European Commission

Food science and techniques

Reports of the Scientific Committee for Food

(44th Series)

OPINIONS OF THE SCIENTIFIC COMMITTEE FOR FOOD ON:

Nitro musk compounds in foods

Principles for the development of risk assessment of microbiological hazards under the hygiene of foodstuffs Directive 93/43/EEC

Microcrystalline cellulose

Derivatives of wood rosin as coating agents for fresh citrus fruits

The relationship between scientific data and the labelling of genetically modified foods and their derived products

A maximum residue limit (MRL) of 0.01 mg/kg for pesticides in foods intended for infants and young children

The potential risk to human health arising from the bulk transport of raw sugar, semi-processed syrups and thick sugar juices intended for the production of white sugar, in non-dedicated ships' tanks and road tankers

The potential microbiological risk arising from the presence of moisture in tea

Papain from papaya fruit (Carica papaya) *used as a meat tenderising agent (examination of additional information)*

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OPINIONS ON:

OPINION ON NITRO MUSK COMPOUNDS IN FOODS

(expressed on 13 June 1997)

Terms of reference

The Committee is requested to evaluate the potential risk to human health arising from the presence of certain nitro musk compounds in foods.

Background

Nitro musk compounds are used as fragrance substances in detergents, cleaning agents and cosmetic products. They are not easily biodegradable and accumulate in the environment. Reports of the presence of traces of nitro musk substances in a number of foodstuffs and in human milk and adipose tissue prompted the Federal Republic of Germany to request the Commission to consult the Scientific Committee for Food in the light of the reported levels of occurrence in foods and the toxicological evaluation of these substances made by the Scientific Committee for Cosmetology.

Discussion

Nitro musk compounds have been found as contaminants in some foodstuffs, human milk and adipose tissue. Maximum concentrations of musk xylene, musk ketone and musk ambrette in farmed fish (mainly trout) and fish originating from rivers amount to about 90, 68 and 1 µg/kg fresh weight (1, 2, 3, 4, 5). Human milk has been found to contain up to 1.2 mg musk xylene and 0.2 mg musk ketone/kg fat (6, 7).

From the concentrations found in human adipose tissue and the elimination half-life of 63 -107 days determined in volunteers, a total average daily intake of about 11 µg of musk xylene was estimated (4). The mean intake from fish or other contaminated foodstuffs, however, is much lower. It is quantitatively negligible in comparison with the contribution to body burden of cosmetic products and household detergents.

A long-term feeding study with musk xylene in mice for 80 weeks resulted in an increased incidence of liver adenomas in both sexes and liver carcinomas in males and harderian gland adenomas in males as compared with the controls at doses of 91 and 170 mg/kg b.w./day for males and 101 and 192 mg/kg b.w./day for females (8). Carcinogenicity data in rats are not available.

Ames test, chromosome aberration assay with CHO cells, mouse lymphoma assay and *in vitro* and *in vivo* UDS assays did not reveal genotoxicity of musk xylene (9). However, genotoxic intermediates such as aromatic amines can be formed *in vivo* since the nitrogroups of musk xylene are metabolically reduced to amino groups in rats (10) and humans (11).

Musk xylene induces cytochrome P 450 enzymes in rats, particularly those in the CYP 1A family (12, 13, 14). In mice, musk xylene causes generalised hepatic changes similar to classical CYP 2B inducers like phenobarbital. However, in contrast to phenobarbital, musk xylene is also a potent inhibitor of the CYP 2B enzymes such that there is no measurable increase in CYP 2B enzyme activity, even when CYP 2B protein levels are very high (15).

Musk ambrette is neurotoxic and its use in cosmetic products has been banned in the EU. Furthermore it has been found to be mutagenic in *Salmonella typhimurium* in the presence of metabolic activation (16). Musk ketone, like musk xylene, is a strong inducer of toxifying liver enzymes (17,18).

Conclusion

Musk xylene is carcinogenic in mice and given that a number of tests did not reveal a genotoxic potential it is probably acting through a non-genotoxic mechanism in mice. On the other hand, it must be taken into account that musk xylene is metabolised in rats and humans to aromatic amines. In addition, musk xylene is an enzyme inducer and accumulates in body tissues because of its lipophilic nature. It is found in human milk and adipose tissue. The half-life in humans is extremely long in contrast to rats and mice. For these reasons, in the opinion of the Committee, contamination of food with musk xylene should be reduced as much as possible.

The toxicological data on musk ambrette, musk ketone, musk tibetene and musk moskene are insufficient to allow a reliable evaluation or to provide a basis for the setting of tolerable levels in food. These nitro musk compounds must also be expected to have a high tendency to accumulate. It is therefore the opinion of the Committee that, as a matter of prudence, contamination of food with these compounds should also be reduced as much as possible.

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PRINCIPLES FOR THE DEVELOPMENT OF RISK ASSESSMENT OF MICROBIOLOGICAL HAZARDS UNDER THE HYGIENE OF FOODSTUFFS DIRECTIVE 93/43/EEC (1)

(expressed on 13 June 1997)

Terms of reference

To prepare for the Commission guidance on the principles to be considered when assessing the potential risks caused by micro-organisms and their toxins in foodstuffs and the scientific basis for risk assessment for the development of hygiene requirements for certain classes of foodstuffs under Article 4 of the hygiene of foodstuffs Directive 93/43/EEC.

1. Background

1.1. Under Article 4 of the hygiene of foodstuffs Directive 93/43/EEC without prejudice to more specific Community rules, the Commission, assisted by the Standing Committee for Foodstuffs, after consultation with the SCF, may adopt microbiological criteria and temperature criteria for certain classes of foodstuffs.

In order to advise the Commission in this area the Scientific Committee for Foods has given this opinion on the 'Principles for the development of microbiological criteria for foodstuffs as covered by the hygiene of foodstuffs Directive 93/43/EEC'.

1.2. Under the Sanitary and Phytosanitary (SPS) Agreement reached within the Uruguay Round of the multilateral trade negotiations under the General Agreement on Tariffs and Trade (GATT), food regulations outside of those contained in internationally recognised food standards may be required to be justified in relation to, amongst other issues, the level of health protection provided by the measure in question. (OJ L 336, 23 December 1994, Annex 1A: p. 41 Art. 3.)

1.3. Risk assessment for foodborne microbiological hazards is a new activity and there have been different approaches to its methodology. Due to its importance in the international context, the process should be undertaken in a transparent and comparable way by different risk assessors and there is a need for a common understanding of its basic elements. For harmonisation and transparency, risk assessments should be developed according to a structured and universally accepted framework. However, within this framework, some flexibility should be recognised in relation to the detail of application and use of tools which may vary depending on the purpose of the risk assessment.

1.4. These guidelines identify the essential elements of a risk assessment framework for foodborne microbiological hazards, incorporating the standard risk assessment paradigm ('the four steps paradigm') agreed upon at the WHO/FAO consultation on risk assessment (2), and which constitutes the basis of the Codex discussions on risk assessment (Alinorm 97/13A, Appendix IV).

In addition, they provide an outline of the diverse elements and factors that may be considered at each stage and of the possible sources of information and techniques that may be used. These are not offered as formal guidance as they are not exhaustive, nor will all of them be relevant in every assessment.

1.5. In the following sections, the essential elements of a risk assessment framework are presented in frames and printed in bold letters. Text which is not in bold type refers to explanatory notes or identifies areas where some flexibility in details of application is recognised.

2. Definitions

(Origin Codex Alimentarius Commission) (3)

Hazard: A biological, chemical or physical agent in, or condition of, food with the potential to cause an adverse health effect.

Risk: A function of the probability of an adverse health effect and the severity of that effect, consequential to a hazard(s) in food.

Risk analysis: A process consisting of three components: risk assessment, risk management and risk communication.

Risk assessment: A scientifically based process consisting of the following steps: (i) hazard identification, (ii) hazard characterisation, (iii) exposure assessment, and (iv) risk characterisation.

Hazard identification: The identification of biological, chemical and physical agents capable of causing adverse health affects and which may be present in a particular food or group of foods.

Hazard characterisation: The qualitative and/or quantitative evaluation of the nature of the adverse health effects associated with biological, chemical and physical agents which may be present in food. For chemical agents, a dose-response assessment should be performed. For biological or physical agents, a dose-response assessment should be performed if the data are obtainable.

Dose-response assessment: The determination of the relationship between the magnitude of exposure (dose) to a chemical, biological or physical agent and the severity and/or frequency of associated adverse health effects (response).

Exposure assessment: The qualitative and/or quantitative evaluation of the likely intake of biological, chemical, and physical agents via food as well as exposures from other sources if relevant.

Risk characterisation: The qualitative and/or quantitative estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterisation and exposure assessment.

Risk management: The process of weighing policy alternatives in the light of the results of risk assessment and, if required, selecting and implementing appropriate control options, including regulatory measures.

Risk communication: The interactive exchange of information and opinions concerning risk among risk assessors, risk managers, consumers and other interested parties.

3. Microbiological risk assessment in the context of risk analysis

3.1. ***Risk analysis*** is a structured and multidisciplinary approach to identifying and, where necessary, reducing risk.

A broad consensus recognises that the process of risk analysis consists of three essential components (Figure 1):

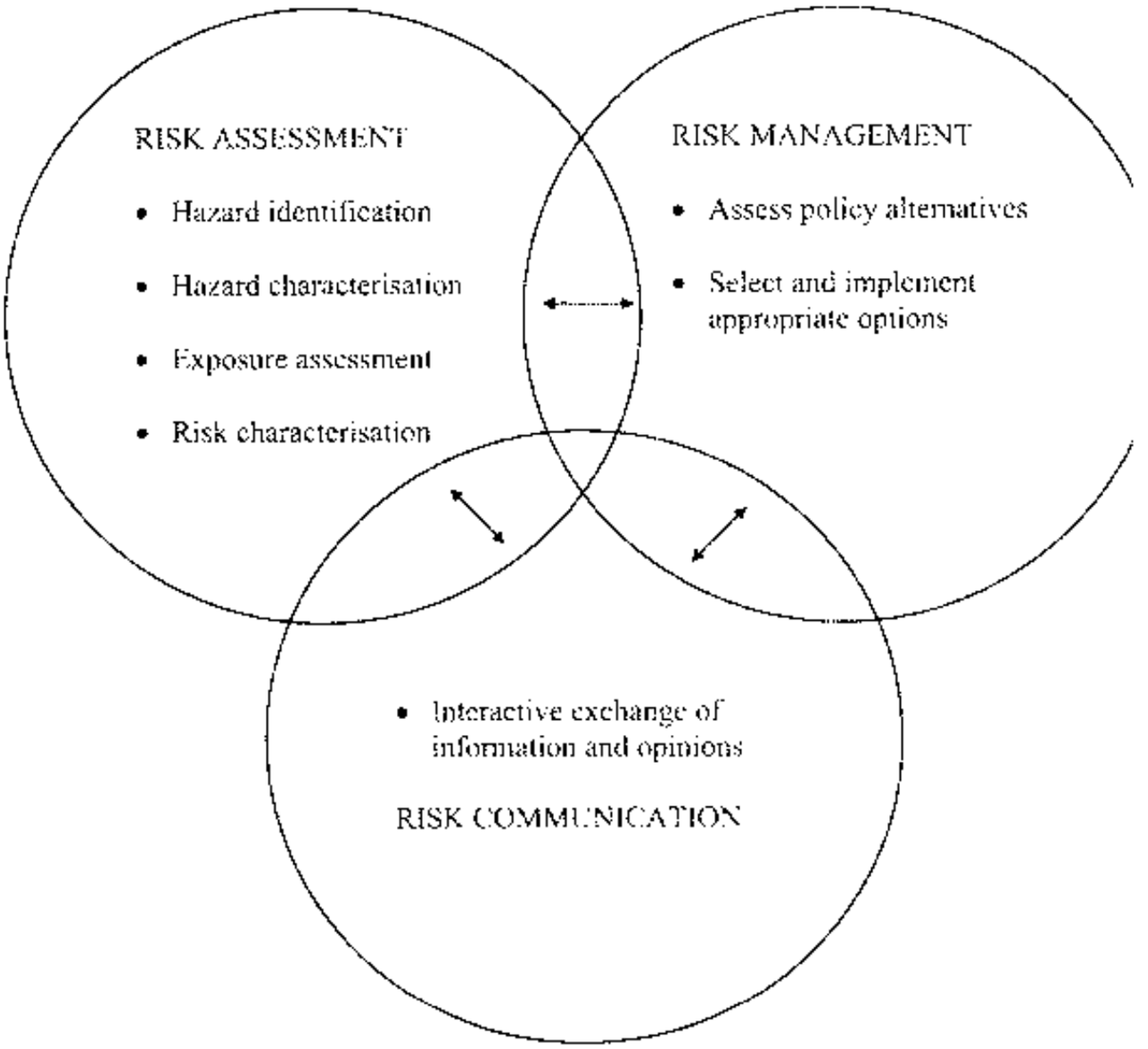
-- risk assessment
--- risk management
— risk communication.

3.2. ***Risk assessment*** is the scientific evaluation of known or potential adverse health effects resulting from human exposure to (foodborne) hazards.

The purpose of risk assessment is documentation and analysis of scientific evidence to measure risk and identify factors that influence it, for use by risk managers.

The outcome of the risk assessment is called the **risk estimate.**

Figure 1: Risk analysis framework (modified from Lammerding, A., 1996)



3.3. ***Risk management*** is the process of weighing policy alternatives to accept, minimise or reduce assessed risks and to select and implement appropriate options.

The purpose of risk management is to identify acceptable risk levels, develop and implement control options within the framework of public health policy. A cost-benefit analysis of options would also support risk management.

3.4. ***Risk communication*** is an interactive process of exchange of information and opinion on risk among risk assessors, risk managers and other interested parties.

In particular, communicating foodborne risk to the public involves an informational exchange between risk managers, those concerned with production and the consumers about risk, potential control options and the cost of control options. Risk communicators also interface with those involved through educational programmes to enhance the effectiveness of selected management strategies.

3.5. This paper deals with risk assessment. Risk management and risk communication should be dealt with in future documents.

4. Risk assessment for microbiological hazards in foods — general principles

4.1. Risk assessment for microbiological hazards must be soundly based on science

For the purpose of this document the term microbiological hazard includes hazards caused by bacteria, viruses, yeasts, moulds, algae, parasitic protozoa, their toxins and metabolites. All available scientific data relevant to the risk assessment should be considered. These data are likely to come from different sources. For example, data may include clinical and epidemiological studies such as disease symptoms, severity and dose-response data; microbiological studies including the physiology, biochemistry and ecology of micro-organisms and the biochemistry and stability of their toxins; sources and prevalence of micro-organisms and their toxins in foods and the effect of processing and food handling operations on them; data on food production and consumption patterns. Where scientific data are limited, otherwise incomplete or conflicting, informed judgements may be made on the basis of the best information available.

4.2. There must be a functional separation between risk assessment and risk management

Risk assessment of microbiological hazards is a scientific process aimed at identifying and characterising a microbiological hazard and estimating the risk of that hazard to a population. Risk management is a separate process aimed at identifying options for action(s) needed to manage that risk and has a policy function. However, certain interactive elements are essential for a systematic risk analysis process. For example, these may include the ranking of hazards in the risk assessment process and risk management policy issues. Where risk management issues may affect the decision-making process used in risk assessment, the implications of this must be made clear in the final report.

4.3. A structured approach must be used when conducting a risk assessment of microbiological hazards

This structured approach must include four components: hazard identification, hazard characterisation, exposure assessment and risk characterisation. The sequence of use of these may vary depending on the purpose of the risk assessment.

4.4. A risk assessment of microbiological hazards must clearly state both the purpose of the assessment and the form of the risk estimate that will be the output

The objective might be to estimate the risk associated with a microbiological hazard in the total food supply to a population or the risks associated with a number of microbiological hazards associated with a specific food commodity. The output might take the form of an estimate of the annual occurrence of illness, or an estimate of the annual rate of illness per 100 000 population or an estimate of the rate of illness per eating occurrence.

4.5. Risk assessment must be transparent

This requires that the assessment is documented in full and that a complete and formal record is made of the assessment. The formal record must include any constraints imposed by costs, resources or time and an evaluation of the possible effect of these on the quality of the risk estimate. Any assumptions or judgements made during the assessment, and which may have affected the outcome of the estimate, should also be described and the rationale explained and fully documented in the report. Where appropriate, the record should include an evaluation of the impact of the resource constraint(s) on the risk assessment. The formal record, including a summary must be made available, on request, to independent parties so that other risk assessors can evaluate the assessment and repeat it if deemed necessary.

4.6. The risk estimate must contain a detailed description of uncertainty and where this arose during the risk assessment process

To ensure transparency in the decision-making process it is essential that there is a clear understanding of any limitations in the data or models used in the risk assessment and how these limitations influenced the risk estimate. Such limitations should be recorded in the report.

4.7. Data must be of sufficient quality and precision such that uncertainty in the risk estimate is minimised as far as possible

It is important that the best available information and expertise is applied to a risk assessment in order to reduce uncertainty and increase reliability of the risk estimate. Quantitative information should be used to the extent possible, but where this is not available good qualitative information should be used.

4.8. Where appropriate, a risk assessment of microbiological hazards must consider the fate of the hazard(s) in food(s) and the disease process following infection

It should explicitly consider the dynamics of microbial growth, survival and death. Where applicable the dynamics of microbial toxin formation and destruction should also be considered together with distribution of the agent, in appropriate foodstuffs. The interactions between humans and the agent (including possible sequelae) following consumption, and the potential for horizontal or vertical spread of the agent are part of the assessment.

4.9. Risk estimates, where possible, must be re-evaluated over time against human health data, and when new data become available

For microbiological agents human health data relating to the results of exposure to a microbiological agent may be available. This may provide the opportunity to compare a risk estimate of such an agent with the actual occurrence of human disease, thereby providing a gauge as to the reliability of a risk estimate. If there is a significant discrepancy between the risk estimates and the human data there must be a re-evaluation of the risk assessment.

5. Recommended scheme for risk assessment of foodborne microbiological hazards

Risk assessment is a scientifically based process consisting of the following steps: (i) hazard identification; (ii) hazard characterisation; (iii) exposure assessment; and (iv) risk characterisation.

Based on this definition, the following scheme is recommended (Figure 2):

- statement of purpose of risk assessment
- hazard identification
- hazard characterisation (including a dose–response assessment)
- exposure assessment
- risk characterisation
- production of a formal report

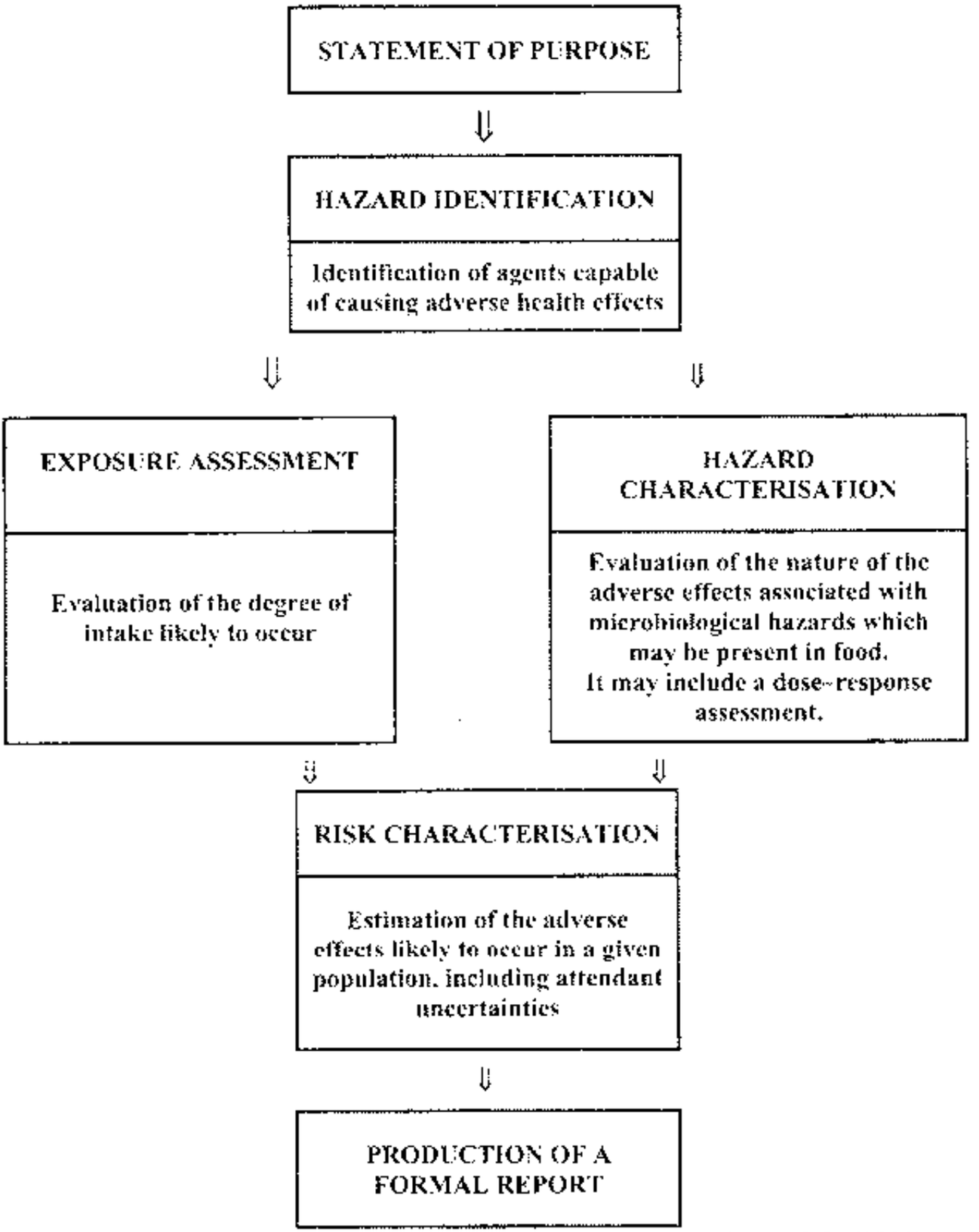
The following sections will consider in turn the elements of this recommended scheme. The recommended scheme for risk assessment for foodborne microbiological hazards provides a working agenda. However, the stages listed may not necessarily be considered in sequence but rather in an orderly manner, as suggested in Figure 2.

These stages are the same for microbiological or chemical risk assessment. However, the emphasis among such stages and the elements to be considered at each stage is likely to differ. For example, the hazard identification phase needs less investigation for already known foodborne pathogenic bacteria than for new chemicals. Alternatively, carrier state and potential secondary spread are not factors to be considered when assessing chemical risks but are important when considering microbiological risk assessment.

Risk assessment is the science of understanding hazards, how likely they are to occur and the consequences if they do occur. Therefore, the product of risk assessment, i.e. the 'risk estimate', is a statement that links the probability that exposure to a pathogenic agent will occur and that such exposure will affect the host. For microbiological risk assessment of foodborne pathogens, this may often be coupled to a consideration of severity (or magnitude) of the adverse effects.

The scope, detail and complexity of a given risk assessment may vary depending on factors such as the availability of time, availability of data, resources, perceived seriousness of the hazard or the outcome and possible consequences of any decision. Risk assessment should be comprehensive but remain feasible given the available time and resources.

Figure 2: Risk assessment scheme for foodborne microbiological hazards



Jouve, J. L. (1996)

5.1. Statement of purpose

5.1.1. The specific purpose of the risk assessment should be clearly stated; the output form and possible output alternatives should be defined

5.1.2. This stage refers to problem formulation. During this stage, the cause of concern, the goals, breadth and focus of the risk assessment should be defined. The statement may also include data requirements, as they may vary depending on the focus and the use of the risk assessment and the questions relating to uncertainties that need resolving.

5.1.3. Entry into a risk assessment process for foodborne microbiological hazards may be triggered in different ways, for example, by:

- emerging and re-emerging pathogens
- public concern
- the need to establish or to evaluate control options, for example microbiological criteria, etc.

5.1.4. Depending on its purpose, a microbiological risk assessment process may be focused on either the agent, the food vehicle or the treatment/process (the latter may cover, for a given product, all the stages of the food chain, one segment of specialised activity, e.g. production or processing or wholesale/retail activities, a multistep process or a single treatment, e.g. different pasteurisation temperatures). Such a focus may in turn influence the information and data requirements.

As an example, if the focus is on the agent, there is a need to collect data which identifies if foodborne transmission plays an important role in the aetiology of disease and which foods are implicated. If the focus is on food, data are necessary to determine which pathogens have been, or potentially could be, associated with the product. Where the focus is on the treatment/process, there is a need to understand the possible food handling practices and consumers' preferences and habits to identify their possible consequences and determine how likely are these consequences in specific situations.

5.1.5. The output might, for example, take the form of an estimate of:

- annual occurrence of illness
- annual rate of illness per 100 000 population
  rate of human illness per eating occurrence

which facilitate in particular the comparison with human health data.

5.2. Hazard identification

5.2.1. Hazard identification is the identification of biological, chemical and physical agents which are capable of causing adverse health affects and may be present in a particular food or group of foods.

The purpose of hazard identification is to identify the micro-organism or microbial toxin of concern and to evaluate whether the micro-organism or the toxin is a potential hazard when present in food.

5.2.2. The key to hazard identification is the availability of public health data and a preliminary estimate of the amount, frequencies and sources of the micro-organism.

5.2.3. The necessary information can be obtained from scientific literature, from databases such as those maintained in governmental agencies and in the food industry and through experts' advice.

5.2.4. Areas of relevant information may include, among others:

- clinical studies
- epidemiological studies and surveillance
- laboratory animal studies
- investigation of the characteristics and properties of micro-organisms (e.g. genotype, phenotype and behaviour)
  interaction between micro-organisms and their environment through the food chain from primary production up to and including consumption
- information on analogous micro-organisms, situations or contexts.

5.2.5. For many established foodborne pathogens, hazards are already well documented and the formal requirements for information and data are minimal. However, there is a perceived need for better identification of newly emerging (or re-emerging) foodborne pathogens and to develop for that purpose targeted medical studies, epidemiological monitoring (e.g. sentinel or case/control studies) and microbiological techniques (e.g. improved detection and identification techniques, differentiation of strains).

5.3. Exposure assessment

5.3.1. Exposure assessment is the qualitative and/or quantitative evaluation of the likely intake of biological, chemical and physical agents via food as well as exposure from other sources if relevant.

The ultimate goal of exposure assessment is to evaluate the level of micro-organisms or microbial toxins in the food at the time of consumption. This may include an assessment of actual or anticipated human exposure.

For foodborne microbiological hazards, exposure assessment might be based on the possible extent of food contamination by a particular hazard and on consumption patterns and habits (i.e. 'dietary information').

5.3.2. Assessing the potential extent of food contamination involves consideration of the frequency or likelihood of contamination of foods by the pathogenic agent and its prevalence and/or level in those foods over time, up to the time of consumption.

In addition to the characteristics of the pathogenic agent information of interest may include:

- the microbial ecology of the food
- the initial contamination of the raw materials
- the effect of the production, processing, handling, distribution steps and preparation by the final consumer on the microbial agent. (i.e. the impact of each step on the level of the pathogenic agent of concern)
- the variability in processes involved and the level of process control
  the level of sanitation
- the potential for (re)contamination (e.g. cross-contamination from other foods; recontamination after a killing treatment)
  the methods or conditions of packaging, distribution and storage of the food (e.g. temperature of storage, relative humidity of the environment, gaseous composition of the atmosphere)
- the characteristics of the food that may influence the potential for growth of the pathogen (and/or toxin production) in the food under various conditions, including abuse (e.g. pH, moisture content or water activity, nutrient content, presence of anti-microbial substances, competitive flora).

5.3.3. To gain this information several techniques may be used, for example:

- data collection on prevalence and distribution of micro-organisms in food(s) including foods involved in outbreaks
- storage testing
- challenge testing

— historical performance data of a food process or laboratory studies of such performance (e.g. 'D' values of survivors to a heat treatment)
— mathematical modelling to predict the growth, death or survival of micro-organisms in response to environmental conditions and the likely number of micro-organisms present in food at the time of consumption
— examination of foods involved in outbreaks.

Such exposure assessment includes various levels of uncertainty. This uncertainty can be estimated using various techniques, e.g. event tree analysis, fault tree analysis, HAZOP (hazard analysis and operability study) and probabilistic scenario analysis (PSA) (6, 7).

5.3.4. Information on consumption patterns and habits ('dietary information') may include:

— socioeconomic and cultural background, ethnicity
consumer preferences and behaviour as they influence the choice and the amount of the food intake (e.g. frequent consumption of high risk foods)
— average serving size and distribution of sizes
— amount of food consumed over a year considering seasonality and regional differences
— food preparation practices (e.g. cooking habits and/or cooking time, temperature used, extent of home storage and conditions, including abuse)
— demographics and size of exposed population(s) (e.g. age distribution, susceptible groups).

5.4. Hazard characterisation

5.4.1. Hazard characterisation is the qualitative and/or quantitative evaluation of the nature of the adverse effects associated with biological, chemical and physical agents that may be present in food. A dose–response assessment should be performed if data are obtainable.

The purpose of hazard characterisation is to provide an estimate of the nature, severity and duration of the adverse effects associated with harmful agents in food. Factors important to consider relate to the micro-organisms, the dynamics of infection and the sensitivity of the host.

5.4.2. Factors relating to the micro-organisms may include the following:

microbial replication

e.g. self-replication, generation time

— virulence factors

e.g. synthesis of various toxins; presence of attachment factors on the cell surface, antigenic properties, ability to circumvent host's immune response

— dynamic evolution of virulence of micro-organisms depending on their interaction with environment and host

— microbial variability in response to environmental factors or natural mutation that may result in changes in pathogenicity

e.g. altered biochemical activity

genetic changes

— antigenic variation

— DNA transfer leading to transfer of characteristics such as antibiotic resistance

— tolerance to adverse conditions

transmissibility that may allow spread.

5.4.3. Factors relating to dynamics of infection may include:

— rate of infection

latency (delayed onset of clinical infection following exposure)

— disease pattern

- infection (asymptomatic) versus clinical disease
- disease: acute, chronic, persistent, latent
- incubation period
- severity and duration of episode(s)
- possible diseases outcome (e.g. recovery, mortality, chronic sequelae)
- persistence of the micro-organism in certain individuals leading to continued excretion and risk of spread.

5.4.4. Factors relating to the host may include:

— genetic factors that may influence the immune response (e.g. human leucocyte antigen (HLA) type)

— immune status of subpopulation (e.g. infants, the elderly, pregnant women, immuno-compromised individuals); as well as previously exposed or unexposed populations

— breakdown of physiological barriers leading to increased susceptibility (e.g. concomitant infections, consumption of antibiotics, antacids, excessive level of iron in the blood, reduced liver/kidney function)

— diet and social behaviour (e.g. nutrition deficiencies, poor hygiene, stress).

5.4.5. Specific to risk assessment of foodborne microbiological hazards, consideration should also be given to the interaction between the food matrix, the micro-organism and the host which may influence the survival of the agent through the hostile environment of the stomach. Related factors may include:

- increase of stomach pH (e.g. age, use of antacids)
- decreased residence time (e.g. initial rapid transit of liquids in empty stomach)
- increased acid tolerance (e.g. pre-exposure of bacteria to moderately acid conditions, entrapment of bacteria in lipid droplets, highly buffered foods).

5.4.6. Not all factors listed above will be important for all foodborne microbiological hazards, depending on the purpose of the risk assessment.

5.4.7. A key aspect of hazard characterisation is establishing a **dose–response relationship.**

Dose–response assessment is the process of obtaining quantitative information on the probability of human illness following exposure to a hazard; it is a translation of exposure into harm.

5.4.8. In general, dose–response assessment is carried out for the population (or sub-population) exposed to the hazard but it should be taken into account that the dose-response relationship depends on the sensitivity of the exposed group and that there exists a large variation in the human population.

5.4.9. Information on which to base quantitative dose–response estimates is difficult to obtain, due to, for instance, the variability in virulence and pathogenicity of micro-organisms, the variation in attack rates, the large variation in host susceptibility and the type of food vehicle which modulate the ability of bacteria to infect and otherwise affect the host.

Data sources, where available, could possibly include results of:

- foodborne disease analysis
- population characteristic surveys
- animal trials
- human volunteer studies.

5.4.10. Mathematical models have been developed (beta-Poisson distribution, exponential distribution) to provide assistance in developing dose–response relationship, in particular at low levels. It is recognised that the development of such mathematical models may facilitate this approach, but the assumptions on which they are based, their usefulness and limitations still need to be carefully considered. Since minimum infective dose (MID) may vary widely from person to person, this concept may not be appropriate for risk assessment in a population.

5.5. Risk characterisation

5.5.1. Risk characterisation is the quantitative and/or qualitative estimation including attendant uncertainties of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterisation and exposure assessment.

Bringing together the information of the previous stages, it provides an estimate, qualitative or quantitative, of risk to a given population or subpopulation.

The degree of confidence of the final estimation of risk will depend on the factors considered and their uncertainty identified in all the previous stages.

5.5.2. Risk characterisation is the last step in risk assessment from which a risk management strategy can be formulated.

5.5.3. Risk characterisation has been defined as the integration of the hazard identification, hazard characterisation, and exposure assessment determinations, previously described, into qualitative or quantitative estimates of the likelihood of the adverse effects occurring in a given population, including a description of the uncertainties and variability.

5.5.4. These estimates can be assessed by comparison with independent epidemiological data that relate hazards to disease prevalence.

Risk characterisation brings together all of the qualitative or quantitative information of the previous steps to provide a soundly based estimate of risk for a given population or subpopulation. The weight of evidence integrating quantitative and qualitative data may permit only a qualitative estimate of risk.

5.5.5. The degree of confidence in the final estimation of risk will depend on the variability, uncertainty, and assumptions identified in all previous steps. Uncertainty is associated with the data themselves, and with the choice of model. Data uncertainties include those that might arise in the evaluation and extrapolation of information obtained from epidemiological, microbiological, and laboratory animal studies. Uncertainties arise whenever attempts are made to use data concerning the occurrence of certain phenomena obtained under one set of conditions to make estimations or predictions about phenomena likely to occur under other sets of conditions for which data are not available. Biological variation includes the differences in virulence that exist in microbiological populations and variability in susceptibility within the human population and particular subpopulations. It is important to demonstrate the influence of the estimates and assumptions used in risk assessment, for quantitative risk assessment this can be done using sensitivity and uncertainty analyses.

5.6. Produce a formal report

5.6.1. The risk assessment should be fully and systematically documented. To ensure transparency the final report should indicate, in particular, any constraints and assumptions relative to the risk assessment. The report should be made available to independent parties on request.

5.6.2. The specific format should indicate all the elements of a scientific report.

6. Conclusions and recommendations

The field of risk assessment of foodborne microbial hazards is a dynamic developing scientific discipline. The principles and guidance for risk assessment presented in this document are recommended for use by the European Commission, EC member countries and may form the basis for refinement of the risk assessment procedure.

Experiences gained from such usage as well as scientific experiences, for example, from ongoing scientific cooperation projects will need to be taken into account in an update of this document as well as global experiences assembled within the Codex system.

The SCF recommends revising this document in five years' time in order to refine and focus the scientific procedures for qualitative and quantitative microbial risk assessment to be applied in the European Union.

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OPINION ON MICROCRYSTALLINE CELLULOSE

(expressed on 19 September 1997)

Terms of reference

To re-evaluate the safety in use of microcrystalline cellulose (MC) in the light of additional information received with respect to its general uses as set out in Directive 95/2/EC on food additives other than colours and sweeteners.

Background

The Committee established in 1978 an ADI 'not specified' for MC (1) but expressed a wish to be kept informed of any ongoing work to elucidate the problem of the persorption of ingested particulates which had been raised in connection with the safety assessment of MC. In 1990, the Committee agreed that the use of MC as an additive in weaning foods and gluten-free cereal-based weaning foods was acceptable (2). In 1993, the Committee reconsidered microcrystalline cellulose in the light of the request to use material of particle size below 5 µm in infant formula (3). The Committee remained concerned about the possibility of increased persorption in infants, considering the immaturity of the gut mucosa at that age, and its altered absorptive capacity in babies suffering from bowel disease, and withdrew its earlier acceptance of the use of microcrystalline cellulose in gluten-free weaning foods. It was unable to give any view on the safety of microcrystalline cellulose of particle size below 5 µm as no toxicity data relevant to such material had been submitted. At that time the Committee also commented that a limit of 5 µm should be introduced into the specification to ensure that only microcrystalline cellulose for which adequate toxicity data existed be permitted for food use. Further information has since been submitted and is considered here.

New information submitted

The new information on biochemistry included a study on three types of cellulose, administered orally to rats at 5 % in their diet, which used glucose generation *in vitro* and *in vivo* as indicator of the digestibility of the celluloses tested. MC was found to be the least digestible of the three celluloses examined (4). Furthermore, a recent study in rats on the determination of the available energy from ingested MC and other incompletely digested carbohydrates was also supplied (45).

The earlier results of acute toxicity, irritancy and sensitisation studies were resubmitted (5- 13) together with some recent similar studies on another MC preparation (47–52, 62, 64).

Genotoxicity was examined in several mutagenicity tests using different genetic endpoints. Three bacterial microsomal reversion tests, using *Salmonella typhimurium* strains TA 98, TA 100, TA 1535, TA 1537 and TA 1538 with MC suspended in DSMO +/- S9 mix, produced no increase in revertants at doses up to 5 000 µg/plate (14, 15, 53). Forward gene mutation tests in cultured L5178Y mouse lymphoma cells did not show any increase in mutants over a dose range of 100–1 000 µg/ml (16, 54). MC did not induce any unscheduled DNA synthesis in cultured primary hepatocytes up to doses of 1 000 µg/ml. Some insolubility was noted with doses >5 µg/ml (17). Several *in vivo* micronucleus tests in mice showed no increase in micronuclei induced by MC doses up to 5 000 mg/kg b.w. (18, 55, 56). MC was thus found to be non-genotoxic in a series of adequately performed mutagenicity tests using different genetic endpoints.

A recent study on subacute toxicity has also become available. A 28-day gavage study in Sprague-Dawley rats used doses of 1 000, 2 000, 3 000, 4 000 and 5 000 mg/kg b.w./day in groups of five animals/sex. No adverse toxicological effects occurred at any of the dose levels tested. No persorbed particles of MC were detected in the gut or in the Peyers' patches at the highest dose level tested. The administered MC had a median particle size of 6 µm and contained 28 % of particles of size <5 µm (19).

Several new subchronic toxicity studies in Sprague-Dawley rats were also submitted (63). One of these was a 90-day feeding study using 25 000 mg/kg feed and 50 000 mg/kg feed of MC in the diet of the test animals. No adverse effects on body weight gain, haematological and clinical chemical parameters, organ weights of six major organs and the histopathology of 26 tissues including the GI tract, ileal lymphnodes and Peyers' patches were noted. Inconsistent increases in food consumption occurred in both test groups. The NOAEL was 50 000 mg/kg feed in the diet or approximately 4 000 mg/kg b.w. as actually measured. The MC tested had a median particle size of 21 µm but contained only 1 % of material of a particle size <5 µm (20).

Another 90-day feeding study used 5 % and 10 % of MC in the diet. No adverse effects were noted on body weight gain, clinical chemical and haematological parameters, organ weights of six major organs and the histopathology of 33 tissues. Food consumption was increased dose-dependently. The NOAEL was 10 % or approximately 6 000 mg/kg b.w. as actually measured. The MC tested had a mean particle size of 32 µm but contained only 1 % of material of a particle size <5 µm (21).

A further 90-day study used administration of MC by gavage and doses of 500 mg, 2 500 mg and 5 000 mg/kg b.w./day. No significant adverse effects were produced on survival, body weight gain, haematological and clinical chemical parameters, organ weights of five major organs, and the histopathology of 33 tissues. Only the high dose males showed reduced body weight gain, most probably the result of a nutritional effect. No specific pathological lesions were reported in spleen, gut wall and gut-associated lymphoid tissue (GALT). The NOAEL was 5 000 mg/kg b.w./day. The MC tested had a median particle size of 6 µm and contained 28 % of material of particle size <5 µm (22).

In a six months' study, groups of random bred rats of both sexes received either a control diet or a diet with 330 ppm of MC. At the end of this time six rats in each group were killed, their organs examined and tissues examined histopathologically. No adverse effects were observed (57).

Teratogenicity was examined in two studies using Sprague-Dawley rats. In one study MC was fed at doses of 25 000 mg/kg feed and 50 000 mg/kg feed in the diet from days 6 to 15 of gestation. No treatment-related adverse effects were noted on pregnancy, parturition and litter parameters. The NOAEL was 4 410 mg/kg b.w. as determined from food consumption. The MC tested had a median particle size of 21 µm and only 1 % of the material was particles of size <5 µm (23). The second study used 25 000 mg/kg feed and 50 000 mg/kg feed of another MC product in the feed from days 6 to 15 of gestation. No treatment-related adverse effects were seen on pregnancy, parturition and litter parameters. The NOAEL was 4 589 mg/kg b.w. as determined from actual food consumption. The MC tested had a mean particle size of 32 µm and contained only 1 % of material of particle size <5 µm (24).

The effects of cellulose fibre on tumour growth were investigated again by feeding artificial diets containing varied concentrations of either wheat bran or pure cellulose fibre to female F344 rats treated with i.v. 40 mg/kg b.w. N-nitrosomethylurea to induce mammary tumours. The wheat bran diet appeared to possess anti-promotion properties not observed with pure cellulose. The concentrations of serum oestrogens, urinary oestrogens and faecal oestrogens did not vary in a consistent, statistically significant manner (58).

The human clinical studies on various ingested MCs submitted were all concerned with changes of gastrointestinal function and nutrient balance and examined essentially faecal output, faecal composition, effects on blood biochemistry, the digestibility of the major nutrients and the bioavailability of essential micronutrients. Up to 30 g MC/day in the diet had no adverse effect on the function of the gastrointestinal tract, or haematological and on clinical chemical parameters except for the production of an increased faecal output (25, 35–39). These findings were supplemented by recent metabolic studies with MC (46) and with various cellulosic fibres (59, 60, 65–67).

Persorption aspects

Since the early publications in the 1960s on the persorption of ingested particulates and on the demonstration of their presence in the circulating bloodstream, further research has been carried out which confirmed, that MC particles ranging in size from 5–150 µm could be persorbed and detected in venous blood samples taken 1–2 hours after ingestion by rats, dogs, guinea-pigs and in one human volunteer (26–28).

Further experiments, using i.v. administration to rats, showed some effects on haematology and renal function. MC particles could be identified in various tissues but these studies were of little relevance for assessing the biological significance of persorption following ingestion. However, a combined one-generation reproduction/chronic toxicity study in rats, in which the F1 generation was fed MC containing 90 % of particles of size <20 µm at 0, 3 %, 10 %, and 20 % in their diet for two years, showed no adverse effects on litter parameters except some growth depression of the F1 weanlings at the top dose during the early growth phase only. Food consumption was increased in all MC-treated rats. After 12 months, MC particles were said to be detected in some organs and no microemboli were identified (summary report only available). Reports of some impairment of renal function without any associated histopathological changes and of some haematological changes in the highest dose group could not be confirmed in the surviving rats of the same study, which had been treated for a further year, (29, 30). In a more recent 90-day feeding study in rats, in which special precautions against contamination were taken, no MC particles were detected in any organ or tissue examined and no adverse histopathological effects were found. In particular, no kidney lesions were seen (22).

From the numerous studies reported in the literature it appears that persorption is a universal physiological process similar in mammals, the rat being a good model for man in this respect. Man and animals do not show accumulated particles in the intestines, or in the GALT, despite daily exposure to large numbers of persorbable particles in the diet throughout life. In recent appropriate studies, persorption has been shown to be an inefficient process. In single dose tests persorbed particulates are cleared from tissues within a few hours and they do not accumulate on repeated dosing even for several months (31). Interestingly, macrophages appear to be able to take up particles of size <2 µm while particles >16 µm do not appear to enter GALT (32). Some more recent studies using either biodegradable microspheres or other non-MC particulates confirmed uptake by GALT and systemic transfer to other tissues (40–44, 61).

Reassessment of the techniques used in the early studies on persorption also revealed the need for taking meticulous precautions to avoid extraneous sample contamination, which could be misinterpreted as evidence for persorption. The absence of these precautions in the early studies therefore makes their results difficult to interpret. This point was examined specifically in a gavage study in rats using polystyrene particles under appropriate experimental conditions. The results confirmed intestinal persorption to be a very inefficient process in adult rats as only 0.05 %–0.1 % of the ingested particles could be recovered in the Peyers' patches (33). It should also be remembered that many naturally occurring particulates are ingested frequently by man throughout life without causing any apparent harm (34).

Conclusions

This opinion applies only to general food uses of MC and does not apply to use in foods specially prepared for infants and young children including foods for special medical purposes for the same age group.

The additional toxicological information now submitted confirms the validity of the ADI 'not specified' for MC previously established by the Committee. There is now evidence that MC has neither genotoxic nor teratogenic potential in the rat.

Early studies on the intestinal persorption of MC of varying particle size suggested that MC is persorbed, particularly if the particle size is <5 μm. This process is, however, very inefficient, at least in adult animals, and does not result in microembolic phenomena, nor does it appear to interfere with the immune function of the GALT. Recent studies on persorption in several species have shown that the rat provides an adequate model for this process in man. The two-year feeding study in rats showed no evidence of any histopathological or functional effects ascribable to accumulation of MC particles in any tissue as a consequence of persorption. The available human data on particles other than MC and animal studies on MC and the GALT suggest that in normal adults exposed over a comparatively short period the intestinal persorption of MC of particle size even down to at least 5 μm would be unlikely to cause any adverse pathology in the gut and GALT. The Committee wishes to stress that there are no data available on the existence and the extent of persorption in very young animals or in human infants.

As a precautionary measure however, the Committee reiterates its view of 1993 (3) that the specification of MC should include a restriction on the content of material of particle size <5μm. The Committee is aware that a tolerance of 10 % by number of particles is achievable. Otherwise the Committee's views on MC remain unchanged.

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OPINION ON DERIVATIVES OF WOOD ROSIN AS COATING AGENTS FOR FRESH CITRUS FRUITS

(expressed on 19 September 1997)

Terms of reference

To evaluate the safety of certain wood rosin derivatives as coating agents for fresh citrus fruits not listed at present in the directive on food additives other than colours and sweeteners.

Background

The directive on food additives other than colours and sweeteners (1) does not include in its Annex IV among the coating agents listed therein any rosin derivatives as coating agents for fresh citrus fruits. However, these materials have been in use for years in some EU Member States as protective coating agents on citrus fruits to prevent transpiration of moisture with resulting weight loss, to delay fruit ageing and to improve the appearance of the fruits by increasing the shine of the peel. An amendment to this directive has now been requested to permit the use of certain rosin derivatives as surface treatment of citrus fruits at a rate of application of 50 mg/kg fruit.

Another rosin derivative, Ester Gum 8BG (a glycerol ester of wood rosin), used as an emulsifier and stabiliser in soft drinks, was previously evaluated by the SCF in 1990 (2) and allocated a temporary ADI of 0 -0.5 mg/kg b.w, provided that the only rosin present is wood rosin and that the results of an adequate 90-day feeding study in rats using a well-specified commercial product would be submitted in due course. The same compound was subsequently re-evaluated by JECFA in 1995 (3) and allocated an ADI of 0–25 mg/kg b.w.

Information submitted

The Committee was provided with specifications, technological information on use levels and biological data on the following three specific rosin derivatives: partially hydrogenated rosin, rosin esterified with pentaerythritol and rosin modified with maleic anhydride and esterified with pentaerythritol (4).

The specifications submitted do not specify wood rosin as the basic rosin, modified for the production of the three coating agents put forward for inclusion in the present directive. However, all the biological data submitted relate entirely to modified wood rosins.

For partially hydrogenated wood rosin a 90-day feeding study in Sprague-Dawley rats was submitted. It encompassed five test and two control groups, each consisting of 10 animals/sex/group and covered the dietary dose levels 0 %, 0.01 %, 0.05 %, 0.2 %, 1 % and 5 % of the test substance suspended in corn oil. All control and test groups were adjusted to a corn oil content of 2.33 %, the 5 % test group had a dietary corn oil level of 11.7 %. The investigations carried out covered the usual parameters except that no clinical chemistry parameters were investigated. Organ weights were determined for seven major organs and histopathology was performed on 20 different tissues. All animals of the 5 % test group had died by day 11 from inanition due to food refusal as a consequence of unpalatability of the diet. Reduced body weight gain and slight increase in relative liver weight were noted at the 1 % dose level. The NOAEL was 0.2 % (= 100 mg/kg b.w.) (5)

In addition a two-year chronic feeding study in Sprague-Dawley rats was submitted. It used three test and two control groups, each comprising 30 animals/sex/group. The dietary dose levels tested were 0 %, 0.05 %, 0.2 % and 1 % of the test substance suspended in corn oil. All diets including that of the controls were adjusted to a total corn oil level of 2.33 %. The investigations carried out covered the usual parameters but did not include any clinical chemistry. Organ weights were determined for eight major organs and histopathology examined 24 different tissues. Apart from lower body weights in the 1 % test group compared with controls, not accompanied by reduced food consumption, no other significant adverse toxicological effects were noted in any test or control group. The NOAEL was 0.2 % (= 100 mg/kg b.w.) (6).

Furthermore, a two-year chronic feeding study in beagle dogs was supplied, which used two test groups with three animals/sex/group and a control group of six animals/sex/group. The dietary dose levels investigated were 0 %, 0.05 % and 1 %. The diet of all groups was adjusted to a corn oil content of 2.33 % as the test substance was suspended in corn oil. None of the standard investigations showed any toxicologically significant findings compared with controls. The NOAEL was 1 % in the diet (= 250 mg/kg b.w.), the highest dose level tested (7).

For the pentaerythritol ester of wood rosin the submission contained the results of acute toxicity tests in rats and guinea-pigs (8, 9). The respective LD_{50}s were >20 g/kg b.w. and >18 g/kg b.w.

A 90-day feeding study in Sprague-Dawley rats was also supplied. It used five test groups and two control groups, each consisting of 10 animals/sex/group and the

following dietary dose levels: 0 %, 0.01 %, 0.05 %, 0.2 %, 1 % and 5 %. The test material was suspended in corn oil and each group diet was adjusted to contain 2.33 % corn oil except for the 5 % group which had 11.7 %.

One rat died in each of the control and test groups up to the 1 % dose level, two rats died in the 5 % dose group. There were no significant adverse toxicological findings in all standard investigations in the test groups compared to the controls. The NOAEL was the highest level tested, i.e. 5 % in the diet (= 2 500 mg/kg b.w.) (10).

In addition, the results of a two-year feeding study in Sprague-Dawley rats were submitted. This study was inadequate in design as it used only one rather low test dose level and two control groups, each of 30 animals/sex/group. There were a few unscheduled deaths in the three groups due to respiratory disease. No significant adverse toxicological effects were noted in the test group compared to the controls. Tumour incidence and type in the test group were also comparable to those of the controls. The NOAEL was 0.05 % (= 25 mg/kg b.w.), the only dose level tested (11).

Furthermore, the results of a two-year study in beagle dogs were supplied. This study was inadequate because it used only one rather low dose level. The test group consisted of 3 animals/sex/group, the control group of 6 animals/sex/group. There was no mortality and no significant differences were noted between the test and control group in all standard parameters investigated. The NOAEL was 0.05 % (= 12.5 mg/kg b.w.) the only dose level tested (12).

For the rosin modified with maleic anhydride and esterified with pentaerythritol only an inadequate specification was supplied which did not clarify whether the basic unmodified rosin was of the wood rosin type. It is therefore not possible to use the 90-day feeding study in Sprague-Dawley rats also submitted for the safety assessment of this particular modified rosin, although the design of this feeding study was reasonably adequate, until the identity of the material tested becomes available (13).

The Committee has received an intake estimate of 0.00075 mg/kg b.w./person/day as the likely worst case from assumed non-standard use of rosin esters on the peel of bitter oranges. This estimate is based on import figures for certain EC countries and assumed consumption of all imported fruit by their total population (14). The Committee considered this to be an unsatisfactory and unrealistic approach. It has now been supplied with intake estimates based on dietary surveys in the United Kingdom which suggest that the estimated total dietary intake of wood rosins ranges for adults from a mean of 0.04 mg/kg b.w./day to a 97.5 percentile of 0.17 mg/kg b.w./day. The equivalent figures for pre-school children range from a mean of 0.08 mg/kg b.w./day to a 97.5 percentile of 1.16 mg/kg b.w./day. The only significant intake of citrus peel is taken to come from the consumption of orange juice made from comminuted crushed whole oranges and from marmalade (40 % fruit) made from bitter oranges.

Conclusion

The question whether the coating materials requested for inclusion in Annex IV of the directive on food additives other than colours and sweeteners are in fact produced from appropriately modified wood rosin cannot be verified by the Committee until the revised specifications become available. Meanwhile, the Committee is of the opinion, that coatings made from partially hydrogenated wood rosin are **temporarily acceptable** as coatings for fresh citrus fruits at an application rate of 50 mg/kg fruit. This decision is based on the available, though limited, feeding studies in rats and dogs, which indicate a safety margin of 75–500 between likely intakes and the NOAEL. The Committee requires information on reproductive effects, teratogenicity, mutagenicity and an adequate specification defining the source of the rosin within the next three years.

For coatings made from the pentaerythritol ester of wood rosins the Committee considers that these are **temporarily acceptable** for use on fresh citrus fruits at an application rate of 50 mg/kg fruit. This decision is based on the available, though inadequate, long-term studies in the rat and dog and the reasonably adequate 90-day rat study, none of which disclose any significant adverse toxicological effects. The acute toxicity is also very low and hydrolysis is unlikely in view of the stable chemical structure of the ester. The safety margin between likely intakes and the NOAEL lies between 10 and 60. However, appropriate information on reproductive effects, teratogenicity and mutagenicity is required within the next three years and an adequate two-year oral feeding study in rats is required within five years. An adequate specification defining the source of the rosin is also required.

The Committee is unable to evaluate the safety of rosin modified by maleic anhydride and esterified with pentaerythritol because of the grossly inadequate toxicological database and the uncertainty regarding the specification of this modified wood rosin. The Committee therefore considers this modified resin **unacceptable** for food use.

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OPINION ON THE RELATIONSHIP BETWEEN SCIENTIFIC DATA AND THE LABELLING OF GENETICALLY MODIFIED FOODS AND THEIR DERIVED PRODUCTS.

(expressed on 19 September 1997)

Terms of reference

The Committee is asked to advise on:

- the factors to be taken into consideration to demonstrate that the composition of a novel food or a novel food ingredient is different in comparison with a conventional food or food ingredient based upon an appropriate analysis of existing data and having regard to the control methods currently available and the current variations within the family of foods or food ingredients when they are obtained by conventional means.

- the qualitative and/or quantitative conditions that such factors would have to fulfil.

Background

Authorisations for placing on the market have been given in conformity with the provisions of Directive 90/220/EEC (1) concerning the deliberate release into the environment of genetically modified organisms for Monsanto's soybeans (1) and for Ciba-Geigy's maize (2). These authorisations were given before the entry into force of Regulation (EC) No 258/97 (2) without requiring any specific labelling provisions because Directive 90/220/EEC did not provide for such provisions except if justified for safety reasons.

The Commission has deemed it necessary to lay down additional labelling provisions for foods and food ingredients derived from the genetically modified soybeans or maize according to Article 8 in Regulation (EC) No 258/97.

In view of the above and having regard to the fact that the Scientific Committee for Food has already given its opinion concerning the guidelines for the scientific evaluation of novel foods and novel food ingredients and, conscious of the major role that the Committee will have during the implementation of this Community regulation, the Commission has considered it desirable to consult the Committee on

(1) Commission Decision of 5 April 1996.
(2) Commission Decision of 23 January 1997

the scientific evaluation of the term 'equivalence' as used in Article 8, §1a), in Regulation (EC) No 258/97.

Approach

In considering this question the Committee felt that it might be best answered by addressing some generic issues relating to 'substantial equivalence' and 'equivalence', rather than issues specific for genetically modified maize and soya beans.

The notion of safety

It should be emphasised that all novel foods accepted as being in accordance with requirements of the SCF's opinions on the assessment of novel foods (3, 4, 5) are, on the basis of current knowledge, safe for human consumption. This statement applies regardless of whether the particular novel food must be labelled according to the pertinent section of the regulation. The objective of the SCF's opinions mentioned above is primarily to provide guidelines for safety and nutritional evaluation of novel foods and ingredients in order to avoid ambiguity and to achieve coherence of the regulatory process within the entire EC.

The principle of substantial equivalence

The concept of 'substantial equivalence' in the context of the SCF opinions on the assessment of novel foods (3, 4, 5) embodies the idea that existing organisms or products used as foods or food sources, can serve as a basis for comparison when assessing the safety and nutritional value of a food or food ingredient that has been modified or is new. If a new food or food ingredient is found to be substantially equivalent to an existing food or food ingredient, it can be treated in the same manner with respect to safety and nutritional value, keeping in mind that establishment of substantial equivalence is not a safety or nutritional assessment in itself, but an approach to compare a potential new food with its conventional counterpart.

The application of the principle of substantial equivalence can be extended to the evaluation of foods from novel sources and processes. Substantially equivalent novel foods and novel food ingredients are thus comparable, in terms of safety and nutritional value, to their conventional counterparts. Substantial equivalence may be established either for the whole food or food component including the introduced 'new' change, or it might be established for the food or food component except for the specific 'new' change introduced. If a novel food or novel food ingredient has not been found to be substantially equivalent to an existing food or food component, this does not imply that it is unsafe. It simply indicates that such a novel food or novel

food ingredient should be evaluated on the basis of its unique composition and properties.

The demonstration of substantial equivalence contains a dynamic element, as the continuing modification of a food requires that the basis of comparison will evolve in a way that the most recent novel food or novel food ingredient is compared with an appropriate predecessor and not necessarily with the most traditional counterpart.

The technical approach to substantial equivalence is addressed in detail in the SCF opinions but essentially leads to one of three scenarios:

(i) **Substantial equivalence to a traditional counterpart:**
If substantial equivalence to a traditional counterpart is established, the novel food or novel food ingredient can be regarded as wholesome and to be toxicologically and nutritionally acceptable for use in the overall diet in a manner comparable to its counterpart or as replacement of its counterpart. When judging the comparability of the novel food or novel food ingredient to its counterpart, the limits of known and measurable natural diversity of any conventional counterpart are taken into account.

(ii) **Substantial equivalence except for one or more defined traits:**
If substantial equivalence except for one or more defined traits is demonstrated, the assessment focuses on these traits. These are evaluated on a case-by-case basis and may in certain cases require information, matching that needed for the safety evaluation of food additives (6).

(iii) **No substantial equivalence:**
If substantial equivalence to a traditional food or food ingredient is not established, the novel food requires an extensive database as outlined in the SCF opinions.

Comparison of the legal term 'equivalence' with the concept of 'substantial equivalence'

The term 'equivalence' is not explicitly defined in Regulation (EC) No 258/97 concerning novel foods and novel food ingredients, but Article 8 sets out the conditions under which a novel food or novel food ingredient can no longer be considered to be equivalent to an existing food or ingredient:

A novel food or food ingredient shall be deemed to be no longer equivalent for the purpose of this Article if scientific assessment, based upon an appropriate analysis of existing data, can demonstrate that the characteristics assessed are different in

comparison with a conventional food or food ingredient, having regard to the accepted limits of natural variations for such characteristics.

Essentially the legal term 'equivalence' relates to inherent and analytical variance in composition and supports the consumer's entitlement to know about the origin and composition of the novel food, whereas the scientific concept of 'substantial equivalence' embraces an assessment of safety and nutritional adequacy. The SCF emphasises the importance of differentiating between labelling issues and those relating to safety and nutritional value.

Use of data submitted for safety and nutritional evaluation for the specific labelling of novel foods

The SCF advises that safety and nutritional data used for the evaluation of substantial equivalence may also contribute to the identification of measures to monitor the correct implementation of labelling and the spread of novel foods in the market place. The application of the data for this purpose will have to be established on a case-by-case basis paying particular attention to key macronutrients and micronutrients and to potential toxic and anti-nutritional factors which might be either inherently present or process-derived.

Foods which have been shown to be substantially equivalent and to be as safe as their traditional counterparts may contain modified DNA. In such cases, this DNA, although it does not change the composition and safety of the final food product, may facilitate monitoring and control. It may be relevant to use the presence of residues of the marker genes and of their expression products along with the primarily targeted modification as a logical handle for labelling. Account should be taken of the nature and possible persistence of the primary modification.

For foods where substantial equivalence is established except for certain defined traits, the defined changes provide a logical starting point for the selection of parameters for monitoring and control of labelling and trade as wished. These indicators of novelty may embody introduced changes of the genetic material, derived novel proteins and new secondary metabolites to be chosen on a case-by case basis.

For foods where no substantial equivalence to existing foods can be established, but the wholesomeness has been confirmed on the basis of submitted data, there will be a variety of analytical possibilities, again to be determined on a case-by-case basis.

The control of labelling: possibilities and limitations

The correct labelling of a novel food or novel food ingredient cannot be verified if no differences to the conventional counterpart can be detected.

The following situations are examples for the limitations of labelling:

Advances in the sampling and analytical procedures used during the control procedures might in the future reveal previously unrecognised structural and compositional differences; these might allow identification of new markers of the novel product.

- As new techniques will probably lead to higher sensitivities, it is recommended that validated methods with defined limits of determination be used.

- In the case of methods based on the detection of recombinant DNA it is recommended that regulating authorities be informed of the introduced sequences including unique border sequences suitable for PCR techniques.

- During the harvesting, transportation and processing of food, cross-contamination may occur between a substantially equivalent novel food and its traditional counterpart. Such technological carry-overs would be acceptable from a safety point of view but for management purposes defined tolerable limits are recommended. For example, in accordance with Regulation (EEC) No 2731/75 amended by Regulation (EEC) No 2094/87, contamination of common wheat, durum wheat, rye, barley or maize by grains of other cereals is accepted at levels ranging from 1,5 to 4 %.

At the present time, methods for quantitative determination of functional/transcriptional DNA sequences are still developing. It is recommended that validated standards containing defined concentrations of GM markers only should be supplied to facilitate sensitive and validated methods for sampling and monitoring.

It should also be appreciated that the final product might not contain any detectable markers of an earlier modification or process, because such markers have been removed during processing. This would render the regulation of such products difficult. None the less it might be desirable for the product to be monitored for the absence of such markers as an aspect of control.

Conclusions

This opinion delineates the presently known technical possibilities for monitoring and control as well as the associated limitations for labelling purposes.

The SCF emphasises that 'equivalence' is a legal term which applies to the inherent analytical compositional characteristics of a food or food ingredient, whereas 'substantial equivalence' represents a safety and nutritional evaluation of such products in comparison to appropriate predecessors.

The SCF advises that safety and nutritional data used for the evaluation of substantial equivalence may also contribute to the basis for the identification of measures to monitor the correct implementation of labelling and the spread of novel foods in the market place. The application of the data for this purpose will have to be established on a case-by-case basis paying particular attention to key macronutrients and micronutrients and to potential toxic and anti-nutritional factors which might be either inherently present or process derived.

The Committee suggests based on its considerations, that if obligatory labelling requirements for novel foods which from a legal point of view are no longer equivalent to traditional foods are introduced, they should for practical reasons be combined with a management decision to introduce an acceptable level for the accidental mixing of the safe novel food with its conventional counterpart.

Furthermore, analytical methods should be employed that are standardised and validated. For determination of recombinant DNA in a food or food ingredient, all available information concerning unique sequences should be revealed for use by control laboratories.

The Committee also points out that foods which have been shown to be substantially equivalent and to be as safe as their traditional counterparts, may contain modified DNA but otherwise be identical to their traditional counterpart. In such cases, this DNA, although it does not change the composition and safety of the final food product, may facilitate monitoring and control.

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OPINION ON A MAXIMUM RESIDUE LIMIT (MRL) OF 0.01 MG/KG FOR PESTICIDES IN FOODS INTENDED FOR INFANTS AND YOUNG CHILDREN

(expressed on 19 September 1997)

Terms of reference

The Committee is asked to advise the Commission as to whether a maximum residue limit (MRL) of 0.01 mg/kg for pesticides in manufactured foods intended for infants and young children (dietetic foods) would be adequate to protect the health of this section of the population or whether there are instances where there are reasons to be concerned that the presence of even lower levels might constitute a risk. In the latter case, the Committee is invited to provide criteria for the identification of the pesticide residues concerned and for the establishment of appropriate residue limits for them.

Background

In its opinion on the essential requirements for weaning foods (1), the Committee defined 'infants' as children aged less than 1 year and 'young children' as children aged between 1 and 3 years. For the purposes of the present opinion, 'older infants' are those aged between 4 and 12 months and 'childhood' is understood as the period from 1 year to 12 years (young child 1–3, older child 3–12 years).

Foods for particular nutritional uses (dietetic foods) intended for infants and young children are covered by two directives: Directive 91/321/EEC (2) as amended by Directive 96/4/EC (3) on infant formulae and follow-on formulae and Directive 96/5/EC (4) on processed cereal-based foods and baby foods. Article 6 of each of these directives specifies that the products covered 'shall not contain any substance in such a quantity as to endanger the health of infants and young children. Necessary maximum levels shall be established without delay.'

The terms used in these directives are consistent with those defined by the Committee.

Pesticide residues are regulated by Directives 76/895/EEC (5), 86/362/EEC (6), 86/363/EEC (7) and 90/642/EEC (8) and their amendments. These directives do not harmonise the situation for foods intended for infants and young children, however, the Commission declared to the Council during the adoption of these directives its intention to present proposals for maximum levels of pesticides in foods intended for infants and young children by 1 January 1999.

Taking account of the various scientific, practical and socioeconomic factors, the Commission has asked the Committee to advise it on the health implications of a limit of 0.01 mg/kg for pesticides in manufactured foods intended for infants and young children in the light of current scientific knowledge.

Current procedures for establishing maximum residue levels (MRLs) for pesticides

The use of pesticides is regulated on the basis of the MRLs established for residues on various crops. The establishment of an MRL should, among other things, take into account that the acceptable daily intake (ADI) for humans for that particular pesticide is not exceeded when the foods are ingested by the consumer. The ADI is defined as 'an estimate of the amount of a residue, expressed on a body weight basis, that can be ingested daily over a lifetime without appreciable health risk' (9). The ADI is intended to cover all vulnerable groups (including different age groups) within the human population. It has been stated that the ADI is applicable to children older than 12 weeks of age (10). JMPR (Joint FAO/WHO Meeting on Pesticide Residues) has been establishing ADIs since the early 1960s.

MRLs are subsequently derived based on GAP (*) supervised trials and compared with the ADI. In the EC there is a tiered approach in the setting of the MRLs (Directives 86/362/EEC, 86/363/EEC, 90/642/EEC and 91/414/EEC (11)). Firstly, the TMDI (theoretical maximum daily intake) is calculated from the MRL proposals based on the results of the GAP supervised trials and the estimated food consumption per person. If the ADI is exceeded according to this calculation, more refined methods are used to calculate a more realistic intake using e.g. the actual median residue levels determined after GAP supervised trials, and reduction factors from the processing of food. If the ADI is still exceeded after use of the refined calculation methods, then the proposed MRLs cannot be endorsed.

Differences in susceptibility between infants, children and adults

In contrast to adults, children and, in particular, infants are in a progressive stage of development and growth. Potential differences in susceptibility to pesticides are dependent on toxico-kinetic and toxico-dynamic parameters (such as organ sensitivities), including genetic, physiological, and metabolic factors, mechanism of action of the chemical and dose-effect and dose-response relationships. Special concerns for infants and children relate to the early developmental state of their biochemical and physiological processes. Therefore it needs to be considered whether exposure of these

(*) Good Agricultural Practice

age groups to pesticides may lead to more serious toxicological effects or even effects not induced in the adult.

The susceptibility of the developing foetus, neonate, infant and child to delayed functional toxicity becoming manifest in adult life, as a result of exposure to apparently subtoxic doses of pesticides during a developmental period of high susceptibility (critical window), is of particular concern. Developmental functional toxicity may be particularly relevant for the developing central nervous system, but also applies to other systems, such as the endocrine, reproductive (e.g. reduced semen quality due to impairment of Sertoli cell development), and immune systems. Although delayed neurotoxicity has been observed in experimental animals after exposure to some pesticides, the current databases do not allow any unified conclusions about the potential for delayed toxicity in humans from exposure to pesticides.

The overall experience gained from toxicological studies in experimental animals strongly suggests that it is not possible to make general statements about age-related differences in toxico-dynamic parameters, such as organ sensitivity. For some chemicals, immature animals are more sensitive than adults while in other cases they are less sensitive, depending on the compound and its effects. In humans, the same picture emerges from experimental and clinical data on pharmaceuticals, while knowledge about age-related differences in susceptibility to pesticides is virtually absent. Therefore, the issue of age-related differences in susceptibility to pesticides should be addressed on a case-by-case basis.

Adequacy of current animal testing protocols for the risk assessment of pesticide residues in the diet of infants and young children

The reproduction studies cover different developmental periods up to weaning, and in the case of multigenerational studies from conception to adulthood, while the usual chronic two-year toxicity/carcinogenicity tests, starting at 6–8 weeks of age in the rat, cover only the late period of juvenile growth. The ADI derived from these studies is thus intended to cover exposure of older infants and children as well as exposure of the foetus during pregnancy and the neonate and young infant during the nursing period.

An examination of age-related differences in toxico-kinetics has shown that there are no major systematic differences between neonatal and young animals and their human counterparts for several toxico-kinetic parameters, and that an increased uncertainty factor is not required for inter-species differences provided that the toxico-dynamic endpoints have been adequately studied and considered carefully.

In several respects, the human neonate is more developed at birth than the neonatal rat. For instance, the major growth of the brain takes place before birth in humans while this occurs after birth in the rat. During lactation, the human infant will therefore probably

not be as vulnerable as the neonatal rat toward effects on the development of the central nervous system. Therefore, the new-born rat is not developmentally parallel to the new-born human, and studies using new-born pigs or monkeys may provide better models for the exposure situation for young human infants.

Carcinogens will generally be detected in regular carcinogenicity studies. The United States Environmental Protection Agency has made a comparison of carcinogenicity studies with perinatal and adult exposure, and adult exposure only (12). It found that the incidence of tumours may increase, and the latency period may be reduced in studies with combined perinatal and adult exposure compared to adult exposure only. Perinatal exposure, however, rarely identifies carcinogens that are not found in standard carcinogenicity studies.

An area of particular concern is the possibility that interactions of chemicals with specific endocrine receptors during foetal life and infancy may have profound effects on morphological and functional properties of these systems after maturation. This raises the question of whether the current toxicological database for pesticides is sufficient to assess potential developmental adverse effects fully. This may not always be the case, as for instance impairment of the central nervous system, leading to behavioural, memory and learning deficits is rarely examined in conventional studies, and delayed toxicity resulting from exposure to low levels of a toxicant during a particularly sensitive developmental period may not always be adequately addressed by current testing procedures.

At present, no single test approach for developmental behavioural toxicity has been identified as the most appropriate.

Although the clinical examinations performed in the currently used toxicity tests, including multigenerational studies, may reveal obvious signs of functional deficits, this aspect deserves more attention in the future. It would be expected, that many, but not all substances having a toxic effect in the nervous system of the new-born, would show some effect in the adult at least at higher doses. In the light of the present knowledge, the standard test package ought to be refined in both design of studies and the choice of parameters examined. More attention should be given to parameters that adequately address the function of the nervous, reproductive, endocrine, and immune systems. A new guideline regarding developmental neurotoxicity is being prepared within the OECD test guideline programme in order to obtain more information about these effects.

None of the present standard toxicological tests mimics the situation where a human infant is exposed to chemicals via infant formulae. Therefore special considerations are needed for pesticides likely to be found in infant formulas for infants below the age of 16 weeks.

Exposure of infants and young children to pesticides from commercial infant formulae, cereals and other weaning foods

Infants and young children have a higher food intake than adults when expressed on a per kg body weight basis. The dietary exposure of infants in their first few months of life to pesticides arises primarily from breast-feeding (human milk), infant formulae, and water. From the age of about 4 months, infants are exposed to pesticides through consumption of manufactured foods including infant formulae, follow-on formulae and weaning foods and also from 'family food' and drinking water used to reconstitute dry products.

Infant formulae can be divided into 'ready to feed' products and those consisting of dry powder for mixing with water immediately before use. Water is the major ingredient in infant formula and the water used for the 'ready to feed' formulations during manufacturing is understood to be purified by for example active carbon filtration and is thus anticipated not to contain pesticide residues of concern. Tap water is most commonly used to reconstitute infant formula in the home although bottled and natural mineral water may also be used. In this risk assessment, the Committee has taken note of the current and proposed EU limits for pesticides in drinking water (13, 14) which are 0.1 µg/l for individual substances and 0.5 µg/l for the total pesticide content. The Committee estimated that the contribution to the overall pesticide content arising from the use of drinking water containing pesticides at these maximum permissible levels to reconstitute dry products would be one or two orders of magnitude lower than that which could result from the products themselves if they contained pesticides at the MRL of 0.01 mg/kg.

The solid fraction of liquid infant formula typically constitutes about 13 % of the finished product. The main part is processed cows' milk or soy products and corn syrup. All raw materials used have been processed which should reduce the pesticide content. It has been stated that, in general, none or very small amounts of pesticides are found in infant formulas (15).

The estimation of the potential exposure from manufactured food was made by adopting a worst case approach, i.e. assuming that these foods constitute the total diet of a reference child. The calculation uses the physiological requirements of infants at various ages for energy and macronutrients to determine the amount of 'solid matter' being consumed daily in formulas and weaning foods. As they mature, infants consume smaller volumes of formulas as their intake of weaning foods increases, i.e. the energy density of their diet increases and the hydration factor for the solids consumes falls. On this basis a worst case scenario for exposure to solids can be hypothesised for 12-month old infants. For such infants, using a hydration factor of 33 % and an energy requirement of 1 000 kcal/day, an energy density of 3 kcal/g can be derived which in turn gives an

intake of 30 g/kg body weight per day for a 10 kg infant. By applying two standard deviations (the standard deviation from the literature for these data is 30 %) to this mean, the value of 48 g/ kg/day is obtained.

The Committee had the opportunity to test this approach by comparing this calculated value with an estimate made from the results of the Donald study (Forschungsinstitut für Kinderernährung, Dortmund) which employs consecutive three-day weighed diet records to study the food consumption patterns of infants and young persons in families from favourable social backgrounds in the Dortmund area of Germany. The study provided data for the consumption of manufactured infant formulae (dry), cereals and milk cereals (dry), and other weaning foods (ready-to-eat) as sold.

The data from the Donald study were used to generate a frequency distribution for the total daily consumption of manufactured infant formulae (dry), cereals and milk cereals (dry), and other weaning foods (ready-to-eat) as sold based on the individual dietary records of children in each age category.

The 95-percentiles of consumption estimated from the Donald study were judged to be consistent with the value of 48 g/kg body weight as calculated above on the basis of energy requirements. A worst case intake estimate was made by assuming this level of daily consumption for all infants and young children and that all the commercial products consumed were appropriately hydrated and contained a pesticide residue at 0.01 mg/kg. This would lead to a maximum estimated intake of a pesticide of about 0.0005 mg/kg b.w./day. On the other hand, if the infant's intake were derived from a commercial manufactured dry product which was reconstituted as recommended (customarily 2 parts dry food product to 1 part water), the resultant exposure from a residue of 0.01 mg/kg would be 0.0003 mg/kg. b.w./day.

Conclusions

The Committee is asked to advise the Commission as to whether a maximum residue limit (MRL) of 0.01 mg/kg for pesticides in manufactured foods intended for infants and young children (dietetic foods) would be adequate to protect the health of this section of the population or whether there are instances where there are reasons to be concerned that the presence of even lower levels might constitute a risk. It reaches the following conclusions.

The ADI covers all groups of the population. The Committee does not recommend the use of special uncertainty factors for infants and children or the establishment of special ADIs for this age group. The toxicological database should adequately cover the most sensitive effects and the most sensitive age groups and the ADI should cover all sensitive segments of the population, irrespective of age. If there is scientific evidence

that infants and children are the most sensitive populations to a particular pesticide, that evidence must drive the derivation of the ADI.

The Committee recognised that the currently used data package for the establishment of the ADI was not in all respects optimal to reflect a particular sensitivity of infants towards the potential toxicity of a given pesticide. However, it was the opinion that in most cases the toxicological studies would have provided indications if such special sensitivities were to exist. The Committee concluded that the current ADIs would provide a reasonable basis for evaluating the health impact of pesticides in foods intended for infants and young children.

The fact that infants and children have a relatively higher intake of some food items than adults should clearly be considered in the risk assessment. This is not always taken into consideration when setting MRLs.

The Committee considered 0.0005 mg/kg b.w to be a realistic worst case estimate for the upper limit for the daily intake of a pesticide arising from the consumption of manufactured infant formulae (dry), cereals and milk cereals (dry), and other ready-to-eat weaning foods. The estimate assumes that all infants and young children consume commercial products at the highest recorded 95-percentile every day and that all commercial products contain the pesticide at a level of 0.01 mg/kg in the products as sold.

The Committee concluded that if the maximum residue limit were to be set at 0.01 mg/kg in foods intended for infants and young children, there is a possibility that an infant could exceed the ADI for pesticides having an ADI at 0.0005 mg/kg b.w. or lower.

This would imply that the Commission and the Member States should carefully reconsider pesticides that have been allocated ADIs at 0.0005 mg/kg b.w. or lower as to the health impact of their presence in baby food. This consideration should include an examination of their actual use and the basis on which the ADIs was set, i.e. whether the toxicological data package gives any reason for special concerns for infants and children.

The Committee was also aware that some pesticides share a common mechanism for their critical toxic effect which determined the ADI, but do not necessarily share a group ADI. The Committee recommends that further consideration be given by the appropriate bodies to the potential for additive effects and whether the risk management of residues in foods specially manufactured for infants and young children needs to take these into account.

In giving its opinion, the Committee wishes to note that the limit of 0.01 mg/kg has not been proposed on the basis of toxicological evaluation. Therefore, for those pesticides

having an ADI greater than 0.0005 mg/kg b.w., their presence in foods intended for infants and young children at levels exceeding 0.01 mg/kg does not necessarily imply a risk to their health.

When setting MRLs for pesticides in foods intended for infants and young children, the Committee draws attention to limitations of current routine analytical methods for determination of some pesticides particularly at levels around 0.01 mg/kg.

The Committee notes that pesticides are subject to continuous re-evaluation within the EC and elsewhere, and recommends that special attention is paid to the potential higher susceptibility of infants and children to certain compounds during this process. This will require further research which may lead to improved test strategies.

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OPINION ON THE POTENTIAL RISK TO HUMAN HEALTH ARISING FROM THE BULK TRANSPORT OF RAW SUGAR, SEMI-PROCESSED SYRUPS AND THICK SUGAR JUICES INTENDED FOR THE PRODUCTION OF WHITE SUGAR, IN NON-DEDICATED SHIPS' TANKS AND ROAD TANKERS

(expressed on 19 September 1997)

Terms of reference

The Committee is asked to examine the potential risk to public health associated with a derogation for the transport of raw sugar from the specific requirement of Directive 93/43/EEC on the hygiene of foodstuffs that bulk foodstuffs in liquid, granulate or powdered form be transported in containers reserved for the transport of foodstuffs only. In assessing the risk the Committee is asked to consider:

— the indeterminate nature of the previous cargo

the likelihood and potential level of contamination in raw sugar, semi-processed syrups or thick sugar juices, taking account of cleaning procedures

the control procedures employed by industry to ensure effective cleaning prior to shipment of the unrefined products

— the physico-chemical nature of the refinement process and its capacity to eliminate contaminants

the control procedures applied to the final product.

Background

Currently, some 1.8Mt of raw sugar are imported into the European Union in non-dedicated ships. In addition, a considerable quantity of semi-processed syrups and thick sugar juices are transported between factories in the European Union by non-dedicated road tankers.

Chapter IV of the Annex to Directive 93/43/EEC on the hygiene of foodstuffs requires however, that bulk foodstuffs in liquid, granulate or powdered form be transported in containers reserved for the transport of foodstuffs only. Article 3 of Directive 93/43/EEC allows the Commission to derogate from the provisions of the

Annex subject to the agreement of Member States. The Commission's services have considered the possibility of such a directive, the objective of which would be to permit the bulk transport of raw sugar, semi-processed syrups and thick sugar juices in containers which are not dedicated to the transport of foodstuffs. It would, however, still require all other provisions of the hygiene and foodstuffs directive, and in particular, those relating to hazard analysis and critical control point (HACCP) principles (Article 3), the cleaning of transport containers and conveyances, and the avoidance of contamination during transport to be applied.

Adoption of the derogating directive is dependent on assurance that the proposed measure would not give rise to risk to human health and therefore the Committee has been asked for its opinion.

Evaluation

The Committee stresses that the present evaluation is restricted to the bulk transport of raw sugars, semi-processed syrups and thick sugar juices which will undergo a full and effective refining process before use as foods or food ingredients.

Industry's request for a derogation would allow continuation of current practice which permits a wide range of cargoes to be used prior to the transport of raw sugar or semi-processed syrups and thick sugar juices. In view of the indeterminate nature of the contaminants which may result from a previous cargo, the Committee requested information on the effect of the various steps in transport, cleaning and processing on various classes of contaminants.

It is to be noted that since different considerations apply to the bulk transport of raw (solid) sugar and of semi-processed syrups and thick sugar juices, they are treated separately to some extent in the following risk assessment.

Nature of previous cargoes

Transport of raw sugar (solid cargoes)

The Committee is aware that ships used for the transport of raw sugar are also used for the bulk transport of a very wide range of previous solid cargoes such as cereals, grains, ores, coke, coal and general mixed cargoes. The Committee was informed that, in practice, ships used for bulk transport of raw sugar are generally unsuitable for bulk transport of liquids. It did not therefore give consideration to the potential for contamination of raw sugars from the previous transport of liquid cargoes by ship. It was understood by the Committee that cargoes consisting of substances that are

classified as noxious, pesticides for example, must be transported in accordance with international rules which should prevent accidental spillage and eliminate potential for contamination of the raw sugar. A relatively small proportion of raw sugar is transported by road in lorries which, the Committee was informed, are also used at peak demand to transport other raw materials such as coal, coke and limestone to the sugar refinery.

Transport of unrefined liquid sugars (semi-processed syrups and thick sugar juices)

The Committee was informed that semi-processed syrups and thick sugar juices are normally transported in non-dedicated road tankers. Refinery operators restrict previous cargoes to liquids, decide on their acceptability and maintain records.

Cleaning and inspection procedures

Transport of raw sugars

The Committee noted that the hygiene of foodstuffs Directive 93/43/EEC requires conveyances and or containers used for the transport of foodstuffs to be kept clean and where they are used for anything other than a foodstuff there must be effective cleaning between loads. In addition, the directive requires through the principles of the hazard analysis and critical control point system contained in Article 3 of the directive, hazards to health to be identified, and control and monitoring measures applied at the most effective 'critical point' in the process (Annex, Chapter VI).

Cleaning and inspection procedures for ships are defined by the Sugar Charter-Party (1) (revised in 1977), Article 17 of which requires ship's holds to be physically clean and only to be washed with sea water followed by fresh water if the previous cargo may be 'injurious to sugar'. Cleaning is subject to independent inspection prior to permission to load the following cargo. Records of cleaning and inspection are retained by the ship's master. The Committee is not aware of the existence of a similar charter governing transport of raw sugar by land but was informed that lorries used under peak demand for the transport of coal, coke and limestone are washed with hot water under pressure and checked for cleanliness prior to the transport of raw sugar.

Transport of unrefined liquid sugars

The Committee was informed that non-dedicated road tankers used for the transport of semi-processed syrups and thick sugar juices are subjected between consignments

(1) The conventional agreement between shipowners and charterers

to cleaning with hot water under pressure and to visual inspection and microbiological control. It was also informed that records of cleaning are kept by the refinery operator.

Removal of contaminants during refining

The sugar refining is a multistage and continuous process which is designed to produce a highly refined product (circa 99.95 % purity, the remaining 0.05 % comprising mainly water and minerals). The critical steps are affination, dissolution, carbonation, filtration through ion-exchange resins and active carbon, evaporation, crystallisation and drying.

Each step has the potential to reduce the level of specific contaminants in the final product (white sugar) and is associated with dilution of any contaminant in the total process volume.

The quantitative effect of the critical steps mentioned above on the reduction of certain classes of contaminant was evaluated in a worst case scenario, where, in spite of the cleaning procedures, 1 kg of a potentially toxic chemical found its way into the refinery process. On the basis of the dilution during the process and reasoned factors which took account of the physic-chemical behaviour of the contaminant during each step, it was concluded that it was unlikely that such contamination would lead to residue levels of concern to public health in the refined sugar.

Having regard to the nature of the individual steps in the process, the Committee paid particular attention to contaminants such as heavy metals, arsenic and non-hydrolisable herbicides. The analytical data provided indicated that the levels of such contaminants were low and consistent with the levels to be expected following refining of the original materials. Further, limited analytical data provided by industry for white sugar produced in different parts of the Community over recent years indicate that the levels of these substances are considerably lower than those in foodstuffs in general. Analytical data for molasses were provided which further demonstrated that the refinery process was very effective in the removal of contaminants. The Committee notes that the levels of contaminants reported in the literature and by industry for refined sugar using analytical methods which were considered to be modern and appropriate for the task, are generally below their limits of detection and are consistent with the expected efficiency of the refining process.

Conclusions

The Committee notes that this request for a derogation relates to a well-established industrial practice with a long history of safe use. It concludes that, on the basis of the

information available to it, it has no reason to believe that the transport of raw sugar or of semi-processed syrups and thick sugar juices in non-dedicated vessels and in accordance with best industrial practices is likely to give rise to risks to public health.

The Committee was informed that, in practice, ships used for bulk transport of raw sugar are generally unsuitable for bulk transport of liquids.

It noted that the cleaning and control procedures applied during transport of raw solid and unrefined liquid sugars are not well defined in all cases. Furthermore, it appeared that judgement of the acceptability of the cargoes carried prior to bulk semi-processed syrups and thick sugar juices is to some extent discretionary.

In view of the above considerations, the Committee recommends that any derogation be subject to the following additional safeguards.

Transport of raw sugars

Effective cleaning procedures should be introduced to ensure that contamination from transport containers or previous cargoes does not result in a risk to health arising from the consumption of refined sugar. This may be achieved by considering cleaning to be a critical control point within the terms of Article 3 of the hygiene of foodstuffs directive which refers to the principles of HACCP systems.

- The prohibition of the use of liquid previous cargoes in bulk for the transport of raw sugar.

Transport of unrefined liquid sugars (semi-processed syrups and thick sugar juices)

- Effective cleaning procedures should be introduced to ensure that contamination from transport containers or previous cargoes does not result in a risk to health arising from the consumption of refined sugar. This may be achieved by considering cleaning to be a critical control point within the terms of Article 3 of the hygiene of foodstuffs directive which refers to the principles of HACCP systems.

- A list of acceptable previous cargoes.

The Committee's conclusions are applicable to the bulk transport of raw sugars and semi-processed syrups and thick sugar juices which will undergo a full and effective refining process before use as food or food ingredients.

OPINION ON THE POTENTIAL MICROBIOLOGICAL RISK ARISING FROM THE PRESENCE OF MOISTURE IN TEA
(expressed on 19 September 1997)

Terms of reference

To advise the Commission on the potential microbiological risk associated with the presence of moisture in tea and to indicate in general terms an acceptable upper limit from the point of view of public health.

Background

In 1995, the FAO (Food and Agriculture Organisation) international group established a standard on black tea (1). This standard includes a paragraph specifically on moisture content and states that tea should be packed with a moisture content of less than 4 %. The document also states that it is likely that during transport to the point of export and further shipment to the importing country, tea absorbs more moisture and that tea with a moisture content of 6 % and above deteriorates in quality.

Discussion

The preservation of foods by a reduction in water content is based on the fact that micro-organisms and enzymes need water in order to be active. Yeasts and moulds are adapted to low-moisture foods and the limits for growth depend on available water and temperature. Traditionally, 'moisture content' has been the parameter used to identify appropriate levels of moisture for the safe storage of low-moisture foods. However, this measure is usually regarded as inaccurate in determining inhibitory levels for mould growth. More recent literature refers to levels of moisture being expressed as water activity (Aw). Water activity of a food is proportional to relative humidity (RH) and indicates the amount of free water that can be used for microbial growth. Water activity also take into account 'hysterisis' an effect characterised by differences in water activity in a drying and a wetting system with similar moisture content. A literature review of tea shows that tea is strongly hygroscopic and easily absorbs moisture from the atmosphere (2).

Many mould species are known for their potential to produce mycotoxins. In many cases this occurs in inaccurately dried and stored low-moisture foods. After harvest black tea undergoes a step-by-step technical process including withering, maceration, fermentation and firing/drying. Moulds and bacteria have the opportunity to grow under this process (3). However, with respect to tea the literature does not identify organisms causing health hazards. The drying process before packaging prevents the further growth of contaminating micro-organisms, and drying at high temperatures inactivates parts of contaminating micro-organisms. The high content of anti-microbial active polyphenolic compounds in tea will contribute to an additional safety margin (4, 5).

The FAO document CCP TE 95/7 on quality standards refers to mould growth in respect of deterioration but does not mention the growth of mycotoxinogenic variants (1). The ISO standards 1573 and 3720 mentioned in the FAO document specify levels for moisture content (6, 7).

A review of available literature identifies the lack of data to underpin explicit advice to the Commission on the potential microbiological risk with the presence of moisture in tea and acceptable upper limits. Tea seems to have a safe history of use. Because of the lack of data concerning associated fungi in tea, it has not been possible to identify health hazards due to elevated moisture content in tea, and moisture levels of up to 10 % seem to give an acceptable safety margin.

On the other hand, occurrence of moulds and mycotoxins in similar commodities such as spices, herbs and grain products, is quite frequent and there appears to be a need to review acceptable water levels in low moisture foods. These levels should be related to the water activity. Very few mould species are able to grow below Aw < 0.65. Mycotoxin production occurs at Aw> 0.80.

Conclusion

Tea has a long history of safe use and the Committee is not aware of any safety problems related to moisture in tea. This may be attributed to low moisture content (i.e. water activity) and the high content of anti-microbial substances. Moisture levels of up to 10 % seem to give an acceptable safety margin for the storage of tea. A lower level may be needed in order to restrict quality defects.

However, a general review is recommended for acceptable levels of water in low moisture foods. Assessment of acceptable levels should focus on potential growth of mycotoxicogenic moulds. Acceptable levels should be based on water activity (Aw) and follow the general principles for safe storage.

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PAPAIN FROM PAPAYA FRUIT (*CARICA PAPAYA*) USED AS A MEAT TENDERISING AGENT (EXAMINATION OF ADDITIONAL INFORMATION)

(expressed on 20 September 1997)

Terms of reference

To examine the additional information submitted in response to the Committee's opinion on papain expressed on 2 June 1995 (1) and, if appropriate, to issue an opinion in respect to the bacteriological safety of papain treated meat and the formation of biogenic amines.

Background

Papain has been previously evaluated and found to be acceptable for chill proofing of beer on the basis that it is a constituent of a part of a plant (papaya fruit) commonly consumed as a food source (80th meeting of the Scientific Committee for Food, October 1991).

In its opinion on papain from papaya fruit (*Carica papaya*) used as a meat tenderising agent, expressed in June 1995, the SCF considered that the use of papain as a meat tenderiser, administered to stunned and pithed animals before bleeding, was acceptable from the point of view of the safety of papain *per se*, provided the general provisions of the guidelines on enzymes (2) were followed.

In this opinion, the SCF also considered that the bacteriological safety of meat, where papain is injected into beef as a meat tenderiser, should be confirmed by pilot testing under different conditions, representative of actual hygiene conditions in slaughterhouses in different Member States of the EC.

In its 1995 opinion, the Committee raised the question of whether the use of papain-treated meat in fermented sausages might affect the levels of biogenic amines in the final product. The petitioner subsequently submitted further information for evaluation by the SCF to address the concerns raised in the 1995 opinion. The Committee concluded as follows.

Microbiological safety

The Committee remains concerned that any process involving the physical introduction of material into the deep tissue layers of the animal prior to bleeding, under slaughterhouse conditions, increases the risk of contamination and propagation of micro-organisms into other parts of the body/meat, whether this is through injection of papain or other substances, or through the pithing process.

Further, the Committee remains concerned that the delay in bleeding necessary to facilitate the spread of papain throughout the body, may increase the opportunity for micro-organisms introduced in the way outlined above or in the papain solution itself, to be disseminated.

The Committee is also concerned about the relationship between the delay in bleeding and pH values in the tissues.

Formation of biogenic amines

The Committee notes the following in relation to the potential levels of biogenic amines in fermented sausages made from meat treated in this way.

In its 1995 opinion, the Committee raised the question of whether the use of papain-treated meat in fermented sausages might affect the levels of biogenic amines in the final product. In a report submitted by the applicant, it was shown that there was no difference in amine production in sausages prepared from meat from animals treated with papain compared with ones prepared from untreated meat. However, the Committee is aware of one recently published study in which papain was added at two different levels to experimentally prepared, fermented, dried sausages. The study showed an increase in the levels of free amino acids and biogenic amines, such as histamine and putrescine, in sausages with added papain compared with controls.

However, it is not clear how the amounts of papain added to the experimental sausages might relate to residues of papain which may be present in meat if it were used during the slaughtering process and furthermore, although there was a clear dose-related effect in the release of free amino acids, this was not the case for the amines.

The Committee was therefore not able to draw a firm conclusion on the likelihood of an increase in amine production after papain treatment, but such an effect cannot be excluded.

Summary and conclusion

The Committee remains concerned about the microbiological safety of the meat injected with papain under slaughterhouse conditions, particularly in relation to the increased risk of contamination through the injection site and the subsequent risk of propagation of micro-organisms into other parts of the body. The Committee is also concerned that the delay in bleeding necessary to facilitate the spread of papain throughout the body may increase the opportunity for micro-organisms introduced in the way outlined above or in the papain solution itself to be disseminated. The Committee recommends that the issues raised relating to veterinary hygiene in slaughterhouses and in particular to the pithing and other processes involving the introduction of materials into deep tissue layers are examined by the Scientific Committee on Veterinary Measures relating to Public Health.

In its 1995 opinion, the Committee raised the question of whether the use of papain-treated meat in fermented sausages might affect the levels of biogenic amines in the final product. After consideration of the information provided in the report submitted by the applicant, the Committee was not able to draw a firm conclusion on the likelihood of an increase in amine production after papain treatment, but such an effect could not be excluded.

In these circumstances, the Committee is unable to give a favourable opinion on the use of papain as a meat tenderiser, injected after stunning and before bleeding under slaughterhouse conditions.

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- Certain additives for use in foods for infants and young children in good health and in foods for special medical purposes for infants and young children (expressed on 21 March 1997 and amended on 13 June 1997)
- An additional list of monomers and additives used in the manufacture of plastics materials intended to come into contact with foodstuffs (expressed on 13 June 1997)
- Clarification and explanation of the SCF's opinion of 7 June 1996 on BADGE (expressed on 13 June 1997)

Forty-second Series (1999)
(Catalogue No: GT-29-98-001-EN-C)

Report on:

- Compilation of the evaluations of the Scientific Committee for Food on certain monomers and additives used in the manufacture of plastics materials intended to come into contact with foodstuffs until 21 March 1997

Forty-first Series (1997)
(Catalogue No: CF 07 97660-EN-DE-FR)

Opinions on:

- Colours in foods for special medical purposes for young children (Opinion expressed on 13 December 1996)
- Maximum limits for vitamins and minerals in processed cereal-based foods and baby foods (Opinion expressed on 13 December 1996)
- The potential for adverse health effects from the consumption of genetically modified maize (*Zea mays L.*) (Opinion expressed on 13 December 1996)
- ß-cyclodextrin manufactured by the action of the enzyme cycloglycosyltransferase obtained from *Bacillus circulans* on partially hydrolysed starch (Opinion expressed on 13 December 1996)
- Foods for special medical purposes (FSMPS) (Opinion expressed on 13 December 1996)
- The safety in use of konjac gum as a food additive (Opinion expressed on 13 December 1996)
- The safety in use of konjac glucomannan as a food additive (Opinion expressed on 13 December 1996)

Fortieth Series (1997)
(Catalogue No: CF 07 97652-EN-DE-FR)

Report on:

- Endocrine disruptors and food (adopted on 7 June 1996)

Opinions on:

- Additives in nutrient preparations for use in infant formulae, follow-on formulae and weaning foods (Opinion expressed on 7 June 1996)
- Bisphenol A diglycidyl ether (Opinion expressed on 7 June 1996)
- The potential risk to human health arising from the transport in ships' tanks of oil and fats from substances proposed as acceptable previous cargoes (Opinion expressed on 20 September 1996)
- The microbiological safety of modified atmosphere packaged (MAP) and controlled atmosphere packaged (CAP) foods (Opinion expressed on 20 September 1996)
- Propane-1,2-diol (Opinion expressed on 20 September 1996)

The assessment of novel foods:

- Part II: Recommendations concerning the scientific aspects of the presentation of information necessary to support applications for placing on the market of novel foods and novel food ingredients (Opinion expressed on 13 December 1996)

- Part III: Recommendations concerning the scientific aspects of the preparation of the initial assessment reports on applications for placing on the market of novel foods and novel food ingredients (Opinion expressed on 13 December 1996)

Thirty-ninth Series (1997)
(Catalogue No: GT 07 97644-EN-DE-FR)

Opinions on:
- The scientific basis of the concept of threshold of regulation in relation to food contact materials (Opinion expressed on 8 March 1996)
- Products derived from bovine tissues, especially gelatin, tallow and di-calcium-phosphate in relation to bovine spongiform encephalopathy (Opinion expressed on 15 April 1996)
- The use of ozone for the removal of unstable elements such as iron, manganese and arsenic from natural mineral waters (Opinion expressed on 7 June 1996)
- Dimethyldicarbonate (DMDC, VELCORIN) (Response to comments of the French authorities) (Opinion expressed on 7 June 1996)
- Phthalates in infant formulae (Opinion expressed on 7 June 1996)
- The calculation of vitamin E content in infant formulae and follow-on formulae (Opinion expressed on 7 June 1996)

The assessment of novel foods:
- Part I: Recommendations concerning the scientific aspects of information necessary to support applications for placing on the market of novel foods and novel food ingredients (Opinion expressed on 7 June 1996)

Report on:
- Principles for the development of microbiological criteria for foodstuffs as covered by the hygiene of foodstuffs Directive 93/43/EEC — Recommendation of the Scientific Committee for Foods (Opinion expressed on 7 June 1996)

Thirty-eighth Series (1997)
(Catalogue No: GT 07 97620-EN-DE-FR)

Opinions on:
- Nitrate and nitrite (Opinion expressed on 22 September 1995)
- Draft Commission Directive laying down specific purity criteria on food additives other than colours and sweeteners (Opinion expressed on 14 December 1995)

- Cyclamic acid and its sodium and calcium salts (Opinion expressed on 14 December 1995)
- The safety in use of 1,1,1,2-tetrafluorethane as a solvent for flavour extraction (Opinion expressed on 14 December 1995)
- Bovine spongiform encephalopathy (Opinion expressed on 8 March 1996)

Thirty-seventh Series (1997)
(Catalogue No: CO-04-97-226-DA-DE-EN-ES-GR-FR-IT-NL-PT-C)

Report on:
- Adverse reactions to foods and food ingredients

Opinion on:
- Mineral and synthetic hydrocarbons

Thirty-sixth Series (1997)
(Catalogue No: CO-02-96-868-DA-DE-EN-ES-GR-FR-IT-NL-PT-C)

Opinions on:
- Coumarin
- Carnauba wax
- Ammonia caramel as a food colour
- Caustic sulphite caramel
- Iso-ascorbic acid (including D-isoascorbic (Erythorbic) and its sodium, potassium and calcium salts)
- 3-monochlorpropane-1,2-diol (3-MCPD)
- Cadmium
- The food safety implications of surveillance systems employing neutron scanning (interrogation) devices
- Di-ethylhexyladipate (DEHA)
- Di-ethylhexyladiphthalate (DEHP)
- Papain from papaya fruit (*Carica papaya*) used as a meat tenderising agent
- Acetylated oxidised starch
- Polyethyleneglycol 6000

Report on:
- Certain esters used in plastics for food contact applications

Thirty-fifth Series (1996)
(Catalogue No: CO-91-95-253-DA-DE-EN-ES-GR-FR-IT-NL-PT-C)

Opinions on

- Propylene glycol
- Alternatively refined carrageenan produced from *Eucheuma cottonii* and *Eucheuma spinosum*
- p-Hydroxybenzoic acid alkyl esters and their sodium salts
- Specifications for food additives
- Sorbic acid and its calcium and potassium salts
- Sulphur dioxide and other sulphiting agents
- Benzoic acid and its salts
- Hexane used as an extraction solvent
- Lindane in baby foods
- Cross-linked sodium carboxymethylcellulose (modified cellulose gum)
- Invertase derived from *Sachcharomyces cerevisiae*
- Aflatoxins, ochratoxin A and patulin

Thirty-fourth Series (1995)
(Catalogue No: CO-85-94-907-DA-DE-EN-ES-GR-FR-IT-NL-PT-C)

Reports on:

- Smoke flavouring (adopted on 25 June 1993)
- Essential requirements for infant formulae and follow-on formulae. (Opinion expressed on 17 September 1993)

Opinions on:

- Microcrystalline cellulose (adopted on 17 September 1993)
- Polyoxyethylene(20)sorbitan mono-oleate (polysorbate 80) (Opinion expressed on 17 September 1993)
- Dimethylerephthalate recovered from PET bottles (Opinion expressed on 17 September 1993)
- Three chymosins from genetically modified organisms (Opinion expressed on 25 June and 10 December 1993)

Thirty-third Series (1995)
(Catalogue No: CO-86-94-852-DA-DE-EN-ES-GR-FR-IT-NL-PT-C)

- First report of the Scientific Committee for Food on certain additives used in the manufacture of plastic materials intended to come into contact with foodstuffs (Opinion expressed on 3 May 1992)

Thirty-second Series (1994)
(Catalogue No: CO-80-93-589-DA-DE-EN-ES-GR-FR-IT-NL-PT-C)

Opinions on:

- An activated lactoperoxidase system (Opinion expressed on 19 June 1992)
- Re-evaluation of 5 modified celluloses (Opinion expressed on 13 March 1992)
- Addendum to the opinion on modified celluloses concerning enzymatically hydrolised carboxymethylcellulose (Opinion expressed on 11 December 1992)
- The potential risk to health presented by lead in food and drink (Opinion expressed on 19 June 1992)
- The evaluation of sucrose acetate isobutyrate (SAIB) (Opinion expressed on 3 May 1992)
- The acceptability of wines treated with certain ion-exchange resins (Opinion expressed on 11 December 1992)
- Certain additives for use in infant formulae, follow-on formulae and weaning foods (Opinion expressed on 11 December 1992)
- Carrageenan (Opinion expressed on 11 December 1992)

Revisions of previous opinions on:

- Alginate (Opinion expressed on 19 October 1992)
- Modified starches – starch sodium octenyl succinate (Opinion expressed on 19 October 1992)
- Extraction solvents – dichlormethane (Opinion expressed on 10 April 1992)
- Glycerol esters of wood rosin (Opinion expressed on 19 June 1992)
- Food irradiation: use in relation to Camembert cheeses (Opinion expressed on 19 June 1992)

Thirty-first Series (1993)
(Catalogue No: CO-80-93-242-DA-DE-EN-ES-GR-FR-IT-NL-PT-C)

- Nutrient and energy intakes for the European Community (Opinion expressed on 11 December 1992)

Thirtieth Series (1993)
(Catalogue No: EUR 14769 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- Third addendum to the first report of the Scientific Committee for Food on certain monomers and other starting substances to be used in the

manufacture of plastic materials and articles intended to come into contact with foodstuffs (Opinion expressed 19 June 1991)

Twenty-ninth Series (1992)
(Catalogue No: EUR 14482 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- Second report on extraction solvents (adopted on 21 June 1991)
- Recommendation on ammonium chloride in liquorice products (Opinion expressed on 11 October 1991)
- Recommendation on glycyrrhizin in liquorice products (Opinion expressed on 11 October 1991)
- Guidelines for the evaluation of flavourings for use in foodstuffs:
  1. Chemically defined flavouring substances (Opinion expressed on 10 December 1991)

Twenty-eighth Series (1993)
(Catalogue No: EUR 14452 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- Report on infant formulae claimed to be 'hypoallergenic' or 'hypoantigenic' (adopted on 9 December 1991)
- Second addendum concerning the essential requirements of infant formulae and follow-up milks based on cows' milk proteins and the mineral requirements for soya-based infant formulae and follow-up milks (adopted on 9 December 1991)
- Report on foods for particular nutritional uses whose sodium content has been modified. Low sodium foods and salt substitutes (adopted on 9 December 1991)

Twenty-seventh Series (1992)
(Catalogue No: EUR 14181 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- Foods intended for weight control diets (Opinion expressed on 19 October 1990)
- Guidelines for the presentation of data on food enzymes (Opinion expressed on 11 April 1991)
- Recommendation on cyclamates (Opinion expressed on 21 June 1991)
- Report on the risks of hypervitaminosis A (Opinion expressed on 21 June 1991)

Twenty-sixth Series (1992)
(Catalogue No: EUR 13913 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- Second series of food additives of various technological functions (Opinion expressed on 19 October 1990)
- Nitrates and nitrites (Opinion expressed on 19 October 1990)
- Health aspects of the release of lead from capsules for wine (Opinion expressed on 7 December 1989)
- Toxicity of lead and cadmium in ceramics (Opinion expressed on 7 December 1989)
- Guidelines for presentation of data for toxicological evaluation of a substance to be used in materials and articles intended to come into contact with foodstuffs (Opinion expressed on 18 May 1990)

Twenty-fifth Series (1991)
(Catalogue No: EUR 13416 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- First series of food additives of various technological functions (Opinion expressed on 18 May 1990)

Twenty-fourth Series (1991)
(Catalogue No: EUR 13140 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- First Addendum (Opinion expressed on 27 October 1989)
  to the Reports of the Scientific Committee for Food concerning
  — the essential requirements of infant formulae and follow-up milks based on cows' milk proteins (Opinion expressed on 27 April 1983)
  — the minimum requirements for soya-based infant formulae and follow-up milks (Opinion expressed on 9 December 1988)
- First Report of the Scientific Committee for Food concerning the essential requirements for weaning foods (Opinion expressed on 27 October 1989 and 30 March 1990)

Twenty-third Series (1989)
(Catalogue No: EU-12536 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- The minimum requirements for soya-based infant formulae and follow-up milk (Opinion expressed on 9 December 1988)

Twenty-second Series (1989)
(Catalogue No: EU-12535 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- Antioxidants (Opinion expressed on 11 December 1987)

Twenty-first Series (1989)
(Catalogue No: EUR 11617 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- Colouring matters (Opinion expressed on 10 December 1987)
- Sweeteners (Opinion expressed on 11 December 1987 and 10 November 1988)
- Quinine (Opinion expressed on 19 February 1988)
- Emusifiers, stabilizers, thickeners and gelling agents (Opinion expressed on 11 November 1988)

Twentieth Series (1989)
(Catalogue No: EUR 11558 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- **Reports on**
  Second Addendum to the first Report of the Scientific Committee for Food on certain monomers and other starting substances to be used in the manufacture of plastic materials and articles intended to come into contact with foodstuffs (adopted on 10 December 1987) First Addendum, Nineteenth Series of SCF reports

  Opinion on
- Nitrosamines in babies dummies and teats (Opinion expressed on 10 December 1987)

Nineteenth Series (1988)
(Catalogue No: EUR 11322 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

- First Addendum to the first report of the Scientific Committee for Food on certain monomers and other starting substances to be used in the manufacture of plastic materials and articles intended to come into contact with foodstuffs (Opinion expressed on 28 November 1986)
  — first report of the SCF Seventeenth Series -

Eighteenth Series (1986) (1989)

(Catalogue No: EU-10840 -DA-DE-EN-ES-GR-FR-IT-NL-PT)

(The English version of 1989 of this publication replaces the published version of 1986)

- Irradiated foods (Opinion expressed on 13 March 1986)

Seventeenth Series (1986)
(Catalogue No: EU-10778 -DA-DE-EN-GR-FR-IT-NL)

- Certain monomers and other starting substances to be used in the manufacture of plastic materials and articles intended to come into contact with foodstuffs (Opinion expressed on 14 December 1984)

Sixteenth Series (1985)
(Catalogue No: EU-10210 -DA-DE-EN-GR-FR-IT-NL)

- Sweeteners (Opinion expressed on 14 September 1984)

Fifteenth Series (1984)
(Catalogue No: EU-9357 -DA-DE-EN-GR-FR-IT-NL)

- Emusifiers, stabilizers, thickeners and gelling agents (Opinion expressed on 8 July 1983)

Fourteenth Series (1984)
(Catalogue No: EUR 8752 -DA-DE-EN-FR-IT-NL)

- Di-2-ethylhexylphthalate and Di-2-ethylhexyladipate (Opinion expressed on 1 October 1982)
- Certain anabolic agents used in animal production (Opinion expressed on 3/4 February 1983)
- Essential requirements of infant formulae and follow-up milks based on cows' milk proteins (Opinion expressed on 27 April 1983)
- Butylated hydroxyanisole (Opinion expressed on 29 April 1983)
- Caffeine (Opinion expressed on 7 July 1983)
- Colouring matters authorized for use in foodstuffs intended for human consumption (Opinion expressed on 7 July 1983)

Thirteenth Series (1982)
(Catalogue No: EUR 7982 -DA-DE-EN-FR-IT-NL)

- Acrylonitrile monomer (Opinion expressed on 15 January 1981)
- Vinylidene chloride monomer (Second report) (Opinion expressed on 15 January 1981)
- Hydrolised lecithin (Opinion expressed 12 June 1981)
- Modified starches (Second Report) (Opinion expressed 12 June 1981)
- Flavourings (Second Report) (Opinion expressed on 11 December 1981)
- Styrene monomer (Opinion expressed on 5 March 1982)

Twelfth Series (1982)
(Catalogue No: EUR 7823 -DA-DE-EN-FR-IT-NL)

- Sensitivity of individuals to food components and food additives (Opinion expressed on 22 October 1981)

Eleventh Series (1981)
(Catalogue No: EUR 7421 -DA-DE-EN-FR-IT-NL)

- Extraction solvents (Opinion expressed on 15 January 1981)
- Sulphiting agents (Opinion expressed on 15 January 1981)

Tenth Series (1980)
(Catalogue No: EU-6892 -DA-DE-EN-FR-IT-NL)

- Guidelines for the safety assessment of food additives (Opinion expressed on 22 February 1980)

Ninth Series (October 1979)
(Catalogue No: CB-NW-79-009-EN-C -DA-DE-EN-FR-IT-NL)

- Flavourings (Opinion expressed on 21 September 1979)
- Asbestos (Opinion expressed on 31 October 1979)
- Natamycin (Opinion expressed on 31 October 1979)

Eighth Series (May 1979)
(Catalogue No: CB-28-79-827-EN-C -DA-DE-EN-FR-IT-NL)

- Use of certain emulsifiers in chocolate and related products (Opinion expressed on 7 February 1979)

- Certain colouring matters for use in food (Opinion expressed on 23 March 1979)

Seventh Series (December 1978)
(Catalogue No: CB-NW-78-007-EN-C -DA-DE-EN-FR-IT-NL)

- Emulsifiers, stabilizers, thickeners and gelling agents (Opinion expressed on 30 November 1978)

Sixth Series (October 1978)
(Catalogue No: CB-NW-78-006-EN-C -DA-DE-EN-FR-IT-NL)

- Second Report of the Scientific Committee for food on thiabendazole (Opinion expressed on 23 June 1978)
- Positive list of substances to be authorized in the manufacture of regenerated cellulose films intended to come into contact with foodstuffs (Opinion expressed on 28 September 1978)

Fifth Series (May 1978)
(Catalogue No: CB-AH-78-005-EN-C -DA-DE-EN-FR-IT-NL)

- Elements of information given to the Commission on the use of additives for which no acceptable daily intake has been allowed (Opinion expressed on 16 March 1978)
- Provisions relating to additives and processing aids in the draft proposal for a Council Directive concerning the approximation of the laws of the Member States relating to fine bakers' wares, rusks, pastries and biscuits (Opinion expressed on 1 May 1978)

Fourth Series (December 1977)
(Catalogue No: CB-AH-77-004-EN-C -DA-DE-EN-FR-IT-NL)

- Saccharin (Opinion expressed 24 June 1977)
- Calcium disodium ethylenediamine tetra-acetate (Opinion expressed on 24 June 1977)
- Colouring matters (Opinion expressed on 16 September 1977)
- Formaldehyde in 'Grana Padano' Cheese (Opinion expressed on 20 October 1977)

Third Series (January 1977)
(Catalogue No: CB-AH-77-001-EN-C -DA-DE-EN-FR-IT-NL)

- Toxicological evaluation of a substance for materials and articles intended to come into contact with foodstuffs (Opinion expressed on 1 October 1976)

Second Series (December 1976)
(Catalogue No: 8843 -DA-DE-EN-FR-IT-NL)

- Amaranth (Opinion expressed on 27 February 1976)
- Some chemically modified starches (Opinion expressed on 27 February 1976)
- Research necessary on long chain fatty acids and oils and fats used in food (Opinion expressed on 2 April 1976)
- Thiabendazole (Opinion expressed on 2 April 1976)
- Propyl gallate (Opinion expressed on 2 July 1976)

First Series (December 1975)
(Catalogue No: 8801 -DA-DE-EN-FR-IT-NL)

- Sodium methyl parahydroxybenzoate, potassium nitrite and potassium propionate (Opinion expressed on 15 November 1974)
- Mercury in food (Opinion expressed on 16 November 1974)
- Rapeseed oils (Opinion expressed on 16 November 1974)
- Revision of the Directive on colouring matters authorized for use in foodstuffs intended for human consumption (Opinion expressed on 27 June 1975)
- Vinyl chloride monomer (Opinion expressed on 27 June 1975)
- Ethoxyquin (Opinion expressed on 13 November 1975)

European Commission

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The Scientific Committee for Food was established by Commission Decision 74/234/EEC of 16 April 1974 (OJ L 136, 20.5.1974, p. 1), replaced by Commission Decision 95/273/EC of 6 July 1995 (OJ L 167, 18.7.1995, p. 22), to advise the Commission on any problem relating to the protection of the health and safety of persons arising or likely to arise from the consumption of food, in particular on nutritional, hygienic and toxicological issues.

The members are independent persons, highly qualified in the fields associated with medicine, nutrition, toxicology, biology, chemistry, or other similar disciplines.

Responsibility for the Secretariat of the Scientific Committee for Food was transferred from Directorate-General III 'Industry' to Directorate-General XXIV 'Consumer Policy and Consumer Health Protection' with effect from 1 April 1997.

The present report deals with:

* Nitro musk compounds in foods
* Principles for the development of risk assessment of microbiological hazards under the hygiene of foodstuffs Directive 93/43/EEC
* Microcrystalline cellulose
* Derivatives of wood rosin as coating agents for fresh citrus fruits
* The relationship between scientific data and the labelling of genetically modified foods and their derived products
* A maximum residue limit (MRL) of 0,01 mg/kg for pesticides in foods intended for infants and young children
* The potential risk to human health arising from the bulk transport of raw sugar, semi-processed syrups and thick sugar juices intended for the production of white sugar, in non-dedicated ships' tanks and road tankers
* The potential microbiological risk arising from the presence of moisture in tea
* Papain from papaya fruit (*Carica papaya*) used as a meat tenderising agent (examination of additional information)