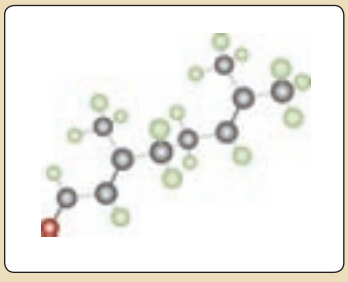
BY R.L. SMITH, S.M. COHEN, J. DOULL, V.J. FERON, J.I. GOODMAN, L.J. MARNETT, P.S. PORTOGHESE, W.J. WADDELL, B.M. WAGNER, & T.B. ADAMS

GRAS

FLAVORING SUBSTANCES 22

The **22nd publication** by the FEMA Expert Panel presents safety and usage data on 185 new **generally recognized as safe** flavoring ingredients and describes an approach to assessing the safety of natural flavor complexes.



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The Flavor and Extract Manufacturers Association's GRAS Program is now in its 45th year of continuous operation. During that time, the FEMA Expert Panel, as an independent scientific body, has rigorously evaluated the safety of food flavors with the goal of protecting human health.

The GRAS program was established to respond to the provision in the 1958 Food Additives Amendment to the Federal Food, Drug, and Cosmetics Act—Public Law 85-929, 72 Stat. 1784 (1958), codified at 21 USC Section 348 (1988)—that exempted from food additive status those substances "generally recognized by experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures . . . to be safe under the conditions of intended use." Based on this provision, substances "generally recognized as safe" (GRAS) by the FEMA Expert Panel are not considered to be food additives, and are excluded from mandatory premarket approval by the Food and Drug Administration (Hallagan and Hall, 1995).

For most of the Program's history, the Expert Panel has concentrated on the evaluation and regularly scheduled reevaluation of data related to the safe use of approximately 1,900 chemically identified flavor ingredients. However, over the past decade, the Panel recognized that a comprehensive GRAS program for food flavorings entails not only the consideration of chemically identified flavoring substances, but also the assessment of natural flavor complexes such as essential oils, extracts, and oleoresins.

The Panel also recognized that other chemical substances with non-flavor function—such as emulsifiers, antioxidants, and flavor modifiers—are used in the preparation of finished flavors. Most finished flavors are a combination of chemically identified substances, natural flavor complexes, and those substances (stabilizers, solvents, and emulsifiers) required to process the flavor into the finished food product. Since finished flavorings function optimally at such low levels in foods, intake of these three types of substances normally represents a minute contribution to the diet compared to direct food additives and food itself.

As one of its principal long-term goals, the Panel strives to develop scientifically rigorous criteria and procedures that can be used to evaluate the safety of all substances used in the production of food flavors. Over the past four decades, criteria have been developed to evaluate the safety of nearly 1,900 substances (Woods and Doull, 1991; Smith et al., 2005b). The scientific criteria used by the Panel to reach its GRAS conclusions were last addressed in 1991 (Woods and Doull, 1991). Scientific advances since 1991 in the areas of DNA adduct formation, experimental pathology, and molecular mechanism of genotoxicity and

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mixture safety evaluation now play a major role in understanding the chemical, biochemical, and biological fate of flavoring substances consumed in food.

Given the impact of these recent scientific advances, primarily in fields related to molecular reactions in vivo, revised guidelines for current and future GRAS decisions have recently been published (Smith et al., 2005b). These criteria are vigorously applied to evaluate chemically identified substances, natural flavor complexes, and substances exhibiting non-flavor function used in the preparation of finished food flavors.

Because of the rich database of safety data available, the evaluation of substances needed to stabilize, emulsify, acidify, etc., compounded flavorings followed more-traditional lines of safety evaluation. Almost without exception, these substances possess extensive toxicity data. These data provide enormous margins of safety for the intake of low levels of these substances from use in flavors. These margins of safety are orders of magnitude lower than those for the same substances added directly to food.

The most difficult aspect of safety evaluation for flavors involves naturally occurring mixtures or natural flavor complexes. The development of scientifically based criteria to evaluate naturally occurring mixtures such as essential oils provides a significant challenge, one that mixture toxicology has faced for decades. The recent publication of a guide to evaluate natural flavor complexes (NFCs), specifically essential oils (Smith et al., 2005a), is a major step forward. The practical procedure is based mainly on the evaluation of the chemical composition of the NFC and the variability of that composition in the commercially available product. It represents the first attempt to evaluate the safety of a naturally occurring complex chemical mixture based on its actual chemical composition and safety data available for those constituents.

Scientific advances since 1991 ... play a major role in understanding ***the chemical, biochemical, and biological fate of flavoring substances*** *consumed in food.*

The GRAS Reaffirmation Program

In 1994, the Panel initiated its third comprehensive review of data relevant to the safety of all chemically identified GRAS flavoring substances. As in the previous comprehensive review (GRAS affirmed or GRASa) performed between 1979 and 1988, the Panel evaluated each flavoring substance within the context of safety data on the group of structurally related substances. This group approach involves the evaluation of data available for the specific substance and a much larger volume of data for structurally related substances that are anticipated to exhibit similar chemical, biochemical, and biological fate, especially at low levels of intake from their intended use as flavors.

Using newly revised evaluation criteria (Smith et al., 2005a), the Panel reaffirmed the GRAS status of more than 98% of chemically identi-

FEMA GRAS LISTS

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fied GRAS substances. In relatively few cases, the Panel requested that additional safety studies be performed for representative substances (e.g., verbenone and nootkatone) in a selected chemical group (bridged and fused bicyclic ketones) prior to successful completion of the GRASr evaluation of that chemical group.

The GRASr program is now essentially complete, and the results are presented in this article. Through 2004, more than 1,900 chemically identified flavoring substances have been reevaluated and recognized as GRASr.

As part of the GRASr program, the key scientific data on which the GRASr decisions are based is published in the peer-reviewed literature. These published data have been organized according to chemical group. For example, the safety data for chemical groups such as aliphatic and aromatic lactones, cinnamyl, phenethyl alcohol, benzyl, and hydroxybenzyl derivatives have been published (Adams et al., 1996, 1997, 1998, 2004; Newberne et al., 1999; Smith et al., 2002a, b). These publications contain an analysis of food and flavor exposure data; data on absorption, distribution, metabolism, excretion, and molecular reactions with proteins and DNA; and reports of toxicology, carcinogenicity, and genotoxicity studies for groups of structurally related flavoring substances. These are, in addition >>> to expert judgment, the key data on which GRAS and GRASr decisions are made.

The Most New Substances Since 1965

In addition to the reevaluation of safety data on existing GRAS substances, a significant number of new candidates have been evaluated as GRAS for their intended use as flavoring substances. The main reason for the recent influx of GRAS candidates is related to international interest in developing a global positive list of flavoring substances. Flavor safety evaluation programs begun by the World Health Organization/Food Agriculture Organization (WHO/FAO) Joint

Expert Committee on Food Additives (JECFA) and in Europe are based on scientific principles similar to those used by the FEMA Expert Panel over the past four decades. Therefore, in the spirit of globalization, FEMA recommended that the current GRAS system that had previously been limited to United States FEMA-member companies should be expanded to allow foreign producers of flavors to submit flavoring substances for GRAS evaluation and eventual sale in the U.S. marketplace.

As a result, FEMA created the International Group GRAS Program. In this program, flavor companies that are members of the International Organization of Flavor Industries (IOFI) or their national flavor trade associations can submit groups of structurally related flavoring substances for GRAS evaluation by the FEMA Expert Panel. Since its inception in 2002, the Group GRAS Program is the major reason that GRAS 22 contains the most new chemically identified flavoring substances (185) since the first GRAS list (GRAS 3) was published in 1965.

For the vast majority of substances in the GRASr Program, the conclusions concerning the GRAS status of chemically identified flavoring substances have been reaffirmed by another evaluating body. Beginning in 1996, JECFA began a program to evaluate chemically identified flavoring substances. Through 2004, it has evaluated approximately 1,500 flavoring substances.

JECFA has annually evaluated groups of structurally related chemically identified flavoring substances (130–220/year) using a procedure presented at JECFA in 1995 and formally adopted in 1996 (JECFA, 1997). Initial evaluations during 1996 were time consuming, in that each substance was evaluated individually. However, JECFA determined that efficient but effective evaluations could be performed on groups of chemically related substances similar to but not identical to those used by the Expert Panel. Based on this group approach and use of a formal evaluation procedure, JECFA has reached the conclusion that the reviewed flavoring substances are safe under current conditions of intake.

In this, the 22nd GRAS publication, 185 new GRAS flavoring substances are identified—FEMA Nos. 4069–4253 (Tables 1 and 2, pp. 40–60). In addition, the Panel determined that new use levels and food categories for five flavoring substances are consistent with their current GRAS status (Table 3). Of these 185 new flavoring substances, four (Nos. 4219–4222) are NFCs, and six (Nos. 4223–4229) are substances with a non-flavor function that are used in the preparation of finished food flavors.

GRAS 22 also presents elements of the guide for the safety evaluation of NFCs composed exclusively of volatile constituents (essential oils and distillates) and its application to the GRAS evaluation of corn mint oil, *Mentha arvensis* L. and the GRASr evaluation of lemongrass oil, *Cymbopogon citratus* (DC) Stapf. and *Cymbopogon flexuosus* (Nees ex. Steud.).

Safety Assessment of Natural Flavor Complexes

Publication of GRAS 18 (Newberne et al., 1998) provided the first insights into the Panel's approach to the safety evaluation of NFCs. Fundamentally, biological responses are the result of the in-vivo interactions of one or more molecules in an NFC or their metabolites with macromolecules (proteins, enzymes, etc.). Molecules exert their flavor function by binding to receptor proteins of the gustatory or olfactory systems at extremely low levels of exposure. It has been estimated that as few as 40 molecules produces an identifiable sensation (Devries and Stuiver, 1961). When distributed in the body at much higher levels, these same molecules—and, in some cases, their metabolites—bind an assortment of proteins and other macromolecules, potentially leading to toxicity.

Based on years of experience reviewing the database of information on NFCs and their chemically identified constituents, the Panel has concluded that a scientifically based evaluation of an NFC should involve a comprehensive evaluation of available data for the NFC and the chemical constituents that make up the NFC. The method for a constituent-based safety evaluation of essential oils is the subject of recent publications (Smith et al., 2004, 2005a).

Previous safety evaluations of NFCs have followed more-traditional approaches. Typically, a representative sample of the NFC with recognized physical specifications was subjected to a battery of toxicology tests. If sufficient margins of safety existed between estimated intakes of the NFC and no-effect levels in animal studies, intake of the NFC was concluded to be safe. Of course, key assumptions are inherent in the standard toxicologic approach: (1) the sample of an NFC to be tested is representative of the product in the marketplace now or at some point in the future; (2) NFCs are derived from nature and subjected to further physical processing (i.e., distillation, blending, etc.); and (3) there is without exception variability in the composition that is not accounted for in the testing of a single sample. Treating an NFC as a single chemical entity leaves no flexibility for evaluating the safety of the full range of product used in the marketplace over an extended period of time.

The recent influx of GRAS candidates is related to international interest in ***developing a global positive list of flavoring substances.***

For certain NFCs, a comprehensive chemical characterization may not always be practical or even possible. In these instances, the standard toxicological approach may be the only viable option for determining safety in use. However, given the advances in low-cost, high-throughput technology to identify and quantify NFC constituents, it is more often feasible to chemically

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characterize a full range of commercial samples of an essential oil over an extended period of time than to subject the mixture to a standard battery of toxicity tests for a product that may not be fully representative of the product in commerce now or in the future.

The guide is a chemically based procedure for the safety evaluation of existing GRAS NFCs and new candidate GRAS NFCs for their intended use as flavoring substances (Smith et al, 2005b). In its current form, the guide is limited to essential oils and distillates in which essentially all of the mass of the NFC is composed of volatile constituents. The procedure will almost certainly undergo revisions and refinements, given its early stage of development and, more importantly, this endeavor is the first practical but exhaustive attempt to evaluate naturally occurring complex mixtures based on their actual chemical composition and the variability of that composition for the product in commerce.

The guide considers the safety of all chemically identified and unidentified chemical constituents of the essential oil with the intent that no significant part of the oil goes unevaluated. Since experience in toxicology, biochemistry, chemistry, and pathology and a thorough knowledge of natural products chemistry and structure–activity relationships all play a major role in the evaluation, a broad range of scientific expertise and judgment are required to successfully apply this guide to essential oils.

Extensive data on botanical origin, physical properties, isolation processes, intake of the essential oil, and qualitative and quantitative analytical data for the chemical composition of the product in commerce are required for the successful use of the guide. To effectively evaluate an essential oil, attempted complete analyses (analyses for all of the constituents) must be available for the product intended for the marketplace. The industry is therefore obligated to collect analytical data on many different samples of a commercial essential oil to ensure that the evaluation is representative of the flavoring product used worldwide.

Additional quality control data of key flavor constituents is useful, since it demonstrates consistency in the chemical composition of the product being marketed over time. These composition data are not to be confused with analytical data collected for the crude oil isolated in the field. These analytical data are used mainly to improve field crop yields and oil yields. Only those data collected on the finished essential oil intended for their addition as flavorings to food are used as the basis for the safety evaluation.

Steps in Safety Evaluation

Smith et al. (2005a) provides a detailed discussion of each step of the guide. The discussion below is an outline of the guide and a summary of the results of the evaluation for a new GRAS essential oil, corn mint oil, and the GRAS reaffirmation of lemongrass oil. Basically, the guide consists of five parts:

1. Comparison of the intake of an essential oil (e.g., basil oil) intentionally added to food and the intake of the oil as the result of consuming the plant source as a food (e.g., basil). Presumably, if the intake of the oil occurs principally through consumption as a food and not from added flavor use, then the concern for safety of the flavor use of the oil is significantly reduced. »»

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However, in cases such as corn mint oil, in which the plant is not consumed primarily as a food, a more rigorous set of criteria are applied to the evaluation, especially the unidentified constituents. This step is followed by a series of steps that organize and prioritize the constituents for further evaluation.

2. The chemically identified constituents are assigned to congeneric groups, and each group is prioritized according to its relative intake from consumption of the oil as a flavor, its metabolic fate, and its potential toxicity (Structural Classes I, II, or III; Cramer et al., 1978; Munro et al., 1996). For more than a decade, the Panel has used toxicity and metabolic data to organize the large number of chemically identified GRAS substances (>1,900), the majority of which are naturally occurring, into congeneric groups (e.g., aliphatic terpene hydrocarbons; limonene, campene, myrcene, pinene, etc.) that exhibit similar metabolic fate and toxic potential. Biochemical data support the conclusion that substances in the group undergo enzyme-catalyzed reactions to yield metabolites that are readily excreted or further metabolized to carbon dioxide and water. Toxicity data support the conclusion that the differences in toxic potency between members of a congeneric group are small compared to the large differences between intake of members of the group as flavorings and toxic dose levels. Additionally, consistent toxicity and genotoxicity data demonstrate that small molecular changes among members of a congeneric group generally do not significantly alter toxic potency (Table 4).

3. In the next part, the intake of each congeneric group is evaluated with respect to metabolic pathways available for the safe disposition of the members of the group. If an intoxication pathway has been identified that may play a significant role in the safe disposition of the substance, this is cause to separate that substance or substances into a different congeneric group (see pulegone, below).

The congeneric group is assigned to a structural class (Cramer et al., 1978) that relates structure to potential toxicity. If the group (e.g., aliphatic monoterpene hydrocarbons) has structural features that allow for its efficient and rapid detoxication, it is assigned to Structural Class I. If its structural features or those of a principal metabolite indicate intoxication (e.g., 2-isopropylidenecyclohexanones, pulegone), it is assigned to Structural Class III. Chemicals of questionable biochemical and biological fate are assigned to Structural Class II.

Based on these three structural classes, the intake of the congeneric group is then compared to thresholds for toxicity (human exposure thresholds) obtained from a large database of no-observable-effect levels (NOELs) for a wide range of chemical substances (Munro et al., 1996). This step involves a comparison of intake for the congeneric group to no-effect levels for a large group of substances in the same structural class. If the intake exceeds 100 times the 5th-percentile NOEL (i.e., only 5% of the substances in the structural class have lower NOELs), toxicity data for representative members of the group are required.

The NOELs for these substances (e.g., menthol and menthone) are compared to the intake of the group (alicyclic secondary alcohols/ketones and related esters) to ensure that adequate margins of safety exist between intake of the group and no-effect levels in toxicity studies. At no point does the evaluation involve isolated consideration of data on an individual constituent. Rather, congeneric groups are evaluated in the context of all data available for members of the group.

In terms of effort, instead of individually evaluating each of the chemically identified constituents in isolation (e.g., 150 constituents of corn mint oil), the guide focuses on the comprehensive evaluation of a few congeneric groups (3–8) containing these constituent chemicals.

4. Subsequently, the total intake of unidentified constituents is evaluated by comparing intake through added flavor use to intake from consumption of food. If intake through food use exceeds added flavor use, there is little concern for the intake of the unidentified constituents. However, if intake of the essential oil is not principally from intake of food, the intake is compared to the most conservative exposure threshold (90 μg/person/day for Structural Class III).

If intake is toxicologically insignificant (<90 µg/person/day), then safety concern for intake of unidentified constituents is reduced. If intake of the unidentified constituents exceeds this level, then toxicity data on the essential oil or an oil of similar composition is required, or additional analyses must be obtained to reduce the number and intake of unidentified constituents in the essential oil.

Although the unidentified constituents are placed in the highest class of toxicological concern, it does not necessarily mean that the structures of these substances present a safety concern. In reality, many of the unidentified constituents are expected to belong to the same congeneric groups in the NFC. They often represent shoulders on a gas or liquid chromatographic peak for a constituent of known structure, possibly a double-bond isomer or dihydro derivative. It is noteworthy that most newly identified naturally occurring constituents (Nijssen et al., 2003) are structurally related to constituents previously identified in that NFC. Therefore, the assignment of these substances to Structural Class III is a conservative default feature of the guide.

5. When the evaluation of the intake of each congeneric group and the total intake of unidentified constituents is completed, the essential oil itself is evaluated in the context of the combined intake of all congeneric groups and the total of unidentified constituents, plus any other related data (e.g., data on the essential oil itself or on an essential oil of similar composition). The guide organizes the extensive database of information on the NFC to efficiently evaluate the essential oil under conditions of intended use. It is, however, not intended to be a rigid checklist. The Panel will continue to evaluate each essential oil on a case-by-case basis, applying their scientific judgment to ensure that no significant part of the NFC goes unevaluated.

An important issue for the flavor industry is the relationship of the results of the safety evaluation to the specifications for the essential oil placed into commerce. An essential oil produced under good manufacturing practices (GMPs) should be of a purity (quality) and chemical composition sufficiently high to represent a reasonable certainty of safety under conditions of intended use. In addition to specifying the biological origin, physical and chemical properties, and other identifying characteristics of the essential oil, specifications must include the chemical assay for the essential oil in commerce to link the chemical composition of the essential oil to the safety evaluation.

The chemical assay requirements should not create an undue burden on the industry and should be easily incorporated into an ongoing quality control program that monitors key constituents reflecting flavor function of an essential oil. They should be consistent with other published specifications for chemical assay such as those listed for essential oils in the 5th edition of *Food Chemicals Codex* (FCC, 2003) and those of the International Organization for Standardization (ISO).

To meet the above conditions and be consistent with the results of the safety evaluation, the chemical assay should specify (1) upper limits of concentrations for key congeneric groups that constitute the vast majority of the oil; (2) key constituents in congeneric groups that would be monitored in an ongoing quality control program that also reflect the technical flavor function of the product (e.g., linalool in coriander oil or menthol in peppermint oil); and (3) information on constituents exhibiting a higher order of toxicity or the group of unidentified constituents that may be of a safety concern at sufficiently high levels of intake (e.g., pulegone in peppermint oil, *Mentha piperita*).

The scope of a specification should be sufficient to ensure safety in use, but not impose an obligation on the industry to perform ongoing analyses for constituents unrelated to the safety or to the flavor function of the essential oil.

This approach is illustrated below by the safety assessment of corn mint oil and lemongrass oil. The daily per capita intake is calculated by the equation shown in the accompanying graphic.

EQUATION

$$\text{mg/person/day} = \frac{(\text{anticipated annual volume, kg/year})(10^6\ \text{mg/kg})}{(\text{population} \times 0.1)(365\ \text{days/year})}$$

where U.S. population = 2.8×10^8 in 2003 and 0.1 represents "eaters only" (10% of the population.)

$$\text{mg/kg bw/day} = \frac{\text{mg/person/day}}{\text{60-kg body weight}}$$

Safety Assessment of Corn Mint Oil

Corn mint oil (FEMA No. 4219) is produced by the steam distillation of the flowering herb of *M. arvensis*. The crude oil contains more than 70% (–)-menthol, some of which is isolated by crystallization at low temperature. The resulting dementholized oil is corn mint oil.

Although produced mainly in Brazil during the 1970s and 1980s, corn mint oil is now produced predominantly in China and India. Corn mint oil has a more stringent taste compared to that of peppermint oil, *M. piperita*, and therefore is a cheaper substitute for peppermint oil.

Corn mint oil isolated from various crops undergoes subsequent "clean up," further distillation, and blending to produce the finished commercial oil. The analytical data cited below are representative of samples of commercial oil intended for use in flavorings. Although there may be significant variability in the concentrations of

individual constituents in different samples of crude essential oil, there is far less variability in the concentration of constituents and congeneric groups in the finished commercial oil. Also, corn mint oil is not normally consumed as a food. Therefore, the total of unidentified constituents must be considered in light of data on intake, toxicity thresholds, and actual toxicity data for the oil or an oil of similar chemical composition.

• **Principal Congeneric Group.** In corn mint oil, the principal congeneric group is composed of terpene alicyclic secondary alcohols, ketones, and related esters, as represented by the presence of (–)-menthol, (–)-menthone, (+)-isomenthone, (–)-menthyl acetate, etc. Samples of triple-distilled commercial corn mint oil may contain up to 95% of this congeneric group. The biochemical and biological fate of this group of substances has been previously reviewed (Adams et al., 1996; JECFA, 1999). Key data on metabolism, toxicity, and carcinogenicity are cited in Table 5 to complete the evaluation.

Corn mint oil is anticipated to develop a market of 200,000 kg/year, or approximately 10% of the market for peppermint oil, which corresponds to a daily per capita intake ("eaters only") of approximately 20 mg/person/day (0.333 mg/kg bw/day) of corn mint oil. Although constituents in this group are effectively detoxicated via conjugation of the corresponding alcohol or ω-oxidation followed by conjugation and excretion (Yamaguchi et al., 1994; Madyastha and Srivatsan, 1988; Williams, 1940), the intake of the congeneric group (19 mg/person/day) is higher than the exposure threshold of 0.54 mg/person/day for Structural Class II. Therefore, toxicity data are required for this congeneric group.

In both long- and short-term studies (Madsen et al., 1986; NCI, 1979), menthol, menthone, and other members of the group exhibit no-observable-adverse-effect levels (NOAELs) at least 1,000 times the daily per capita intake ("eaters only") (0.32 mg/kg bw/day) of this congeneric group resulting from intake of the essential oil. Numerous in-vitro and in-vivo genotoxicity assays are consistently negative (Heck et al., 1989; Sasaki et al., 1989; Muller, 1993; Florin et al., 1980; Rivedal et al., 2000, Zamith et al., 1993; NTP, 2003a) for members of this group. Therefore, the intake of this congeneric group from consumption of *M. arvensis* is not of a safety concern.

• **Pulegone.** Although it is a constituent of corn mint oil and is also a terpene alicyclic ketone structurally related to the above congeneric group, pulegone exhibits a unique structure (i.e., 2-isopropylidenecyclohexanone) that participates in a well-recognized intoxication pathway (McClanahan et al., 1989; Thomassen et al., 1992; Adams et al., 1996; Chen et al., 2001) leading to hepatotoxicity at intake levels at least an order of magnitude less than the NOELs for structurally related alicyclic ketones and secondary alcohols (menthone, carvone, and menthol). Therefore, pulegone and its metabolite (menthofuran) that account for <2% of commercial corn mint oil are considered separately. In this case, the daily per capita intake ("eaters only") of 0.40 mg/person/day (0.0067 mg/kg bw/day) exceeds the 0.09 mg/kg bw/day threshold for Class III. However, a 90-day study on pulegone (NTP, 2002) showed a NOAEL (9.375 mg/kg bw/day) that is approximately 1,000 times the intake of pulegone and its metabolites as constituents of corn mint oil.

Also, in a 28-day study (Serota, 1990) with peppermint oil, *M. piperita,* containing approximately 4% pulegone and menthofuran, a NOAEL of 200 mg/kg bw/day for male rats and a NOAEL of 400 mg/kg bw/day for female rats were established, which corresponds to a NOAEL of 8 mg/kg bw/day for pulegone and menthofuran. In a 90-day study with a mixture of *M. piperita* and *M. arvenesis* peppermint oils (Splindler and Madsen, 1992; Smith et al., 1996a), a NOAEL of 100 mg/kg bw/day was established, which corresponds to a NOAEL of 4 mg/kg bw/day for pulegone and menthofuran.

Photo courtesy of David Michael & Co.

• **Terpene Hydrocarbons.** The only other congeneric group that accounts for >2% of the composition of corn mint oil is a congeneric group of terpene hydrocarbons: (+) and (–)-pinene, (+) limonene, etc.). Although these may contribute up to 8% of the oil, upon multiple redistillations during processing the hydrocarbon content can be significantly reduced (<3%) in the finished commercial oil. Using the 8% figure to determine a conservative estimate of intake, the intake of terpene hydrocarbons is 1.6 mg/person/day (0.027 mg/kg bw/day).

This group is predominantly metabolized by CYP P-450–induced hydroxylation and excretion in conjugated form (Ishida et al., 1981; Madyastha and Srivatsan, 1987; Crowell et al., 1994; Poon et al., 1996; Vigushin et al., 1998; Miyazawa et al., 2002). The daily per capita intake (1.60 mg/person/day) is slightly less than the exposure threshold (1.80 mg/person/day) for Structural Class I. Although no additional data would be required to complete the evaluation of this group, NOAELs (300 mg/kg bw/day) from long-term studies (NTP, 1990) on principal members of this group are orders of magnitude greater than the daily per capita intake ("eaters only") of terpene hydrocarbons (0.025 mg/kg bw/day). Therefore, all

Photo courtesy of Takasago Corp.

congeneric groups in corn mint oil are considered safe for use when consumed in corn mint oil.

• **Unidentified Constituents.** The total of unidentified constituents in commercial corn mint oil range from a low of 2.9% up to 4%. This corresponds to a daily per capita intake ("eaters only") of up to approximately 0.80 mg/person/day). This exceeds the 0.09 mg/person/day for the structural class of highest toxic concern (Class III). Therefore toxicity data are required on the essential oil or one of a similar chemical composition. A 28-day study on peppermint oil containing essentially the same constituents as corn mint oil shows NOAELs of 100 mg/kg/day for the oil, equivalent to 5 mg/kg bw/day for the unidentified constituents (Serota, 1990), which is at least 100 times the intake (0.0133 mg/kg bw/day) of unidentified constituents present in corn mint oil. Hence the total of unidentified constituents is also not a safety concern.

• **The Essential Oil.** Finally, the essential oil itself is evaluated in the context of the combined intake of all congeneric groups and the total of unidentified constituents, and any other related data. Interestingly, members of the terpene alicylic secondary alcohols, ketones, and related esters, multiple members of the monoterpene hydrocarbons, and peppermint oil itself show a common nephrotoxic effect recognized as α-2u-globulin nephropathy. The pathologists on the Panel evaluated kidney data for male rats in the mint oil study and determined that the data were consistent with the presence of α-2u-globulin nephropathy.

In addition, a standard immunoassay for detecting the presence of α-2u-globulin was performed on kidney sections from male and female rats in the mint oil study (Serota, 1990). Results of the assay confirmed the presence of α-2u-globulin nephropathy in male rats (Swenberg and Schoonhoven, 2002). This effect is found only in male rats and is not relevant to the human health assessment of corn mint oil. Other toxic interactions between congeneric groups are expected to be minimal, given that the NOELs for the congeneric groups and those for finished mint oils are on the same order of magnitude.

• **Criteria for GRAS Status.** Based on the above assessment and the application of the scientific judgment of the FEMA Expert Panel, corn mint oil is concluded to be "generally recognized as safe" under conditions of intended use as a flavoring substance. Given the criteria used in the evaluation, recommended specifications should include the following chemical assay: (1) <95% alicyclic secondary alcohols, ketones, and related esters, typically measured as (–)-menthol; (2) <2% 2-isopropylidenecyclohexanones and their metabolites, measured as (–)-pulegone; and (3) <10% monoterpene hydrocarbons, typically measured as limonene.

Safety Assessment of Lemongrass Oil

Lemongrass oil (FEMA No. 2624) is produced by the steam distillation of the freshly cut or slightly dried grasses of *Cymbopogon citratus* or *Cymbopogon flexuosus*. The two oils were formerly the main source of natural citral containing upward of 75% of a mixture of neral and geranial in a ratio of approximately 1:4. However, the commercial importance of lemongrass oil has declined as a result of competition from synthetic citral and natural citral from *Litsea cubeba* oil. *C. citratus*, the West Indian Type, is produced in Central and South America as well as in Africa and East Asian countries, while *C. flexuosus* is primarily a product of India.

***Corn mint oil is** concluded to be **"generally recognized as safe"** under conditions of intended use as a flavoring substance.*

Lemongrass oil has a lemon-like aroma characteristic of citral. The analytical data cited below are representative of samples of commercial oil intended for use in flavorings. Although consumption of lemongrass as a food in the United States has sharply risen in the past few years, quantitative data on its consumption are not available.

The annual volume of use of lemongrass oil as a flavoring substance has decreased from approximately 5,100 kg in 1975 to 1,470 kg in 1999 (NAS, 1975; Lucas et al., 1999). Based on the most recent data, the daily per capita intake ("eaters only") is 0.194 mg/person/day (0.0032 mg/kg bw/day).

• **Principal Congeneric Group.** The principal congeneric group in either the West or East Indian types of lemongrass oil is terpene branched-chain primary alcohols (geraniol, nerol, citronellol), aldehydes (citral as a mixture of geranial and neral),

GRAS

acids, and related esters. Analyses of distilled commercial oils reveal that lemongrass oil typically contains 80% of this congeneric group, with citral accounting for the majority.

The biochemical and biological fate of this group of substances has been previously reviewed (JECFA, 2004) and indicates that the major constituents of this congeneric group are effectively detoxicated via oxidation of the corresponding alcohol or aldehyde or ω-oxidation of the branched chain to yield polar polyoxygenated metabolites that are readily excreted either free or in conjugated form (Chadha and Madyastha, 1982; Boyer and Petersen, 1990; Diliberto et al., 1990). The intake of the congeneric group (0.155 mg/person/day) is less than the exposure threshold (1.80 mg/person/day) for Structural Class I. Given the extremely low intake from use of lemongrass oil as a flavoring substance, no toxicity data are required for this congeneric group. Therefore, the intake of this congeneric group from consumption of lemongrass oil is not a safety concern.

In the event that intake of lemongrass oil were to increase significantly (e.g., 20 times the current level of 0.155 mg/person/day for this congeneric group and exceed the human exposure threshold (>1.80 mg/person/day) for Structural Class I, there are numerous subchronic and chronic toxicity and carcinogenicity studies for citral (Hagan et al., 1967; NTP, 2003b), geraniol (Hagan et al., 1967), citronellol (Oser, 1958), and other members of the group (NTP, 1987) that show NOAELs at least three orders of magnitude greater than the hypothetical daily per capita intake ("eaters only") (3.1 mg/person/day) of this congeneric group resulting from 20 times the current intake of the essential oil.

• Terpene Hydrocarbons. Like corn mint oil, the only other congeneric group that accounts for >2% of the composition of lemongrass oil is a congeneric group of terpene hydrocarbons: (+) limonene, myrcene, etc. This group may account for approximately 10% of lemongrass oil. The intake of terpene hydrocarbons is approximately 0.019 mg/person/day. The metabolism of this group has been discussed previously. The daily per capita intake (0.019 mg/person/day) is approximately 100 times lower than the exposure threshold (1.80 mg/person/day) for Structural Class I. Because intake of this group does not exceed the threshold, no additional data are required. The intake of this congeneric group from consumption of lemongrass oil does not present a safety concern.

• Unidentified Constituents. The total of unidentified constituents in lemongrass oil is less than 3%. This corresponds to a daily per capita intake ("eaters only") of up to approximately 0.006 mg/person/day. This intake is lower than the 0.09 mg/person/day threshold for the structural class of highest toxic concern (Class III). Therefore, the total of unidentified constituents does not present a safety concern.

• Criteria for GRAS Status. In the context of the combined intake of all congeneric groups and the total of unidentified constituents, and any other related data, there is no evidence of any interaction that would present a safety concern. Based on the above assessment and the application of the scientific judgment of the FEMA Expert Panel, lemongrass oil is reaffirmed as "generally recognized as safe" under conditions of intended use as a flavoring substance (Table 6).

Lemongrass oil is reaffirmed as "generally recognized as safe" *under conditions of intended use as a flavoring substance.*

Given the criteria used in the evaluation, recommended specifications should include the following chemical assay: (1) <92% terpene aliphatic branched-chain primary alcohols, aldehydes, carboxylic acids, and related esters, typically measured as citral; and (2) <20% monoterpene hydrocarbons, typically measured as (+)-limonene or myrcene. **FT**

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***Robert L. Smith**, Chairman of the FEMA Expert Panel, is Professor, Molecular Toxicology, Imperial College School of Medicine, University of London, South Kensington, London SW7 2AZ, United Kingdom. Other members of the FEMA Expert Panel are **Samuel M. Cohen,** Professor and Chair, Dept. of Pathology and Microbiology, University of Nebraska Medical Center, Omaha; **John Doull**, Professor Emeritus, University of*

Corrections & Changes

The chemical name for FEMA No. 2563 in GRAS 3 (Hall and Oser, 1965) was incorrectly listed as 3-hexen-1-ol; the correct name is *cis*-3-hexen-1-ol.

The chemical name for FEMA No. 2564 in GRAS 3 was incorrectly listed as 2-hexen-1-yl acetate; the correct name is *trans*-2-hexen-1-yl acetate.

2,2′-(Dithiodimethylene)-difuran (FEMA No. 3146) reported in GRAS 4 (Hall and Oser, 1970) and bis(2-furfuryl) disulfide (FEMA No. 3257) reported in GRAS 5 (Oser and Hall, 1972) are identical materials. Consequently, FEMA No. 3257 has been deleted from the GRAS list.

The chemical name for FEMA No. 3283 in GRAS 5 was incorrectly listed as furfuryl 2-methylbutanoate; the correct name is furfuryl 3-methylbutanoate.

The chemical name for FEMA No. 3353 in GRAS 6 (Oser and Ford, 1973a) was incorrectly listed as 3-hexenyl formate; the correct name is *cis*-3-hexenyl formate.

The chemical name for FEMA No. 3638 in GRAS 12 (Oser and Ford, 1979) was incorrectly listed as 2-*trans*-4-*cis*-7-*cis*-tridecadienal; the correct name is 2-*trans*-4-*cis*-7-*cis*-tridecatrienal.

The chemical name for FEMA No. 3761 in GRAS 15 (Burdock et al., 1990) was listed incorrectly as 5-methyl-2-hept-4-one; the correct name is 5-methyl-2-hepten-4-one.

The chemical name for FEMA No. 3770 in GRAS 15 was listed incorrectly as 3-oxo-hexanoic acid diglyceride; the correct name is 3-oxo-hexanoic acid glyceride.

The use levels for FEMA 3804, 2-isopropyl-*N*,2,3-trimethybutyramide, were incomplete as reported in GRAS 17 (Smith et al., 1996a); an average usual use level of 3 ppm and an average maximum use level of 8 ppm in non-alcoholic beverages should also have been listed.

The chemical name for FEMA No. 4054 in GRAS 21 (Smith et al., 2003) was listed incorrectly as 1-menthyl methyl ether; the correct name is *l*-menthyl methyl ether.

Bernard Wagner retired from the FEMA Expert Panel in October 2003 after a distinguished tenure but will remain an Emeritus member of the Panel.

John Doull retired as a consultant to the Panel in October 2003 but will remain an Emeritus member of the Panel.

Kansas Medical School, Kansas City; ***Victor J. Feron****, TNO Quality of Life, Professor Emeritus, Biological Toxicology, Utrecht University, Zeist, The Netherlands;* ***Jay I. Goodman****, Professor, Dept. of Pharmacology and Toxicology, Michigan State University, East Lansing;* ***Lawrence J. Marnett****, Dept. of Biochemistry, Center in Molecular Toxicology, School of Medicine, Vanderbilt Institute of Chemical Biology, Nashville, Tenn.;* ***Philip S. Portoghese****, Professor, College of Pharmacy, University of Minnesota, Minneapolis;* ***William J. Waddell****, Professor and Chair, Emeritus, Dept. of Pharmacology and Toxicology, University of Louisville School of Medicine, Louisville, Ky; and* ***Bernard M. Wagner****, Emeritus Research Professor of Pathology, New York University Medical Center, New York, N.Y.* ***Timothy B. Adams*** *is the Scientific Secretary for the FEMA Expert Panel and Scientific Director of the Flavor and Extract Manufacturers Association, 1620 I St., N.W., Suite 925, Washington, DC 20006. Send reprint requests to author Adams (tadams@therobertsgroup.net).*

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Table 1: Primary Names & Synonyms

Primary names(in boldfaced capital letters, listed alphabetically) & Synonyms (in lower case)

FEMA No.	Substance primary name and synonyms
4069	**(+/-)-1-Acetoxy-1-ethoxyethane** Ethanol, 1-ethoxy-, acetate 1-Ethoxy-1-ethanol acetate 1-Ethoxyethyl acetate
4070	**4-Acetyl-2,5-dimethyl-3(2*H*)-furanone** 3(2*H*)-Furanone, 4-acetyl-2,5-dimethyl-
4071	**2-Acetyl-3,5-dimethylfuran** Ethanone, 1-(3,5-dimethyl-2-furanyl)- Ketone, 3,5-dimethyl-2-furyl methyl 3,5-Dimethyl-2-furyl methyl ketone
4072	**Allyl crotonate** 2-Butenoic acid, 2-propenyl ester Crotonic acid, allyl ester
4073	**Allyl propyl disulfide** Disulfide, 2-propenyl propyl Disulfide, allyl propyl 2-Propenyl propyl disulfide 4,5-Dithia-1-octene Propyl allyl disulfide
4074	**Allyl valerate** Pentanoic acid, 2-propenyl ester Valeric acid, allyl ester
4075	**4-Allylphenol** Phenol, 4-(2-propenyl)- Chavicol Phenol, *p*-allyl- 3-(*p*-Hydroxyphenyl)-1-propene *p*-Hydroxyallylbenzene
4076	**Allyl thiohexanoate** Hexanethioic acid, *S*-2-propenyl ester
4077	***o*-Anisaldehyde** Benzaldehyde, 2-methoxy- 2-Anisaldehyde 2-Methoxybenzaldehyde 2-Methoxybenzenecarboxaldehyde 2-Methoxyphenylformaldehyde *o*-Formylanisole *o*-Methoxybenzaldehyde Salicylaldehyde methyl ether
4078	***N*-Benzoylanthranilic acid** 2-Benzoylaminobenzoic acid Dianthramid B Benzoic acid, 2-(benzoylamino)- Anthranilic acid, *N*-benzoyl- 2-Carboxybenzanilide *N*-(2-Carboxyphenyl)benzamide
4079	**Thujyl alcohol** Bicyclo[3.1.0]hexan-3-ol, 4-methyl-1-(1-methylethyl)-, (1*S*,3*S*,4*R*,5*R*)- 3-Thujanol, (1*S*,3*S*,4*R*,5*R*)-(-)- Bicyclo[3.1.0]hexan-3-ol, 4-methyl-1-(1-methylethyl)-, [1*S*-(1.alpha.,3.alpha.,4.alpha.,5.alpha.)]- (-)-3-Neoisothujanol (-)-Thujol 3-Neoisothujanol, (-)- Thujol, (-)-
4080	***L*-Bornyl acetate** (1*S*-endo)-1,7-Trimethylbicyclo[2.2.1]heptan-2-ol acetate Bicyclo[2.2.1]heptan-2-ol, 1,7,7-trimethyl-, acetate, (1*S*,2*R*,4*S*)- (-)-Bornyl acetate
4081	**2-Butylfuran** Furan, 2-butyl-
4082	**Butyl isothiocyanate** Butane, 1-isothiocyanato- Isothiocyanic acid, butyl ester 1-Isothiocyanatobutane Butyl mustard oil *n*-Butyl isothiocyanate
4083	**2-Butyrylfuran** 1-(2-Furyl)-1-butanone 2-Furyl propyl ketone Furyl *n*-propyl ketone 1-Butanone, 1-(2-furanyl)-
4084	**Carvone-5,6-oxide** 7-Oxabicyclo[4.1.0]heptan-2-one, 1-methyl-4-(1-methylethenyl)- (1*S*,4*R*,6*S*)- 1,6-Epoxy-*p*-Menth-8-en-2-one
4085	***beta*-Caryophyllene oxide** 5-Oxatricyclo[8.2.0.04,6]dodecane, 4,12,12-trimethyl-9-methylene-, (1*R*,4*R*,6*R*,10*S*)- Caryophyllene epoxide
4086	**Citronellyl anthranilate** 6-Octen-1-ol, 3,7-dimethyl-, 2-aminobenzoate
4087	***N*-Cyclopropyl-*trans*-2-*cis*-6-nonadienamide** *N*-Cyclopropyl-(*E*2,Z6)-nonadienamide 2,6-Nonadienamide, *N*-cyclopropyl-, (2*E*,6*Z*)-
4088	***trans*-*alpha*-Damascone** *trans*-1-(2,6,6-Trimethyl-2-cyclohexen-1-yl)but-2-en-1-one 2-Buten-1-one, 1-(2,6,6-trimethyl-2-cyclohexen-1-yl)-,(2*E*)-
4089	**2-*trans*-4-*trans*-7-*cis*-Decatrienal** (2*E*,4*E*,7*Z*)-Decatrienal
4090	**2-Decylfuran** Furan, 2-decyl-
4091	**Dehydronootkatone** 2(3*H*)-Naphthalenone, 4,4a,5,6-tetrahydro-4,4a-dimethyl-6-(1-methylethenyl)-, [4*R*-(4.alpha.,4a.alpha.,6.beta.)]- 5,6-Dimethyl-8-isopropenyl bicyclo[4.4.0]-1,9-decadien-3-one 4.beta.H,5.alpha.-Eremophila-1(10),8,11-trien-2-one 8,9-Didehydronootkatone
4092	**Diacetyl tartaric acid esters of mono- and diglycerides** Glycerides, C8-21 and C8-21-unsatd. mono- and di-, 2-(acetyloxy)-3-hydroxybutanedioates 2,3-bis(acetyloxy)butanedioates Glycerides, mixed mono- and di-, esters with diacetyltartaric acid Diglycerides, mixed monoglycerides and diglycerides, esters with diacetyltartaric acid Monoglycerides, mixed monoglycerides and diglycerides, esters with diacetyltartaric acid DATEM Diacetyltartaric acid esters of mono- and diglycerides Panodan 0165 Datem Panodan 150DATEM Panodan DATEM TR Panodan TR-DATEM
4093	**Diethyl disulfide** Disulfide, diethyl Ethyl disulfide 3,4-Dithiahexane Ethyl disulphide Ethyldithioethane NSC 8839
4094	**Mixture of 3,6-Diethyl-1,2,4,5-tetrathiane and 3,5-diethyl-1,2,4-trithiolane** 1,2,4,5-Tetrathiane, 3,6-diethyl- and 1,2,4-Trithiolane, 3,5-diethyl-
4095	**2,4-Difurfurylfuran** Furan, 2,4-bis(2-furanylmethyl)-
4096	**Diisopentyl thiomalate** Butanedioic acid, mercapto-, bis(3-methylbutyl) ester bis(3-Methylbutyl)mercaptosuccinate
4097	**Dimercaptomethane** Methanedithiol
4098	**1,1-Dimethoxy-*trans*-2-hexene** 1,1-Dimethoxy-*E*-2-hexene 2-Hexene, 1,1-dimethoxy-, (2*E*)- 2-Hexenal, dimethyl acetal, (*E*)- 2-Hexene, 1,1-dimethoxy-, (*E*)- (*E*)-2-Hexenal dimethyl acetal *trans*-2-Hexenal dimethyl acetal
4099	**2,4-Dimethyl-1,3-dioxolane** 1,3-Dioxolane, 2,4-dimethyl- Acetaldehyde cyclic propylene glycol acetal Propylene acetal
4100	**3,5- and 3,6-Dimethyl-2-isobutylpyrazine** Pyrazine, 3,5-dimethyl-3-(2-methylpropyl)- and Pyrazine, 3,6-dimethyl-3-(2-methylpropyl)- 3,5-Dimethyl-3-(2-methylpropyl)-1,4-diazine and 3,6-Dimethyl-3-(2-methylpropyl)-1,4-diazine
4101	**2,5-Dimethyl-3(2*H*)-furanone** 3(2*H*)-Furanone, 2,5-dimethyl- 2,3-Dihydro-2,5-dimethyl-3-furanone 2,5-Dimethyl-2,3-dihydrofuran-3-one 2,5-Dimethyl-2*H*-furan-3-one
4102	**(+/-)-*trans*- and *cis*-4,8-Dimethyl-3,7-nonadien-2-ol** (+/-)*E*- and *Z*-4,8-Dimethyl-3,7-nonadien-2-ol 3,7-Nonadien-2-ol, 4,8-dimethyl- (*E*,*Z*)-
4103	**(+/-)-*trans*- and *cis*-4,8-Dimethyl-3,7-nonadien-2-yl acetate** (+/-)*E*- and *Z*-4,8-Dimethyl-3,7-nonadien-2-yl acetate 3,7-Nonadien-2-ol, 4,8-dimethyl-, acetate (*E*,*Z*)-
4104	**2,5-Dimethyl-4-ethoxy-3(2*H*)-furanone** 3(2*H*)-Furanone, 4-ethoxy-2,5-dimethyl- 2,3-Dihydro-2,5-dimethyl-4-ethoxy-3-furanone 2,5-Dimethyl-2,3-dihydro-4-ethoxyfuran-3-one 2,5-Dimethyl-4-ethoxy-2*H*-furan-3-one
4105	**(+/-)-*trans*- and *cis*-5-(2,2-dimethylcyclopropyl)-3-methyl-2-pentenal** (+/-) *E*- and *Z*-5-(2,2-Dimethylcyclopropyl)-3-methyl-2-pentenal 2-Pentenal, 5-(2,2-dimethylcyclopropyl)-3-methyl- (*E*,*Z*)- Acitral
4106	**2,5-Dimethylfuran** Furan, 2,5-dimethyl-
4107	**Divanillin** [1,1'-Biphenyl]-3,3'-dicarboxaldehyde, 6,6'-dihydroxy-5,5'-dimethoxy- 3,3'-Biphenyldicarboxaldehyde, 6,6'-dihydroxy-5,5'-dimethoxy- 6,6'-Dihydroxy-5,5'-dimethoxybiphenyldicarboxaldehyde

FEMA No.	Substance primary name and synonyms
	2,2′-Dihydroxy-3,3′-dimethoxy-5,5′-diformylbiphenyl
	5,5′-Bivanillin
	Dehydrodivanillin
4108	**(+/-)-2,8-Epithio-*cis*-*p*-menthane**
	6-Thiabicyclo[3.2.1]octane, 4,7,7-trimethyl-, (Z)-
	Zestoril
4109	**Epoxyoxophorone**
	7-Oxabicyclo[4.1.0]heptane-2,5-dione, 1,3,3-trimethyl-
	3,5,5-Trimethyl-2,3-epoxycyclohexane-1,4-dione
4110	**Tomato lycopene**
	psi,*psi*-Carotene
	Lycopersicon esculentum
	all-*trans*-Lycopene
4111	**Ethane-1,1-dithiol**
	1,1-Ethanedithiol
4112	**Ethyl *cis*-3-hexenoate**
	Ethyl *Z*-3-hexenoate
	Ethyl (3*Z*)-hexenoate
4113	***N*-Ethyl *trans*-2-*cis*-6-nonadienamide**
	2,6-Nonadienamide, *N*-ethyl-, (2*E*,6*Z*)-
4114	**Ethyl furfuryl ether**
	Furfuryl ethyl ether
	Furan, 2-(ethoxymethyl)-
4115	**Ethyl *N*-ethylanthranilate**
	Benzoic acid, 2-(ethylamino)-, ethyl ester
	Ethyl *o*-(ethylamino)benzoate
4116	**Ethyl *N*-methylanthranilate**
	Benzoic acid, 2-(methylamino)-, ethyl ester
	Anthranilic acid, *N*-methyl-, ethyl ester
	Ethyl 2-(methylamino)benzoate
4117	**(+/-)-4-Ethyloctanal**
	Octanal, 4-ethyl
	Excital
4118	**Eugenyl isovalerate**
	4-Allyl-2-methoxyphenyl isovalerate
	Butanoic acid, 3-methyl-, 2-methoxy-4-(2-propenyl)phenyl ester
4119	**Furfuryl 2-methyl-3-furyl disulfide**
	3-[2-Furanylmethyl)dithio]-2-methylfuran
	2-Methyl-3-[(2-furanylmethyl)-dithio]furan
	(2-Methyl-3-furyl) furfuryl disulfide
	3-(Furfuryldithio)-2-methylfuran
	2-Methyl-3-furyl 2-furylmethyl disulphide
4120	**1-(2-Furyl)butan-3-one**
	1-(2-Furanyl)-3-butanone
	1-(2-Furyl)-3-butanone
	4-(2-Furyl)-2-butanone
	Furfurylacetone
	2-Butanone, 4-(2-furanyl)-
4121	**Geranic acid**
	(*E*2),6-Octadienoic acid, 3,7-dimethyl-
	3,7-Dimethyl-2,6-octadienoic acid, (*E*)-
4122	**Geranyl 2-methylbutyrate**
	Butanoic acid, 2-methyl-, (2*E*)-3,7-dimethyl-2,6-octadienyl ester
	Butanoic acid, 2-methyl-, 3,7-dimethyl-2,6-octadienyl ester, (*E*)-
	Geranyl 2-methylbutanoate
4123	**Geranyl valerate**
	Pentanoic acid, (2*E*)-3,7-dimethyl-2,6-octadienyl ester
	2,6-Octadien-1-ol, 3,7-dimethyl-, valerate, (*E*)-
	Pentanoic acid, 3,7-dimethyl-2,6-octadienyl ester, (*E*)-
	Valeric acid, 3,7-dimethyl-2,6-octadienyl ester, (*E*)-
	Geraniol valerate
	Geranyl pentanoate
4124	**Glyceryl-lacto esters of fatty acids**
	Durlac 100
	Lactylated mono- and diglyceride
	Glyceryl lactopalmitate/stearate
4125	**Hept-*trans*-2-en-1-yl acetate**
	2-Hepten-1-ol, acetate, (2*E*)-
	2-Hepten-1-ol, acetate, (*E*)-
	(*E*)-2-Heptenyl acetate
	trans-2-Heptenyl acetate
4126	**Hept-2-en-1-yl isovalerate**
	Butanoic acid, 3-methyl-, (*E*2)-heptenyl ester
4127	***trans*-2-*trans*-4-Heptadien-1-ol**
	2,4-Heptadien-1-ol, (2*E*,4*E*)-
	2,4-Heptadien-1-ol, (*E*,*E*)-
	(2*E*,4*E*)-Heptadienol
	(*E*,*E*)-Hepta-2,4-dien-1-ol
4128	**2-Heptanethiol**
	(±)-2-Heptanethiol
4129	**(+/-)-1-Hepten-3-ol**
	Hept-1-en-3-ol
	Butyl vinyl carbinol
4130	***cis*- and *trans*-2-Heptylcyclopropanecarboxylic acid**
	Cyclopropanecarboxylic acid, 2-heptyl- (*E*and *Z*)-
4131	**2,4-Hexadienyl propionate**
	Sorbyl propionate
	2,4-Hexadien-1-ol, propanoate
4132	**2,4-Hexadienyl acetate**
	Sorbyl acetate
	2,4-Hexadien-1-ol, acetate
4133	**2,4-Hexadienyl butyrate**
	Sorbyl butyrate
	Butanoic acid, 2,4-hexadienyl ester
4134	**2,4-Hexadienyl isobutyrate**
	Sorbyl isobutyrate
	Propanoic acid, 2-methyl-, 2,4-hexadienyl ester
4135	**2-Hexenyl octanoate**
	Octanoic acid, 2-hexenyl ester, (*E*)-
4136	**Hexyl 3-mercaptobutanoate**
	Butanoic acid, 3-mercapto-, hexyl ester
	3-Mercaptobutanoic acid hexyl ester
4137	**2-Hexylthiophene**
	Thiophene, 2-hexyl-
4138	**4-Hydroxy-2-butenoic acid *gamma*-lactone**
	2(5*H*)-Furanone
	Crotonic acid, 4-hydroxy-, *gamma*-lactone
	alpha, beta-Crotonolactone
	delta, alpha, beta-Butenolide
	gamma-Crotolactone
	gamma-Crotonolactone
	gamma-Hydroxycrotonic acid lactone
	2,5-Dihydrofuranone
	2-Buten-4-olide
	2-Butenoic acid, 4-hydroxy-, *gamma*-lactone
	2-Oxo-2,5-dihydrofuran
	4-Hydroxy-2-butenoic acid lactone
	5-Oxo-2,5-dihydrofuran-3-yl ester
	5*H*-Furan-2-one
	Cratone
	Isocrotonolactone
4139	**3-Hydroxy-2-octanone**
	2-Octanone, 3-hydroxy-
4140	**2-(2-Hydroxy-4-methyl-3-cyclohexenyl)propionic acid *gamma*-lactone**
	Wine Lactone
	2(3*H*)-Benzofuranone, 3a,4,5,7a-tetrahydro-3,6-dimethyl
	3a,4,5,7a-tetrahydro-3,6-dimethylbenzofuran-2(3*H*)-one
4141	**5-Hydroxy-4-methylhexanoic acid *delta*-lactone**
	2*H*-Pyran-2-one,tetrahydro-5,6-dimethyl-
	Hexanoic acid, 5-hydroxyl-4-methyl-, *delta*-lactone
	4-Methyl-5-hydroxyhexanoic acid lactone
	5,6-Dimethyltetrahydropyran-2-one
4142	**1-(3-Hydroxy-5-methyl-2-thienyl)ethanone**
	Ethanone, 1-(3-hydroxy-5-methyl-2-thienyl)
4143	**(+/-)-2-Hydroxypiperitone**
	Piperitone, 2-hydroxy-
	Diosphenol
	Buccocamphor
	2-Hydroxy-6-isopropyl-3-methyl- 2-cyclohexen-1-one
4144	***beta*-Ionone epoxide**
	3-Buten-2-one, 4-(2,2,6-trimethyl-7-oxabicyclo[4.1.0]hept-1-yl)-
	4-(2,6,6-Trimethyl-7-oxabicyclo[4.1.0]heptane, 3-buten-2-one
	beta-Ionone 5,6-epoxide
	beta-Ionone epoxide
	4-(1,2-Oxido-2,6,6-trimethylcyclohexyl)-3-buten-2-one
	4-(2,6,6-Trimethyl-1,2-epoxycyclohexyl)-3-buten-2-one
	5,6-*beta*-Ionone epoxide
	5,6-Epoxy-*beta*-ionone
4145	**Isoambrettolide**
	Oxacycloheptadec-10-en-2-one
	9-Hexadecenoic acid, 16-hydroxy-, *o*-lactone
	Δ9-Isoambrettolic acid, lactone
	Oxacycloheptadec-10-en-2-one
4146	**Isobornyl isobutyrate**
	Propanoic acid, 2-methyl-, (1*R*,2*R*,4*R*)-1,7,7-trimethylbicyclo[2.2.1]hept-2-yl
4147	**Isobornyl 2-methylbutyrate**
	Butanoic acid, 2-methyl-, 1,7,7-trimethylbicyclo[2.2.1]hept-2-yl ester
4148	***N*-Isobutyldeca-*trans*-2-*trans*-4-dienamide**
	N-Isobutyl (*E*2),(*E*4)-decadienamide
	2,4-Decadienamide, *N*-(2-methylpropyl)-, (2*E*, 4*E*)-
	2,4-Decadienamide, *N*-(2-methylpropyl)-, (*E*,*E*)-
	2,4-Decadienamide, *N*-isobutyl-, (*E*,*E*)-
	(*E*,*E*)-*N*-(2-Methylpropyl)-2,4-decadienamide
	N-(2-methylpropyl)deca-*trans*-2-*trans*-4-dienamide
	N-Isobutyl-2-*trans*-4-*trans*-decadienamide
	N-Isobutyl deca-*trans*-2-*trans*-4-dienamide
	Pellitorin
	Pellitorine
	trans-Pellitorine
4149	**Isobutyl *N*-methylanthranilate**
	Benzoic acid, 2-(methylamino)-, 2-methylpropyl ester
4150	**(+/-)-Isobutyl 3-methylthiobutyrate**
	2-Methylpropyl 3-(methylthio)butyrate
	2-Methylpropyl 3-(methylthio)butanoate

Table 1 *continued*: Primary Names & Synonyms

FEMA No.	Substance primary name and synonyms
	Butanoic acid, 3-(methylthio)-, 2-methylpropyl ester
	Isobutyl 3-(methylthio)butyrate
4151	***beta*-Isomethylionone**
	3-Buten-2-one, 3-methyl-4-(2,6,6-trimethyl-1-cyclohexen-1-yl)-
4152	**Isopropenyl acetate**
4153	**Lactylated fatty acid esters of glycerol and propylene glycol**
	Durlac 300
	Lactylated fatty acid esters of glycerol and propane-1,2-diol
	Propylene glycol lactostearate
4154	**2-(*L*-Menthoxy)ethanol**
	Ethanol, 2-[[5-methyl-2-(1-methylethyl)cyclohexy]oxy]-
	2-(*p*-Menthan-3-yloxy) ethanol
	3-(2-Hydroxyethoxy)-*p*-menthane,
	COOLACT5 (trade name)
4155	**Menthyl pyrrolidone carboxylate**
	D- and L-proline, 5-oxo, 5-methyl-2-(1-methylethyl)cyclohexyl ester
	2-Isopropyl-5-methylcyclohexyl 5-oxo-2-pyrrolidine carboxylate
	Questice
4156	**Menthyl valerate**
	Pentanoic acid, (1*R*,2*S*,5*R*)-5-methyl-2-(1-methylethyl)cyclohexyl ester
4157	**4-Mercapto-2-pentanone**
	2-Pentanone, 4-mercapto-
	4-Mercaptopentan-2-one
4158	**(+/-)-4-Mercapto-4-methyl-2-pentanol**
	2-Pentanol, 4-mercapto-4-methyl-
4159	**2-Mercaptoanisole**
	2-Methoxythiophenol
	Benzenethiol, *o*-methoxy-
	Methoxybenzenethiol
	o-Methoxythiophenol
	Thioguaiacol
4160	**Methionyl butyrate**
	1-Propanol, 3-(methylthio)-, butyrate
	Butyric acid, 3-(methylthio)propyl ester
	3-(Methylthio)propyl butyrate
4161	***trans*- and *cis*-1-Methoxy-1-decene**
	(*E*)- and (*Z*)-1-Methoxy-1-decene
	1-Decene, 1-methoxy- (*E*,*Z*)-
	Decanal methyl enol ether
4162	**(*S*1)-Methoxy-3-heptanethiol**
	3-Heptanethiol, 1-methoxy-, (3*S*)
	ARUSCOL
4163	**2-Methoxyacetophenone**
	1-(2-Methoxyphenyl)ethanone
	2-Acetylanisole
	2-Methoxyphenyl methyl ketone
	Methyl 2-methoxyphenyl ketone
	Methyl *o*-methoxyphenyl ketone
	o-Acetylanisole
	o-Methoxyacetophenone
4164	**Methyl *cis*-3-hexenoate**
	Methyl (*Z*)-3-hexenoate
4165	**Methyl *cis*-5-octenoate**
	5-Octenoic acid, methyl ester, (5*Z*)
4166	**Methyl 3-(methylthio)butanoate**
	3-(Methylthio)butyric acid methyl ester
	Butanoic acid, 3-(methylthio)-, methyl ester
	3-Methylsulfanylbutyric acid methyl ester
4167	**Methyl 3-mercaptobutanoate**
	Butanoic acid, 3-mercapto-, methyl ester
	3-Mercaptobutanoic acid methyl ester
4168	**Methyl isopentyl disulfide**
	Disulfide, isopentyl methyl
	Isoamyl methyl disulfide
	Isopentyl methyl disulfide
	Methyl isopentyl disulfide
4169	**Methyl *N*,*N*-dimethylanthranilate**
	Benzoic acid, 2-(dimethylamino)-, methyl ester
	Anthranilic acid, *N*,*N*-dimethyl-, methyl ester
	Methyl 2-(dimethylamino)benzoate
	Methyl *o*-(dimethylamino)benzoate
4170	**Methyl *N*-acetylanthranilate**
	Benzoic acid, 2-(acetylamino)-, methyl ester
	Anthranilic acid, *N*-acetyl-, methyl ester
	Methyl 2-(acetylamino)benzoate
	Methyl 2-acetamidobenzoate
	Methyl *N*-acetoanthranilate
	o-(Methoxycarbonyl)acetanilide
	o-Acetamidobenzoic acid methyl ester
4171	**Methyl *N*-formylanthranilate**
	Benzoic acid, 2-(formylamino)-, methyl ester
	Methyl *o*-formamidobenzoate
	N-Formylanthranilic acid, methyl ester
4172	***S*-Methyl propanethioate**
	Propanethioic acid, *S*-methyl ester
	S-Methyl thiopropionate
4173	**2-Methyl-1-methylthio-2-butene**
	2-Methyl-1-methylsulfanyl-but-2-ene
	Methyl 2-methyl-2-butenyl sulfide
4174	**3-Methyl-2(3-methylbut-2-en-1-yl)furan**
	alpha-Naginatene
	gamma-Clausenane
	Rosefuran
	2-(3-Methyl-2-butenyl)-3-methylfuran
	Furan, 3-methyl-2-(3-methyl-2-butenyl)-
4175	**3-(5-Methyl-2-furyl)prop-2-enal**
	3-(5-Methylfuryl)acrolein
	1-(5-Methyl-2-furanyl)-1-propen-3-al
	3-(5-Methyl-2-furanyl)-2-propenal
	5-Methyl-2-furanacrolein
	2-Propenal, 3-(5-methyl-2-furanyl)-
4176	**5-Methyl-3(2*H*)-furanone**
	3(2H)-Furanone, 5-methyl-
4177	**6-Methyl-5-hepten-2-yl acetate**
	5-Hepten-2-ol, 6-methyl-, acetate
	(±)-Sulcatol acetate
4178	**2-Methylbut-2-en-1-ol**
4179	**2-Methylfuran**
	alpha-Methylfuran
	Silvan
	Sylvan
	Furan, 2-methyl-
4180	**4-Methylpent-2-enoic acid**
	4-Methyl-2-pentenoic acid
4181	**3-(Methylthio)-2-butanone**
	2-Butanone, 3-(methylthio)-
	(+/-)-3-(Methylthio)butanone
4182	**4-(Methylthio)-2-pentanone**
	2-Pentanone, 4-(methylthio)-
4183	**(+/-)-3-(Methylthio)heptanal**
4184	**3-(Methylthio)methylthiophene**
	3-Methylsulfanylmethylthiophene
4185	**Methylthiomethylmercaptan**
	Methanethiol, 1-methylthio-
	(Methylthio)methanethiol
4186	**Mono- and diglycerides of fatty acids**
	ALPHADIM 90 NLK
	Distilled monoglycerides
	Glycerides, C14-18 mono- and di-
	Glycerides, C14-18 and C16-18-unsat. mono- and di-
	Glycerides, C14-22 mono-
	Monoglycerides, C14-22
4187	**Nona-2,4,6-trienal**
4188	**2-Nonenoic acid *gamma*-lactone**
	5-Pentyl-5*H*-furan-2-one
	2(5*H*)-Furanone, 5-pentyl-
	2-Nonenoic acid, 4-hydroxy-, *gamma*-lactone
4189	***cis*-3-Octenyl propionate**
	Pearlate
	3-Octen-1-ol, propanoate, (*Z*)-
4190	***L*-Ornithine monochlorohydrate/Ornithine**
	L(+)-2,5-Diamino valeric acid monohydrochloride
	L-Ornithine, monohydrochloride
	L-Ornithine hydrochloride
	Ornithine hydrochloride
	Ornithine monohydrochloride
4191	**Pent-2-enyl hexanoate**
	2-Penten-1-yl hexanoate
4192	**2-Pentanoylfuran**
	1-(2-Furanyl)-1-pentanone
	Butyl 2-furyl ketone
	1-Pentanone, 1-(2-furanyl)-
	1-Pentanone, 1-(2-furyl)-
4193	**2-Pentenoic acid**
	Pent-2-enoic acid
	Pent-2-en-1-oic acid
4194	**(+/-)-2-Phenyl-4-methyl-2-hexenal**
	Benzeneacetaldehyde, *alpha*-(2 methylbutylidene)-
	2-Hexenal, 4-methyl-2-phenyl-
4195	**Phthalide**
	2-Hydroxymethylbenzoic acid *gamma* lactone,
	alpha-Hydroxy-*o*-toluic acid lactone
	1(3*H*)-Isobenzofuranone
4196	**Phytol**
4197	**Phytyl acetate**
4198	**3-Pinanone**
	Isopinocamphone
	Bicyclo[3.1.1]heptan-3-one, 2,6,6-trimethyl-
4199	**Piperitenone oxide**
	7-Oxabicyclo[4.1.0]heptan-2-one, 6-methyl-3-(1-methylethylidene)-
	p-Menth-4-(8)-en-3-one, 1,2-epoxy-
	Piperitenone oxide
4200	***L*-Piperitone**
	2-Cyclohexen-1-one, 3-methyl-6-isopropyl, (6*R*)-
	2-Cyclohexen-1-one, 3-methyl-6-(1-methylethyl)-, (6*R*)-
	p-Menth-1-en-3-one
	(-)-Piperitone
4201	**Polyglycerol esters of fatty acids**
	9-Octadecanoic acid (9*Z*)-monoester with decaglycerol
	Polyaldo 10-1-0

FEMA No.	Substance primary name and synonyms
	Polyglycerol fatty acid esters
	Glyceran fatty acid esters
	Decaglyceryl monooleate
4202	**Prenyl acetate**
	2-Buten-1-ol, 3-methyl-, acetate
	3-Methyl-2-butenyl acetate
4203	**Prenyl benzoate**
	2-Buten-1-ol, 3-methyl-, benzoate
	3-Methyl-2-butenyl benzoate
	Benzoic acid, 3-methyl-2-butenyl ester
4204	**Prenyl caproate**
	Hexanoic acid, 3-methyl-2-butenyl ester
4205	**Prenyl formate**
	2-Buten-1-ol, 3-methyl-,formate
	Methanoic acid, 3-methyl-2-butenyl ester
4206	**Prenyl isobutyrate**
	Propanoic acid, 2-methyl-, 3-Methyl-2-butenyl ester
	Isobutyric acid, 3-methyl-2-butenyl ester
4207	**Propyl 2-mercaptopropionate**
	2-Mercaptopropanoic acid, propyl ester
	Propyl 2-sulfanylpropanoate
4208	**Propylene glycol mono- and diesters of fatty acids**
	Myverol P-06
	Propane-1,2-diol ester of fatty acids
	Propylene glycol esters of fatty acids
	Propylene glycol esters of fatty acids
	Propylene glycol monostearate (or other appropriate ester)
4209	**Tetradec-2-enal**
4210	**Thioacetic acid**
	Ethanethioic acid
	Thiolacetic acid
	Acetothioic acid
4211	***trans*- and *cis*-2,4,8-Trimethyl-3,7-nonadien-2-ol**
	3,7-Nonadien-2-ol, 2,4,8-trimethyl- (2*E*,4*Z*)-
	Cranberry extra
4212	**(+/-)-2,4,8-Trimethyl-7-nonen-2-ol**
	7-Nonen-2-ol, 2,4,8-trimethyl-
4213	**3,7,11-Trimethyldodeca-2,6,10-trienyl acetate**
	Farnesol acetate
4214	**2,4,6-Trithiaheptane**
	bis-(Methylthiomethyl)sulfide
4215	**Tyramine**
	4-(2-Aminoethyl)phenol
	2-(4-Hydroxyphenyl)ethylamine
	Systogene
	Tocosine
	Uteramine
	Tyrosamine
	p-beta-Aminoethylphenol
	4-Hydroxyphenylethylamine
	4-Hydroxyphenethylamine
	p-Hydroxyphenylethylamine
	p-Hydroxyphenethylamine
	Benzeneethanamine
4216	**Verbenone**
	Pin-2-en-4-one
	4,6,6-Trimethyl-bicyclo[3.1.1]hept-3-en-2-one
	Bicyclo[3.1.1]hept-3-en-2-one, 4,6,6-trimethyl-
4217	**Vetiverol**
	6-Azulenol, 1,2,3,3a,4,5,6,8a-octahydro-4,8-dimethyl-2-(1-methylethylidene)-

FEMA No.	Substance primary name and synonyms
4218	**Vetiveryl acetate**
	6-Azulenol, 1,2,3,3a,4,5,6,8a-octahydro-4,8-dimethyl-2-(1-methylethylidene)-, acetate
4219	**Cornmint oil, *Mentha arvensis* L.**
4220	***Heliopsis longipes* extract**
	Heliopsis longipes S.F. Blake
	Chilcaun extract
	Gold root extract
4221	**Scotch spearmint oil, *Mentha cardiaca* L.**
	Scotch spearmint oil
	Scotch mint oil
4222	**Natural hickory smoke flavor**
	Pyroligneous acids, hickory
	Hickory smoke distillate
	Smoke, hickory, condensate
4223	**Betaine**
	1-Carboxy-*N*,*N*,*N*-trimethylmethanaminium hydroxide inner salt
	(Carboxymethyl)trimethylaminum hydroxide inner salt
	(Trimethylammonio)acetate
	alpha-Earleine
	Glycine betaine
	Glycine, trimethylbetaine
	Glycocoll betaine
	Glycylbetaine
	Oxyneurine
	Lycine
	Trimethylglycocoll
	N,N,N-Trimethylglycine
	Trimethylglycine hydroxide inner salt
	Trimethylglycine
4224	**Adenosine monophosphate; monosodium or disodium adenylate**
	Adenosine monophosphate
	Adenosine 5Ð monophosphate sodium salt
4225	**Isoquercitrin, enzymatically modified**
	alpha-Glycosyl-isoquercitrin
	Isoquercetin
	EMIQ
4226	**Glycerol ester of rosin**
	Rosin, glycerol ester
	Rosin Glycerol Ester
	NovaRes1190
4227	**Gum arabic, hydrogen octenylbutane dioate**
	Modified Gum Acacia
	Gum Arabic, hydrogen octenylbutanedioate
4228	**(-)-Homoeriodictyol, sodium salt**
	HED sodium salt
	4H-1-Benzopyran-4-one, 2,3-dihydro-5,7-dihydroxy-2-(4-hydroxy-3-methoxyphenyl)-, sodium salt
	(+,-)-5,7,4′-Trihydroxy-3′-methoxyflavanone, sodium salt
	(+,-)-Homoeriodictyol sodium salt
4229	**Sugar beet Juice extract**
	Beta vulgaris
4230	**(+/-)-*N*,*N*-Dimethyl menthyl succinamide**
	Butanioc acid, 4-(dimethylamino-4-oxo-, (1*R*,2*S*,5*R*)-5methyl-2-(1-methylethyl)cyclohexyl ester
	Butanoic acid, 4-(dimethylamino)-4-oxo-,[1*R*-(1α,2β,5α)]-5-methyl-2-(1-methylethyl)cyclohexyl ester
4231	***N*1-(2-methoxy-4-methylbenzyl)-*N*2-(2-(pyridin-2-yl)ethyl)oxalamide**

FEMA No.	Substance primary name and synonyms
	Ethanediamide, N-[(2-methoxy-4-methylphenyl)methyl]-N′-[2-(2-pyridinyl)ethyl]-
4232	***N*-(Heptan-4-yl)benzo[d][1,3]dioxole-5-carboxamide**
	1,3-Benzodioxole-5-carboxamide, *N*-(1-propylbutyl)-
	N-(1-propylbutyl)-1,3-benzodioxole-5-carboxamide
4233	***N*1-(2,4-Dimethoxybenzyl)-*N*2-(2-(pyridin-2-yl)ethyl)oxalamide**
	Ethanediamide, *N*-[(2,4-dimethoxyphenyl)methyl]-*N*′-(2-(2-pyridinyl)ethyl]-
4234	***N*1-(2-Methoxy-4-methylbenzyl)-*N*2-(2-(5-methylpyridin-2-yl)ethyl)oxalamide**
	Ethanediamide, *N*-[(2-methoxy-4-methylphenyl)methyl]-*N*′-[2-(5-methyl-2-pyridinyl)ethyl]-
4235	**1,6-Hexalactam**
	epsilon-Caprolactam
	omega-Caprolactam
	1-Aza-2-cycloheptanone
	2-Azacycloheptanone
	2-Ketohexamethylenimine
	2-Oxohexamethylenimine
	2-Perhydrazepinone
	6-Caprolactam
	6-Hexanelactam
	Aminocaproic lactam
	Azepan-2-one
	Caprolactam
	Hexahydro-2-azepinone
	Hexahydro-2*H*-azepin-2-one
	Hexano-6-lactam
	Hexanoic acid, 6-amino-, cyclic lactam
	Hexanolactam
4236	**Ethylamine**
	1-Aminoethane
	Aminoethane
	Monoethylamine
	n-Ethylamine
4237	**Propylamine**
	1-Aminopropane
	1-Propylamine
	Mono-*n*-propylamine
	Monopropylamine
	n-Propylamine
	Propan-1-ylamine
4238	**Isopropylamine**
	1-Methylethylamine
	2-Aminopropane
	2-Propylamine
	Monoisopropylamine
	sec-Propylamine
4239	**Isobutylamine**
	1-Amino-2-methylpropane
	2-Methyl-1-aminopropane
	2-Methyl-1-propanamine
	2-Methylpropanamine
	2-Methylpropylamine
	3-Methyl-2-propylamine
	iso-Butylamine
	Monoisobutylamine
	Valamine
4240	***sec*-Butylamine**
	(+/-)-2-Aminobutane
	(+/-)-2-Butanamine

Table 1 *continued*: Primary Names & Synonyms

FEMA No.	Substance primary name and synonyms
	(+/-)-2-Butylamine
	(+/-)-*sec*-Butylamine
	(*RS*)-*sec*-Butylamine
	1-Methylpropanamine
	1-Methylpropylamine
	2-Aminobutane
	2-Butylamine
	Butafume
	Butan-2-ylamine
	dl-2-Butylamine
	DL-*sec*-Butylamine
	Tutane
4241	**2-Methylbutylamine**
	Butylamine, 2-methyl-
	(+/-)-2-Methylbutylamine
	beta-Methylbutylamine
	1-Amino-2-methylbutane
	2-Ethylpropylamine
	2-Methyl-1-butanamine
	2-Methyl-1-butylamine
	2-Methylbutanamine
	2-Methylbutylamine
	dl-2-Methylbutylamine
4242	**Pentylamine**
	Pentylamine
	1-Aminopentane
	1-Pentylamine
	Amylamine
	Monoamylamine
	Monopentylamine
	n-Amylamine
	n-Pentylamine
	Norleucamine
4243	**Hexylamine**
	1-Aminohexane
	1-Hexylamine
	Mono-*n*-hexylamine
	n-Hexylamine
4244	**2-Methylpiperidine**
	2-Pipecoline
	(+/-)-*alpha*-Pipecoline
	(+/-)-2-Methylpiperidine
	alpha-Methylpiperidine
	alpha-Pipecoline
	DL-2-Methylpiperidine
4245	**Trimethylamine oxide**
	Trimethylamine, *N*-oxide
	N,N-Dimethylmethanamine *N*-oxide
	TMAO
	Triox
4246	**Triethylamine**
	Triethylamine
	(Diethylamino)ethane
	N,N-Diethylethanamine
	TEA
4247	**Tripropylamine**
	N,N-Dipropyl-1-propanamine
	Propyldi-*n*-propylamine
	Tri-*n*-propylamine
4248	***N,N*-Dimethylphenethylamine**
	Benzenemethanamine, *N,N-alpha*-trimethyl-, (*R*)-
	Benzylamine, *N,N,alpha*-trimethyl-, *L*-(+)-
	(+)-(*R*)-*N,N*-Dimethyl-*alpha*-phenethylamine
	(+)-*N,N, alpha*-Trimethylbenzylamine
	(+)-*N,N*-Dimethyl-alpha-methylbenzylamine
	(*R*)-(+)-*N,N*-Diemthyl-1-phenethylamine
	(*R*)-*alpha*-Methylbenzyldimethylamine
	(*R*)-Dimethyl(1-phenylethyl)amine
	(*R*)-*N,N*-Dimethyl-1-phenethylamine
	(*R*)-[1-(Dimethylamino)ethyl]benzene
4249	**2-Acetyl-1-pyrroline**
4250	**Piperazine**
	1,4-Diazocyclohexane
	1,4-Piperazine
	Antiren
	Diethylenediamine
	Dispermine
	Eraverm
	Hexahydropyrazine
	Lumbrical
	Piperizidine
	Pipersol
	Pyrazine hexahydride
	Uvilon
	Vermex
	Worm-a-Ton
	Wurmirazin
4251	**Acetamide**
	Acetic acid amide
	Acetimidic acid
	Ethanamide
	Ethanamidic acid
	Methanecarboxamide
4252	**Butyramide**
	Butyramide
	Butanimidic acid
	n-Butylamide
4253	**Methyl 10-undecenoate**
	10-Undecenoic acid, methyl ester
	Methyl undec-10-enoate
	Methyl undecylenate

Table 2: Average Usual Use Levels/Average Maximum Use Levels

Average usual use levels (ppm)/average maximum use levels (ppm) for new FEMA GRAS flavoring substances on which the FEMA Expert Panel based its judgments that the substances are generally recognized as safe (GRAS)

	(+/-)-1-Acetoxy-1-ethoxyethane	4-Acetyl-2,5-dimethyl-3(2*H*)-furanone	2-Acetyl-3,5-dimethylfuran	Allyl crotonate	Allyl propyl disulfide	Allyl valerate	4-Allylphenol	Allyl thiohexanoate	*o*-Anisaldehyde	*N*-Benzoyl anthranilic acid	Thujyl alcohol	*L*-Bornyl acetate
Category	**FEMA No. 4069**	**4070**	**4071**	**4072**	**4073**	**4074**	**4075**	**4076**	**4077**	**4078**	**4079**	**4080**
Baked goods		5/25	10/50	10/50	0.2/1	10/50	10/50	2.5/12.5	10/50	50/100	5/25	10/50
Beverages (nonalcoholic)	0.2/5			5/25		5/25		0.05/0.5	1/10	20/40		
Beverages (alcoholic)	0.3/10							0.25/1.3	3/30	30/50		
Breakfast cereal		2/10	5/25	5/25	0.1/0.5	5/25	5/25				2/10	5/25
Cheese		3/15	7/35	7/35	0.2/1	7/35	7/35	0.4/2			3/15	7/35
Chewing gum	20/50	4/20					10/50	2/10	30/50	500/1,000		
Condiments/ relishes			5/25	5/25	0.1/0.5	5/25	5/25	0.5/3			2/10	
Confectionery frostings	0.5/10	4/20	10/50	10/50	0.2/1	10/50	10/50		5/20		4/20	10/50
Egg products								0.25/1.3				
Fats/oils		2/10	5/25	5/25	0.1/0.5	5/25	5/25	0.4/2			2/10	5/25
Fish products		1/5	2/10	2/10	0.1/0.2	2/10	2/10	0.3/1.5			1/5	2/10
Frozen dairy	0.5/5	3/15	7/35	7/35	0.2/1	7/35	7/35		5/20		3/15	7/35
Fruit ices	1/10	3/15	10/50	10/50	0.2/1	10/50	10/50		1/10		3/15	10/50
Gelatins/ puddings	0.5/5	3/15		5/25		5/25						
Granulated sugar												
Gravies		2/10	5/25	20/100	0.4/2	20/100	5/25	0.2/1				
Hard candy	1/10	4/20					10/50		10/20	50/1,000	5/25	20/100
Imitation dairy				7/35	0.2/1	7/35		0.4/2			3/15	7/35
Instant coffee/tea	0.5/10								5/50	10/20		
Jams/jellies	1/10	2/10	7/35	5/25		5/25			1/10			
Meat products		1/5	20/100	2/10	0.1/0.2	2/10	2/10	0.3/1.5			1/5	5/25
Milk products	0.5/5	3/15	7/35	7/35	0.2/1	7/35	7/35	0.2/1	5/20		3/15	7/35
Nut products												
Other grains			5/25	5/25	0.1/0.5	5/25	5/25					
Poultry		1/5		2/10	0.1/0.2	2/10	2/10				1/5	2/10
Processed fruits		2/10	7/35	7/35	0.2/1	7/35	7/35				2/10	7/35
Processed vegetables							7/35	0.2/1				
Reconstituted Vegetables							7/35					
Seasonings/ flavors		2/10	5/25	5/25	0.1/0.5	5/25	5/25	0.5/5			2/10	5/25
Snack foods		5/25	10/50	10/50	0.1/0.5	10/50	20/100	0.5/2.5				
Soft candy	0.5/5	4/20					10/50		5/20	50/100	5/25	20/100
Soups		2/10	5/25	5/25	0.1/0.5	5/25	5/25	0.1/1			2/10	5/25
Sugar substitutes												
Sweet sauces	0.8/10			5/25	0.1/0.5	5/25					2/10	5/25

Table 2 *continued*: Average Usual Use Levels/Average Maximum Use Levels

	2-Butylfuran	Butyl isothiocyanate	2-Butyryl-furan	Carvone-5,6-oxide	*beta*-Caryophyllene oxide	Citronellyl anthranilate	*N*-Cyclopropyl-*trans*-2-*cis*-6-nonadienamide	*trans*-*alpha*-Damascone	2-*trans*-4-*trans*-7-*cis*-Decatrienal	2-Decylfuran	Dehydronootkatone	Diacetyl tartaric acid esters of mono- and diglycerides
Category	**4081**	**4082**	**4083**	**4084**	**4085**	**4086**	**4087**	**4088**	**4089**	**4090**	**4091**	**4092**
Baked goods	5/25	2/20	5/25	3/15	3/15	10/50	0.5/3	5/25		5/25	1.5/5	6/100
Beverages (nonalcoholic)						10/100	0.1/1		0.02/0.06		0.5/1.5	
Beverages (alcoholic)						10/100					0.5/1.5	
Breakfast cereal	2/10		2/10	2/10	2/10	1/25		2/10		2/10		6/20
Cheese	3/15	0.5/5	3/15	2/10	2/10		0.1/2	3/15		3/15		
Chewing gum						5/25			0.1/0.3		5/10	
Condiments/ relishes	2/10	0.5/5	2/10	5/25	5/25		0.5/3	2/10		2/10		6/200
Confectionery frostings	4/20		4/20			10/50		4/20		4/20	0.5/2	
Egg products				2/10	2/10							
Fats/oils	2/10	1/10	2/10	2/10	2/10		0.5/2	2/10	0.1/0.3	2/10		
Fish products	1/5		1/5	3/15	3/15		1/4	1/5	0.02/0.06	1/5		
Frozen dairy	3/15		3/15	5/25	5/25	1/5	0.1/2	3/15		3/15	0.5/1.5	
Fruit ices	3/15		3/15	1/5	1/5	20/100		3/15	0.02/0.06	3/15	0.5/1.5	
Gelatins/ puddings						25/50			0.1/0.3			
Granulated sugar											0.1/0.5	
Gravies		1/10					0.5/5					60/400
Hard candy						10/100		5/25	0.02/0.06		1/5	
Imitation dairy		1/10					0.5/3	3/15				
Instant coffee/tea											0.1/0.5	
Jams/jellies						10/100					0.5/1.5	
Meat products	1/5	0.5/5	1/5				1/4	1/5	0.02/0.06	1/5		
Milk products	3/15		3/15				0.1/2	3/15	0.02/0.06	3/15	0.5/1.5	
Nut products												
Other grains	2/10		2/10	3/15	3/15		1/10			2/10		
Poultry	1/5		1/5				1/4	1/5		1/5		
Processed fruits	2/10		2/10	1/5	1/5	10/100		2/10		2/10		
Processed vegetables		0.5/5					0.5/3					
Reconstituted Vegetables		0.5/5					0.5/2		0.01/0.03			
Seasonings/ flavors	2/10	5/50	2/10				10/15	2/10		2/10	0.5/1.5	2.3/15
Snack foods	5/25	1/10	5/25			5/25	1/10			5/25		0.2/40
Soft candy				2/10	2/10	10/100		5/25	0.1/0.3		1/5	
Soups	2/10	0.5/5	2/10				0.5/3	2/10		2/10		
Sugar substitutes												
Sweet sauces						1/25		2/10				

	Diethyl disulfide	Mixture of 3,6-diethyl-1,2,4,5-tetrathiane and 3,5-diethyl-1,2,4-trithiolane	2,4-Difurfurylfuran	Diisopentyl thiomalate	Dimercapto-methane	1,1-Dimethoxy-*trans*-2-hexene	2,4-Dimethyl-1,3-dioxolane	3,5- and 3,6-Dimethyl-2-isobutylpyrazine	2,5-Dimethyl-3(2*H*)-furanone	(+/-)-*trans*- and *cis*-4,8-Dimethyl-3,7-nonadien-2-ol	(+/-)-*trans*- and *cis*-4,8-Dimethyl-3,7-nonadien-2-yl acetate	2,5-Dimethyl-4-ethoxy-3(2*H*)-furanone
Category	**4093**	**4094**	**4095**	**4096**	**4097**	**4098**	**4099**	**4100**	**4101**	**4102**	**4103**	**4104**
Baked goods	0.2/1	10/30	10/50	0.4/2	0.05/0.1	10/50	20/50	1.5/2	5/25			5/25
Beverages (nonalcoholic)		1/5		0.2/1		5/25	10/30			2/10	2/10	
Beverages (alcoholic)		5/10		0.2/1			10/50			5/50	5/50	
Breakfast cereal	0.1/0.5		5/25	0.2/1		5/25		1.5/2	2/10	5/25	5/25	2/10
Cheese	0.2/1	10/30	7/35	0.4/2		7/35			3/15			3/15
Chewing gum							30/50		4/20			4/20
Condiments/ relishes	0.1/0.5		5/25	0.2/1		5/25						
Confectionery frostings	0.2/1		10/50	0.4/2		10/50			4/20	5/20	5/20	4/20
Egg products												
Fats/oils	0.1/0.5	5/20	5/25	0.2/1		5/25			2/10			2/10
Fish products	0.1/0.2		2/10	0.1/0.4		2/10			1/5			1/5
Frozen dairy	0.2/1	5/10	7/35	0.4/2		7/35	5/20		3/15			3/15
Fruit ices	0.2/1		10/50	0.4/2		10/50	1/10		3/15	2/10	2/10	3/15
Gelatins/ puddings						5/25	5/10		3/15	5/20	5/20	3/15
Granulated sugar												
Gravies	0.4/2		5/25	1/5	0.05/0.1	20/100			2/10			2/10
Hard candy		10/20					5/20		4/20	5/25	5/25	4/20
Imitation dairy	0.2/1	5/10		0.4/2		7/35						
Instant coffee/tea							5/40			2/20	2/20	
Jams/jellies			7/35			5/25	1/10		2/10			2/10
Meat products	0.1/0.2	10/20	20/100	1/2	0.05/0.1	2/10			1/5			1/5
Milk products	0.2/1		7/35	0.4/2		7/35	10/30	2/3	3/15			3/15
Nut products												
Other grains	0.1/0.5		5/25	0.2/1		5/25						
Poultry	0.1/0.2			1/2		2/10			1/5			1/5
Processed fruits	0.2/1		7/35	0.2/2		7/35	1/10		2/10			2/10
Processed vegetables		5/20						0.5/1.5				
Reconstituted Vegetables												
Seasonings/ flavors	0.1/0.5	10/30	5/25	1/2		5/25		5/10	2/10			2/10
Snack foods	0.1/0.5	10/20	10/50	1/2		10/50			5/25			5/25
Soft candy							1/10		4/20	5/25	5/25	4/20
Soups	0.1/0.5	5/20	5/25	0.6/2		5/25		0.5/1.5	2/10			2/10
Sugar substitutes												
Sweet sauces	0.1/0.5			0.2/1	0.05/0.1	5/25	1/10	2/3				

Table 2 *continued*: Average Usual Use Levels/Average Maximum Use Levels

	(+/-)-*trans* and *cis*-5-(2,2-Dimethyl-cyclopropyl)-3-methyl-2-pentenal	2,5-Dimethylfuran	Divanillin	(+/-)-2,8-Epithio-*cis*-*p*-menthane	Epoxyoxophorone	Tomato lycopene	Ethane-1,1-dithiol	Ethyl *cis*-3-hexenoate	*N*-Ethyl *trans*-2-*cis*-6-nonadienamide	Ethyl furfuryl ether	Ethyl *N*-ethylanthranilate	Ethyl *N*-methylanthranilate
Category	**4105**	**4106**	**4107**	**4108**	**4109**	**4110**	**4111**	**4112**	**4113**	**4114**	**4115**	**4116**
Baked goods	133/178	5/25	30/50		3/15			5/20	0.5/3	5/25	10/50	10/50
Beverages (nonalcoholic)	17/28		5/15	0.05/0.5		2/20	0.2/2	2/10	0.1/1			
Beverages (alcoholic)	3/6		15/30	0.05/0.5			0.2/2	5/20				
Breakfast cereal		2/10			2/10			2/10		2/10	5/25	5/25
Cheese		3/15			2/10				0.1/2	3/15	7/35	7/35
Chewing gum	147/430		100/200	0.08/0.8				5/25				
Condiments/ relishes	10/10	2/10		0.01/0.1	5/25			2/20	0.5/3	2/10	2/25	2/25
Confectionery frostings		4/20	10/20	0.02/0.2				5/25		4/20	10/50	10/50
Egg products					2/10							
Fats/oils		2/10	15/20		2/10		0.2/2		0.5/2	2/10	5/25	5/25
Fish products		1/5			3/15				1/4	1/5	2/10	2/10
Frozen dairy	22/34	3/15	10/20	0.02/0.2	5/25			5/20	0.1/2	3/15	7/35	7/35
Fruit ices		3/15	10/20	0.05/0.5	1/5			5/20		3/15	10/50	10/50
Gelatins/ puddings	174/210		15/20	0.02/0.2				5/20				
Granulated sugar												
Gravies	1/1			0.005/0.05			0.2/5		0.5/5		5/25	5/25
Hard candy	8/115		30/50	0.08/0.8				10/40				
Imitation dairy			10/30					2/10	0.5/3		7/35	7/35
Instant coffee/tea			10/20					2/10				
Jams/jellies				0.02/0.2				5/25				
Meat products	1/2	1/5		0.02/0.2			1/5		1/4	1/5	5/25	5/25
Milk products		3/15	10/40						0.1/2	3/15	7/35	7/35
Nut products												
Other grains		2/10			3/15				1/10	2/10	5/25	5/25
Poultry		1/5					1/5		1/4	1/5	2/10	2/10
Processed fruits		2/10		0.02/0.2	1/5		0.2/2	1/10		2/10	7/35	7/35
Processed vegetables				0.01/0.1					0.5/3			
Reconstituted Vegetables				0.01/0.1					0.5/2			
Seasonings/ flavors		2/10	10/30	0.01/0.1			1/5	25/100	10/15	2/10	5/25	5/25
Snack foods		5/25		0.03/0.3			1/5		1/10	5/25	20/100	20/100
Soft candy	142/181		20/40	0.05/0.5	2/10			10/40				
Soups		2/10	10/30	0.03/0.3			0.6/5		0.5/3	2/10	5/25	5/25
Sugar substitutes												
Sweet sauces								2/10			5/25	5/25

	(+/-)-4-Ethyloctanal	Eugenyl isovalerate	Furfuryl 2-methyl-3-furyl disulfide	1-(2-Furyl)butan-3-one	Geranic acid	Geranyl 2-methyl butyrate	Geranyl valerate	Glyceryl-lacto esters of fatty acids	Hept-*trans*-2-en-1-yl acetate	Hept-2-en-1-yl isovalerate	*trans*-2-*trans*-4-Heptadien-1-ol	2-Heptanethiol
Category	**4117**	**4118**	**4119**	**4120**	**4121**	**4122**	**4123**	**4124**	**4125**	**4126**	**4127**	**4128**
Baked goods		0.2/1		5/25	10/50	10/50	10/50	6/100	10/50	10/50	10/50	
Beverages (nonalcoholic)					3/15	5/25	5/25		5/25	5/25	5/25	4/10
Beverages (alcoholic)												
Breakfast cereal		0.2/1		2/10	5/25	5/25	5/25	6/20	5/25	5/25	5/25	
Cheese	0.005/0.04	0.5/2.5		3/15	3/15	7/35	7/35		7/35	7/35	7/35	
Chewing gum		1/5										
Condiments/ relishes	0.002/0.01	0.3/1.5	0.005/0.02	2/10	5/25	5/25	5/25	6/200	5/25	5/25	5/25	
Confectionery frostings		0.2/1		4/20	10/50	10/50	10/50		10/50	10/50	10/50	
Egg products												
Fats/oils	0.004/0.02	0.2/1		2/10	2/10	5/25	5/25		5/25	5/25	5/25	
Fish products		0.2/1		1/5	2/10	2/10	2/10		2/10	2/10	2/10	
Frozen dairy		0.5/2.5		3/15	3/15	7/35	7/35		7/35	7/35	7/35	
Fruit ices		0.5/2.5		3/15	3/15	10/50	10/50		10/50	10/50	10/50	
Gelatins/ puddings					5/25	5/25	5/25		5/25	5/25	5/25	
Granulated sugar												
Gravies	0.004/0.02	0.3/1.5	0.005/0.02		15/75	20/100	20/100	60/400	20/100	20/100	20/100	1/5
Hard candy		1/5										
Imitation dairy					3/15	7/35	7/35		7/35	7/35	7/35	
Instant coffee/tea												
Jams/jellies					5/25	5/25	5/25		5/25	5/25	5/25	
Meat products	0.005/0.04	0.2/1	0.005/0.02	1/5	2/10	2/10	2/10		2/10	2/10	2/10	1/5
Milk products	0.002/0.01	0.5/2.5		3/15	3/15	7/35	7/35		7/35	7/35	7/35	
Nut products												
Other grains		0.2/1		2/10	5/25	5/25	5/25		5/25	5/25	5/25	
Poultry		0.2/1		1/5	2/10	2/10	2/10		2/10	2/10	2/10	
Processed fruits		0.4/2		2/10	2/10	7/35	7/35		7/35	7/35	7/35	
Processed vegetables		0.4/2										
Reconstituted Vegetables		0.4/2										
Seasonings/ flavors		0.3/1.5	0.005/0.02	2/10	5/25	5/25	5/25	2.3/15	5/25	5/25	5/25	
Snack foods	0.002/0.01	2/10	0.005/0.002	5/25	10/50	10/50	10/50	0.2/40	10/50	10/50	10/50	
Soft candy		1/5										
Soups	0.002/0.01	0.3/1.5	0.005/0.002	2/10	5/25	5/25	5/25		5/25	5/25	5/25	
Sugar substitutes												
Sweet sauces					5/25	5/25	5/25		5/25	5/25	5/25	

Table 2 *continued*: Average Usual Use Levels/Average Maximum Use Levels

	(+/-)-1-Hepten-3-ol	*cis*- and *trans*-2-Heptylcyclopropanecarboxylic acid	2,4-Hexadienyl propionate	2,4-Hexadienyl acetate	2,4-Hexadienyl butyrate	2,4-Hexadienyl isobutyrate	2-Hexenyl octanoate	Hexyl 3-mercaptobutanoate	2-Hexylthiophene	4-Hydroxy-2-butenoic acid *gamma*-lactone	3-Hydroxy-2-octanone	2-(2-Hydroxy-4-methyl-3-cyclohexenyl) propionic acid *gamma*-lactone
Category	**4129**	**4130**	**4131**	**4132**	**4133**	**4134**	**4135**	**4136**	**4137**	**4138**	**4139**	**4140**
Baked goods		0.01/0.03	0.5/10	0.5/10	0.5/10	0.5/10	10/50		0.2/		5/25	1/5
Beverages (nonalcoholic)		0.003/0.01	2/20	2/20	2/20	2/20	5/25	2/8				0.5/5
Beverages (alcoholic)		0.003/0.01	2/20	2/20	2/20	2/20		4/10		3.5/5		2/1 0
Breakfast cereal		0.003/0.02	0.5/10	0.5/10	0.5/10	0.5/10	5/25	5/10			2/10	2/10
Cheese		0.01/0.03					7/35				3/15	0.5/2
Chewing gum		0.005/0.02	1/20	5/25	1/20	1/20		10/20				1/10
Condiments/relishes							5/25		0.5/		2/10	5/20
Confectionery frostings		0.005/0.015	5/25	5/25	5/25	5/25	10/50	5/10			4/20	2/10
Egg products									1/			
Fats/oils							5/25		0.2		2/10	
Fish products	0.05/0.1	0.005/0.02					2/10		1/		1/5	
Frozen dairy		0.005/0.02	1/20	1/20	1/20	1/20	7/35	5/10			3/15	0.5/5
Fruit ices		0.005/0.015	1/20	1/20	1/20	1/20	10/50	2/8			3/15	
Gelatins/puddings		0.003/0.015	5/25	5/25	5/25	5/25	5/25	2/8				2/10
Granulated sugar												
Gravies	0.1/0.2	0.005/0.02					20/100		1/			
Hard candy		0.1/0.03	1/10	1/10	1/10	1/10		20/50				1/10
Imitation dairy		0.003/0.015					7/35				3/15	1/10
Instant coffee/tea												1/10
Jams/jellies		0.003/0.015	5/25	5/25	5/25	5/25	5/25	5/10				
Meat products	0.1/0.2	0.01/0.03					2/10		1/	3.8/505	1/5	
Milk products		0.003/0.015	5/25	5/25	5/25	5/25	7/35	2/5			3/15	0.5/2
Nut products		0.005/0.02										
Other grains							5/25					
Poultry	0.05/0.1	0.01/0.03					2/10		1/			
Processed fruits			5/25	5/25	5/25	5/25	7/35	2/10			2/10	
Processed vegetables												
Reconstituted Vegetables												
Seasonings/flavors	0.5/0.8	0.01/0.03	5/25	1/10	5/50	1/20	5/25		250/		2/10	50/200
Snack foods	0.05/0.1	0.01/0.03	1/10	5/25			10/50		0.2		5/25	
Soft candy		0.005/0.02	1/10	1/10	5/25	1/10		5/10				2/10
Soups	0.05/0.1	0.003/0.02					5/25		1/		2/10	
Sugar substitutes												
Sweet sauces		0.003/0.015	1/25	1/5		1/25	5/25	5/10			2/10	

	5-Hydroxy-4-methylhexanoic acid *delta*-lactone	1-(3-Hydroxy-5-methyl-2-thienyl)ethanone	(+/-)-2-Hydroxypiperitone	*beta*-Ionone epoxide	Isoambrettolide	Isobornyl isobutyrate	Isobornyl 2-methylbutyrate	*N*-Isobutyldeca-*trans*-2-*trans*-4-dienamide	Isobutyl *N*-methylanthranilate	(+/-)-Isobutyl 3-methylthiobutyrate	*beta*-Isomethylionone	Isopropenyl acetate
Category	**4141**	**4142**	**4143**	**4144**	**4145**	**4146**	**4147**	**4148**	**4149**	**4150**	**4151**	**4152**
Baked goods	20/50	0.2/0.5	5/25	3/15	0.1/1	10/50	10/50		10/50	0.02/2	5/25	10/50
Beverages (nonalcoholic)	5/10	0.1/0.3			0.05/0.5			10/25		0.02/1		5/25
Beverages (alcoholic)	10/20	0.1/0.5			0.2/2			20/100		0.02/1		
Breakfast cereal	15/30	0.2/0.5	2/10	2/10	0.1/1	5/25	5/25		5/25		2/10	5/25
Cheese	20/40		3/15	2/10		7/35	7/35		7/35		3/15	7/35
Chewing gum	20/100	2/5			1/5			300/500		0.02/1		
Condiments/ relishes			2/10	5/25				10/50	2/25		2/10	5/25
Confectionery frostings	10/20	0.2/0.4	4/20		0.2/2	10/50	10/50	10/30	10/50	0.02/1	4/20	10/50
Egg products				2/10								
Fats/oils	10/20		2/10	2/10		5/25	5/25		5/25		2/10	5/25
Fish products			1/5	3/15		2/10	2/10		2/10		1/5	2/10
Frozen dairy	10/20		3/15	5/25	0.1/1	7/35	7/35		7/35	0.02/1	3/15	7/35
Fruit ices	10/20	0.1/0.3	3/15	1/5	0.1/2	10/50	10/50	10/25	10/50	0.02/1	3/15	10/50
Gelatins/ puddings	10/20	0.1/0.3			0.1/1					0.02/1		5/25
Granulated sugar												
Gravies									5/25			20/100
Hard candy	10/30	0.3/0.5			0.2/2	20/100	20/100	25/100		0.02/1	5/25	
Imitation dairy	10/20		3/15			7/35	7/35		7/35	0.02/1	3/15	7/35
Instant coffee/tea								10/20				
Jams/jellies		0.2/0.3			0.1/1					0.02/1		5/25
Meat products			1/5			5/25	5/25	25/50	5/25		1/5	2/10
Milk products	10/20	0.2/0.3	3/15		0.1/1	7/35	7/35		7/35	0.02/1	3/15	7/35
Nut products												
Other grains				3/15					5/25			5/25
Poultry						2/10	2/10		2/10		1/5	2/10
Processed fruits			2/10	1/5	0.2/2	7/35	7/35		7/35	0.02/1	2/10	7/35
Processed vegetables										0.02/1		
Reconstituted Vegetables										0.02/1		
Seasonings/ flavors	20/50	3/5	2/10			5/25	5/25	200/2,000	5/25	0.02/1	2/10	5/25
Snack foods	15/30		5/25					20/100	20/100			10/50
Soft candy	10/20	2/5		2/10	0.2/2	20/100	20/100	25/50		0.02/1	5/25	
Soups			2/10			5/25	5/25	10/30	5/25		2/10	5/25
Sugar substitutes										0.02/1		
Sweet sauces			2/10		0.1/1	5/25	5/25		5/25		2/10	5/25

Table 2 *continued*: Average Usual Use Levels/Average Maximum Use Levels

	Lactylated fatty acid esters of glycerol and propylene glycol	2-(*l*-Menthoxy)-ethanol	Menthyl pyrrolidone carboxylate	Menthyl valerate	4-Mercapto-2-pentanone	(+/-)-4-Mercapto-4-methyl-2-pentanol	2-Mercaptoanisole	Methionyl butyrate	*trans*- and *cis*-1-Methoxy-1-decene	(S1)-Methoxy-3-heptanethiol	2-Methoxy-acetophenone	Methyl *cis*-3-hexenoate
Category	**4153**	**4154**	**4155**	**4156**	**4157**	**4158**	**4159**	**4160**	**4161**	**4162**	**4163**	**4164**
Baked goods	2/250			10/50	10/30	0.02/0.1	0.4/2	2/5	15/25	0.3/0.5	10/50	5/20
Beverages (nonalcoholic)		10/100			1/5	0.01/0.05	0.2/1	1/3	2/10	0.005/0.01	1/10	2/10
Beverages (alcoholic)		10/100			5/10	0.02/0.1		1/3	2/12	0.005/0.01	3/30	5/20
Breakfast cereal	2/50			5/25		0.02/0.1	0.2/1	3/5	4/12	0.3/0.5		2/10
Cheese				7/35	1/10		0.4/2					
Chewing gum		2,500/4,000	3,000/3,000			0.02/0.1				0.2/0.5	30/50	5/25
Condiments/ relishes	2/500	10/100			2/10		0.2/1					2/20
Confectionery frostings		200/500		10/50		0.01/0.05	0.4/2	2/5	5/10	0.05/0.1	5/20	5/25
Egg products												
Fats/oils		5/50		5/25	5/20		0.2/1					
Fish products				2/10			0.1/0.4					
Frozen dairy		10/100		7/35	5/10	0.01/0.05	0.4/2	2/5	10/15	0.2/0.4	5/20	5/20
Fruit ices		10/100		10/50		0.01/0.05	0.4/2	1/3	5/10	0.1/0.3	1/10	5/20
Gelatins/ puddings		5/50				0.01/0.05		2/5	5/15	0.1/0.2		5/20
Granulated sugar						0.02/0.1		2/5				
Gravies	20/1,000	5/50			2/10							
Hard candy		100/1,000	500/500	20/100	5/20	0.01/0.1		2/5	2/8	0.1/0.3	10/20	10/40
Imitation dairy				7/35			0.4/2					2/10
Instant coffee/tea		1/10				0.01/0.05				0.1/0.3	5/50	2/10
Jams/jellies		10/100				0.01/0.05		2/5	5/10	0.05/0.1	1/10	5/25
Meat products				5/25	3/20		0.1/0.4	5/7		0.2/0.5		
Milk products				7/35			0.4/2	3/5		0.2/0.4	5/20	
Nut products												
Other grains							0.2/1					
Poultry				2/10			0.1/0.4					
Processed fruits				7/35		0.01/0.05	0.3/1.5			0.1/0.3		1/10
Processed vegetables					2/10		0.3/1.5					
Reconstituted Vegetables												
Seasonings/ flavors	0.8/37.5			5/25	5/30	10/100	0.2/1	200/500				25/100
Snack foods	0.1/100	10/100			5/30	0.02/0.1						
Soft candy		200/500		20/100		0.02/0.1		2/5	10/20	0.1/0.3	5/20	10/40
Soups		10/100		5/25	1/10		0.2/1					
Sugar substitutes		0.5/5				0.1/0.5						
Sweet sauces		20/100		5/25		0.01/0.05	0.2/1			0.05/0.1		2/10

	Methyl *cis*-5-octenoate	Methyl 3-(methylthio)-butanoate	Methyl 3-mercaptobutanoate	Methyl isopentyl disulfide	Methyl *N,N*-dimethyl-anthranilate	Methyl *N*-acetylanthranilate	Methyl *N*-formylanthranilate	*S*-Methyl propanethioate	2-Methyl-1-methylthio-2-butene	3-Methyl-2(3-methylbut-2-en-1-yl)furan	3-(5-Methyl-2-furyl)prop-2-enal	5-Methyl-3(2*H*)-furanone
Category	**4165**	**4166**	**4167**	**4168**	**4169**	**4170**	**4171**	**4172**	**4173**	**4174**	**4175**	**4176**
Baked goods	0.5/0.6		0.5/1	0.25/0.5	10/50	10/50	10/50	0.5/2		5/25	10/50	5/25
Beverages (nonalcoholic)	0.2/0.2		0.2/0.1	0.5/1				0.2/1				
Beverages (alcoholic)	0.2/0.2	0.001/5	0.2/0.4					0.2/1				
Breakfast cereal	0.5/0.6				5/25	5/25	5/25	0.2/0.5		2/10	5/25	2/10
Cheese	0.5/0.6	0.001/5			7/35	7/35	7/35	0.5/2		3/15	7/35	3/15
Chewing gum	5/6.3		1/2					0.2/2				4/20
Condiments/ relishes			0.2/0.4		2/25	2/25	2/25	0.2/1	0.1/0.25	2/10	5/25	
Confectionery frostings	0.5/0.6				10/50	10/50	10/50	0.2/2		4/20	10/50	4/20
Egg products		0.001/10										
Fats/oils	1/1.3	0.001/10			5/25	5/25	5/25			2/10	5/25	2/10
Fish products					2/10	2/10	2/10			1/5	2/10	1/5
Frozen dairy	0.5/0.6		0.3/0.6	0.25/0.5	7/35	7/35	7/35	0.1/0.5		3/15	7/35	3/15
Fruit ices	0.3/0.3	0.01/10			10/50	10/50	10/50	0.1/0.5		3/15	10/50	3/15
Gelatins/ puddings	0.5/0.6	0.05/10	0.3/0.6	0.25/0.5				0.2/1				3/15
Granulated sugar	0.3/0.3											
Gravies		0.05/10	0.2/0.4		5/25	5/25	5/25		0.1/0.25		5/25	2/10
Hard candy	1/1.3		0.4/0.8					0.5/2				4/20
Imitation dairy	0.3/0.3	0.01/10	0.2/0.4		7/35	7/35	7/35	0.2/1				
Instant coffee/tea	0.2/0.2		0.2/0.4					0.2/1				
Jams/jellies	0.5/0.6							0.2/1			7/35	2/10
Meat products		0.05/10		1/1.5	5/25	5/25	5/25		0.1/0.25	1/5	20/100	1/5
Milk products	0.5/0.6	0.01/10	0.2/0.4		7/35	7/35	7/35	0.1/0.5		3/15	7/35	3/15
Nut products								0.2/1				
Other grains					5/25	5/25	5/25			2/10	5/25	
Poultry		0.1/20			2/10	2/10	2/10			1/5		1/5
Processed fruits		0.05/10			7/35	7/35	7/35	0.1/0.5		2/10	7/35	2/10
Processed vegetables		0.05/10										
Reconstituted Vegetables		0.05/10										
Seasonings/ flavors	0.3/0.3				5/25	5/25	5/25	10/100	0.1/0.25	2/10	5/25	2/10
Snack foods					20/100	20/100	20/100	0.2/1	0.1/0.25	5/25	10/50	5/25
Soft candy	0.5/0.6		0.3/0.6					0.2/2				4/20
Soups	0.3/0.3	0.05/10	0.2/0.4		5/25	5/25	5/25		0.1/0.25	2/10	5/25	2/10
Sugar substitutes												
Sweet sauces	0.3/0.3				5/25	5/25	5/25	0.2/1				

Table 2 *continued*: Average Usual Use Levels/Average Maximum Use Levels

	6-Methyl-5-hepten-2-yl acetate	2-Methylbut-2-en-1-ol	2-Methylfuran	4-Methylpent-2-enoic acid	3-(Methylthio)-2-butanone	4-(Methylthio)-2-pentanone	(+/-)-3-(Methylthio)-heptanal	3-(Methylthio)-methylthiophene	Methylthiomethyl-mercaptan	Mono- and diglycerides of fatty acids	Nona-2,4,6-trienal	2-Nonenoic acid *gamma*-lactone
Category	**4177**	**4178**	**4179**	**4180**	**4181**	**4182**	**4183**	**4184**	**4185**	**4186**	**4187**	**4188**
Baked goods	2/10	10/50	10/50	10/50	0.8/1	0.8/1	10/50	0.02/0.2	0.05/0.1	6/100	5/25	10/30
Beverages (nonalcoholic)	1/10	5/25		3/15	0.5/0.6	0.5/0.6	1/10				2/10	2/5
Beverages (alcoholic)	5/20						1/10					5/10
Breakfast cereal	2/10	5/25	5/25	5/25						6/20	2/10	10/20
Cheese		7/35	7/35	3/15			1/10	0.005/0.05			3/15	10/20
Chewing gum	5/25											20/50
Condiments/ relishes	2/10	5/25	5/25	5/25			2/10	0.005/0.05	1/2.5	6/200	2/10	
Confectionery frostings	5/25	10/50	10/50	10/50							4/20	5/10
Egg products												
Fats/oils		5/25	5/25	2/10				0.01/0.1			2/10	
Fish products		2/10	2/10	2/10							1/5	
Frozen dairy	1/10	7/35	7/35	3/15	0.5/0.7	0.5/0.7					3/15	5/10
Fruit ices	1/5	10/50	10/50	3/15							3/15	10/20
Gelatins/ puddings	2/10	5/25		5/25	0.5/1	0.5/1					3/15	5/10
Granulated sugar												
Gravies		20/100	5/25	15/75			2/10	0.01/0.1	1/2.5	60/400	5/25	
Hard candy	10/40											10/20
Imitation dairy	2/10	7/35		3/15				0.01/0.1			3/15	
Instant coffee/tea	2/10											
Jams/jellies	5/25	5/25	7/35	5/25							3/15	5/10
Meat products		2/10	20/100	2/10	0.2/0.5	0.2/0.5	3/20	0.005/0.05	1/2.5		1/5	
Milk products		7/35	7/35	3/15							3/15	5/20
Nut products	2/20											
Other grains		5/25	5/25	5/25							2/10	
Poultry		2/10		2/10							1/5	
Processed fruits	1/5	7/35	7/35	2/10							2/10	5/10
Processed vegetables							2/10	0.005/0.05				
Reconstituted Vegetables								0.005/0.05				
Seasonings/ flavors	25/100	5/25	5/25	5/25			5/30	0.05/0.5	1/2.5	2.3/15	2/10	
Snack foods	2/10	10/50	10/50	10/50			5/30	0.01/0.1	1/2.5	0.2/40	3/15	5/10
Soft candy	5/25											10/20
Soups		5/25	5/25	5/25			1/10	0.005/0.05	1/2.5		2/10	5/10
Sugar substitutes												
Sweet sauces	2/10	5/25		5/25							2/10	

	cis-3-Octenyl propionate	*L*-Ornithine monochloro-hydrate/ Ornithine	Pent-2-enyl hexanoate	2-Pentanoylfuran	2-Pentenoic acid	(+/-)-2-Phenyl-4-methyl-2-hexenal	Phthalide	Phytol	Phytyl acetate	3-Pinanone	Piperitenone oxide	*l*-Piperitone
Category	**4189**	**4190**	**4191**	**4192**	**4193**	**4194**	**4195**	**4196**	**4197**	**4198**	**4199**	**4200**
Baked goods	0.5/1	300/1,500	10/50	10/50	10/50	2/15	5/25	10/50	10/50	5/25	3/15	1/10
Beverages (nonalcoholic)	0.5/2		5/25					5/25	5/25			0.2/1
Beverages (alcoholic)	0.5/2											0.2/2
Breakfast cereal			5/25	5/25	5/25	1/7	2/10	5/25	5/25	2/10	2/10	
Cheese			7/35	7/35	3/15		3/15	7/35	7/35	3/15	2/10	
Chewing gum	5/10											30/150
Condiments/ relishes	1/3	1,000/3,000	5/25	5/25			2/10	5/25	5/25	2/10	5/25	
Confectionery frostings	5/10		10/50	10/50	10/50	2/12	4/20	10/50	10/50	4/20		0.5/5
Egg products											2/10	
Fats/oils			5/25	5/25	2/10		2/10	5/25	5/25	2/10	2/10	
Fish products			2/10	2/10	2/10		1/5	2/10	2/10	1/5	3/15	
Frozen dairy	1/5		7/35	7/35	3/15	1/8	3/15	7/35	7/35	3/15	5/25	0.5/5
Fruit ices	1/5		10/50	10/50	3/15		3/15	10/50	10/50	3/15	1/5	0.2/2
Gelatins/ puddings	0.5/2		5/25			0.5/5		5/25	5/25			0.2/2
Granulated sugar												
Gravies		300/1,500	20/100	5/25	15/75			20/100	20/100			
Hard candy	1/5				10/50					5/25		5/50
Imitation dairy			7/35			0.5/7.5	3/15	7/35	7/35	3/15		
Instant coffee/tea						2/12						0.2/2
Jams/jellies			5/25	7/35				5/25	5/25			0.2/2
Meat products		100/1,000	2/10	20/100	2/10		1/5	2/10	2/10	1/5		
Milk products			7/35	7/35	3/15	0.5/5	3/15	7/35	7/35	3/15		0.2/5
Nut products												
Other grains			5/25	5/25	5/25			5/25	5/25		3/15	
Poultry		100/1,000	2/10		2/10			2/10	2/10	1/5		
Processed fruits	5/10		7/35	7/35	2/10		2/10	7/35	7/35	2/10	1/5	
Processed vegetables												
Reconstituted Vegetables												
Seasonings/ flavors	1/5	100/500	5/25	5/25	5/25		2/10	5/25	5/25	2/10		
Snack foods	1/5	100/500	10/50	10/50			5/25	10/50	10/50			
Soft candy	5/10				10/50	1/15				5/25	2/10	5/40
Soups		100/500	5/25	5/25	5/25		2/10	5/25	5/25	2/10		
Sugar substitutes												
Sweet sauces			5/25		5/25		2/10	5/25	5/25	2/10		

Table 2 *continued*: Average Usual Use Levels/Average Maximum Use Levels

	Polyglycerol esters of fatty acids	Prenyl acetate	Prenyl benzoate	Prenyl caproate	Prenyl formate	Prenyl isobutyrate	Propyl 2-mercaptopropionate	Propylene glycol mono- and diesters of fatty acids	Tetradec-2-enal	Thioacetic acid	*trans*- and *cis*-2,4,8-Trimethyl-3,7-nonadien-2-ol	(+/-)-2,4,8-Trimethyl-7-nonen-2-ol
Category	**4201**	**4202**	**4203**	**4204**	**4205**	**4206**	**4207**	**4208**	**4209**	**4210**	**4211**	**4212**
Baked goods	6/100	10/100	10/100	10/100	10/100	10/100		6/100	10/50	1/5		
Beverages (nonalcoholic)		0.3/3	0.3/3	0.3/3	0.3/3	0.3/3			5/25	0.1/0.5	2/10	2/10
Beverages (alcoholic)		1.5/15	1.5/15	1.5/15	1.5/15	1.5/15				0.1/0.5	5/50	5/50
Breakfast cereal	6/20	0.3/1.5	0.3/1.5	0.3/1.5	0.3/1.5	0.3/1.5		6/100	5/25	0.5/2.5	5/25	5/25
Cheese									3/15	1/5		
Chewing gum		15/100	15/100	15/100	15/100	15/100						
Condiments/ relishes	6/200						0.04/0.1	6/200	5/25	0.2/1		
Confectionery frostings		1.5/10	1.5/10	1.5/10	1.5/10	1.5/10			10/50	0.1/0.5	5/20	5/20
Egg products		1.5/10	1.5/10	1.5/10	1.5/10	1.5/10				1/8		
Fats/oils		1.5/10	1.5/10	1.5/10	1.5/10	1.5/10			2/10	3/8		
Fish products									2/10	1/5		
Frozen dairy		6/60	6/60	6/60	6/60	6/60			3/15	0.2/1		
Fruit ices		3/30	3/30	3/30	3/30	3/30			3/15	0.2/1	2/10	2/10
Gelatins/ puddings		3/30	3/30	3/30	3/30	3/30			5/25	0.2/1	5/20	5/20
Granulated sugar												
Gravies	60/400						0.04/0.1	60/400	15/75	0.1/0.5		
Hard candy		5/50	5/50	5/50	5/50	5/50				0.2/1	5/25	5/25
Imitation dairy									3/15	0.5/2.5		
Instant coffee/tea		0.6/6	0.6/6	0.6/6	0.6/6	0.6/6				0.1/0.5	2/20	2/20
Jams/jellies		3/30	3/30	3/30	3/30	3/30			5/25	0.1/0.5		
Meat products							0.04/0.1		2/10	1/5		
Milk products		0.6/6	0.6/60	0.6/60	0.6/60	0.6/60			3/15	0.5/2.5		
Nut products										0.1/0.5		
Other grains									5/25			
Poultry									2/10	1/8		
Processed fruits									2/10	0.2/1		
Processed vegetables										0.2/1		
Reconstituted Vegetables										0.1/0.5		
Seasonings/ flavors	2.3/15	1.5/15	1.5/15	1.5/15	1.5/15	1.5/15	0.04/0.1	2.3/15	5/25	1/8		
Snack foods	0.2/40						0.04/0.1	0.2/40	10/50	1/5		
Soft candy		3/30	3/30	3/30	3/30	3/30				0.2/1	5/25	5/25
Soups							0.04/0.1		5/25	0.2/2		
Sugar substitutes												
Sweet sauces									5/25	0.2/1		

	3,7,11-Trimethyldodeca-2,6,10-trienyl acetate	2,4,6-Trithiaheptane	Tyramine	Verbenone	Vetiverol	Vetiveryl acetate	Cornmint oil, *Mentha arvensis* L.	*Heliopsis longipes* extract	Scotch spearmint oil, *Mentha cardiaca* L.	Natural hickory smoke flavor	Betaine	Adenosine monophosphate; monosodium or disodium adenylate
Category	**4213**	**4214**	**4215**	**4216**	**4217**	**4218**	**4219**	**4220**	**4221**	**4222**	**4223**	**4224**
Baked goods	10/50	0.2/2		5/25	10/50	10/50	2,000			1.8/2.5	1,000/5,000	300/800
Beverages (nonalcoholic)	5/25						2,100/4,000	20/100		0.8/1.5	1,000/5,000	300/800
Beverages (alcoholic)							2,240/5,000	25/150		0.8/1.5	1,000/5,000	300/800
Breakfast cereal	5/25			2/10	5/25	5/25					1,000/5,000	300/800
Cheese	7/35	0.05/0.5		3/15	7/35	7/35				600/650	1,000/5,000	400/800
Chewing gum							8,300/16,000	350/800	2,000/8,000	0.17/0.2	1,000/5,000	300/800
Condiments/ relishes	5/25	0.05/0.5	1/3	2/10			500/1,000	25/120	50/250	10/15	1,000/5,000	400/800
Confectionery frostings	10/50			4/20	10/50	10/50	650/1,500				1,000/5,000	
Egg products											1,000/5,000	
Fats/oils	5/25	0.1/1		2/10	5/25	5/25				100/125	1,000/5,000	
Fish products	2/10		1.2/3	1/5	2/10	2/10				210/220	1,000/5,000	400/800
Frozen dairy	7/35			3/15	7/35	7/35	110/200		50/130		1,000/5,000	
Fruit ices	10/50			3/15	10/50	10/50	110/200				1,000/5,000	
Gelatins/ puddings	5/25						2,200/4,000				1,000/5,000	
Granulated sugar											1,000/5,000	
Gravies	20/100	0.1/1	1/3					25/150		10/20	1,000/5,000	400/800
Hard candy				5/25	20/100	20/100	2,000/4,000	200/600	1,500/2,000		1,000/5,000	
Imitation dairy	7/35	0.1/1		3/15	7/35	7/35	100/200				1,000/5,000	
Instant coffee/tea							200/400				1,000/5,000	300/800
Jams/jellies	5/25						500/1,000		100/200		1,000/5,000	
Meat products	2/10	0.05/0.5	1/3	1/5	5/25	5/25	210/20			100/150	1,000/5,000	500/800
Milk products	7/35			3/15	7/35	7/35				210/220	1,000/5,000	
Nut products											1,000/5,000	400/800
Other grains	5/25										1,000/5,000	300/800
Poultry	2/10			1/5	2/10	2/10				250/280	1,000/5,000	500/800
Processed fruits	7/35			2/10	7/35	7/35					1,000/5,000	
Processed vegetables		0.05/0.5								130/150	1,000/5,000	400/800
Reconstituted Vegetables		0.05/0.5								130/150	1,000/5,000	400/800
Seasonings/ flavors	5/25	0.5/5	1/3	2/10	5/25	5/25	2,000/4,000	100/500	1,000/5,000	10/20	1,000/5,000	400/900
Snack foods	10/50	0.1/1	1/3					25/150		3,600/4,000	1,000/5,000	400/900
Soft candy				5/25	20/100	20/100	1,200/2,000	200/600	1,500/2,000		1,000/5,000	
Soups	5/25	0.05/0.5	1/3	2/10	5/25	5/25				10/20	1,000/5,000	400/800
Sugar substitutes											1,000/5,000	400/800
Sweet sauces	5/25			2/10	5/25	5/25	100/200		40/90		1,000/5,000	

Table 2 *continued*: Average Usual Use Levels/Average Maximum Use Levels

	Isoquercitrin, enzymatically modified	Glycerol ester of rosin	Gum arabic, hydrogen octenylbutane dioate	(-)-Homoeriodictyol, sodium salt	Sugar beet juice extract	(+/-)-*N*,*N*-Dimethyl menthyl succinamide	*N*1-(2-methoxy-4-methylbenzyl)-*N*2-(2-(pyridin-2-yl)ethyl)oxalamide	*N*-(Heptan-4-yl)benzo[d]-[1,3]dioxole-5-carboxamide	*N*1-(2,4-Dimethoxybenzyl)-*N*2-(2-(pyridin-2-yl)ethyl)oxalamide	*N*1-(2-Methoxy-4-methylbenzyl)-*N*2-(2-(5-methylpyridin-2-yl)ethyl)oxalamide	1,6-Hexalactam	Ethylamine
Category	**4225**	**4226**	**4227**	**4228**	**4229**	**4230**	**4231**	**4232**	**4233**	**4234**	**4235**	**4236**
Baked goods			5,000/10,000	200/500	350/1,000		1/2	1/2	1/2	1/2	1/5	2/10
Beverages (nonalcoholic)	150/200	100/100	10,000/20,000	100/800	150/400	100/300						
Beverages (alcoholic)		100/100	5,000/10,000	200/800	300/500	100/300						
Breakfast cereal			5,000/10,000	200/800	300/500						0.2/1	0.2/1
Cheese			5,000/10,000	200/800			1/3	1/3	1/3	1/3	0.4/2	0.4/2
Chewing gum	1,500/2,000		28,000/56,000	200/800	500/1,000	4,000/8,000						
Condiments/ relishes			5,000/10,000		250/500		2/4	2/4	2/4	2/4	0.1/0.5	0.1/0.5
Confectionery frostings			62,000/124,000	100/500	300/600	400/1,000					1/5	1/5
Egg products			5,000/10,000									
Fats/oils			7,500/15,000	100/500			2/4	2/4	2/4	2/4	0.1/0.5	0.1/0.5
Fish products			5,000/10,000	200/800			1/3	1/3	1/3	1/3	0.2/1	0.2/1
Frozen dairy	150/200		6,500/13,000	100/500	300/500						0.4/2	0.4/2
Fruit ices			5,000/10,000		250/500	20/50					0.4/2	0.4/2
Gelatins/ puddings	150/200		12,500/25,000	100/500	300/600	20/100						
Granulated sugar			5,000/10,000									
Gravies			5,000/10,000	100/500	500/1,000		2/4	2/4	2/4	2/4		0.1/0.5
Hard candy			232,500/465,000	100/500	500/1,000	800/2,000						
Imitation dairy			5,000/10,000	200/800	300/500							
Instant coffee/tea			5,000/10,000	100/100	150/500							
Jams/jellies			5,000/10,000		250/500							
Meat products			5,000/10,000	200/800			1/3	1/3	1/3	1/3	0.2/1	0.2/1
Milk products			5,000/10,000	100/100	250/400						0.4/2	0.4/2
Nut products			5,000/10,000									
Other grains			5,000/10,000								0.2/1	0.2/1
Poultry			5,000/10,000				1/3	1/3	1/3	1/3	0.2/1	0.2/1
Processed fruits			5,000/10,000								0.4/2	0.4/2
Processed vegetables			5,000/10,000				1/3	1/3	1/3	1/3		
Reconstituted Vegetables			5,000/10,000									
Seasonings/ flavors			5,000/10,000	200/800		100/500	5/10	5/10	5/10	5/10	0.1/0.5	0.1/0.5
Snack foods			20,000/40,000	100/500		30/200	5/10	5/10	5/10	5/10	1/5	1/5
Soft candy	150/200		425,000/850,000		250/500	800/2,000						
Soups			5,000/10,000	100/500	500/1,000		2/4	2/4	2/4	2/4	0.1/0.5	0.1/0.5
Sugar substitutes			5,000/10,000	100/500								
Sweet sauces			5,000/10,000	100/500	250/500							

	Propylamine	Isopropylamine	Isobutylamine	*sec*-Butylamine	2-Methylbutylamine	Pentylamine	Hexylamine	2-Methylpiperidine	Trimethylamine oxide	Triethylamine	Tripropylamine	*N*,*N*-Dimethyl-phenethylamine
Category	**4237**	**4238**	**4239**	**4240**	**4241**	**4242**	**4243**	**4244**	**4245**	**4246**	**4247**	**4248**
Baked goods	2/10	2/10	2/10	2/10	2/10	2/10	2/10	2/10	2/10	2/10	2/10	2/10
Beverages (nonalcoholic)												
Beverages (alcoholic)												
Breakfast cereal	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1
Cheese	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2
Chewing gum												
Condiments/ relishes	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5
Confectionery frostings	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5
Egg products												
Fats/oils	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5
Fish products	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1
Frozen dairy	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2
Fruit ices	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2
Gelatins/ puddings												
Granulated sugar												
Gravies	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5		0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5
Hard candy												
Imitation dairy												
Instant coffee/tea												
Jams/jellies												
Meat products	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1
Milk products	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2
Nut products												
Other grains	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1
Poultry	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1	0.2/1
Processed fruits	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2	0.4/2
Processed vegetables												
Reconstituted Vegetables												
Seasonings/ flavors	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5
Snack foods	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5	1/5
Soft candy												
Soups	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5
Sugar substitutes												
Sweet sauces												

Table 2 *continued*:

Average Usual Use Levels/Average Maximum Use Levels

	2-Acetyl-1-pyrroline	Piperazine	Acetamide	Butyramide	Methyl 10-undecenoate
Category	**4249**	**4250**	**4251**	**4252**	**4253**
Baked goods	2/10	2/10	1/5	1/5	
Beverages (nonalcoholic)					1/2
Beverages (alcoholic)					4/8
Breakfast cereal	0.2/1	0.2/1	0.2/1	0.2/1	
Cheese	0.4/2	0.4/2	0.4/2	0.4/2	
Chewing gum					
Condiments/relishes	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	
Confectionery frostings	1/5	1/5	1/5	1/5	
Egg products					
Fats/oils	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	
Fish products	0.2/1	0.2/1	0.2/1	0.2/1	
Frozen dairy	0.4/2	0.4/2	0.4/2	0.4/2	4/8
Fruit ices	0.4/2	0.4/2	0.4/2	0.4/2	
Gelatins/puddings					
Granulated sugar					
Gravies					
Hard candy					
Imitation dairy					
Instant coffee/tea					
Jams/jellies					
Meat products	0.2/1	0.2/1	0.2/1	0.2/1	
Milk products	0.4/2	0.4/2	0.4/2	0.4/2	
Nut products					
Other grains	0.2/1	0.2/1	0.2/1	0.2/1	
Poultry	0.2/1	0.2/1	0.2/1	0.2/1	
Processed fruits	0.4/2	0.4/2	0.4/2	0.4/2	
Processed vegetables					
Reconstituted Vegetables					
Seasonings/flavors	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	
Snack foods	1/5	1/5	1/5	1/5	
Soft candy					8/16
Soups	0.1/0.5	0.1/0.5	0.1/0.5	0.1/0.5	
Sugar substitutes					
Sweet sauces					

Table 3: Updated Average Use Levels

Updated average usual use levels (ppm)/average maximum use levels (ppm) for flavoring substances previously recognized as FEMA GRAS.

	iso-Pulegol	Thaumatin	Sodium 2-(4-methoxyphenoxy) propanoate	Monomenthyl succinate	Vanillyl ethyl ether
	FEMA No. 2962	3732	3773	3810	3815
Category	**GRAS List No. 3**	**13**	**15**	**17**	**17**
Baked goods	14/19	15/25	100/150	300/900	5/15
Beverages (nonalcoholic)	50[a]/200[a]	9[a]/25[a]	80/130	50[a]/150[a]	30[a]/300[a]
Beverages (alcoholic)	50[a]/200[a]	10[a]/25[a]		50[a]/150[a]	30[a]/300[a]
Breakfast cereal		20[a]/25[a]	100/150		5/10
Cheese		10[a]/25[a]	50/80		
Chewing gum	500[a]/1,000[a]	300/300	80/130	1,250/4,000[a]	200[a]/600[a]
Condiments/relishes		5/30	100/150		
Confectionery frostings	100[a]/500[a]	9[a]/25a[a]	70/100	200/600	100[a]/500[a]
Egg products		7[a]/25[a]			
Fats/oils		10[a]/25[a]			
Fish products		9[a]/25[a]			
Frozen dairy	12/15	7[a]/25[a]	100/150	70/210	3/5
Fruit ices		7[a]/25[a]	75/125	70/210	
Gelatins/puddings	50[a]/200[a]	10[a]/25[a]	85/135	150/450	
Granulated sugar					
Gravies		15[a]/25[a]	90/140		
Hard candy	100[a]/500[a]	10[a]/25[a]	100/150	300[a]/1,000[a]	100[a]/500[a]
Imitation dairy		10[a]/25[a]	80/130		
Instant coffee/tea		9[a]/25[a]			3/10
Jams/jellies		10[a]/25[a]	85/135	150/450	
Meat products		9[a]/25[a]	70/100		
Milk products		9[a]/25[a]	5[a]/50[a]	60/180	20[a]/200[a]
Nut products		10[a]/25[a]			
Other grains		10[a]/25[a]	70/100		
Poultry		9[a]/25[a]			
Processed fruits		10[a]/25[a]	50/80		
Processed vegetables		10[a]/25[a]	50/80		
Reconstituted Vegetables		10[a]/25[a]			
Seasonings/flavors		7[a]/25[a]	100/150		
Snack foods		25/25	100/150		50[a]/500[a]
Soft candy	100[a]/500[a]	10[a]/25[a]	100/150	200/600	100[a]/500[a]
Soups		15[a]/25[a]			
Sugar substitutes					
Sweet sauces		10[a]/25[a]	90/140		

[a] *New use level.*

Table 4: Toxicity Data on Aliphatic Monoterpene Hydrocarbons

Aliphatic monoterpene hydrocarbon	Biochemical fate: Enzyme induction[a]/ Metabolic fate[b]	Lead biochemistry references	Toxicity studies: Target organ (effect[c])/NOAEL (female)[d]	Genotoxicity assays (in-vitro/in-vivo): AMS, ABS, SCE, UDS/MN[e]	Lead toxicity references
Myrcene	Yes/Yes	Miyazawa (2002); DeOliveira et al. (1997)	Kidney (α-2u)/250	–, –, –, –/–	NTP (2003[a])
Limonene	Yes/Yes	Miyazawa et al. (2002); Maltzman (1991); Kodama (1976); Poon (1996)	Kidney (α-2u)/300	–, –, –, –/–	NTP (1990)
Camphene	Yes/Yes	Hoechst (1991); Ishida (1981)	Kidney (α-2u)/250	–, NR, –, –/–	Hoechst (1991)
Pinene	Yes/Yes	Austin et al. (1997); Eriksson (1996)	Kidney (α-2u)/NR	–, NR, –, –/–	Lehman-McKeeman and Caudill (1999)

[a]CYP450 isozymes, epoxide hydrolase.

[b]Oxidation/epoxidation & hydrolysis.

[c]α-2u = α-2u globulin nephropathy.

[d]NOAEL = No observable adverse effect level (mg/kg bw/day).

[e]AMS = Ames; ABS = Chromosomal Aberration; SCE = Sister Chromatid Exchange; UDS = Unscheduled DNA Synthesis; MN = Micronucleus; + = Positive; – = Negative; ± = Equivocal; NR = Not reported.

Table 5: Safety Evaluation of Corn Mint Oil, *Mentha arvensis* (FEMA No. 4219)[a]

Congeneric group	Decision tree class & Human exposure threshold (mg/person/day)	High % from multiple commercial samples	Intake ("eaters only") (mg/person/day)[b]	Metabolic pathway	Is intake of congeneric group or total of unidentified constituents group less than exposure threshold for class?	Relevant toxicity data if intake of group is greater than exposure threshold
Secondary alicyclic saturated and unsaturated alcohol/ketone/ketal/ester (menthol, menthone, isomenthone, menthyl acetate, etc.)	II (0.54)	95	19.00	(1) Glucuronic acid conjugation of the alcohol followed by excretion in the urine. (2) α-Oxidation of the side-chain substituents to yield various polyols and hydroxyacids and excreted as glucuronic acid conjugates.	No, 19.00 mg/person/day > 0.54 mg/person/day	NOAEL of 600 mg/kg bw/day for menthol (103-week dietary study in mice; NCI, 1979) NOAEL of 400 mg/kg bw/day for menthone (28-day gavage study in rats; Madsen et al., 1986)
Aliphatic terpene hydrocarbon (limonene, pinene, etc.)	I (1.80)	8	1.60	α-Oxidation to yield polar hydroxy and carboxy metabolites excreted as glucuronic acid conjugates.	Yes, 1.60 mg/person/day < 1.80 mg/person/day	Not required
2-Isopropylidene cyclohexanone and metabolites (pulegone, etc.)	III (0.09)	2	0.40	(1) Reduction to yield menthone or isomenthone, followed by hydroxylation of ring or side-chain positions and then conjugation with glucuronic acid. (2) Conjugation with glutathione in a Michael-type addition leading to mercapturic acid conjugates that are excreted or further hydroxylated and excreted. (3) Hydroxylation catalyzed by cytochrome P-450 to yield a series of ring- and side-chain-hydroxylated pulegone metabolites, one of which is a reactive 2-ene-1,4-dicarbonyl derivative; this intermediate is known to form protein adducts leading to enhanced toxicity.	No, 0.40 mg/person/day > 0.09 mg/person/day	NOAEL of 9.375mg/kg bw/day for pulegone (90-day gavage study in rats; NTP, 2002)
Unknown	III (0.09)	4	0.80		No, 0.80 mg/person/day > 0.09 mg/person/day	NOAEL of 200 mg/kg bw/day (males) and 400 mg/kg bw/day (females) for peppermint oil (28-day gavage study in rats; Serota, 1990) NOAEL of 100 mg/kg bw/day for peppermint oil (90-day gavage study in rats; Spindler and Madsen, 1992; Smith et al., 1996)

[a]Based on daily per capita intake ("eaters only") of 20 mg/person/day or 0.33 mg/kg bw/day for corn mint oil.

[b]Daily per capita intake (mg/person/day) = (anticipated annual volume, kg/year)(10^6 mg/kg)/(population x 0.1)(365 days/year), where U.S. population = 2.8 x 10^8 in 2003; 0.1 represents 10% "eaters only"; mg/kg bw/day = (mg/person/day)/body weight, where body weight = 60 kg.

Table 6: Safety Evaluation of Lemongrass Oil, *Cymbopogon citratus* DC (West Indian type) and *Cymbopogon flexuosus* Stapf (East Indian type) (FEMA No. 2624)[a]

Congeneric group	Decision tree class & Human exposure threshold (mg/person/day)	High % from multiple commercial samples	Intake ("eaters only") (mg/person/day)[b]	Metabolic pathway	Is intake of congeneric group or total of unidentified constituents group less than exposure threshold for class?	Relevant toxicity data if intake of group is greater than exposure threshold
Terpene aliphatic branched-chain primary alcohols, aldehydes, carboxylic acids, and related esters (citral)	I (1.80)	80	0.155	(1) Oxidation to carboxylic acid and excretion. (2) α-Oxidation of the side chain substituents to yield various polyols and hydroxyacids and excreted as glucuronic acid conjugates.	Yes, 0.155 mg/person/day < 1.80 mg/person/day	Not required
Aliphatic terpene hydrocarbon (limonene, pinene, etc.)	I (1.80)	10	0.019	α-Oxidation to yield polar hydroxy and carboxy metabolites excreted as glucuronic acid conjugates.	Yes, 0.019 mg/person/day < 1.80 mg/person/day	Not required
Unknown	III (0.09)	3	0.006		Yes, 0.006 mg/person/day < 0.09 mg/person/day	Not required

[a]Based on daily per capita intake ("eaters only") of 0.194 mg/person/day or 0.0032 mg/kg bw/day for lemongrass oil.

[b]Daily per capita intake (mg/person/day) = (anticipated annual volume, kg/year)(10^6 mg/kg)/(population x 0.1)(365 days/year), where U.S. population = 2.8×10^8 in 2003; 0.1 represents 10% "eaters only"; mg/kg bw/day = (mg/person/day)/body weight, where body weight = 60 kg.

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