



Regulatory View

The Taste Test

Global safety evaluation of flavoring ingredients

Tim Adams, Flavor Extract Manufacturers Association

In the 1990s, the flavor industry became increasingly global. Since 1993, the flavor industry has committed to an international program in which all flavoring substances in use in the global marketplace will be recognized as safe for their intended use in food. The globalization of the flavor industry has had a significant impact on the activities of the FEMA Expert Panel, the US Food and Drug Administration (FDA), and international committees such as the World Health Organization Joint Expert Committee on Food Additives (JECFA), the Food Agriculture Organization (FAO), and the European Food Safety Authority (EFSA). During the last decade, these committees and panels have become actively involved in the safety evaluation of flavoring substances.

FEMA Expert Panel

For its part, the FEMA Expert Panel has engaged in an extensive review of all scientific data relevant to the safety evaluation of existing FEMA GRAS substances. Beginning in 1994, the Expert Panel has re-evaluated all relevant scientific information and reaffirmed the GRAS status (GRASr) of almost 1,500 flavoring substances. When necessary, the Panel has requested that additional studies be performed in order to complete the GRASr process.

Evaluation of such a large number of substances has been a monumental task. Based on more than four decades of experience, the Panel has concluded that structurally related substances exhibiting similar biological, biochemical and chemical properties, can be effectively evaluated as a chemical group. Over the last decade, the Panel has organized more than 1,500 flavoring substances according to relatively few (ca. 40) chemical groups. The Panel then evaluates each substance based on the data available for that substance and on structurally related substances.

The Expert Panel recognizes that the GRASr program and the scientific database of information on flavoring substances must be readily available and transparent worldwide. Therefore, they have initiated

Flavor Safety on the Web

FEMA Expert Panel: www.femaflavor.org

US Food and Drug Administration: www.fda.gov

World Health Organization Joint Expert Committee on Food Additives: www.who.int/ipcs/food/jecfa/en/

Food Agriculture Organization: www.fao.org

European Food Safety Authority: efsa.eu.int/

European Flavor and Fragrance Association: www.effa.be



a program to publish in the peer-reviewed literature, scientific reviews of the data on chemical groups that provide the scientific basis for the Panel's GRASr decisions.^{1-4,6-8}

During the last three years, the Panel has expanded the application of the group assessment approach to the safety evaluation of natural flavor complexes (NFCs). NFCs are mixtures of constituents, most of which have been chemically identified, that belong to a limited number of chemical groups. Studies on the biochemical fate and toxicologic potential along with intake data for members of each of these chemical groups provide the scientific basis to perform a comprehensive safety evaluation of NFCs. Because

of the complexities involved in the evaluation of a mixture, the Panel has developed a scheme for the systematic evaluation of the chemical composition of an NFC. The principles, details and examples of this novel approach to safety evaluation are the subject of a soon to be published article.

WHO JECFA/ FAO Activities

Since 1995, the JECFA has been engaged in a scientific program to evaluate the safety of flavor substances and prepare specifications for these approved substances (FAO). In 1995, a systematic procedure was developed to evaluate the relatively large number (>2,000) of substances used as flavor materials. The safety evaluation procedure was adopted by JECFA in 1996 following a trial evaluation of 46 flavor substances.⁵ Following the 1996 review of individual material monographs and chemical group monographs, JECFA concluded that the safety evaluations be based on the chemical group approach. This approach would facilitate and strengthen the evaluation process. Typically, groups of 20 to 60 flavoring agents were assigned

to a chemical group based on the similar chemical and biological properties. Since beginning in 1997, JECFA has annually evaluated two to seven such chemical groups containing between 120 and 225 flavoring agents. Through 2004, 1,450 flavoring substances have

been successfully evaluated by JECFA and specifications for each substance have been developed by FAO (JECFA, 1997-2003).

During 2003 and 2004, JECFA has also begun an evaluation of naturally occurring mixtures. The history of chemical group reviews performed from 1996 through 2004 contains many of the constituents found in these mixtures. Based on its experience evaluating groups of chemically identified flavoring substances, JECFA is developing a procedure to evaluate naturally occurring mixtures used as flavoring substances.



Globalization of the flavor industry has created a multifaceted international program of safety evaluation of flavoring substances that will eventually provide a global list of flavoring substances recognized as safe for their intended use in food.

EFSA Activities

In 2000, the European Union Scientific Committee on Food (SCF), now recognized as the European Food Safety Authority (EFSA), initiated a program to evaluate the safety of flavoring substances in use in the EU. Following a comprehensive review of the JECFA procedure and prior JECFA activities related to flavor safety evaluation, the SCF adopted the JECFA procedure and provisionally adopted the list of flavoring substances already approved by JECFA. They also began a program to evaluate flavoring substances used in Europe that were not yet used in the US and had not

been evaluated by JECFA. The European Flavor and Fragrance Association (EFFA) submitted data related to these substances. In the last four years, EFFA has submitted data on more than 400 flavoring substances.

Globalization of the flavor industry has created a multifaceted international program of safety evaluation of flavoring substances that will eventually provide a global list of flavoring substances recognized as safe for their intended use in food.

References

1. T.B. Adams, J.B. Hallagan, J.M. Putman, T.L. Gierke, J. Doull, I.C. Munro, P.M. Newberne, P.S. Portoghese, R.L. Smith, B.M. Wagner, C.S. Weil, L.A. Woods and R.A. Ford, *The FEMA GRAS assessment of alicyclic substances used as flavor ingredients*. Food Chem. Toxicol., **34**: 763-828 (1996).
2. T.B. Adams, J. Doull, J.I. Goodman, I.C. Munro, P.M. Newberne, P.S. Portoghese, R.L. Smith, B.M. Wagner, C.S. Weil, L.A. Woods and R.A. Ford, *The FEMA GRAS assessment of furfural used as a flavor ingredient*. Food Chem. Toxicol., **35**: 739-751 (1997).
3. T.B. Adams, D.B. Greer, J. Doull, I.C. Munro, P.M. Newberne, P.S. Portoghese, R.L. Smith, B.M. Wagner, C.S. Weil, L.A. Woods and R.A. Ford, *The FEMA GRAS assessment of lactones used as flavor ingredients*. Food Chem. Toxicol., **36**, 249-278 (1998).
4. T.B. Adams, S. Cohen, J. Doull, V.J. Feron, J.I. Goodman, L.J. Marnett, I.C. Munro, P.S. Portoghese, R.L. Smith, W.J. Waddell, and B.M. Wagner, *The FEMA GRAS assessment of cinnamyl derivatives used as flavor ingredients*. Food Chem. Toxicol., **42**, 157-185 (2004).
5. JECFA (1997-2003) Joint FAO/WHO Expert Committee on Food Additives. <http://www.who.int/ipcs/food/jecfa/en/>.
6. P. Newberne, R.L. Smith, J. Doull, J.I. Goodman, I.C. Munro, P.S. Portoghese, B.M. Wagner, C.S. Weil, L.A. Woods, T.B. Adams, C.D. Lucas and R.A. Ford, *The FEMA GRAS assessment of trans-anethole used as a flavoring substance*. Food and Chem. Toxicol., **37**, 789-811 (1999).
7. R.L. Smith, J. Doull, V.J. Feron, J.I. Goodman, L.J. Marnett, I.C. Munro, P.M. Newberne, P.S. Portoghese, W.J. Waddell, B.M. Wagner and T.B. Adams, *The FEMA GRAS assessment of pyrazine derivatives used as flavor ingredients*. Food Chem. Toxicol., **40**, 429-451 (2002a).
8. R.L. Smith, T.B. Adams, J. Doull, V.J. Feron, J.I. Goodman, L.J. Marnett, P.S. Portoghese, W.J. Waddell, B.M. Wagner, A.E. Rogers, J. Caldwell and I.G. Sipes, *Safety assessment of allylalkoxybenzene derivatives used as flavoring substances - Methyleugenol and estragole*. Food Chem. Toxicol., **40**, 851-870 (2002b).

Address correspondence to Tim Adams, The Roberts Group LLC, 1620 I Street, N.W. Suite 925, Washington, DC 20006; tadams@therobertsgroup.net. ■