR THE IDENTITY
AND PURITY OF FOOD ADDITIVES
AND THEIR TOXICOLOGICAL EVALUATION**

**Some Food Colours, Emulsifiers, Stabilizers,
Anticaking Agents, and Certain Other Substances**

**Thirteenth Report of the
Joint FAO/WHO Expert Committee on Food Additives
Rome, 27 May - 4 June 1969**



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Specifications for the substances considered in this report, as well as monographs containing summaries of relevant biological data and toxicological evaluations, will be issued by FAO and WHO in separate publications entitled:

1. *Toxicological evaluation of some food colours, emulsifiers, stabilizers, anticaking agents and certain other substances*

FAO Nutrition Meetings Report Series

No. 46A

WHO/Food Add./70.36

2. *Specifications for the identity and purity of some food colours, emulsifiers, stabilizers, anticaking agents and certain other substances*

FAO Nutrition Meetings Report Series

No. 46B

WHO/Food Add./70.37

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OF FOOD ADDITIVES AND THEIR TOXICOLOGICAL EVALUATION :
SOME FOOD COLOURS, EMULSIFIERS, STABILIZERS,
ANTICAKING AGENTS, AND CERTAIN OTHER SUBSTANCES**

**Thirteenth report of the Joint FAO/WHO
Expert Committee on Food Additives**

CORRIGENDA

Page v, under *Observers*, the correct title of Professor
M. J. L. Dols is :

Chairman, Codex Committee on Food Additives.

Page 10, footnote ³ should read : Annex 1, ref. 13.

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**THIRTEENTH SESSION OF THE JOINT FAO/WHO EXPERT COMMITTEE
ON FOOD ADDITIVES**

Rome, 27 May - 4 June 1969

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- Dr J. M. Coon, Department of Pharmacology, Jefferson Medical College, Philadelphia, Pennsylvania, U.S.A. (*Chairman*)
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- Dr L. Golberg, Research Professor of Pathology, Albany Medical College of Union University, Albany, New York, U.S.A. (*Rapporteur*)
- Dr H. Lange, Chairman, Food Chemistry Section, Society of German Chemists, c/o Nestlé Sarotti AG, Hattersheim, Federal Republic of Germany
- Professor R. Monacelli, Superior Institute of Health, Rome, Italy
- Professor M. J. Rand, Department of Pharmacology, University of Melbourne, Australia
- Professor J. F. Reith, Department of Food Chemistry and Toxicology, University of Utrecht, Netherlands (*Vice-Chairman*)
- Professor A. I. Stenberg, Head, Food Hygiene Department, Institute of Nutrition, Academy of Medical Sciences of the U.S.S.R., Moscow, U.S.S.R. (unable to attend)
- Professor R. Truhaut, Director, Toxicological Research Centre, Faculty of Pharmacy of the University of Paris, France

Observers (invited by FAO)

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INTRODUCTION

The thirteenth session of the Joint FAO/WHO Expert Committee on Food Additives met in Rome from 27 May to 4 June 1969. The meeting was opened by Mr A. Adomakoh, Assistant Director-General, FAO, on behalf of the Directors-General of the Food and Agriculture Organization of the United Nations and the World Health Organization. Dr J. M. Coon was unanimously elected Chairman and Professor J. F. Reith, Vice-Chairman. Dr L. Golberg agreed to serve as Rapporteur.

As a result of the recommendations of the Joint FAO/WHO Conference on Food Additives held in September 1955, twelve meetings of the Joint FAO/WHO Expert Committee on Food Additives have been held (Annex 1).

The present meeting was convened on the recommendations made in the eleventh report of the Joint FAO/WHO Expert Committee on Food Additives. The terms of reference were to draw up specifications for and to make a toxicological evaluation of certain food additives (Annex 2). The substances considered had been suggested by the Codex Committee on Food Additives, to which the Expert Committee acts also as an advisory body on questions of toxicity, specifications for identity and purity, and methods of analysis.

In order to facilitate the discussions, the Committee constituted itself into two groups, one of which gave major attention to chemical specifications and the other to toxicological evaluation.

1. PRINCIPLES GOVERNING ESTABLISHMENT OF CHEMICAL SPECIFICATIONS

The specifications of a food additive play an important role in the safety evaluation, as stressed in previous reports.

1.1 Scope

The specifications have been developed for the use of toxicologists and others concerned with the identity and purity of the additive (Annex 1, ref. 9), to prescribe what can be regarded as a satisfactory degree of purity which should be met by such a substance. Thus the specifications do not necessarily include criteria solely of interest to the commercial user (and which can be assumed not to affect significantly the biological behaviour), although these commercial criteria may be of interest if specifications are needed internationally for trade in the food additives themselves.

It is noted that many of the materials on the list appended to the agenda (Annex 2) are being examined at the request of Member Nations through the Codex Alimentarius Commission and its Committee on Food Additives. In view of the fact that these specifications for additives prescribing the satisfactory degree of purity in the above context are intended for international use, they should be so drawn up as to encompass all suitable food additives produced in various parts of the world, which could properly be included in the designation.

As at previous meetings (Annex 1, ref. 7), it was agreed that specifications would be developed for those substances for which there were known manufacturers and which had been recognized by the Committee at those meetings as being presently used in foods. The Committee continued to be guided by this decision.

Where a complete specification could not be developed, it will be

published as a tentative specification indicating where additional information is necessary. This will make possible further toxicological work henceforth on the material meeting the specifications and encourage receipt of comments for the improvement and completion of the specifications.

The Committee prepared the specifications for some of the substances listed in Annex 2, along with the methods of analysis for identification and for determination of purity, and these are to be found in a separate publication.¹

1.2 Development and improvement of analytical methods

Analytical methods are continually being developed to improve their sensitivity, specificity, accuracy and reproducibility. Newer methods or refinements of those described may be available in the future. However, the methods cited should be acceptable at the international level, whether or not improved methods are available.

¹ *Specifications for the identity and purity of some food colours, emulsifiers, stabilizers, anticaking agents and certain other substances.* FAO Nutrition Meetings Report Series No. 46B, 1970; WHO/Food Add/70.37.

2. PRINCIPLES GOVERNING THE TOXICOLOGICAL EVALUATION

2.1 General guidelines

The Committee reviewed the general principles for the establishment of acceptable daily intakes (ADIs) set out in previous relevant reports of the Joint FAO/WHO Expert Committee on Food Additives, and paid particular attention to the emphasis put on the more recent advances in toxicological and biochemical methodology and interpretation set forth in the report of the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives.¹

It was considered desirable that, once an ADI or a temporary ADI has been established on the basis of the available scientific evidence, this action be followed up by controlled observations in man, as suggested in the above-mentioned report of the WHO Scientific Group.

2.2 Special considerations

2.2.1 FOOD COLOURS

An advance has taken place in our understanding of the mechanism of the development of subcutaneous sarcoma in rats and mice at the site of repeated injection of food colours and other additives. This development has made possible a reevaluation of colours such as Brilliant Blue FCF and Fast Green FCF, previously placed in Category B.² The demonstration that many additives produce local sarcomagenic effect by virtue of physical properties, such as surface activity rather than carcinogenic potential, has made possible the acceptance of such materials for use in food.

In the light of new information and new criteria, reassessment of colours that were formerly placed in Categories B and C I has made possible, in some instances, an allocation of ADIs or temporary ADIs. The status of the remaining colours not considered by the present session

¹ World Health Organization: Technical Report Series No. 348, 1967.

² Annex 1, ref. 8.

of the Committee remains unchanged and their previous classification into Categories C. II to E has not been superseded. In due course a re-examination of these categories of colours may be undertaken.

2.2.2 MODIFIED STARCHES

In evaluating the safety of modified starches, the Committee considered that the following three aspects need to be borne in mind:

- (a) The possibility that one or more of the products of digestion of a modified starch may prove deleterious to, or provoke manifestations of intolerance in, various segments of the human population: the very young (and the unborn child by transplacental transfer); the old; patients with malabsorption syndromes or other pathological states of, or within, the gastrointestinal tract.

The Committee did not subscribe to the assumption that metabolism of a modified starch involves nothing more than metabolism of the unmodified starch and the separate modifying groups, or that metabolism in the body can be predicted from studies on the *in vitro* hydrolysis by chemical or enzymatic means, or to such opinion as "it is unlikely that an ether of glucose and glycerol, both of which are nontoxic and common food constituents, could itself be toxic."³ The intestinal milieu is a complex environment about which relatively little is known. It is impossible at present to forecast chemical changes undergone by the ingested material during passage through the human gut, or the reactions of the human consumer to the products of these changes, on the basis of analogy, of *in vitro* enzyme studies, or of evidence of metabolism in the rat based on calorie equivalence studies.

- (b) Despite repeated emphasis on "minor modifications of starch structure" and on the negligible proportions of other entities introduced into the starch molecules, the fact remains that many of the modified starches are capable of inducing diarrhoea and/or caecal enlargement when fed to rats, usually but not invariably at high levels. Increased weight of the full and empty caecum has been considered as a nonspecific effect (which may also be brought about by other substances such as sorbitol, lactose, raw potato starch, etc.), possibly stemming from low digestibility of the modified starch or

³ Turner, A. W. Unpublished report to WHO. 1961.

caused by its high water-retaining capacity. In fact, a further important consideration is that caecal enlargement may reflect a major change in the balance of the intestinal flora. Thus Turner (1961),⁴ in examining the composition of the gut contents in rats fed modified starches, found a loss of *E. coli* and yeasts and an overgrowth of lactobacilli with a corresponding shift of pH from 7.5 to 5.0 in the caecum. A somewhat similar clinical situation develops in the human gut as a result of lactose intolerance and related mal-absorptive conditions. Since the presence of such states in man, and particularly in children, may be a source of serious concern, the analogous effect in experimental animals cannot be dismissed.

- (c) Persorption has been established as a mechanism whereby solid particles, including starch granules, with diameters of 5-100 μ , may be taken up intact into the body. Subsequently they may be found in body fluids and tissues (see 4.2). The persorption of food starches in animals and man does not appear to have produced untoward effects. One cannot, however, assume that all modified starches will therefore be equally safe if absorbed into the body as intact particles.

For modified starches as a whole, the Committee deemed it advisable to outline a scheme of research comprising studies that are germane to the use of these food additives in the human diet. While recognizing the difficulties involved in many of the proposed investigations, the Committee nevertheless stresses the need for the type of information that such studies will provide, a need rendered all the more urgent by the fact that many of the starches under consideration are already in widespread use, and may constitute a substantial proportion of certain foods. In the belief that there has not been a general recognition of the full nature of the toxicological problems involved in the use of some modified starches in food, the Committee draws attention to the need for research in the following areas:

Analysis of the products of digestion

- (a) The precise nature and relative proportions of the products at various stages of digestion of each modified starch should be determined, under conditions corresponding as closely as possible to those prevailing in the gastrointestinal tract of healthy human adults.

⁴ Turner, A. W. Unpublished report to WHO. 1961.

- (b) On the basis of identified products of digestion that are not formed from the original unmodified starch ("novel digestion products," NDP), a check should be made of NDP formed in children, the aged, in patients suffering from malabsorption syndromes or other pathological states of the gastrointestinal tract.

Experimental studies in animals

- (a) The biological effects of NDP should be ascertained in specifically designed tests of adequate duration (at least 90 days) carried out in several mammalian species, including a rodent and a nonrodent.
- (b) The modified starch itself should be administered to two species in long-term feeding studies at three or more levels in the diet, using the parent (unmodified) starch as control.

Human studies

- (a) Assessment of the tolerance of NDP in human subjects, in the various categories listed under "Analysis of the products of digestion (b)."
- (b) Studies involving consumption of diets containing adequate levels of modified starch, in the form normally consumed, by human volunteers over a suitable period of time.

2.2.3 CERTAIN NATURALLY OCCURRING SUBSTANCES

A number of the additives considered by the Committee were substances with a long history of use. Turmeric has been employed traditionally as a spice and condiment. The amounts ingested depend on ethnic traditions and are prescribed and limited by personal taste. Although there is no evidence of objectionable effects from turmeric used in this traditional manner, a different set of circumstances arises when turmeric, or the colour extracted from it, is used for colouring manufactured staple foods; in this case turmeric is being considered as an additive because the consumer is no longer aware of ingesting it and the colour is therefore subject to the same scrutiny and standards of evaluation as other food colours.

Some edible gums have also long been consumed by certain ethnic groups. The opinion of the Committee was that traditional use of a material does not constitute evidence of safety. Hence, at the risk of ap-

plying what appear to be absurd limitations, the Committee felt bound to base its decisions on the experimental evidence available. Allowance was made for traditional use by applying a lower safety factor than in the case of other additives.

In those instances where no limit is set by the Committee except for good manufacturing practice, as with gum arabic, provision exists for setting limits through the machinery of Codex Alimentarius standards and national legislations that ensure freedom from adulteration of food through excessive use of additives of this sort.

The Committee wished to draw attention to the fact that some additives produced from natural sources may be contaminated with harmful microbes or their spores. Such substances are cochineal, curcuma, vegetable gums, clay, kaolin, and diatomaceous earth.

The Committee also discussed the possibility that additives produced from marine plants may contain *toxic amounts of certain elements or compounds*. It was suggested that most of the products in question would be sufficiently purified so that the problem did not arise but that this question should be studied at a future meeting of this Committee.

2.3 Acceptable daily intakes

It is generally recognized that all chemicals are toxic to animals and man if large enough amounts are administered. Even the so-called innocuous substances, when given in excessive doses, may induce untoward effects as a result of various nonspecific actions, for example physical obstruction of the gastrointestinal tract, alteration of osmotic pressure, and nutritional imbalance. A limit on the daily intake of a substance is thus essential for the protection of the health of the consumer. The Committee therefore followed previous practice where appropriate in allocating acceptable daily intakes (ADI) to the food additives considered.

An *unconditional* ADI was allocated only to those substances for which the biological data available included either the results of adequate short-term and long-term toxicological investigations or information on the biochemistry and metabolic fate of the compound, or both.

A *conditional* ADI was allocated for specific purposes arising from special dietary requirements.

A *temporary* ADI was allocated when the available data were not fully adequate to establish the safety of the substance and it was considered

necessary that additional evidence be provided within a stated period of time. If the additional data requested do not become available within the stated period, the temporary ADI may be withdrawn by a future session of the Committee.

Whereas all ADIs are subject to periodic review, especially when additional data are available, reconsideration of temporary ADIs is *obligatory* after the date specified. The decision arrived at will depend on the information available at the time of review. It is not intended to maintain indefinitely the temporary status of ADI for a food additive.

For those additives for which the available information was grossly inadequate to establish safety, no ADI was allocated.

On the other hand, the Committee took cognizance of the facts that certain food additives have a very low toxicity and that their level of use in foods is limited if good manufacturing practice is followed.

A few chemicals were considered, on the basis of available toxicological information, to be unsuitable for use as food additives. These are indicated in the following section and annexes. These decisions are naturally subject to revision in the light of new evidence.

3. COMMENTS ON SUBSTANCES ON THE AGENDA

Detailed considerations of most of the compounds in Annex 2 are given in the individual specifications and monographs.¹ The following section summarizes the results of the deliberations of the Committee on all the substances on the agenda.

3.1 Food colours

Food colours were evaluated by this Committee at its eighth meeting² and three of them were given ADIS. Since then, five other colours have been given ADIS.³ For various technological and other reasons, the Codex Alimentarius Committee on Food Additives referred to this Committee for reevaluation a number of additional colours, including all those placed originally in categories B and C I, and certain colours derived from natural sources.

A summary of the decisions including the acceptable daily intake figures is given in Annex 3. Details on the colours are given in the monographs, except that no monograph was prepared on curcumin or Yellow 2G, since there was virtually no information available about these colours, or about caramel, for the reasons given below.

3.1.1 FOOD COLOURS DERIVED FROM NATURAL SOURCES

Specifications for five natural colours (annatto, chlorophyll, chlorophyll copper complex, curcumin [turmeric] and riboflavin) have been published previously (Annex 1, ref. 4). The specifications for annatto extracts, chlorophyll and chlorophyll copper complex were suitably modified to

¹ See p. ii.

² Annex 1, ref. 8.

³ Annex 1, ref. 10.

cover the products actually in use for which toxicological data were available, and these supersede the previous specifications. In addition, a separate tentative specification was developed for the sodium or potassium salt of chlorophyllin copper complex.

As a result of toxicological evaluations and the availability of specifications, the present Committee was able to recommend one type or another of acceptance for the following natural colours: annatto extracts, chlorophyll, chlorophyll copper complex, chlorophyllin copper complex, sodium or potassium salt, riboflavin, and turmeric.

The biological data on turmeric were far from complete and none was available for the isolated colouring principle, curcumin. The toxicological assessment of turmeric took into account the established use of this material and the available experimental data. However, no ADI was established for curcumin.

Caramel refers to a large number of ill-defined and complex products formed from various carbohydrates by heating with any of a wide range of acids, bases and salts, under different conditions of temperature and pressure. Specifications could not be developed for caramel and much additional information is needed on the chemical nature of commercially available caramels.

It might be argued that caramel can be considered as a natural constituent of the diet as it can be formed when certain foods are cooked or when sucrose is heated. The Committee, however, considered that it was unable to delineate degrees of difference, and that a toxicological discrimination was unwarranted between such caramel and caramels produced commercially, with the exception of caramel prepared by processes using ammonia or ammonium salts.

The Committee considered that the use of ammonium hydroxide or ammonium salts for the production of caramel for edible purposes was not acceptable. Various imidazoles and pyrazines have been isolated from the products of the reaction of glucose with aqueous ammonia.⁴ One of these compounds, 4-methylimidazole, is a powerful convulsant,⁵ which elicits neurological signs in rabbits, mice and chicks that are similar to the "violent hysteria" produced in cattle and the "madness"

⁴ Hough, L., Jones, J. K. N. and Richards, E. L. *J. chem. Soc.*, 1952: 3854-3857, 1952; *Chem. Ind.*, 1954: 545-546, 1954. — Komoto M. *J. agric. Chem. Soc. Japan*, 36: 305, 407, 461, 1962. — Fujii, S., Tsuchida, H. and Domoto, M. *Agric. biol. Chem.* 30: 73-77, 1966.

⁵ Loeper, M., Mougeot, A. and Parrod, J. *C.r. Soc. Biol.*, 118: 405-406, 1935. — Nishie, K., Waiss, A. C. Jr and Keyl, A. C. *Toxic. appl. Pharmac.*, 14: 301-307, 1969.

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in chickens fed with ammoniated invert molasses.^{6, 7} Molasses treated with ammonia contain imidazoles and pyrazines at levels, by weight, of 10 and 20 percent respectively.⁶ The only imidazole isolated was the 4-methyl derivative.

Until the questions raised by these findings have been resolved, the safety of caramel produced with ammonia or ammonium salts cannot therefore be evaluated.

The Committee was unable to arrive at values for the acceptable intake of quercetin and quercitron. The data were inadequate and there was a report of cataract being produced by a commercial sample.

3.1.2 SYNTHETIC FOOD COLOURS

Specifications of these colours were available.⁸ They were reexamined by the Committee. The specification for Erythrosine was amended to exclude the presence of fluorescein, a substance with known nephrotoxicity. It will be published.⁹

Brilliant Blue FCF and Fast Green FCF were given unconditional acceptable daily intakes following the clarification of the significance of local sarcomata after repeated subcutaneous injections of these colours (see 2.2.1).

Temporary values of acceptable daily intake were assigned to Erythrosine, Indanthrene Blue, Indigotine, Patent Blue V, Ponceau 4R, Quinoline Yellow and Woolgreen BS, since the available information was nearly adequate to establish their safety. The further work required and the time by which this should be submitted are specified in the respective monographs.⁹ In arriving at these evaluations, the Committee adopted the recommendations of the Scientific Group¹⁰ for the allocation of temporary acceptable daily intake.

The available data were inadequate for the evaluation of Brilliant Black BN, Orange I and Yellow 2G, and the Committee was unable to assign figures for acceptable daily intake to these colours.

Citrus Red No. 2 has been shown to have carcinogenic activity and the toxicological data available were inadequate to allow the determina-

⁶ Wiggins, L. F. *Sugar J.*, 18: 18-20, 1956.

⁷ Bartlett, S. and Broster, W. H. *J. agric. Sci.*, 50: 60-63, 1958.

⁸ Annex 1, ref. 10.

⁹ See p. ii.

¹⁰ World Health Organization: Technical Report Series No. 348, 1967.

tion of a safe limit; the Committee therefore recommends that it should not be used as a food colour.

The Committee decided not to establish a limit on the intake of titanium dioxide since the evidence indicates that it is free from toxic effects on account of its insolubility and inertness. The intake in food would be limited by good manufacturing practice.

3.2 Emulsifiers and stabilizers

Some of the emulsifiers and stabilizers placed on the agenda were covered by tentative specifications.¹¹ These were reexamined by the Committee for completeness and for certain toxicological requirements. In addition a number of other emulsifiers and stabilizers were considered. These substances may be regarded as belonging to three main classes, namely, starches, gums, and modified fats. In addition there is a group of miscellaneous emulsifiers and stabilizers.

3.2.1 STARCHES AND MODIFIED STARCHES

The processes for the production of stabilizers by the treatment of starches may be classified into the following three types:

- (a) Treatment by *physical means* is any treatment of starches in the dry or wet state by heat, or pressure, or mechanical action, or any combination of these, including fractionation. No specifications were drawn up for starches treated by physical means.
- (b) Treatment by *enzymatic means* is any treatment of starches in the presence of small amounts of enzymes to obtain partly hydrolyzed products. No specifications were drawn up for starches treated by enzymatic means, but it may be desirable to draw up specifications on the enzymes used and residues remaining in the product.
- (c) Treatment by *chemical means* is any treatment of starches in the dry or wet state and in the presence of one or more of the chemical compounds listed in the specification and subject to conditions mentioned therein.¹² The modified starches produced by various chemical treatments are also indicated in the specifications.

¹¹ FAO. *Tentative specifications for identity and purity of food additives, some emulsifiers and stabilizers and certain other substances*. Rome, 1968.

¹² See page ii.

The classification into these three types of treatment is a practical way of distinguishing between various types of treated starches as well as various methods of manufacture. It is not intended to be used to distinguish between "food additives" and "common foods" in a legal sense.

In evaluating the safety of starches and modified starches, the Committee regarded them as falling, in the first instance, into two categories according to the degree of modification.

In the first category are amylose, amylopectin, and yellow and white dextrans, and those substances, equivalent to normal products of digestion, which include acid-treated starches, enzyme-treated starches, and alkali-treated starches. On these grounds, the substances are regarded as being free from toxicological hazard and no limitation on their use as food additives is considered necessary beyond that of good manufacturing practice.

The second category contains the other modified starches. The principles adopted by the Committee in undertaking the toxicological evaluation of these modified starches are dealt with in detail in Section 2.2.2 of this report and the decisions arrived at are summarized in Annex 4. Further details on individual substances for which data are available appear in the monographs.¹³

A number of other modified starches were not considered further because adequate information was not available. These include starch sodium octenyl succinate, starch aluminium octenyl succinate, sodium carboxymethyl distarch glycerol, and acetylated distarch adipate.

3.2.2 NATURAL GUMS

A number of naturally occurring polysaccharides generally designated as gums were considered and the evaluations of the Committee are summarized in Annex 5. With these substances, changes in the position of linkages, and in the monosaccharides that are present, greatly affect the physical, chemical and biological properties. Consequently the Committee thought it unwise to try to predict that any gum was safe on the basis of its structure alone. Furthermore, an established use of a gum in pharmaceutical preparations or as a dietary supplement by various peoples was not in itself sufficient to justify its general use as a food additive.

¹³ See page ii.

In considering natural gums, it is important to emphasize that no parallel exists with natural fats, where a range of related substances behave in so similar a manner biologically that they can justifiably be grouped together for purposes of toxicological evaluation.

No limit on acceptable daily intake except for good manufacturing practice was imposed on gum arabic. Carrageenan and furcellaran were considered as being so similar in chemical structure that the biological data available for carrageenan may be taken to apply to furcellaran, and the substances were grouped together for assignment of values of acceptable daily intake. Since these substances are of marine origin, the Committee considered that they should be the subject of a special study (mentioned in 2.2.3). A temporary acceptable daily intake value was assigned to gum guar. The recommendations and requirements for additional work on these four substances are dealt with in the respective monographs.

The biological data were inadequate for assigning levels of acceptable daily intake to gum karaya, gum tragacanth and carob bean gum.

3.2.3 MODIFIED FATS AND FATTY ACIDS

The specifications for propylene glycol esters of fatty acids, stearyl citrate and sucrose esters of fatty acids developed at the tenth meeting¹⁴ will be published. Tentative specifications were developed for calcium stearoyl lactylate and sodium stearoyl lactylate. Only a temporary acceptable daily intake was established pending further information on specifications. Specifications were also developed for polyglycerol esters of interesterified ricinoleic acid.

Information was not available for drafting specifications for the mono- and diglycerides of either acetylcitric acid or phosphoric acid. Due to the problem mentioned below, specifications for monoglyceride citrate could not be developed since it was not clear whether or not stearic acid would be the sole fatty acid. Much additional information is needed on the chemical nature of the substances concerned.

The Committee considered that food additives belonging to this class would be metabolized in the normal way in digestive processes, and that no toxicological problems were likely to arise other than the ones associated with the individual constituents. However, information on the

¹⁴ Annex 1, ref. 13.

digestibility of certain of these substances is lacking. Where data were incomplete or not available, the Committee considered that they should be provided before an unconditional acceptable daily intake could be assigned.

The main problem with substances containing the stearic and citric acid moieties, which might be the case with a monoglyceride citrate, was the observation that in rats short-term oral administration leads to increased liver weight and calcification of the kidney.¹⁵ It is not known whether these pathological changes would occur if the two acid moieties were present in different molecules.

Propylene glycol esters of fatty acids were evaluated in the tenth report. The biological data were reviewed by the Committee and the assessment arrived at in the tenth report was confirmed.¹⁶

Fatty acid esters with mono- and disaccharides were considered, but the Committee was prepared to evaluate only the sucrose esters of fatty acids. Sucroglycerides were not considered separately because they are composed of sucrose esters of fatty acids and mono- and diglycerides.

In the preparation of these compounds the substance dimethyl formamide is used as a solvent and residues remain. Since sufficient toxicological data on dimethyl formamide were not available, the Committee decided to set the maximum permissible level of the solvent at 50 ppm corresponding to the level present in the sucrose esters studied toxicologically.

In connexion with the evaluation of calcium stearoyl lactylate, the Committee reviewed DL-lactic acid and DL-malic acid, the evaluation of which was given in the ninth report.¹⁷ A conditional acceptable daily intake was then set for the D-isomers of these acids, whereas no limit was set for the L-isomers, on the ground that they are metabolized to a lesser degree than the D-isomers. On the basis of further evidence indicating that adults do metabolize D-lactic and D-malic acids, it was not considered necessary to maintain the distinction previously drawn between the enantiomorphs of the two acids for use by adults. Accordingly, the Committee decided to convert the evaluation for the D-enantiomorphs from a conditional acceptable daily intake value to use limited only by good man-

¹⁵ Verschuuren, H. G. & van Esch, G. J. Unpublished report, 1963; Wheldon G. H., Ginn, H. B., Leaby, J. S. and Mawdeody-Thomas, L. E. Unpublished report, 1966.

¹⁶ Annex 1, ref. 13.

¹⁷ Annex 1, ref. 11.

ufacturing practice. However, the restriction on the use of these acids in the diet of very young infants remains.

More detailed consideration of modified fat and fatty acids used as emulsifiers and stabilizers is given in the individual monographs.

3.2.4 MISCELLANEOUS GROUP OF EMULSIFIERS AND STABILIZERS

The specifications for hydroxypropyl cellulose had been developed at the tenth session and will be published. The additive was considered by this session of the Committee and was placed in the class of modified celluloses evaluated previously.¹⁸ On the basis of the data available, it was concluded that it could be included in the collective acceptable daily intake level for these substances.

Pectin derived from citrus rinds and apples is essentially unchanged by the simple extraction procedures used. In its evaluation the Committee considered pectin to be a normal constituent of the diet and imposed no limit on daily intake except that of good manufacturing practice; a specification was developed.

In its consideration of propylene glycol alginate the Committee noted that the 1,3-diol propylene glycol has been reported to have an embryopathic action in the chick.¹⁹ However, it is the 1,2-diol that is used in the food additive material. Furthermore, the alginate derivative of this glycol had been used in a long-term feeding study at a level of 5 percent in the diet, through two generations, without evidence of ill effects. Pending submission of the results of *in vivo* metabolic studies, the Committee assigned a temporary acceptable daily intake of propylene glycol alginate.

Hydroxylated lecithin had a tentative specification.²⁰ This was re-examined and remains a tentative specification due to the lack of certain chemical data. There was also a lack of adequate biological data to allow evaluation of this material.

The ammonium salts of phosphatidic acids have tentative specifications, and sufficient biological data were available to assign a temporary value of acceptable daily intake.

A summary of the evaluations on all the emulsifiers and stabilizers, except those on modified starches, is given in Annex 5.

¹⁸ Annex 1, ref. 13.

¹⁹ McLaughlin, Marliac, Verrett and Fitzhugh. *Toxic. appl. Pharmac.*, 7: 491, 1965.

²⁰ FAO. *Tentative specifications for identity and purity of food additives, some emulsifiers and stabilizers and certain other substances*. Rome, 1968.

3.3 Anticaking agents

The evaluations of these substances, as far as it was possible to arrive at evaluations, are summarized in Annex 6. Most of the anticaking agents considered fell into two main groups: inorganic substances and salts of fatty acids.

3.3.1 INORGANIC SUBSTANCES

The potassium and sodium salts of ferrocyanic acid are used as anticaking agents in common salt (sodium chloride) and in the production of common salt with a dendritic rather than a cubic crystalline structure. The calcium salt might also be used. The toxicological data on these substances were deficient in several respects and the evaluation was consequently stringent. In particular, ferrocyanides are reabsorbed by the renal tubules in man and have a nephrotoxic action in animals, as demonstrated histologically. Although there was a no-effect level for histopathology in a short-term study in the rat, the Committee considered that tests of longer duration, including tests of kidney function, were required to establish with greater certainty a no-effect level. The specifications were modified to limit the amount of cyanide in the ferrocyanides as an additional safety factor, although there was little toxicological basis for considering any risk from such contamination.

Of the inorganic phosphates used as anticaking agents bone phosphate is judged to be essentially the same as tribasic calcium phosphate, provided it meets the same purity requirements, particularly with respect to fluoride. Various calcium and magnesium phosphates were on the agenda. The Committee only prepared specifications for tribasic calcium phosphate and tribasic magnesium phosphate, which are the phosphates used as anticaking agents. A specification for sodium pyrophosphate had been prepared at the seventh session.²¹ Tribasic calcium and magnesium phosphates were grouped with the monophosphates evaluated previously and the acceptable daily intake was assigned for these phosphates collectively. The Committee noted that insoluble phosphates may be taken up from the gut by persorption. Crystals of tribasic calcium phosphate smaller than 5 microns fed to rats were subsequently found in tissues and body

²¹ Annex 1, ref. 7.

fluids.²² This phenomenon was also considered in relation to starches (page 6) and silica compounds (see below).

Specifications were developed for silicon dioxide (including silicic acid), for aluminium, calcium and magnesium silicates, and for sodium aluminosilicate. No information was available for the other silicates on the list and these are probably not in use as food additives. The Committee recommended that a microscopic test be developed for the identification of asbestos fibres in those anticaking agents which are minerals, for example, talc (magnesium silicate) and kaolin (hydrated aluminium silicate) because they may be absorbed in particulate form by the body and have harmful effects.

The Committee decided that there was no need to distinguish toxicologically between soluble and insoluble forms of silica, as both types are absorbed into the body, although by different mechanisms. On the evidence it seems that soluble silicates are absorbed, but excreted without undue accumulation in the body. Insoluble silicates may gain entry into the body from the gastrointestinal tract by the process of persorption (page 6).²³ It is reported that asbestos fibres are transported to the pleura of rats after subcutaneous injection.²⁴ Particles of silica flour were deposited in the myocardium and elsewhere in the body after oral administration of the material to rats.²⁵ Despite these considerations, the Committee's conclusions, based on the evidence given in the monograph, was that no limit need be set for the use of these materials in food, provided the amounts used are consistent with good manufacturing practice.

3.3.2 SALTS OF FATTY ACIDS

With edible fatty acids and their salts, consideration was confined to salts of myristic, palmitic and stearic acids since neither chemical nor biological data were available for shorter chain fatty acids. The three fatty acids considered were not differentiated; in this, past practice was followed.²⁶ The salts appearing on the list are all prepared from bases which were accepted at the ninth session,²⁷ except those of aluminium.

²² Reimann, H. A., Ducanes, T. and Gatter, R. *Archs envir. Hlth*, 10: 33, 1965.

²³ King, E. J. and Belt, T. H. *Physiol. Rev.*, 18: 329, 1938.

²⁴ Roe, F. J. C., Carter, R. L., Walters, M. A. and Harington, J. S. *Int. J. Cancer*, 2: 628, 1967.

²⁵ Reimann, H. A. and Danes, T. *Fedn Proc.*, 24: 555, 1965.

²⁶ Annex 1, ref. 7.

²⁷ Annex 1, ref. 11.

Salts of myristic, palmitic and stearic acids, as described in the specifications, were held to be equivalent to normal products of digestion of fats with cations that are normally encountered in the diet; consequently the Committee considered it unnecessary to establish an acceptable daily intake.

3.3.3 OTHER ANTICAKING AGENTS

Although they appeared on the agenda, specifications were not developed at this stage for polyethylene glycol and terpene resins, which have a very limited utilization as anticaking agents, being used only in certain food additives.

3.4 Miscellaneous food additives

The evaluations of these substances, as far as it was possible to arrive at them, are summarized in Annex 7.

Monosodium glutamate. Glutamic acid is a normal constituent of dietary proteins and also occurs freely in many natural foods. It is itself used as a condiment and is an important constituent of other condiments (e.g., soy sauce). The present state of knowledge concerning monosodium glutamate was reviewed. Although attention has recently been drawn to adverse acute effects from ingestion of foods high in free glutamate content, the Committee considers that it is unable to advise any restriction on use at the present time. It was considered that self-limitation of intake of foods containing glutamate by susceptible individuals would be possible. Since there is a considerable amount of work in progress, the Committee postponed evaluations of this compound as a food additive until the results of the current work are available. In the meantime no monograph was prepared. A tentative specification was developed.

Dimethylpolysiloxane. A specification was developed. These antifoaming agents, falling into the specified range of polymers, were evaluated by the Committee and assigned a temporary acceptable daily intake for man. Commercial products may contain silicon dioxide and emulsifiers. Although there is no objection to mixtures of silicone fluid and silicon dioxide, emulsifier-silicone fluid mixtures were not evaluated since there were no specifications or adequate toxicological data. Furthermore, it was noted that an emulsifier may influence the absorption of silicone fluid.

Oxystearin. A specification was developed for oxystearin. As it is manufactured by controlled oxidation of fat, the Committee thought it wise to limit the epoxide content of the material.

Ascorbyl stearate. Specifications were developed for ascorbyl stearate. This substance was evaluated in terms of studies previously reviewed for ascorbyl palmitate in the sixth report,²⁸ since the latter substance contained an admixture of the stearate. An acceptable daily intake was established for these two substances singly or in combination.

Nordihydroguaiaretic acid. A specification had been developed for NDGA at the third meeting.²⁹ However, the biological data were inadequate to allow an evaluation.

Tocopherol esters. These were not considered to be effective antioxidants and therefore no specifications were prepared for them.

Isoamyl gallate and ethyl protocatechuate. These substances were not considered as the data were inadequate to proceed to an evaluation and hence no monographs were prepared. A tentative specification for isoamyl gallate and identification tests for ethyl protocatechuate were developed.

Calcium sulfate. A specification was developed for calcium sulfate. No limit was placed on the use of calcium sulfate as a firming agent, except for good manufacturing practice.

Potassium chlorate. This substance was regarded by the Committee to be too toxic to allow its use as a food additive; hence no monograph was prepared for it. Identification tests were drawn up.

Gum guaiac. A specification could not be developed for gum guaiac owing to lack of information and consequently the earlier decision³⁰ was confirmed. No monograph was prepared for it.

²⁸ Annex 1, ref. 6.

²⁹ Annex 1, ref. 3.

³⁰ Annex 1, ref. 8.

4. OTHER OBSERVATIONS

4.1 Evaluation of technological efficacy

In considering the food additives on the agenda, the Committee discussed the need for the evaluation of technological efficacy of food additives as part of its work. In the view of the Committee, information on the technological use of additives should be considered by the Committee and be published in the form of monographs similar to those on the toxicological evaluation and specifications for food additives. This information was considered essential to all concerned with the evaluation of food additives, either as to their toxicology or their efficacy. Developing countries in particular would welcome this information.

It was suggested that the scope of the proposed monographs be limited to scientific information on the efficacy and uses of additives, including the chemical, physical or other mechanism of action based on evaluation of available data. A further subject for study could be possible reactions between additives and nutrients or other food constituents, and the possible occurrence of degradation products. The monographs will not contain any suggestions as to acceptability or permissible levels. This would be the prerogative of governments, the monographs being intended only to facilitate their task. As a practical approach the Committee suggested that additives could be dealt with in groups according to their application. Such groups could be colours, preservatives, antioxidants, and emulsifiers.

4.2 The need for review of past decisions

There is a widespread but fallacious belief that clearance of an additive for use in food constitutes an irrevocable decision. Such a view renders a grave disservice to the cause of consumer protection for it fails to recognize the need for regular review of all safety evaluations.

Periodic review of past decisions on safety is made necessary by one or more of the following developments:

- (a) A new manufacturing process for the food additive.
- (b) A new specification.
- (c) New data on the biological properties of the compound.¹
- (d) New data concerning the nature, or the biological properties, or both, of the impurities present in a food additive.
- (e) Advances in scientific knowledge germane to the nature or mode of action of food additives. A striking instance is the rediscovery of the phenomenon of "persorption." The possibility exists that particulate additives that have hitherto been regarded as totally unabsorbed, since they are, for practical purposes, completely insoluble, may be taken up by a process of persorption. Although excretory mechanisms are known to exist for some persorbed materials, clarification of this aspect is necessary.
- (f) Important developments in methodology. These include the advances in analytical and radioisotope techniques that facilitate the acquisition of information on composition or metabolism formerly difficult or impossible to obtain. Elucidation of metabolic pathways is now considered of primary importance in safety evaluation and increasing emphasis is placed on the desirability of studies of metabolism in man. In this connexion, the Committee decided to reiterate the recommendations of the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives,² which are as follows:

"*Metabolic studies.* There is a need at a relatively early stage to obtain information on the absorption, distribution, metabolism and elimination of the chemical in human subjects, since this makes it possible to compare this information with that obtained in various animal species and to choose the species that are most likely to have a high predictive value for human responses.

"The problems that arise in connexion with such early human studies in the investigation of drug toxicity have been discussed in

¹ In this connexion, the Committee took note of the findings on amaranth reported by Baigusheva (1969) and recommends that this food colour be reevaluated when confirmatory results become available (Baigusheva, M. M. *Vop. Pitan.*, 2: 46-50, 1969).

² World Health Organization: Technical Report Series No. 348 (p. 9), 1967.

a recent report of a WHO scientific group.³ The sooner, in the course of toxicological investigation, these studies at a low dosage level can be undertaken, the better; however, it is necessary to have adequate short-term toxicological information in several species before even low doses of a new chemical are administered to human subjects.^{4, 5}

Among the additives considered by the Committee, triphenylmethane colours were thought to be an appropriate subject of study, since so little is known concerning their metabolism in man.

- (g) Improved standards of safety evaluation. This is made possible by new scientific knowledge, more information on metabolism, and the quantity and quality of safety data considered necessary in the case of new additives. Since the Joint FAO/WHO Expert Committee on Food Additives began evaluation of food additives in 1961, the paucity of information available on many food additives has been such that assessments were often difficult to make. Tests of too short duration, conducted on very small groups of animals, often using only one level of exposure to the test compound, without adequate haematological, clinical, chemical or histopathological examinations, are frequently encountered among the data submitted for evaluation. Tests of this sort cannot be regarded as having permanent validity; with the passing of time they need to be supplemented by studies carried out in full accordance with the recommendations set out in this and earlier reports of the Committee and in the report of the WHO Scientific Group on Procedures for Investigating Intentional and Unintentional Food Additives.

4.3 Need for a Food Additives Conference

In order to discuss the use which governments could make of the conclusions of the previous sessions the Committee considered that it would be desirable to convene a further Joint FAO/WHO Food Additives

³ World Health Organization: Technical Report Series No. 341, 1966.

⁴ Hayes, W. J. Jr. *Research in pesticides*. New York, Academic Press, 1965.

⁵ National Research Council. Food and Nutrition Board. Food Protection Committee. *Ad Hoc Subcommittee on Use of Human Subjects in Safety Evaluation. Some considerations in the use of human subjects in safety evaluation of pesticides and food chemicals*. Washington D. C. Publication 1270.

Conference in the near future. This conference would assess progress made under the mandate given by the second conference, give guidance for the future work of the Committee, and consider decisions made by the sessions of this Committee and the WHO Scientific Group ⁶ held since the Second Joint FAO/WHO Food Additives Conference.

4.4 Additives to be considered in future

While considering the food additives on the agenda, the Committee felt that the list was extremely long. Since most of these additives were proposed by Codex committees, it is suggested that these committees, before proposing the inclusion of food additives in the draft standards, should adhere strictly to the criteria laid down by the Codex Alimentarius Commission ⁷ for supplying adequate data.

⁶ World Health Organization: Technical Report Series No. 348, 1967.

⁷ Joint FAO/WHO Codex Alimentarius Commission, ALINORM 69/12, Appendix II.

5. RECOMMENDATIONS TO FAO AND WHO

1. In view of the large number of food additives requiring consideration, the Committee recommends that further meetings of this Committee be held annually.
2. In future meetings of the Joint FAO/WHO Expert Committee on Food Additives, consideration should also be given to the technological efficacy of additives and/or groups of additives, including their mechanism of action and possible reaction between additives and other food constituents, this information to be included in the monographs. The Committee recommends that ways and means be explored to obtain the data required and to prepare working papers.
3. For the reasons set out in section 4.2, the Committee stresses the need to review past decisions and recommends that the review process be initiated at an early stage.
4. Since the specifications for a large number of intentional food additives have been developed by this Committee over a considerable period of time, these specifications should now be compiled and edited for consistency and published in one compendium to make them readily available.
5. The question of microbiological contamination of additives produced from natural sources should be brought to the attention of an appropriate body for investigation with the view of elaborating respective criteria together with the analytical methods required.
6. A third session of the Joint FAO/WHO Food Additives Conference should be convened in the near future.
7. The problem of the possible presence of toxic amounts of certain elements and compounds in food additives produced from marine plants should be studied at a future meeting.

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

1. *Joint FAO/WHO Conference on Food Additives. Report.* FAO Nutrition Meetings 1956 Report Series No. 11; *General principles governing the use of food additives. First report.* World Health Organization: Technical Report Series No. 129.
2. *Procedures for the testing of intentional food additives to establish their safety for use. Second report.* FAO Nutrition Meetings Report Series No. 17; World Health Organization: Technical Report Series No. 144.
3. *Specifications for identity and purity of food additives (antimicrobial preservatives and antioxidants). Third report.* These specifications were subsequently revised and published as *Specifications for identity and purity of food additives. Vol. I. Antimicrobial preservatives and antioxidants.* Rome, 1962 Food and Agriculture Organization of the United Nations.
4. *Specifications for identity and purity of food additives (food colors). Fourth report.* 1959 These specifications were subsequently revised and published as *Specifications for identity and purity of food additives. Vol. II. Food colors,* 1963 Rome, Food and Agriculture Organization of the United Nations.
5. *Evaluation of the carcinogenic hazards of food additives. Fifth report.* FAO Nutrition Meetings Report Series No. 29; World Health Organization: Technical Report Series No. 220.
6. *Evaluation of the toxicity of a number of antimicrobials and antioxidants. Sixth report.* FAO Nutrition Meetings Report Series No. 31; World Health Organization: Technical Report Series No. 228.
7. *Specifications for the identity and purity of food additives and their toxicological evaluation: emulsifiers, stabilizers, bleaching and maturing agents. Seventh report.* FAO Nutrition Meetings Report Series No. 35; World Health Organization: Technical Report Series No. 281.
8. *Specifications for the identity and purity of food additives and their toxicological evaluation: food colours and some antimicrobials and antioxidants. Eighth report.* FAO Nutrition Meetings Report Series No. 38; World Health Organization: Technical Report No. 309.

28 SPECIFICATIONS FOR IDENTITY AND PURITY OF FOOD ADDITIVES

- *9. *Specifications for identity and purity and toxicological evaluation of some antimicrobials and antioxidants.* FAO Nutrition Meetings Report Series No. 38A; WHO/Food Add/24.65.
- *10. *Specifications for identity and purity and toxicological evaluation of some food colours.* FAO Nutrition Meetings Report Series No. 38B; WHO/Food Add/66.25.
- 11. *Specifications for the identity and purity of food additives and their toxicological evaluation: some antimicrobials, antioxidants, emulsifiers, stabilizers, flour-treatment agents, acids and bases. Ninth report.* FAO Nutrition Meetings Report Series No. 40; World Health Organization: Technical Report Series No. 339.
- *12. *Toxicological evaluation of some antimicrobials, antioxidants, emulsifiers, stabilizers, flour-treatment agents, acids and bases.* FAO Nutrition Meetings Report Series No. 40 A, B, C; WHO/Food Add/67.29.
- 13. *Specifications for the identity and purity of food additives and their toxicological evaluation: some emulsifiers and stabilizers and certain other substances. Tenth report.* FAO Nutrition Meetings Report Series No. 43; World Health Organization: Technical Report Series No. 373.
- 14. *Specifications for the identity and purity of food additives and their toxicological evaluation: some flavouring substances and non-nutritive sweetening agents. Eleventh report.* FAO Nutrition Meetings Report Series No. 44; World Health Organization: Technical Report Series No. 383.
- *15. *Toxicological evaluation of some flavouring substances and non-nutritive sweetening agents.* FAO Nutrition Meetings Report Series No. 44A; WHO/Food Add/68.33.
- 16. *Specifications for the identity and purity of food additives: some antibiotics. Twelfth report.* FAO Nutrition Meetings Report Series No. 45; World Health Organization: Technical Report Series No. 430.
- *17. *Specifications for the identity and purity of some antibiotics and methods of analysis of their residues in food.* FAO Nutrition Meetings Report Series No. 45A; WHO/Food Add/69.34.

* These documents can be obtained on request from: Food Additives, World Health Organization, Avenue Appia, 1211 Geneva, Switzerland, or: Food Science and Technology Branch, Food and Agriculture Organization of the United Nations, Via delle Terme di Caracalla, 00100 Rome, Italy.

LIST OF FOOD ADDITIVES ON THE AGENDA

Part A. For Evaluation

I. FOOD COLOURS

Annatto
Caramel
Chlorophyll
Chlorophyll copper complex
Curcumin (turmeric)
Riboflavin

II. ANTICAKING AGENTS

Bone phosphate
Calcium phosphate, tribasic
Calcium, sodium and potassium ferrocyanides
Magnesium phosphates
Myristic acid, and its potassium and sodium salts
Polyethylene glycol
Silicates including the following:
 Aluminium silicate monohydrate (pyrophyllite)
 Calcium silicate
 Calcium silico-aluminate hydrate
 Diatomaceous earth
 Magnesium silicates (talc)
 Magnesium silico-aluminate
 Magnesium trisilicate
 Silicon dioxide
 Silicic acid (silica gel)
 Sodium calcium aluminium silicate (sodium calcium silico-aluminate)

Sodium and potassium palmitates
Sodium pyrophosphate
Stearic acid and its aluminium, calcium, magnesium, potassium and sodium salts
Terpene resins

30 SPECIFICATIONS FOR IDENTITY AND PURITY OF FOOD ADDITIVES

III. EMULSIFIERS AND STABILIZERS

Ammonium salts of phosphatidic acids
Hydroxylated lecithin
Hydroxypropyl cellulose
Modified starches
Mono- and diglycerides of fatty acids esterified with acetylcitric acid
Mono- and diglycerides of fatty acids esterified with phosphoric acid
Polyglycerol esters of interesterified ricinoleic acid
Propylene glycol esters of fatty acids
Stearoyl lactic acid and its calcium salt

IV. MISCELLANEOUS

Ascorbyl stearate
Calcium sulfate
Dimethylpolysiloxane
Ethyl protocatechuate
Gum guaiac
Isoamyl gallate
Monoglyceride citrate
Monosodium glutamate
NDGA (nordihydroguaiaretic acid)
Oxystearin
Pectin
Potassium chlorate
Stearyl citrate
Tocopherol esters of acetic, succinic, and fatty acids

Part B. For Reevaluation

I. FOOD COLOURS

Brilliant Blue FCF
Brilliant Black BN
Citrus Red
Erythrosine
Fast Green FCF
Idanthrene Blue RS
Indigotine
Orange I
Patent Blue V
Ponceau 4R
Quercetin and Quercitron
Quinoline Yellow
Titanium dioxide
Wool Green BS
Yellow 2G

II. EMULSIFIERS AND STABILIZERS

Arabic gum

Carob bean gum

Carrageenan

Furcelleran

Guar gum

Karaya gum

Mono- and disaccharides esterified with fatty acids (sucroglycerides)

Propylene glycol alginate

Sucrose esters of nonpolymerized fatty acids

Tragacanth

Annex 3

ACCEPTABLE DAILY INTAKES (ADI) FOR MAN OF SOME FOOD COLOURS

Substance	ADI (mg/kg body weight)
Annatto extracts ^a	0 - 1.25 ¹
Chlorophyll ^a	No limit ²
Chlorophyll copper complex ^a	0 - 15
Chlorophyllin copper complex, sodium or potassium salts ^{a, d}	0 - 15 ¹
Quercetin and quercitrin ^b	No ADI
Riboflavin ^c	0 - 0.5
Turmeric ^c	0 - 0.5 ¹
Brilliant Blue FCF ^b	0 - 12.5
Brilliant Black BN ^b	No ADI
Citrus Red No. 2 ^b	Not to be used
Erythrosine ^a	0 - 1.25 ¹
Fast Green FCF ^b	0 - 12.5
Indanthrene Blue RS ^b	0 - 1 ¹
Indigotine ^b	0 - 2.5 ¹
Orange I ^b	No ADI
Patent Blue V ^b	0 - 1 ¹
Ponceau 4R ^b	0 - 0.75 ¹
Quinoline Yellow ^b	0 - 1 ¹
Titanium dioxide ^b	No limit ²
Woolgreen BS ^b	0 - 5 ¹

NOTE: For caramel, curcumin and Yellow 2G no monographs were prepared for the reasons given in section 3.1.

¹ Temporary acceptable daily intakes - details on further information required are given in the respective monographs.

² Not limited except by good manufacturing practice.

^a Specifications will be published for these compounds (see p. ii).

^b Specifications are available for these substances (see Annex 1, ref. 10).

^c Specifications are available for these substances (see Annex 1, ref. 4).

^d Tentative specification.

ACCEPTABLE DAILY INTAKES (ADI) FOR MAN OF MODIFIED STARCHES

Substance ^a	ADI (mg/kg body weight)
Amylose, amylopectin	No limit ²
Enzyme-treated starches	" " ²
White and yellow dextrans	" " ²
Acid-treated starches	" " ²
Bleached starches	" " ²
Oxidized starches	" " ^{1, 2}
Alkali-treated starches	" " ²
Monostarch phosphate	" " ^{2, 4}
Starch acetate	0 - 12.5 ¹
Starch sodium succinate	No ADI
Hydroxypropyl starch	0 - 25 ¹
Distarch phosphate (phosphorus oxychloride)	No ADI
Distarch phosphate (sodium trimetaphosphate)	0 - 25 ^{2, 4}
Phosphated distarch phosphate	0 - 25 ^{2, 4}
Acetylated distarch phosphate	No ADI
Hydroxypropyl distarch phosphate	No ADI
Distarch glycerol	No ADI
Acetylated distarch glycerol	No ADI
Hydroxypropyl distarch glycerol	0 - 12.5 ¹
Acetylated distarch adipate	0 - 12.5 ¹

NOTE: No monographs were prepared for other modified starches (see section 3.2.1.).

¹ Temporary acceptable daily intakes - details on further information required are given in the respective monographs.

² Not limited except by good manufacturing practice.

³ As distarch phosphate (sodium trimetaphosphate) or phosphated distarch phosphate or the sum of both.

⁴ Subject to limits of phosphorus load (see Annex 1, ref. 7).

^a Specifications will be published for these compounds (see p. ii) except for the first three items. The specifications are tentative for those items which have not been given an ADI.

Annex 5

ACCEPTABLE DAILY INTAKES (ADI) FOR MAN OF SOME EMULSIFIERS AND STABILIZERS

Substance ^a	ADI (mg/kg body weight)
Carrageenan	} 0 - 500 ³
Furcellaran	
Arabic gum	No limit ²
Carob bean gum	No ADI
Guar gum	0 - 125 ¹
Karaya gum	No ADI
Tragacanth gum	No ADI
Polyglycerol esters of interesterified ricinoleic acid	0 - 3.75 ¹
Propylene glycol esters of fatty acids	0 - 20 ⁴
Stearoyl lactylate, calcium ^b	} 0 - 2.5 ¹
Stearoyl lactylate, sodium ^b	
Stearyl citrate	0 - 1.25 ¹
Sucrose esters of fatty acids ^c	0 - 2.5 ¹
Hydroxylated lecithin ^b	No ADI
Ammonium salts of phosphatidic acids ^b	0 - 15 ¹
Hydroxypropyl cellulose	0 - 30 ^{5, 6}
Pectin	No limit ²
Propylene glycol alginate	0 - 12.5 ¹

NOTE: No specifications or monographs were prepared for mono- and diglycerides of fatty acids esterified with acetylcitric acid, mono- and diglycerides of fatty acids esterified with phosphoric acid and monoglyceride citrate because of lack of information (see section 3.2.3). For the monograph on propylene glycol esters of fatty acids, see Annex 1, ref. 12.

¹ Temporary acceptable daily intakes; details on further information required are given in the respective monographs.

² Not limited except by good manufacturing practice.

³ As carrageenan or furcellaran, or the sum of both.

⁴ As propylene glycol.

⁵ As any of the acceptable cellulose derivatives or any combination of them (see Annex 1, ref. 13).

⁶ Higher levels for dietetic or calorie control purposes.

^a Specifications will be published for these compounds (see page ii).

^b Tentative specification.

^c Containing not more than 50 ppm of dimethylformamide.

ACCEPTABLE DAILY INTAKES (ADI) FOR MAN OF SOME ANTICAKING AGENTS

Substance ^a	ADI (mg/kg body weight)
Ferrocyanide, calcium	} 0 - 0.00125 ¹
Ferrocyanide, potassium	
Ferrocyanide, sodium	
Phosphate, calcium, tribasic	} 0 - 30 ²
Phosphate, magnesium, tribasic	
Salts of myristic, palmitic and stearic acid with bases accepted for food use	No limit ³
Silicon dioxide, amorphous (includes silica aerogel; hydrated silica; silicic acid; dehydrated silica gel)	} No limit ³
Aluminium silicate (includes kaolin)	
Calcium silicate	
Magnesium silicate (includes talc, magnesium tri-silicate)	
Sodium alumino silicate	

NOTE: No specifications or monographs were prepared for a number of substances listed in the agenda (Annex 2) for reasons given in section 3.3.

¹ Temporary acceptable daily intakes; details on further information required are given in the respective monographs.

² As total dietary phosphorus intakes from both food and food additives (see Annex 1, ref. 7).

³ Not limited, except by good manufacturing practice.

^a Specifications will be published for these compounds.

Annex 7

ACCEPTABLE DAILY INTAKES (ADI) FOR MAN OF CERTAIN OTHER FOOD ADDITIVES

Substance ^a	ADI (mg/kg body weight)
Monosodium glutamate ^b	Decision postponed
Calcium sulfate	No limit ¹
Potassium chlorate ^c	Not to be used
Ascorbyl palmitate ^d	0 - 1.25 ²
Ascorbyl stearate	0 - 1.25 ²
Dimethylpolysiloxane ^e	0 - 0.25 ³
Oxystearin	0 - 25
NDGA (nordihydroguaiaretic acid)	No ADI

NOTE: No monographs were prepared for certain substances for reasons given in section 3.4. However, a tentative specification was prepared for isoamyl gallate and identification tests for ethyl protocatechuate were described.

¹ Not limited, except by good manufacturing practice.

² As ascorbyl palmitate or stearate or the sum of both.

³ *Temporary* acceptable daily intakes; details on further information required are given in the respective monographs.

^a Specifications will be published for these compounds.

^b Tentative specifications.

^c Identification tests only.

^d Specifications are available for this compound (see Annex 1, ref. 3).

^e As dimethylpolysiloxane fluid with or without added silicon dioxide.