Donald F. Schmitt, MPH
ToxStrategies, Inc.
931 W. 75th St., Suite 137, PMB 255
Naperville, IL 60565

Re: GRAS Notice No. GRN 001018

Dear Mr. Schmitt:

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 001018. We received the notice that you submitted on behalf of Cargill, Inc. (Cargill) on June 11, 2021, and filed it on October 28, 2021. Cargill submitted an amendment to the notice on February 7, 2022, which discussed the extent of denaturation of myoglobin in cooked meat, the weight-to-gas volume ratio for typical packages of ready-to-eat (RTE) meats used in the dietary exposure estimate, and the dates of Cargill's review of the scientific literature addressing safety.

The subject of the notice is carbon monoxide (CO) for use at levels up to 0.48% as a component of a modified atmosphere packaging (MAP) system for fully cooked, sliced, pre-packed, RTE deli meats and poultry (RTE deli meats and poultry). The notice informs us of Cargill's view that this use of CO is GRAS through scientific procedures.

Cargill describes CO, CAS Registry Number 630-08-0, as a colorless, odorless, gas. Cargill describes the typical production method for CO and states that it can be produced by steam methane reforming; sulfur-free hydrocarbons and superheated steam are passed over a nickel catalyst. The hydrocarbon/steam mixture is converted to hydrogen and carbon oxides, which are then separated from each other.

Cargill states that the CO will be "food-grade," with a 98% minimum purity. The remaining 2% are components found in the atmosphere (e.g., nitrogen, oxygen, carbon dioxide, argon, water, hydrogen and/or methane).

Cargill states that CO is included in the MAP system to stabilize the color of the RTE deli meats and poultry. CO is not intended to affect microbial growth and will not extend the shelf life of RTE deli meats and poultry.[1] Cargill provides a shelf-life study for cooked beef using the MAP system over a 70-day period. Cargill states that the indicators of spoilage were similar for both the control and the sample using the MAP system, regardless of the color of the product.

[1] In the February 7, 2022, amendment, Cargill further clarifies that CO in these formulations stabilizes the undenatured meat and poultry pigment myoglobin in RTE deli meats and poultry, and the utility of CO in RTE deli meats and poultry will be dependent upon cooking temperature and formulation.

Cargill estimates dietary exposure to CO in a manner similar to that described in GRN 000143.[2] Cargill notes that the dietary exposure scenarios are based upon three different package sizes typically used for cooked RTE deli meats and poultry, actual package volumes, and an ingestion scenario where 100% of the CO in the package is absorbed by the meat or poultry and 100% of the CO is ingested by the consumer. Cargill estimates that the dietary exposure to CO would range from 0.31 to 0.42 mg of CO per portion of the RTE deli meats or poultry, depending upon the package volume and weight of the packaged RTE deli meats or poultry.[3,4] Cargill notes that this estimated intake of CO from these uses in packaging meat is small compared to the amount that is presently accepted as a safe exposure limit by the Environmental Protection Agency (EPA) and the Occupational Safety and Health Administration (OSHA).[5]

Cargill cites the safety information in several previous GRAS notices[6] that received no questions letters from FDA for the use of CO up to 0.48% in MAP packaging in support of their GRAS conclusion. Cargill also states that it conducted literature searches through May 2022 and notes that they did not find information that would contradict their conclusion of safety.

Based on the totality of the data and information, Cargill concludes carbon monoxide is GRAS for its intended use.

Use in Products under USDA Jurisdiction

As provided under 21 CFR 170.270, during our evaluation of GRN 001018, we coordinated with the Food Safety and Inspection Service (FSIS) of the United States Department of Agriculture. Under the Federal Meat Inspection Act, the Poultry Products Inspection Act, and the Egg Products Inspection Act, FSIS determines the efficacy and suitability of ingredients used in meat, poultry, and egg products, and prescribes safe conditions of use. Suitability relates to the ingredient's effectiveness in performing its intended technical effect and the assurance that the ingredient's use will not result in products that are adulterated or misleading for consumers.

---

[2] CO for use as a component of a MAP system for case-ready fresh beef and pork was the subject of GRN 000143. FDA evaluated this notice and responded in a letter dated July 29, 2004, stating that FDA had no questions at that time regarding the notifier's GRAS conclusion.

[3] Cargill defines 2 ounces (56 g) as a standard portion size (serving size) for RTE deli meats and poultry.

[4] Using food consumption data from the 2015-2018
and the maximum amount of CO absorbed in packaged deli meat and poultry (7.48 mg CO/kg meat or poultry, Table 1 in the February 7, 2022, amendment), FDA estimates dietary exposure for CO to be 0.36 mg/p/d at the mean and 0.73 mg/p/d at the 90th percentile. This is consistent with the dietary exposure estimates provided by Cargill.

[5]

[6] CO was the subject of GRNs 000083, 000143, 000167, and 000251. We evaluated these notices and responded in letters dated February 21, 2002, July 29, 2004, September 29, 2005, and January 25, 2012, respectively, stating that we had no questions at that time regarding the respective notifier's GRAS conclusion.

FSIS has advised the following with respect to the statutes it administers:

> FSIS has completed its review of the GRN 1018 and has determined that it could not evaluate the suitability of CO as a component of a modified atmosphere packaging system in fully cooked, sliced, pre-packed, RTE deli meats and poultry. In their request, Cargill provided an expert opinion letter and a study completed on cooked beef, however there was no data presented to support its effectiveness on RTE poultry. Additionally, the notifier did not support how CO for this use would constitute a processing aid.
>
> If Cargill intends for this use of CO to be included in Directive 7120.1, FSIS will require additional support to demonstrate efficacy and suitability in the identified USDA-regulated products.[7]

FSIS requested that we advise you to seek regulatory guidance from its Risk Management and Innovations Staff (RMIS) about the use of CO in meat, poultry, and egg products. You should direct such an inquiry to Dr. Melvin Carter, Director, RMIS, Office of Policy and Program Development, FSIS by email at Melvin.Carter@usda.gov.

Section 301(ll) of the Federal Food, Drug, and Cosmetic Act (FD&C Act)

Section 301(ll) of the FD&C Act prohibits the introduction or delivery for introduction into interstate commerce of any food that contains a drug approved under section 505 of the FD&C Act, a biological product licensed under section 351 of the Public Health Service Act, or a drug or a biological product for which substantial clinical investigations have been instituted and their existence made public, unless one of the exemptions in section 301(ll)(1)-(4) applies. In our evaluation of Cargill's notice concluding that CO is GRAS under its intended conditions of use, we did not consider whether section 301(ll) or any of its exemptions apply to foods containing CO. Accordingly, our response should not be construed to be a statement that foods containing CO, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

[7] FDA expects that Cargill will copy us on any communication or data provided to FSIS.

Conclusions

Based on the information that Cargill provided, as well as other information available to FDA, we have no questions at this time regarding Cargill's conclusion that CO is GRAS under its intended conditions of use. This letter is not an affirmation that CO is GRAS under 21 CFR 170.35. Unless noted above, our review did not address other provisions of the FD&C Act. Food ingredient manufacturers and food producers are responsible for ensuring that marketed products are safe and compliant with all applicable legal and regulatory requirements.

In accordance with 21 CFR 170.275(b)(2), the text of this letter responding to GRN 001018 is accessible to the public at www.fda.gov/grasnoticeinventory.

Sincerely,

Susan J. Carlson -S

Digitally signed by Susan JCarlson -S
Date: 2022.08.11 17:53:43 -04'00'

Susan Carlson, Ph.D.
Director
Division of Food Ingredients
Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition

cc: Melvin Carter, Ph.D.
Director
USDA/FSIS/OPPD/RMIS
Stop Code 3782, Patriots Plaza III
1400 Independence Ave. SW
Washington, DC 20250-3700