Timothy Adams

The evolution of FEMA GRAS, FEXPAN and the flavorist's palette

When it was first released in January 2011, the GRAS (Generally Recognized as Safe) 25 list of flavoring substances issued by the Flavor and Extract Manufacturers Association (FEMA) was notable for the number and diverse types of flavors and flavor modifiers it included. The composition of these regular publications has evolved since the FEMA Expert Panel (FEXPAN) published its first GRAS publication (GRAS 3) in 1965, reflecting the evolution of the flavor industry's palette, the sophistication of instrumentation, and national and international regulatory concerns.[a] For more than 30 years Timothy Adams, current scientific director of FEMA and scientific secretary of FEXPAN, has held leading positions in the assessment of flavor ingredient safety. For these efforts he will receive FEMA's 2011 Richard L. Hall Distinguished Service Award. Working initially as a consultant for FEMA in the 1970s, Adams participated in the preparation of scientific literature reviews (SLR) regarding the safety of flavor ingredients. In the 1980s he was responsible for the updating of SLRs and the perparation of the Flavor and Fragrance Information Data Sheets (FFIDS). During the 1990s he worked with FEXPAN to perform the second comprehensive reevaluation of the safety of FEMA GRAS substances. In 2000 he became FEMA scientific director and was appointed scientific secretary by FEXPAN. "The panel is composed of an extremely diverse group of experts from many different scientific disciplines," says Adams. The composition of this independent body has evolved as its needs have grown. Today, FEXPAN's expertise includes metabolism, toxicology, DNA adducts, biostatistics, pathology and biochemistry. "That means all the aspects related to the safety of flavorings are being considered during GRAS evaluations," says Adams. The conclusions of this group are published in open, peer-reviewed journals. Adams' initial work with FEMA centered on the collection of data on existing flavoring materials, reaching back to 1900. The initial data on individual substances was organized according to chemical groups of structurally related substances. This provided the basis for FEXPAN to evaluate the safety of a substance in the context of data for the substance and all structurally related substances. The "chemical group approach" is now a cornerstone of safety evaluation for FEXPAN. Beginning in 1992, seeking to broaden the scope of FEMA GRAS acceptance, Adams and his colleagues began a project to create a global recognition for the safety of flavor ingredients. Based on the chemical group approach, Adams' group supplied the data support to the FDA, which placed FEMA GRAS substances on the agenda of the World Health Organization (WHO) for evaluation by the Joint Expert Committee on Food Additives (JECFA). "From 1995 to 2010 WHO and its affiliate, JECFA, have evaluated more than 2,000 flavor substances for safety," says Adams of the ongoing program, "and in the vast majority of cases they've come to the same conclusions as those of our Expert Panel." In 1995, as natural flavors and ingredients grew in popularity and sophistication, FEXPAN began to develop a constituent-based evaluation for natural flavoring complexes—essential oils, extracts and oleoresins. The group eventually published its procedure.[b] And so today, says Adams, FEXPAN evaluates both individual materials and natural flavor complexes. "The industry is changing," says Adams. "Recently—with the advent of work on the human genome in the late 1990s—our industry began to develop receptor-designed flavoring substances that bind to specific taste receptors." These substances often act as flavor modifiers, an area that has become increasingly important for the industry as it seeks to manufacture flavors that provide a more complete flavor profile. Flavor modifiers that modulate sweetness, saltiness, herbal, fruity, creamy and other effects are becoming available "We are now in the stages of evaluating flavor modifiers that by themselves are not exerting a flavoring effect, but tend to modify the flavoring effect of formulated flavorings," says Adams, discussing GRAS 25. "We're now at the advent of a new [era] of flavor development that adds greater fullness to the flavor experience." Yet even as the range of ingredients available to flavor manufacturers diversifies, FEXPAN's challenges multiply. "As always, there are challenges," says Adams. "One of them is chemically identifying materials at extremely low levels which have extremely potent flavor effects. We have materials now that can be detected at 1 in 1,000 trillion. You're getting down to the point now where insignificant amounts of substance have an impact on flavor." He adds, "Another [challenging] area is the production of molecules that bind directly to individual taste receptors to produce an effect," such as cooling. "These substances are really breaching on the edge of a pharmaceutical industry approach. As [ingredient manufacturers] look at the structure of receptors, they're designing molecules to fit them." These emerging materials require new and expanded types of safety testing, says Adams. "The studies being performed on these various receptor-designed materials are [similar] to ones used in the pharmaceutical industry." These include in vivo and in vitro metabolism studies, 90-day studies in animals, genotoxicity assays and more. However, Adams points out, "The biggest difference between our industry and the pharmaceutical industry is that the levels [of ingredients] needed to affect flavor are orders of magnitude less than those needed for a particular drug to exert pharmacological activity."

Adams will be honored during FEMA's annual business meeting during its 102nd annual convention taking place May 1–4, 2011 at The Breakers in Palm Beach, Florida. For more information, visit www.femaflavor.org.

[a] *In the wake of the US Food Additives Amendment of 1958, the US Food and Drug Administration (FDA) published a GRAS list of flavoring materials, which was included in the Code of Federal Regulations, Title 21 (commonly known as CFR 21). Faced with industry's requests for amendments and a cumbersome ingredient review process, FDA cooperated with FEMA's Dick Hall—the namesake of the organization's distinguished service award—to create FEXPAN, which assumed responsibility for the safety assessment of flavor ingredients.*

[b] *RL Smith, SM Cohen, J Doull, VJ Feron, JI Goodman, LJ Marnett, PS Portoghese, WJ Waddell, BM Wagner, RL Hall, NA Higley, C Lucas-Gavin and TB Adams, A procedure for the safety evaluation of natural flavor complexes used as ingredients in food: essential oils.* Food and Chemical Toxicology, ***43***(3), 345–363 (2005)