

5 Safety Evaluation and Legal Aspects

5.1 Flavoring Substances

Flavoring substances are used to compose special tastes, e.g., strawberry. When flavor compounds are added to foods, no health hazards should arise from the concentration used. The flavor contains flavoring substances and solvents or carriers; the concentration of a single flavoring substance in the food does not usually exceed 10–20 ppm. Because of the taste and smell of the substances, high concentrations cannot be used, i.e., flavoring substances are self-limiting.

Normal toxicological testing for food additives is not necessary and would be too expensive in view of the relatively small amounts of substance used. Nevertheless, toxicological testing of flavoring substances has provided very useful data. Those substances which may cause adverse effects on human health (including allergens) have been identified and have been prohibited or limited in use.

The JECFA (Joint FAO/WHO Expert Committee on Food Additives/FAO Food and Nutrition Paper No. 30 Rev. 1 and amendments (Food and Agriculture Organisation of the UN, Via della Terme di Caracalla, Rome/Italy)) has made recommendations for the ADI (acceptable daily intake (in mg/kg body weight)) of food additives based on toxicological tests; these include flavoring substances.

Another international body which has dealt with the safety of flavoring substances for human health is the 'Partial Agreement in the Social and Public Health Field' of the 'Council of Europe'. Lists of flavoring substances have been published in the 'blue book' (*Flavouring Substances and Natural Sources of Flavours*, Vol. 1, 4th Edition (Council of Europe, Strassbourg 1992)), which contains 900 flavoring substances with their structures, use levels in beverages and food, main natural food occurrence, and main toxicological data.

Furthermore the IOFI (International Organisation of the Flavor Industry (Square Marie-Louise 49, B-1000 Brussels)) has compiled a list of artificial flavoring substances (approved by experts) in the 'Code of Practice' and a short restrictive list of natural and nature-identical flavoring substances with recommended maximum concentrations for foods and beverages. Natural flavoring substances are obtained by physical, microbiological, or enzymatic processes from a foodstuff or material of vegetable or animal origin. Nature-identical substances

are obtained by synthesis or isolated by chemical processes from a raw material and are chemically identical to their natural counterparts present in natural products. Artificial flavoring substances are made in the same way, but have not yet been identified in a natural product.

Lists of approved flavoring substances have been compiled in the United States since 1959. According to the American Federal Food, Drug, and Cosmetic Act, every natural and artificial flavoring substance has to be approved by the US FDA or a reliable expert panel. Lists of approved and 'GRAS' (generally recognized as safe) flavor substances are published in the CFR (Code of Federal Regulations of USA (US Government Printing Office, Washington, DC)) and by the FEMA (Flavor and Extract Manufacturers Association of the United States (1620 Eye Street, N.W., Washington, DC)). These lists have been adopted by other countries.

In the European Union a Regulation (EC) No. 2232/96 of the European Parliament and of the Council laying down a Community procedure for flavoring substances used or intended for use in or on foodstuffs has been issued (*Official Journal of the European Communities* No. L 299, 1–4, 23.11.1996).

This regulation, under Article 3, should provide a list of flavoring substances by the year 2004, whereby member States will notify the Commission of all flavoring substances which may be used in products marketed on their territory. These flavoring substances have been entered into a register of about 2800 substances which has been adopted by the Commission as Commission Decision 1999/217/EC, and updated by Commission Decision 2000/489/EC.

Amendments to the register are possible, the intellectual property rights of the flavor manufacturers will be protected. The register forms the basis of a five-year evaluation program. This program defines the order of priorities according to which the flavoring substances are to be examined, the time limits, the flavoring substances which are subject to scientific cooperation, and the technical and toxicological data which have to be provided by the flavor industry. Commission Regulation 1565/2000/EC lays down the details of the evaluation program. After completion of the evaluation a positive list of flavoring substances for use in foodstuffs will be established [844c].

5.2 Fragrance Materials

Fragrance materials are used in a wide variety of products, e.g., cosmetics, soaps, detergents, etc. As is the case for flavoring substances, the concentrations of fragrances used must not cause any adverse effects on human health. Contrary to flavoring substances, special legislative regulations do not exist for fragrance materials. However, with respect to the handling and application of chemicals, cosmetic and other regulations are affecting fragrance materials and compounds

more and more. Safety evaluation and regulation for fragrance materials and compounds is mostly done on the basis of voluntary self-control by the industry. Increasing awareness of possible risks has initiated extensive toxicological testing, which has, in turn, generated useful data on many fragrance ingredients. Hundreds of monographs on fragrance materials and essential oils have been published by the Research Institute for Fragrance Materials (RIFM*) [845] in 'Food and Chemical Toxicology' (formerly 'Food and Cosmetics Toxicology'); they report specifications, data on biological activity, and testing results [845a–845m]. Based on RIFM and other data, the International Fragrance Association (IFRA**) has published industrial guidelines for limiting or prohibiting the use of certain fragrance ingredients.

Some years ago an indicative, nonexhaustive list of fragrance ingredients used in cosmetics was published by the EC Commission (Resolution 96/335/EG of May 8, 1996 published in OJL 132 of June 1, 1996). This is noteworthy, since it is the first time that fragrance ingredients as a group appeared in an official piece of legislation. The sole purpose of this list is to enhance transparency of the generic term 'perfume,' which has to be used for ingredient labeling of cosmetic products as prescribed by the EC Cosmetic Directive.

During the last few years, discussions about the environmental fate of fragrance materials, as used in consumer products, roused some interest after residual amounts of certain fragrance ingredients have been identified in various biota. This has triggered extensive environmental testing of the major, high-volume fragrance ingredients. Based on these data, risk assessments are carried out by IFRA and certain task forces. On the basis of these results, limited use of two nitromusk fragrances has been recommended by the Scientific Committee of Cosmetology and Non Food Products (SCCNFP). Other nitromusks have been banned because of the lack of data. At present the risk assessments of polycyclic musks are being carried out. Because there are a lot of new developments in the application and interpretation of risk assessments it can be expected that some fragrance materials will require further action to be taken.

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