



Safety Evaluation of Fragrance Materials

Ingredient Evaluation

Fragrance ingredients that deviate from generally accepted quality standards should be used only after satisfactory evaluation according to the requirements set forth in this guidance document.

The IFRA Scientific Committee will collect and make available to RIFM data that are relevant for the safety evaluation of fragrance ingredients. This may include ingredient volume of use, ingredient use level in fragrance compositions, as well as data from the scientific literature, results of testing programs made available by the originators of such programs, and validated reports of adverse reactions to fragrance materials.

Safety data for all fragrance ingredients that are commercially available and offered for sale as such must be submitted by the ingredient manufacturer to RIFM for inclusion in the Fragrance Ingredient Database. Manufacturers must provide all available information on specifications, use and use levels as well as copies of test reports and other safety related information for examination by the REXPAN (RIFM Expert Panel). In particular, when fragrance manufacturers have evidence that warrants creation or modification of a Standard, they shall inform IFRA and supply the data to RIFM.

Nature of Human Health and Environmental Effects Evaluation

The human health and environmental safety evaluations of ingredients require the review of consumer and environmental exposure information, respectively, and supporting safety data. An important component in establishing priorities, applicable to a thorough safety assessment, is a survey of the total usage of individual fragrance ingredients. IFRA generally carries out a worldwide survey of fragrance ingredient usage every four years. This survey is conducted by requests made to all suppliers or compounders of fragrance ingredients on record, whether members of IFRA or not.

Also, critical to a thorough human health safety assessment of individual fragrance ingredients are data on levels of use, and routes of exposure of consumers. These data are determined from a collaborative effort of IFRA and various cosmetic companies or trade associations, with the data being analyzed and summarized in documents prepared by IFRA.

Possible environmental fate and effects should also be considered in the assessment of a substances' use including route of environmental exposure, possible degradation, metabolism and the environmental safety of their metabolites/degradates.

For the evaluation of a fragrance ingredient, consideration should be given to possible effects on the skin, including skin irritation and sensitization, with special attention paid to the effect of sunlight in cases where the ingredient reveals UV-absorbing properties.

Systemic toxicity should be considered in relation to the quantities of a fragrance ingredient used and its likelihood of entry into the human body.

All data collected as described above are communicated routinely to RIFM, for consideration by the Expert Panel.

If there are inadequate data from the sources mentioned above, a testing program must be designed, which includes dermatological, systemic and environmental endpoints as described in the RIFM "Criteria Documents" (see section 'Guidance documents').



As a result of safety assessments, the usage of certain fragrance ingredients may be restricted and these restrictions are set forth in IFRA Standards.

IFRA Human Health Standards

Standards that impose a quantitative limit on the use of fragrance materials are expressed as a maximum concentration of fragrance material in the consumer product. This implies knowledge of (a) the concentration of the restricted fragrance material in the compound and (b) the concentration of the compound in the final consumer product. It is therefore essential that fragrance suppliers inform manufacturers of consumer products, who use or intend to use a fragrance compound, that due to the presence of a restricted ingredient, the compound should only be used up to a specified maximum concentration or in well-defined applications. Unless otherwise specified, "concentrations" are expressed in weight-weight percent.

IFRA Environmental Standards

Two types of IFRA Environmental Standards have been developed: hazard based and risk based. Presently, any fragrance material which has been determined by IFRA to be PBT (Persistent & Toxic & Bioaccumulative) or vPvB (very Persistent & very Bioaccumulative) based on current definitions under the EU REACH legislation shall be banned. The current risk-based Standard is based on an evaluation using the RIFM Framework (Salvito, Senna and Federle, 2002). Risk management measures, applied in a non-discriminatory manner, will be developed, if necessary, for materials whose Predicted Environmental Concentration/ Predicted No Effect Concentration ratio is greater than 1.

Guideline for Communicating IFRA Status

Whenever the IFRA status of a fragrance compound is communicated, the following aspects should be considered:

- the identification of the supplier;
- the identification of the fragrance compound;
- the intended application in consumer products;
- a (realistic) use concentration for the intended application;
- a written statement that the fragrance complies with the requirements of the Code of Practice including the Standards for the specified application and use concentration;
- the maximum use concentration allowed by IFRA;
- a date-specific reference to the version of the IFRA Code of Practice and Standards at the time the statement is made;
- the comment that the use of a higher concentration or a different product application will require another safety evaluation; and
- the date of assessment.

In order to effectively apply the Code of Practice to the manufacture and handling of all fragrance materials, fragrance manufacturers should take all measures to assure that any fragrance compound offered for sale is in full compliance with the requirements of the Code of Practice and all applicable Standards.

In cases where an Amendment to the Code of Practice (and the therein contained Standard(s)) changes the status of a fragrance compound, it is the responsibility of the manufacturer to inform the fragrance purchaser of the change and to provide all information relevant to the user's determination of the conditions under which the material(s) can be used in full compliance with the Code of Practice and the applicable new or revised Standard(s). If required, the manufacturer should offer the purchasing party an alternative fragrance compound that complies with the new or revised Standard(s).



Guidance Documents

The following guidance documents relate to the specifics for human health and environmental effects evaluations as well as to IFRA procedures on how to provide estimates of consumer exposure to fragrance ingredients:

1. Human Health Evaluation

Evaluation of the potential effects of fragrance materials on the skin, for irritation and sensitization, as well as sunlight-mediated effects, systemic toxicity, etc., should utilize the Human Health Criteria Document which has been published as "Criteria for development of a database for safety evaluation of fragrance ingredients", R.A. Ford, B. Domeyer, O. Easterday, K. Maier, and J. Middleton, *Regulatory Toxicology and Pharmacology*, 31: 166-181 (2000).

2. Environmental Effects

A methodology for conducting a preliminary aquatic risk assessment for fragrance materials can be found in the Environmental Framework Document which has been published as "A framework for prioritizing fragrance materials for aquatic risk assessment", D.T. Salvito, R.J. Senna, and T.W. Federle, *Environmental Toxicology and Chemistry*, 21(3): 1301-1308 (2002).

3. Safety Assessment of Fragrance Materials

A description of the process applied for fragrance material safety evaluation by the RIFM Expert Panel has been published as "The safety assessment of fragrance materials", D.R. Bickers, P. Calow, H.A. Greim, J. M. Hanifin, A. E. Rogers, J.H. Saurat, I.G. Sipes, R.L. Smith and H. Tagami, *Regulatory Toxicology and Pharmacology*, 37: 218-273 (2003).

4. Exposure Assessment

A description on how fragrance industry's procedures for estimating exposure to fragrance ingredients through different routes and leading to different potential endpoints has been published as "Consumer exposure to Fragrance Ingredients: Providing Estimates for Safety Evaluation", P.A. Cadby, W.R. Troy, and M.G.H. Vey, *Regulatory Toxicology and Pharmacology*, 36: 246-252 (2002).