



# **Federal Regulation of Substances Generally Recognized As Safe (GRAS) and the Use of Carbon Monoxide in Packaging for Meat and Fish**

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## Summary

The use of carbon monoxide (CO) in the packaging of meat and fish has generated considerable debate. The presence of CO results in the meat turning a bright red color that lasts longer than the color in untreated meat. Additionally, fish treated with CO gain a fresher appearance and a red tint. The meat industry, consumer groups, scientists, and policy makers disagree as to whether the use of CO in meat and fish packaging should be regulated by the Food and Drug Administration (FDA) and the United States Department of Agriculture (USDA), through labeling or otherwise, and whether CO should be a substance Generally Recognized As Safe (GRAS) under current and proposed FDA rules.

Two bills have been introduced in the 110<sup>th</sup> Congress regarding the use of carbon monoxide in meat, poultry products, and seafood: H.R. 3115 and H.R. 3610. The discussion draft of the Food and Drug Administration Globalization Act of 2008, issued by Representatives Dingell, Pallone, and Stupak, similarly addresses the issue. The bills and the discussion draft propose to amend section 201 of the Federal Food, Drug, and Cosmetic Act (FFDCA). Under the proposals, if CO is used to treat meat, poultry, or seafood that is intended for human consumption, and if the conditions of that use would affect the color of the products, CO must be treated as a color additive under FFDCA, unless the product's label includes a statement that is prominently and conspicuously placed to notify the consumer of the use of CO and to warn the consumer of proper factors to judge the safety of the product. The bills and the discussion draft would allow the Secretary of Health and Human Services (HHS) to establish alternative labeling requirements five years after the effective date of the labeling requirement, if the Secretary finds that the labeling requirement is no longer necessary to prevent consumer deception. The discussion draft contains an additional provision related to GRAS determinations that would require the Secretary to publish, in the *Federal Register*, notice of receipt of a request for a substance to be determined by the Secretary to be GRAS. The Secretary would then have 90 days after publication of the notice to determine whether the substance is GRAS; the Secretary's determination would also be published in the *Federal Register*. Other bills also address GRAS substances: H.R. 2633, H.R. 3290, H.R. 3580, H.R. 6635, and S. 1342.

This report provides an overview of the FDA's regulation of GRAS substances, which are exempt from the premarket approval process for food additives. The report next discusses the FDA's 1997 proposed rule, which would create a notification procedure for GRAS substances through which manufacturers can notify the FDA of their "determination that a particular use of a substance is GRAS." The FDA has been using this GRAS notification procedure since the publication of the proposed rule on an "interim policy" basis. The roles of the USDA and FDA are also discussed, including the 2000 Memorandum of Understanding regarding review of substances used in the production of meat and poultry products. Finally, the report examines GRAS notices regarding intended uses of carbon monoxide.

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## Introduction

The use of carbon monoxide (CO) in the packaging of meat and fish has generated considerable debate. Carbon monoxide, in combination with nitrogen and carbon dioxide, is used in a packaging process for fresh meat called Modified Atmosphere Packaging (MAP).<sup>1</sup> In the MAP process, the meat is placed in a container with an “impermeable film similar to a vacuum package but ... the air [is evacuated] from the package and replac[ed] ... with a specified mixture of gases that provides for better control of product properties.”<sup>2</sup> The presence of CO results in the meat turning a bright red color that lasts longer than the color in untreated meat. Additionally, fish treated with CO (for example, as part of a gas mixture called “tasteless smoke”)<sup>3</sup> gain a fresher appearance and a red tint.<sup>4</sup> Conflicting studies have shown that consumers rely primarily on the appearance, including the red color of meat or fish, when choosing which package to purchase,<sup>5</sup> and alternatively, that consumers rely mostly on “sell by” dates.<sup>6</sup> The meat industry, consumer groups, scientists, and policy makers disagree as to whether the use of CO in meat and fish packaging should be regulated by the Food and Drug Administration (FDA) and the United States Department of Agriculture (USDA), through labeling or otherwise, and whether CO should be a substance Generally Recognized As Safe (GRAS) under current and proposed FDA rules.

The meat industry, some scientists, and other supporters argue that MAP reduces shrinkage of the meat, allows for a longer shelf life, “keep[s] meat fresh, protect[s] meat, [and] prevent[s] cross-contamination” because MAP packages are tamper resistant and leak-proof.<sup>7</sup> One scientist believes that MAP offers “better flavor, greater tenderness, and suppression of bacterial growth.”<sup>8</sup> Supporters of MAP also assert that such products are more sustainable, less wasteful, and more flexible in terms of distribution because more packages can be transported per truck.<sup>9</sup> Additionally, they note that consumers prefer the bright red color of meat achieved in MAP.<sup>10</sup> Finally, MAP system supporters dispute the scientific basis for claims that the use of carbon

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<sup>1</sup> Agency Response Letter GRAS Notice No. GRN 000083 from Alan M. Rulis, Director, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, FDA, to Eric Greenberg, Ungaretti and Harris (on behalf of Pactiv Corp.) (Feb. 12, 2002), <http://www.cfsan.fda.gov/~rdb/opa-g083.html>, [hereinafter GRAS Notice No. 83].

<sup>2</sup> To Review Technologies in the Meat Industries: Hearing before the H. Comm. on Agriculture, 110<sup>th</sup> Cong. 2 (2007) (statement of Joe Sebranek, Dep’t of Animal Science and Dep’t of Food Science, Iowa State Univ.), <http://agriculture.house.gov/testimony/110/h71030/Sebranek.doc>.

<sup>3</sup> Agency Response Letter GRAS Notice No. GRN 000015 from Janice F. Oliver, Deputy Director, Center for Food Safety and Applied Nutrition, FDA, to Martin J. Hahn, Hogan & Hartson LLP (on behalf of Hawaii International Seafood, Inc.) (Mar. 10, 2000), <http://www.cfsan.fda.gov/~rdb/opa-g015.html>, [hereinafter GRAS Notice No. 15].

<sup>4</sup> Harold McGee, *The Red-Meat Miracle, and Other Tales from the Butcher Case*, N.Y. Times, Dining, 4 (Apr. 4, 2007).

<sup>5</sup> Press Release, Consumer Federation of America, Most Consumers Are Concerned About Practice of Adding Carbon Monoxide to Meat, New Survey Finds (Sept. 25, 2006), [http://www.consumerfed.org/pdfs/CO\\_Meat\\_Consumer\\_Press\\_Release\\_9.25.06.pdf](http://www.consumerfed.org/pdfs/CO_Meat_Consumer_Press_Release_9.25.06.pdf). (“Sixty-three percent (63%) agreed with the statement that ‘the freshness of meat is directly related to the color of the meat.’”).

<sup>6</sup> To Review Technologies in the Meat Industries: Hearing before the H. Comm. on Agriculture, 110<sup>th</sup> Cong. 11, 21 (2007) (statement of Phil Minerich, Vice President, Research and Development, Hormel Foods Corp.), <http://agriculture.house.gov/testimony/110/h71030/Minerich.pdf> (A 2005 Food Marketing Institute study cited by Minerich in his testimony concluded that “81% of consumers rely on sell by dates.”).

<sup>7</sup> GRAS Notice No. 83, *supra* note 1; Minerich, *supra* note 6, at 6.

<sup>8</sup> Sebranek, *supra* note 2, at 3.

<sup>9</sup> Minerich, *supra* note 6, at 17; GRAS Notice No. 83, *supra* note 1.

<sup>10</sup> See Minerich, *supra* note 6, at 30 (quoting Dr. Gary Acuff, Professor of Microbiology, Texas A&M University in a May 26, 2006, letter to the editor of *Meating Place* magazine); Sebranek, *supra* note 2, at 1.

monoxide is misleading or dangerous and declare the consumers use “sell by” dates when determining the freshness of many products.<sup>11</sup>

Opponents allege that the use of CO misleads consumers into thinking meat and fish are fresher than they are; that certain populations, such as those with a reduced sense of smell, will be at increased risk if they consume spoiled meat or fish that still appears fresh due to the use of CO; that consumers may eat undercooked meat because meat packed in MAP systems may brown faster when cooked than untreated meat; that “sell by” dates are not adequate to assist consumers in determining freshness; that consumers will be exposed to CO; that such MAP products are misbranded and adulterated under the Federal Food, Drug, and Cosmetic Act; and that the FDA is violating its own regulations on CO.<sup>12</sup> Another concern of consumer groups and some scientists is that CO provides a cover for spoiled or “temperature abused” meat and fish, meaning that the use of CO conceals visual cues of decomposition caused in part by exposure to changes in temperature or storage or transport at improper temperatures. Fish, such as tuna, may develop toxic levels of scombrototoxin (histamine) through time and/or temperature abuse, which can make consumers ill.<sup>13</sup> Opponents of the use of CO on meat and fish note that the European Union, Canada, Singapore, and Japan have prohibited or decided not to recognize or approve CO for use in fresh meat or fresh fish packaging.<sup>14</sup> Additionally, certain grocery store chains—including Giant, Safeway, Kroeger, and Publix—either do not sell or have announced that they will no longer sell MAP products.<sup>15</sup> Others have taken different steps. At a March hearing, a Target Corporation executive testified that its primary meat supplier had received approval from FSIS to add a label to its packaging that would state: “Color is not an accurate indicator of freshness. Refer to Use or Freeze By [date].”<sup>16</sup>

## **Legal Regulation of Food Additives and GRAS Substances**

Both the FDA and USDA play a role in food safety and the types of substances that can be added to food. This section will focus on the FDA’s regulation of food additives and GRAS substances, which the agency is responsible for under the Federal Food, Drug, and Cosmetic Act (FFDCA) and parts of Title 21, Code of Federal Regulations. FFDCA § 201(s) defines a food additive as:

any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing,

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<sup>11</sup> Sebranek, *supra* note 2, at 1; Minerich, *supra* note 6, at 25.

<sup>12</sup> Citizen Petition from Donald R. Berdahl, Executive Vice President, Kalsec, Inc., to Laura M. Tarantino, Director, Office of Food Safety, Center for Food Safety and Applied Nutrition, FDA (Nov. 20, 2006), [http://www.co-meat.com/Kalsec\\_November\\_2006\\_filing.PDF](http://www.co-meat.com/Kalsec_November_2006_filing.PDF) at 5-6, 8; Sebranek, *supra* note 2, at 2-3; McGee, *supra* note 4.

<sup>13</sup> Center for Food Safety and Applied Nutrition, FDA, Fish and Fisheries Products Hazards and Controls Guidance, ch. 7, (June 2001), <http://www.cfsan.fda.gov/~comm/haccp4g.html>.

<sup>14</sup> Carbon Monoxide in Fresh Meat, Selected Countries Prohibiting Carbon Monoxide (CO) Gas in Fresh Meat and Fresh Fish Packaging, <http://www.co-meat.com/countries.html>.

<sup>15</sup> Julie Schmidt, *Carbon Monoxide Keeps Meat Red Longer; Is that Good?*, USA Today, Oct. 30, 2007.

<sup>16</sup> Regulatory Failure: Must America Live with Unsafe Food? Hearing before the H. Comm. on Energy and Commerce, Subcomm. on Oversight and Investigations, 110<sup>th</sup> Cong. (Mar. 12, 2008) (statement of Danielle Lachman, Divisional Merchandise Manager, Target Corporation), [http://energycommerce.house.gov/cmte\\_mtgs/110-oi-hrg.031208.Lachman-Testimony.pdf](http://energycommerce.house.gov/cmte_mtgs/110-oi-hrg.031208.Lachman-Testimony.pdf).

processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for such use)....<sup>17</sup>

The latter half of the above definition includes “food contact substances,” which the FFDCA defines as “any substance intended for use as a component of materials used in manufacturing, packing, packaging, transporting, or holding food if such use is not intended to have any technical effect in such food.”<sup>18</sup>

The definition of food additive excludes certain classes of substances: (1) pesticide chemical residues in or on a raw agricultural commodity or processed food, (2) pesticide chemicals, (3) color additives, (4) substances used in accordance with their sanction or approval under FDA and USDA laws prior to 1958, (5) new animal drugs, (6) dietary ingredients in dietary supplements, and (7) substances GRAS under the conditions of the substances’ intended use. These seven categories of substances are exemptions to FFDCA § 201(s) and do not have to obtain FDA approval as food additives before they can enter the market.<sup>19</sup> If a food additive does not meet one of the exemptions under the FFDCA, a rule must be in place that details the circumstances under which the food additive can be safely used.<sup>20</sup>

GRAS substances must be “generally recognized, among experts qualified by scientific training and experience to evaluate [their] safety.”<sup>21</sup> FDA regulations recognize the difficulty of establishing the harmlessness of a substance and therefore define safety as “a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.”<sup>22</sup> The person seeking GRAS status for a substance has the burden of proving the substance is GRAS under conditions of the substances’ use.<sup>23</sup> A determination that a substance has GRAS status is not limited to FDA scientists. Experts may base their view of a general recognition of safety on either (1) scientific procedures or (2) common use of a substance in food prior to January 1, 1958.

The first type of GRAS substances is those that have “been adequately shown through scientific procedures ... to be safe under the conditions of [their] intended use.”<sup>24</sup> Scientific procedures include published and unpublished human, animal, analytical, and other scientific studies that are “appropriate to establish the safety of a substance.”<sup>25</sup> A GRAS determination based on scientific procedures “require[s] the same quantity and quality of scientific evidence as is required to obtain approval of a food additive regulation for the ingredient.”<sup>26</sup> The GRAS determination must “ordinarily” be based on published studies, but can be corroborated by unpublished studies and other information.<sup>27</sup> FDA regulations do not require a unanimous opinion from the scientific

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<sup>17</sup> FFDCA § 201(s); 21 U.S.C. § 321(s).

<sup>18</sup> FFDCA § 409(h)(6); 21 U.S.C. § 348(h)(6).

<sup>19</sup> FFDCA § 409; 21 U.S.C. § 348.

<sup>20</sup> FFDCA § 409(a)(2); 21 U.S.C. § 348(a)(2).

<sup>21</sup> FFDCA § 201(s); 21 U.S.C. § 321(s).

<sup>22</sup> 21 C.F.R. § 170.3(I). This reasonable certainty of no harm standard applies to food additives, color additives, and food contact substances, in addition to GRAS substances.

<sup>23</sup> *See* Substances Generally Recognized as Safe, 62 Fed. Reg. 18937, 18939 (proposed Apr. 17, 1997).

<sup>24</sup> FFDCA § 201(s); 21 U.S.C. § 321(s).

<sup>25</sup> 21 C.F.R. § 170.3(h).

<sup>26</sup> 21 C.F.R. § 170.30(b).

<sup>27</sup> 21 C.F.R. § 170.30(b).

community that a substance is GRAS under the conditions of its intended use; rather, the person seeking GRAS status “must show that there is a consensus of expert opinion regarding the safety of the use of the substance.”<sup>28</sup> However, “a severe conflict among experts regarding the safety of the use of a substance, precludes a finding” that a substance is GRAS.<sup>29</sup>

The second type of GRAS substances is those that were “used in food prior to January 1, 1958, [and shown] through either scientific procedures or experience based on common use in food[] to be safe under the conditions of [their] intended use.”<sup>30</sup> FDA regulations define the phrase “common use in food” as “a substantial history of consumption of a substance for food use by a significant number of consumers.”<sup>31</sup> In this instance, a GRAS determination ordinarily turns on “generally available data and information.”<sup>32</sup> These substances are known as prior-sanctioned substances. They can include substances used in food where the use prior to January 1, 1958, “occurred exclusively or primarily outside of the United States if the information about the experience establishes that the use of the substance is safe.”<sup>33</sup> Published information regarding substances used outside the United States must be corroborated.<sup>34</sup>

The FDA lists some GRAS substances in 21 C.F.R. Part 182. However, this list of GRAS substances is not exhaustive as “[i]t is impracticable to list all substances that are [GRAS] for their intended use.”<sup>35</sup> The list of GRAS substances in 21 C.F.R. Part 182 includes spices, essential oils, natural extracts, synthetic flavoring substances, substances that migrate from dry food packaging and paper products, multipurpose substances, anticaking agents, chemical preservatives, emulsifying agents, stabilizers, sequestrants, and nutrients.<sup>36</sup>

The FDA Commissioner can affirm the GRAS status of a substance based on a petition from a manufacturer or others or on his or her own initiative.<sup>37</sup> Substances affirmed as GRAS, listed in 21 C.F.R. Part 184, differ from the GRAS substances listed in Part 182 because their GRAS status has been sustained through a notice-and-comment rulemaking. The concept of affirming the GRAS status of substances began in 1969, when questions arose about whether cyclamate salts, a substance that had been considered GRAS, were safe because “they were implicated in the formation of bladder tumors in rats.”<sup>38</sup>

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<sup>28</sup> Substances Generally Recognized as Safe, 62 Fed. Reg. 18937, 18939 (proposed Apr. 17, 1997).

<sup>29</sup> *Id.*

<sup>30</sup> FFDCa § 201(s); 21 U.S.C. § 321(s).

<sup>31</sup> 21 C.F.R. § 170.3(f).

<sup>32</sup> 21 C.F.R. § 170.30(c)(1).

<sup>33</sup> 21 C.F.R. § 170.30(c)(2).

<sup>34</sup> 21 C.F.R. § 170.30(c)(2).

<sup>35</sup> 21 C.F.R. § 182.1(a).

<sup>36</sup> See 21 C.F.R. § 170.3 (providing definitions of several of the above terms). Sequestrants are “[s]ubstances which combine with polyvalent metal ions to form a soluble metal complex, to improve the quality and stability of products.” 21 C.F.R. § 170.3(o)(26).

<sup>37</sup> 21 C.F.R. § 170.35(a). “The rulemaking process in § 170.35(c) whereby manufacturers may petition FDA to affirm that a substance is GRAS under certain conditions of use was designed as a voluntary administrative process whose purpose was to provide a mechanism for official recognition of lawfully made GRAS determinations.” 62 Fed. Reg. 18941.

<sup>38</sup> Substances Generally Recognized as Safe, 62 Fed. Reg. 18937, 18939 (proposed Apr. 17, 1997). The FDA Commissioner “conclude[d] that cyclamates c[ould] no longer be regarded as generally recognized as safe for use in food” and amended the Code of Federal Regulations to delete such substances from the GRAS list. 34 Fed. Reg. 17063 (Oct. 21, 1969).

The affirmation of GRAS status occurs through the notice and comment rulemaking process, in which the Commissioner publishes a notice of the substance proposed to be affirmed as GRAS in the *Federal Register*, allows 60 days for comments, evaluates the comments (and the petition, if one was filed), and either (1) publishes a notice in the *Federal Register* affirming the substance is GRAS if there is “convincing evidence” or (2) “concludes that there is a lack of convincing evidence that the substance is GRAS and that it should be considered a food additive” subject to premarket approval by the FDA under FFDCA § 409.<sup>39</sup> If the agency affirms that the use of a substance is GRAS, the substance is added to a list in the *Code of Federal Regulations* as a substance affirmed as GRAS “for the purposes and under the conditions prescribed,”<sup>40</sup> allowing for the possibility that use of a substance under a condition other than the one specified in the regulation may not be GRAS.<sup>41</sup> The FDA has reviewed the direct food substances on the list in Part 184 and determined that they are GRAS “for the purposes and under the conditions prescribed.”<sup>42</sup> These ingredients are also GRAS as indirect food ingredients, also known as food contact substances, within certain limitations.<sup>43</sup> Part 186 of Title 21, Code of Federal Regulations, lists the indirect food substances/food contact substances affirmed as GRAS, such as wrappers, containers, and other food-contact surfaces.<sup>44</sup>

If the Commissioner reviews a food ingredient and finds that it is a GRAS substance, under 21 C.F.R. § 184.1, the final rule approving the GRAS substance for the purposes and under the conditions prescribed may contain limits on the application and use of the substance. First, the regulation identifies the characteristics of the ingredient in such a way that it can be differentiated from other versions of the ingredient that the FDA has not affirmed as GRAS.<sup>45</sup> Second, the substance affirmed as GRAS “must be used in accordance with current good manufacturing practices.”<sup>46</sup> Third, a FDA regulation affirming GRAS status “when the safety of an ingredient has been evaluated on the basis of limited conditions of use” will specify the limited conditions of use. Use of the ingredient under a condition other than the one specified in the regulation may not be GRAS.<sup>47</sup> In such a case, the manufacturer must “independently establish that that use is GRAS

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<sup>39</sup> 21 C.F.R. § 170.35.

<sup>40</sup> 21 C.F.R. § 170.35(b), (c); Substances Generally Recognized as Safe, 21 C.F.R. Part 182; Direct food substances affirmed as generally recognized as safe, 21 C.F.R. Part 184; Indirect food substances affirmed as generally recognized as safe, 21 C.F.R. Part 186.

<sup>41</sup> 21 C.F.R. § 184.1(b)(1); 21 C.F.R. § 170.30(I). In such a case, a manufacturer or other person must “independently establish that that use is GRAS or shall use the ingredient in accordance with a food additive regulation.” 21 C.F.R. § 184.1(b)(1); *see also* 21 C.F.R. § 170.30(I).

<sup>42</sup> 21 C.F.R. § 184.1(a). Presently, the FDA is evaluating a Citizen’s Petition with regard to the affirmed GRAS status of diacetyl, “a primary component of butter flavoring in a number of foods, including microwave popcorn,” that has been linked to bronchiolitis obliterans, “a rare, sometimes fatal respiratory disease.” E-mail from FDA Office of Legislation, Feb. 8, 2008 (on file with author); Andrew Schneider, *Flavoring Additive Puts Professional Cooks at Risk*, Seattle Post-Intelligencer, (Dec. 21, 2007), [http://seattlepi.nwsource.com/national/344277\\_diacetyl21.html](http://seattlepi.nwsource.com/national/344277_diacetyl21.html). While 21 C.F.R. § 184.1278 does not place any limits on the use of diacetyl, and the FDA has stated it is “not aware of any evidence that consumption of diacetyl (as opposed to inhalation) is unsafe,” the FDA would have the power to prescribe limits under 21 C.F.R. § 184 on the purposes and conditions for which diacetyl could be used—for example, not as a component of flavoring for microwave popcorn or butter substitutes that release a potentially harmful vapor from diacetyl when heated. Schneider, *supra*.

<sup>43</sup> *Id.*

<sup>44</sup> 21 C.F.R. § 186.1(b).

<sup>45</sup> 21 C.F.R. § 184.1(a).

<sup>46</sup> 21 C.F.R. § 184.1(b).

<sup>47</sup> 21 C.F.R. § 184.1(b)(1).



or shall use the ingredient in accordance with a food additive regulation.”<sup>48</sup> Fourth, the substance affirmed as GRAS for the purposes and conditions prescribed cannot be used “in a manner that may lead to deception of the consumer” or FFDCA violations.<sup>49</sup> Finally, ingredients listed as GRAS cannot be combined, in order to achieve the same technological effect in a food, at levels greater than were permitted for a single ingredient.<sup>50</sup>

## **The FDA’s 1997 Proposed Rule**

The procedure outlined in a FDA proposed rule from 1997 would eliminate the notice and comment rulemaking process described above for substances affirmed as GRAS.<sup>51</sup> The proposed rule would also end the GRAS petition process and create a new GRAS notification procedure.<sup>52</sup> Although the notice and comment rulemaking process for GRAS substances is still in effect in the FDA regulations, the FDA has effectively been using the GRAS notification procedure outlined in the proposed rule since 1998 without issuing a final rule. Since the FDA has not issued a final rule, it is important to note that the FDA’s procedure set forth in the 1997 proposed rule is only guidance and not law. The agency has also issued guidance for industry in the form of frequently asked questions about GRAS that includes a discussion of the GRAS notification program.<sup>53</sup> More than 250 GRAS notifications have been submitted under the procedure outlined in the 1997 proposed rule. The FDA has issued one of the three responses described below for most of these notices, and both a numerical and alphabetical list of notices received and agency responses can be found on the FDA’s website.<sup>54</sup>

Under the notification procedure in the proposed rule, industry submits a GRAS notification to the FDA that states the company’s view that the substance is GRAS. These notifications identify the notifier and describe the substance that is the subject of the notice, the applicable conditions of use, and the basis for the GRAS determination, including a summary of supporting information “that forms the basis for an exemption from a statutory requirement.”<sup>55</sup> The notifier “explicitly accepts responsibility for the GRAS determination,” unlike the protocol in the current regulations, in which such responsibility falls on the agency because an interested person has petitioned the

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<sup>48</sup> 21 C.F.R. § 184.1(b)(1).

<sup>49</sup> 21 C.F.R. § 184.1(c).

<sup>50</sup> 21 C.F.R. § 184.1(d).

<sup>51</sup> Substances Generally Recognized as Safe, 62 Fed. Reg. 18937, 18939 (proposed Apr. 17, 1997); *see also* Agency Information Collection Activities; Proposed Collection; Comment request; Notice of a Claim for Generally Recognized as Safe Exemption Based on a Generally Recognized as Safe Determination, 70 Fed. Reg. 73009 (Dec. 8, 2005).

<sup>52</sup> The FDA’s notification procedure outlined in the 1997 proposed rule is not unique. The Food and Drug Administration Modernization Act of 1997 (FDAMA) created a notification procedure for food contact substances, and developers of genetically engineered crops need to obtain authorization from USDA’s Animal and Plant Health Inspection Service through either a permit or notification process.

<sup>53</sup> Center for Food Safety and Applied Nutrition, FDA, Guidance for Industry: Frequently Asked Questions About GRAS (Dec. 2004), <http://www.cfsan.fda.gov/~dms/grasguid.html>.

<sup>54</sup> Center for Food Safety and Applied Nutrition, FDA, Numerical Listing of GRAS Notices (October 2007), <http://www.cfsan.fda.gov/~rdb/opa-gras.html>; Center for Food Safety and Applied Nutrition, FDA, Alphabetical Listing of GRAS Notices (Oct. 2007), <http://www.cfsan.fda.gov/~rdb/opagras1.html>.

<sup>55</sup> 62 Fed. Reg. 18947. “[T]he notifier must consent to grant the FDA access to the data and information that are the basis of the GRAS determination,” and the agency has stated that it “intends to conduct random audits of [this] data and information.” *Id.*

FDA to affirm a use of a substance as GRAS or the FDA itself has affirmed a substance's use as GRAS.<sup>56</sup>

Rather than requiring that the FDA affirm that a substance is GRAS through a notice-and-comment rulemaking, the 1997 proposed rule provides that the FDA does not make a finding that a substance in a GRAS notification made under the proposed rule process actually is a GRAS substance. Instead, the agency states that (1) it has “no questions” about the notifier’s conclusion that a substance is GRAS, (2) the notice does not provide a basis for a GRAS status determination, or (3) the notifier has stopped the GRAS notification process.<sup>57</sup> If the agency’s review of a GRAS notification does not furnish appropriate information to find a basis for a GRAS determination, it will issue such a response, potentially in light of the following reasons to question the use of the substance:

FDA may question the GRAS status of use of a substance if the information provided in a notice: (1) Does not adequately establish technical evidence of safety; (2) is not generally available; (3) does not convince the agency that there is the requisite expert consensus about the safety of the substance for its intended use; or (4) is so poorly presented that the basis for the GRAS determination is not clear. FDA also may be aware of information that is not included in the notice but raises important public health issues that lead the agency to question GRAS status of use of the substance.<sup>58</sup>

The FDA notes that notifiers “receive as a benefit a response that documents the agency’s awareness of the [GRAS] determination” by the notifier.<sup>59</sup>

If, as in the majority of the FDA’s responses to GRAS notification submissions, the FDA has no questions about the notification, this determination does not mean that the FDA has approved the substance in the notification as GRAS.<sup>60</sup> In other words, none of the uses of the substances reviewed by the FDA through a GRAS notification are deemed to actually be GRAS by the FDA.<sup>61</sup> Moreover, in contrast to the FDA’s GRAS affirmation regulations, which allow the FDA to place potential limits on the use of a GRAS substance, the GRAS notification procedures in the FDA’s proposed rule do not appear to allow this, as the FDA only responds in one of three ways noted above. Nonetheless, an FDA response of “no questions” could give a substance an imprimatur of safety from the federal government. Such a response may also give manufacturers confidence that the substance is acceptable, and they would be able to tell their suppliers and others of the FDA’s response to the notification. Additionally, an FDA response of “no questions” may convey to manufacturers a feeling of less uncertainty and less potential liability about using such a GRAS substance that has been through the GRAS notification process, as the agency may not be as likely to seize a substance or find a product adulterated or misbranded if the FDA itself has said it has “no questions.”<sup>62</sup>

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<sup>56</sup> 62 Fed. Reg. 18946.

<sup>57</sup> Substances Generally Recognized as Safe, 62 Fed. Reg. 18937 (proposed Apr. 17, 1997).

<sup>58</sup> 62 Fed. Reg. 18950.

<sup>59</sup> 62 Fed. Reg. 18947.

<sup>60</sup> 62 Fed. Reg. 18951.

<sup>61</sup> The use of the term ‘review’ here does not mean that the agency will necessarily “conduct its own detailed evaluation” of, for example, raw data of toxicological studies or data used to support the notifier’s GRAS determination. 62 Fed. Reg. 18948-49.

<sup>62</sup> See *Community Nutrition Institute v. Young*, 818 F.2d 943, 949 n.10 (D.C. Cir. 1987) (characterizing, in a case where the FDA set levels above which it could take action on adulterated corn, the U.S. Supreme Court’s description of (continued...))

As mentioned above, the agency has yet to issue a final rule on the notification procedure; however, the FDA has “invite[d] interested persons” to submit such notifications as described in the proposed rule on an “interim policy” basis until the publication of the final rule.<sup>63</sup> The agency has accepted more than 250 notification submissions under the proposed rule procedures.<sup>64</sup> In its proposal, the FDA has stated that it “will determine whether its experience in administering such notices suggests modifications to the proposed procedure.”<sup>65</sup> The agency’s description and adoption of the new GRAS notification process (as delineated in the proposed rule) on an interim policy basis may be characterized as the equivalent of a guidance document.<sup>66</sup>

## Statistics on FDA GRAS Notices

The chart below provides the number of FDA response letters in each of the three categories discussed above, as well as a fourth category for the number of GRAS notices that are awaiting a response from the FDA, and the percent of the total number of letters issued by the FDA under its procedure in the 1997 proposed rule. One GRAS notification, GRN No. 13, was counted twice—once in the “FDA has no questions” category and once in the “Notice does not provide a basis for a GRAS determination” category—because the FDA had no questions for three botanical substances in the notice (Chrysanthemum, Licorice, and Jellywort) but the FDA stated that the notice did not provide a basis for a GRAS determination for six other substances (Honeysuckle; Lophatherum; Mulberry leaf; Frangipani; Selfheal; Sophora flower bud).

The FDA’s response to GRAS notifications that were initially submitted, but then were either withdrawn or determined not to provide a basis for a GRAS determination, were only included for the resubmitted notices for the same substances. For example, Hawaii International Seafood, Inc. initially submitted its GRAS notification for tasteless smoke as GRAS Notice No. 5, but then at the company’s request, the FDA ceased to evaluate the notice. Hawaii International Seafood, Inc. then resubmitted its GRAS notification for tasteless smoke as GRAS Notice No. 15, and the FDA had no questions. Only the FDA’s response to the resubmitted notification is included on the chart below. There were 18 instances of GRAS notifications being resubmitted, which explains

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(...continued)

action levels as “agency assurance”: “In setting an action level, the FDA essentially assures food producers that it ordinarily will not enforce the general adulteration provisions of the Act against them.”)(internal citations omitted).

<sup>63</sup> 62 Fed. Reg. 18954-55.

<sup>64</sup> The FDA’s acceptance of GRAS notifications since the publication of the 1997 proposed rule could be seen as an “experiment[] while the rulemaking is in progress” that could bolster the need for a subsequent notice-and-comment period before the agency publishes a final rule. JEFFREY S. LUBBERS, *A GUIDE TO FEDERAL AGENCY RULEMAKING* 292-93 (4<sup>th</sup> ed. 2006). Agencies frequently publish requests for additional rounds of notice-and-comment during the rulemaking process. The FDA’s NPRM on GRAS substances asked for the submission of written comments by July 16, 1997. 62 Fed. Reg. 18938.

<sup>65</sup> 62 Fed. Reg. 18954.

<sup>66</sup> If the interim policy procedures are considered to be a guidance document, which is a type of general statement of policy under the Administrative Procedure Act (APA), 5 U.S.C. § 553(b), then the FDA arguably would not need to complete the rulemaking because the notice and comment provisions of the APA would not apply. *See* LUBBERS, *supra* note 64, at 94. Thus the agency would not appear to be violating the APA if the guidance document procedures are prospective and voluntary and if the interim policy preserves the FDA’s discretion. Moreover, the GRAS affirmation regulations are still law and may still be used by interested persons. However, completing the rulemaking may clarify agency policy. Additionally, although the APA does not impose a limit on the time between an agency’s publication of a proposed rule and its issuance of a final rule, the 1997 proposed rule may be considered to be stale, and a new rulemaking may be necessary. 5 U.S.C. § 555(b); LUBBERS, *supra* note 64, at 293, n. 82, 357-58.

the difference in the chart's total number of notices (238) and the number of GRAS notifications listed on the FDA website (256).

<b>Categories of FDA Responses or Response is Pending<sup>a</sup></b>	<b>FDA has no questions<sup>b</sup></b>	<b>Notice does not provide a basis for a GRAS determination</b>	<b>At notifier's request, FDA ceased to evaluate the notice</b>	<b>Pending</b>	<b>Total</b>
<b>Number of FDA Letters in Each Category<sup>a</sup></b>	179	10	22	27	238
<b>Percentage of Total Letters<sup>c</sup></b>	75.21	4.20	9.24	11.34	99.99 <sup>c</sup>

- a. The categories of FDA letters and the number of FDA letters in each category were obtained from the FDA Center for Food Safety and Applied Nutrition's Numerical Listing of GRAS Notices for July 2008. <http://www.cfsan.fda.gov/~rdb/opa-gras.html>.
- b. This category includes notices in which the FDA had no questions but stated that some uses of a GRAS substance may require a color additive listing.<sup>67</sup>
- c. Percentages were calculated by CRS and rounded to two decimal points.

## The Role of USDA in Food Additive Safety Determinations

Under the current legislative and regulatory schemes, the FDA shares responsibility for some food safety issues with the United States Department of Agriculture (USDA). While the FDA is responsible for safety of the vast majority of food categories, the USDA is specifically authorized to regulate the safety and wholesomeness of meat and poultry products that are intended for use as human food.<sup>68</sup> Under this authority, the USDA, and consequently the Food Safety and Inspection Service (FSIS),<sup>69</sup> is required to provide a mark of inspection on meat and poultry products.<sup>70</sup> The mark of inspection reflects a determination that the product is not adulterated<sup>71</sup> or misbranded.<sup>72</sup>

## Dual Process of Review for Meat and Poultry Products

There is a two-step process for approving the use of additive substances in meat and poultry products: (1) FDA determines the safety of substances and prescribes safe conditions of use, and

<sup>67</sup> See, e.g., Agency Response Letter GRAS Notice No. GRN 000156 from Laura M. Tarantino, Director, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, FDA, to George Burdock, Burdock Group (on behalf of LycoRed Natural Products Industries, Ltd.), Feb. 7, 2005, <http://www.cfsan.fda.gov/~rdb/opa-g156.html>.

<sup>68</sup> This authority is provided for by the Federal Meat Inspection Act (21 U.S.C. § 601 et seq.) and the Poultry Products Inspection Act (21 U.S.C. § 451 et seq.), respectively.

<sup>69</sup> The Secretary of the USDA delegates this authority to FSIS under 9 C.F.R. § 300.2.

<sup>70</sup> See 21 U.S.C. § 606; 21 U.S.C. § 457.

<sup>71</sup> A product can be considered "adulterated" if it "bears or contains any poisonous or deleterious substance which may render it injurious to health;" contains any additives considered unsafe; "consists in whole or in part of any filthy, putrid, or decomposed substance or is for any other reason unsound, unhealthful, unwholesome, or otherwise unfit for human food;" or "has been prepared, packed, or held under insanitary conditions." See 21 U.S.C. § 601(m).

<sup>72</sup> A product can be considered "misbranded" if its label is false or misleading; contains an inaccurate description of the product; does not identify its manufacturer, packer or distributor and an accurate statement of quantity of the contents; or does not contain other information that may be required by the act. See 21 U.S.C. § 601(n).

(2) FSIS determines whether new substances or new applications of substances are suitable for use in meat and poultry products.<sup>73</sup> In other words, FDA makes determinations based on the safety of the substance itself, while FSIS approves the substance's application to the meat or poultry product.

In 2000, the roles of FDA and FSIS in this joint review process of substances used in meat and poultry products were laid out in a Memorandum of Understanding (MOU).<sup>74</sup> The MOU provides for standard operating procedures regarding submissions to FDA or FSIS that, for example, petition for the approval of food and color additives intended for use in meat or poultry products, as well as GRAS notifications "regarding the use of a substance in the production of meat or poultry products."<sup>75</sup> The MOU generally instructs the agency that receives a request for review of a substance used in meat or poultry products to seek review by the other agency regarding the substance as well. For example, when FSIS receives a request for an acceptability determination regarding the application of a substance in the production of meat or poultry products, it confirms the status of the substance's safety with FDA.<sup>76</sup> Conversely, if FDA receives a request for a suitability determination regarding the use of a substance in meat or poultry products, the request must be transferred to FSIS.<sup>77</sup>

The MOU provides that when FDA receives a GRAS Notice regarding the use of a substance in the production of meat or poultry products, FDA and FSIS proceed jointly, as they would regarding requests for approval of a food or color additive intended for use in the production of meat or poultry products. FDA informs and consults with FSIS, and FSIS provides written comments to FDA within 60 days. FDA's response to the notifier includes information regarding the notifier's responsibilities under the Federal Meat Inspection Act and Poultry Products Inspection Act and "may include concerns about the suitability of the use of the substance in the production of meat or poultry products and, when applicable, any restrictions or conditions of use in the production of meat or poultry products that FSIS recommends in writing."<sup>78</sup>

## **FSIS Review of Substances in Meat or Poultry Products**

Under the dual review process, if FDA approves a substance, such as a food or color additive, or lists the substance as GRAS for use in food, the substance is not automatically acceptable for use in meat and poultry products. If FDA's approval of a food or color additive, or if the FDA's GRAS listing does not specifically mention meat or poultry products, FSIS needs an affirmative written statement from FDA that it did consider the substance's use in meat or poultry or that it has no objections with regard to safety when the substance is used in meat or poultry.<sup>79</sup> FSIS then

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<sup>73</sup> See 9 C.F.R. § 424.21.

<sup>74</sup> Memorandum of Understanding Between the Food Safety and Inspection Service United States Department of Agriculture and the Food and Drug Administration United States Department of Health and Human Services Regarding the Listing or Approval of Food Ingredients and Sources of Radiation Used in the Production of Meat and Poultry Products, [http://www.fsis.usda.gov/Regulations\\_&\\_Policies/Labeling\\_FDA\\_MOU/index.asp](http://www.fsis.usda.gov/Regulations_&_Policies/Labeling_FDA_MOU/index.asp).

<sup>75</sup> *Id.*

<sup>76</sup> Standard Operating Procedures D, [http://www.fsis.usda.gov/Regulations\\_&\\_Policies/Labeling\\_FDA\\_MOU/index.asp](http://www.fsis.usda.gov/Regulations_&_Policies/Labeling_FDA_MOU/index.asp).

<sup>77</sup> Standard Operating Procedures E, [http://www.fsis.usda.gov/Regulations\\_&\\_Policies/Labeling\\_FDA\\_MOU/index.asp](http://www.fsis.usda.gov/Regulations_&_Policies/Labeling_FDA_MOU/index.asp).

<sup>78</sup> Standard Operating Procedures C, [http://www.fsis.usda.gov/Regulations\\_&\\_Policies/Labeling\\_FDA\\_MOU/index.asp](http://www.fsis.usda.gov/Regulations_&_Policies/Labeling_FDA_MOU/index.asp).

<sup>79</sup> Safe and Suitable Ingredients Used in the Production of Meat and Poultry Products, FSIS Directive 7120.1, (continued...)

needs to determine suitability and whether rulemaking is required.<sup>80</sup> Whether a substance is suitable depends on “the effectiveness of the substance in performing the intended technical purpose of use, at the lowest level necessary, and the assurance that the conditions of use will not result in an adulterated product or one that misleads customers.”<sup>81</sup>

To satisfy the requirement of suitability, FSIS needs certain data as evidence that the substance or use of the substance is suitable for its intended technical purposes.<sup>82</sup> The data must show the effectiveness of the substance in achieving the intended purpose of its use.<sup>83</sup> The data must show that the use is at the lowest level necessary to achieve the intended effect under the proposed conditions of use.<sup>84</sup> The data must show that the use cannot result in adulteration or misbranding.<sup>85</sup> FSIS regulations currently prohibit the use of substances that conceal damage or inferiority or make a product appear better or of greater value than it is.<sup>86</sup> The regulations also provide that substances that are intended to be used to impart color in any meat or poultry product cannot be used unless approved as a color additive (under FDA regulations) or approved by FSIS regulations.<sup>87</sup> This data must be provided for each separate product in which the use of the substance is intended.<sup>88</sup> Based on the merits of these data, FSIS can permit the use of the substance or the new use of a substance under the proposed conditions of use and in conformance with standards and labeling requirements.

With respect to whether rulemaking is required, if FDA has found or confirmed the safety of the substance, FSIS regulations are not amended.<sup>89</sup> If rulemaking is not required, FSIS notifies the requestor in writing of its determination in what is known as an acceptability determination.<sup>90</sup> If the use of the substance is prohibited or limited or if the substance is not normally found in the product, FSIS regulations may be necessary.<sup>91</sup> If rulemaking is required, the substance is added to the current list of approved substances after the formal rulemaking process is completed.<sup>92</sup> Because not all approved substances are listed in the published regulations under this process,

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December 17, 2002, part V, <http://www.fsis.usda.gov/OPPDE/rdad/FSISDirectives/7120.1.pdf>.

<sup>80</sup> *Id.*

<sup>81</sup> Guidance on the Procedures for Joint Food Safety and Inspection Service and Food and Drug Administration Approval of Ingredients and Sources of Radiation Used in the Production of Meat and Poultry Products, <http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-022N/ApprovalofIngredients.htm>.

<sup>82</sup> See Guidance on the Procedures for Joint FSIS and FDA Approval of Ingredients and Sources of Radiation Used in the Production of Meat and Poultry Products, <http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-022N/ApprovalofIngredients.htm>.

<sup>83</sup> *Id.*

<sup>84</sup> *Id.*

<sup>85</sup> *Id.*

<sup>86</sup> See 9 C.F.R. § 424.23.

<sup>87</sup> See 9 C.F.R. § 424.21(b)(3).

<sup>88</sup> FSIS has accepted data that has not been specifically applied to all categories if the data can be easily extrapolated to all species. See GRAS Notice No. 83, *supra* note 1.

<sup>89</sup> *Id.*

<sup>90</sup> Safe and Suitable Ingredients Used in the Production of Meat and Poultry Products, FSIS Directive 7120.1, December 17, 2002, part V, <http://www.fsis.usda.gov/OPPDE/rdad/FSISDirectives/7120.1.pdf>.

<sup>91</sup> *Id.*

<sup>92</sup> Specific substances that FSIS has approved by regulation are listed in 9 C.F.R. § 424.21(c).

FSIS maintains a directive system of all approved substances that are accepted as safe and suitable by FSIS on its website.<sup>93</sup>

## **GRAS Substances**

As discussed above, a determination that a substance is GRAS may be made by the FDA, through the affirmation of the GRAS status of a substance, or by industry (including via a GRAS notification), based on scientific procedures or common use of a substance in food prior to January 1, 1958.<sup>94</sup> FSIS cannot rely on the industry's determination of a substance as GRAS because of statutory requirements requiring USDA inspection of meat and poultry products.<sup>95</sup> Meat and poultry products are required to have a mark of inspection that "reflects a determination by FSIS that the food product is not adulterated, and thus that all substances used to make the product are safe and suitable."<sup>96</sup> As a result, "FSIS must have from FDA, at the very least, a written statement of no objection with regard to the safety of the use of the substance."<sup>97</sup>

## **GRAS Notices Regarding Intended Uses of Carbon Monoxide**

Under the process outlined in the FDA's 1997 proposed rule, manufacturers have submitted GRAS notifications to the FDA that state their view that carbon monoxide is a GRAS substance. The FDA has responded that it has "no questions" about the conclusion that CO is GRAS. The FDA's responses to the GRAS notifications informed the industry that it had the continuing responsibility to ensure the substance's safety and compliance with other legal and regulatory requirements.

The FDA first determined that it had no questions regarding a GRAS notification for the use of carbon monoxide in March 2000. The notifier, Hawaii International Seafood, Inc., stated its determination that the use of "tasteless smoke" (of which carbon monoxide is a component) on raw seafood is GRAS.<sup>98</sup> The company defined its intended use as involving a procedure before the fish is frozen that would preserve the color, taste, aroma, and texture of raw seafood.<sup>99</sup> In addition to determining that it had no questions, the FDA stated that the company's use of

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<sup>93</sup> Safe and Suitable Ingredients Used in the Production of Meat and Poultry Products, FSIS Directive 7120.1, Dec. 17, 2002, <http://www.fsis.usda.gov/OPPDE/rdad/FSISDirectives/7120.1.pdf>. An amended version (dated Oct. 23, 2007) can be found at <http://www.fsis.usda.gov/OPPDE/rdad/FSISDirectives/7120.1Amend13.pdf>.

<sup>94</sup> Guidance on the Procedures for Joint FSIS and FDA Approval of Ingredients and Sources of Radiation Used in the Production of Meat and Poultry Products, <http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-022N/ApprovalofIngredients.htm>.

<sup>95</sup> See 21 U.S.C. § 601 et seq.; 21 U.S.C. § 451 et seq.

<sup>96</sup> Guidance on the Procedures for Joint FSIS and FDA Approval of Ingredients and Sources of Radiation Used in the Production of Meat and Poultry Products, <http://www.fsis.usda.gov/OPPDE/rdad/FRPubs/00-022N/ApprovalofIngredients.htm>.

<sup>97</sup> *Id.*

<sup>98</sup> The company first submitted a notification regarding tasteless smoke as a GRAS substance in 1998, but asked the FDA to cease to evaluate the notice and then resubmitted the notice in 1999. See GRAS Notice No. 15, *supra* note 3; Agency Response Letter GRAS Notice No. GRN 000005 from Linda S. Kahl, Regulatory Policy Branch, Division of Product Policy, Office of Premarket Approval, Center for Food Safety and Applied Nutrition, FDA, to Martin J. Hahn, Hogan & Hartson LLP (on behalf of Hawaii International Seafood, Inc.) (Dec. 11, 1998), <http://www.cfsan.fda.gov/~rdb/opa-g005.html>.

<sup>99</sup> GRAS Notice No. 15, *supra* note 3.

tasteless smoke constituted a preservative and noted that the fish must be labeled so that it complies with misbranding provisions of the FFDCA and the FDA's labeling regulations.

The FDA next determined that it had no questions regarding the use of carbon monoxide as a GRAS substance in meat packaging in a letter to Pactiv Corporation in February 2002.<sup>100</sup> The agency also stated that it had not made an independent determination of the GRAS status of the use of CO described in the notification.<sup>101</sup> FDA noted the industry's conclusion that the use of carbon monoxide allows meat to maintain a desirable red color during storage but once the product was removed from storage, the color of the meat "deteriorates at a similar rate to that of meat that has not been exposed to CO."<sup>102</sup> FSIS concluded that the use of carbon monoxide in the MAP system as it had been described by Pactiv in its GRAS notification "would be acceptable for packaging red meat cuts and ground meat."<sup>103</sup> FSIS agreed with the company that "there is no lasting functional effect in the food and there is an insignificant amount of carbon monoxide present in the finished product under the proposed conditions of use."<sup>104</sup> FDA restated that it had no questions regarding the industry's determination that carbon monoxide is GRAS in July 2004 and September 2005 in response letters to Precept Foods, LLC, and Tyson Foods, Inc., respectively.<sup>105</sup> Currently, two additional GRAS notifications regarding carbon monoxide are pending.<sup>106</sup>

Although notifiers seeking a response from the FDA on GRAS notices for CO have submitted notices describing other conditions of use of CO, it appears possible that a manufacturer could potentially rely on a FDA response that the agency "has no questions" to use a GRAS substance in a manner other than the use described in the GRAS notice for which the FDA had no questions. For example, two of the CO GRAS notices, 83 and 143, discuss a level of CO that is 0.4 percent in a MAP system. Conceivably, a company could interpret the agency's lack of questions regarding the 0.4 CO level and use a CO level of 0.45 percent in a MAP system. However, if the FDA made a determination that the use of 0.45 percent CO, or even 0.4 percent CO, violated the FFDCA, the agency could attempt to seek criminal and civil penalties for violations such as

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<sup>100</sup> See GRAS Notice No. 83, *supra* note 1.

<sup>101</sup> See GRAS Notice No. 83, *supra* note 1.

<sup>102</sup> GRAS Notice No. 83, *supra* note 1.

<sup>103</sup> GRAS Notice No. 83, *supra* note 1. FDA response letters include FSIS conclusions on the substance. Although FSIS did not approve the use of carbon monoxide based on the original information provided, it did ultimately approve the use after receiving additional data. See Letters from Robert C. Post, Director, Labeling and Consumer Protection Staff, FSIS, to Lane Highbarger, Office of Food Additive Safety, FDA (Apr. 28, 2004 and June 2, 2004).

<sup>104</sup> See GRAS Notice No. 83, *supra* note 1.

<sup>105</sup> See Agency Response Letter GRAS Notice No. GRN 000143 from Laura M. Tarantino, Director, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, FDA, to Gary J. Kushner and Anne M. Boeckman, Hogan and Hartson (on behalf of Precept Foods, LLC) (July 29, 2004), <http://www.cfsan.fda.gov/~rdb/opa-g143.html>, [hereinafter GRAS Notice No. 143]; Agency Response Letter GRAS Notice No. GRN 000167, from Laura M. Tarantino, Director, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, FDA, to Mark L. Itzkoff, Olsson, Frank and Weeda, PC (on behalf of Tyson Foods, Inc.), <http://www.cfsan.fda.gov/~rdb/opa-g167.html>, [hereinafter GRAS Notice No. 167]. The FDA ceased to evaluate another GRAS notification regarding carbon monoxide, GRAS Notice No. 167, at the request of the notifier, Freezing Machines, Inc. Agency Response Letter GRAS Notice No. GRN 000166 from Antonia Mattia, Director, Division of Biotech and GRAS Notice Review, Office of Food Additive Safety, Center for Food Safety and Applied Nutrition, FDA, to Mark L. Itzkoff, Olsson, Frank and Weeda, PC (on behalf of Freezing Machines, Inc.) (Oct. 12, 2005), <http://www.cfsan.fda.gov/~rdb/opa-g166.html>.

<sup>106</sup> See listings for GRAS Notifications 188 and 194. Center for Food Safety and Applied Nutrition, FDA, Numerical Listing of GRAS Notices (Oct. 2007), <http://www.cfsan.fda.gov/~rdb/opa-gras.html>.



adulteration and misbranding. The FFDCA also provides the FDA with other enforcement mechanisms such as seizure and injunctions.

## **Proposed Legislation in the 110<sup>th</sup> Congress**

Two bills have been introduced in the House of Representatives regarding the use of carbon monoxide in meat and poultry products: H.R. 3115 (the Carbon Monoxide Treated Meat, Poultry, and Seafood Safe Handling, Labeling, and Consumer Protection Act) and H.R. 3610 (the Food and Drug Import Safety Act of 2007). Additionally, the discussion draft of the Food and Drug Administration Globalization Act of 2008, issued by Representatives Dingell, Pallone, and Stupak, similarly addresses the issue. Other bills also address GRAS substances: H.R. 2633, H.R. 3290, H.R. 3580, H.R. 6635, and S. 1342.

H.R. 3115, H.R. 3610, and the discussion draft propose to amend FFDCA § 201.<sup>107</sup> Under the proposals, if carbon monoxide is used to treat meat, poultry or seafood that is intended for human consumption and if the conditions of that use would affect the color of the products, carbon monoxide must be treated as a color additive under FFDCA,<sup>108</sup> unless the product's label includes a statement that is "prominently and conspicuously" placed to notify the consumer of the use of carbon monoxide and to warn the consumer of proper factors to judge the safety of the product.<sup>109</sup> The bills and the discussion draft would allow the Secretary of Health and Human Services (HHS) to establish alternative labeling requirements five years after the effective date of the labeling requirement, if the Secretary finds that the labeling requirement is no longer necessary to prevent consumer deception.

The discussion draft contains an additional provision related to GRAS determinations that would require the Secretary to publish, in the *Federal Register*, notice of receipt of a request for a substance to be determined by the Secretary to be GRAS. The Secretary would then have 90 days after publication of the notice to determine whether the substance is GRAS; the Secretary's determination would also be published in the *Federal Register*. It is unclear if the discussion draft is referring to a petition for affirmation of GRAS status under 21 C.F.R. § 170.35 as the "request for a substance to be determined by the Secretary to be a GRAS substance," or an alternate situation. (See page 5 in the PDF version of this report.) If the FDA Commissioner receives a petition to affirm the GRAS status of a substance "that directly or indirectly become[s] [a] component[] of food," the Commissioner must publish a notice of the filing of the petition in the *Federal Register* within 30 days after the date of filing of the petition.<sup>110</sup> There is a 60-day comment period after the notice of filing in the current regulations.<sup>111</sup> The current regulations state that the FDA Commissioner will publish an order listing the substance as GRAS if the petition and all available information "provide[s] convincing evidence that the substance is

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<sup>107</sup> H.R. 3115, 110<sup>th</sup> Cong. § 3 (2007); H.R. 3610, 110<sup>th</sup> Cong. § 14 (2007).

<sup>108</sup> See H.R. 3115 § 3(a); H.R. 3610 § 14(a).

<sup>109</sup> The statement provided by the bills reads as follows: "SAFETY NOTICE: Carbon monoxide has been used to preserve the color of this product. Do not rely on color or the 'use or freeze by' date alone to judge the freshness or safety of the product. Discard any product with an unpleasant odor, slime, or a bulging package." H.R. 3115 § 3(a); H.R. 3610 § 14(a). The statement provided by the discussion draft would remove the last sentence and slightly alter the wording as follows: "CONSUMER NOTICE: Carbon monoxide has been used to preserve the color of this product. Do not rely on color or the 'use or freeze by' date alone to judge the freshness of the product." Discussion Draft, § 132.

<sup>110</sup> 21 C.F.R. § 170.35(c)(2).

<sup>111</sup> 21 C.F.R. § 170.35(c)(4).

GRAS.”<sup>112</sup> Alternatively, if the Commissioner “concludes that there is a lack of convincing evidence that the substance is GRAS and that it should be considered a food additive subject to” FFDCA § 409, the Commissioner must publish a notice of this determination in the *Federal Register*.<sup>113</sup>

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<sup>112</sup> 21 C.F.R. § 170.35(c)(5).

<sup>113</sup> 21 C.F.R. § 170.35(c)(4)-(6).

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