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OLSSON, FRANK AND WEEDA, P.C.

ATTORNEYS AT LAW
SUITE 400
1400 SIXTEENTH STREET, N.W.
WASHINGTON, D.C. 20036-2220
(202) 789-1212
FACSIMILE (202) 234-3550

PHILIP C. OLSSON
RICHARD L. FRANK
DAVID F. WEEDA (1948-2001)
DENNIS R. JOHNSON
ARTHUR Y. TSIEN
JOHN W. BODE*
STEPHEN D. TERMAN
MARSHALL L. MATZ
MICHAEL J. O'FLAHERTY
DAVID L. DURKIN
NEIL F. O'FLAHERTY
PAMELA J. FURMAN
BRETT T. SCHWEMER
TISH E. PAHL
ROBERT A. HAHN

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STEPHEN L. LACEY
EVAN P. PHELPS
VALERIE B. SOLOMON
JOLYDA O. SWAIM
KATHRYN E. BALMFORD

COUNSEL
NAOMI J. L. HALPERN

OF COUNSEL
JUR T. STROBOS
JACQUELINE H. EAGLE
KENNETH D. ACKERMAN
MARK L. ITZKOFF
DAVID A. BIEGING

SR. GOVERNMENT AFFAIRS ADVISOR
JOHN R. BLOCK
CHARLES W. STENHOLM
BRIAN E. JOHNSON
SALLY S. DONNER
BRENT W. GATTIS

Sender's Direct Phone (202) 518-6327
Sender's Direct Facsimile (202) 234-2686

December 22, 2005

RECEIVED
DEC 2 3 2005
OFFICE OF
FOOD ADDITIVE SAFETY

BY FEDERAL EXPRESS

Office of Food Additive Safety (HFS-200)
Center for Food Safety and Applied Nutrition
Food And Drug Administration
5100 Paint Branch Parkway
College Park, MD 20740-3835

Dear Sirs:

On behalf of our client, Tyson Foods, Inc., we are hereby submitting four copies of the enclosed Generally Recognized As Safe (GRAS) Notification for the use of carbon monoxide (CO) in modified atmosphere packaging (MAP) for red meat products. As discussed in this Notice, the application discussed herein is a modification of the application previously reviewed by FDA under GRASN 167. More specifically, Tyson Foods is hereby notifying the agency of its determination that the use of CO in Modified Atmosphere Packaging (MAP) for "case-ready" red meat products where the concentration of CO in the MAP gases does not exceed 5.5 mg per pound of packaged meats is GRAS.

Should you have any questions regarding this notice, please do not hesitate to contact us.

Sincerely,

Mark L. Itzkoff

MLI:jdm
Enclosures

GRAS Claim for the Use of Carbon Monoxide In Modified Atmosphere Packaging For Red Meat Products

Submitted by Tyson Foods, Inc.

December 22, 2005

Section I

GRAS Claim

Tyson Foods, Inc. hereby submits this GRAS claim for the use of carbon monoxide (CO) in modified atmosphere packaging (MAP) for red meat products.

A. Name and Address of Notifier:

Tyson Foods, Inc.
2210 Oaklawn Drive
Springdale, Arkansas 72765

B. Common or Usual Name of Substance:

The common or usual name of the substance is carbon monoxide. The Chemical Abstract Services Registration Number (CASRN) for this substance is 630-08-0.

C. Conditions of Use:

In this Notification, CO will be used in Modified Atmosphere Packaging (MAP) for "case-ready" red meat products where the concentration of CO in the MAP gases does not exceed 5.5 mg per pound of packaged meats.[1] This application is the same end use and technical purpose, MAP packaged red meat products, described in GRAS Notices GRASN 167, 83 and 143. This Notice differs only in the consumable amount of CO.

The meat packaged using the MAP described herein will be labeled with a "use-or-freeze-by" date. The package dating is designed to minimize the impact of spoilage organisms, and is the same system used for meats packaged using the MAP system detailed in GRASN 167.

D. Basis for GRAS Determination:

Tyson Food has commissioned a panel of experts (the GRAS Panel) to review the safety of the proposed use of CO. The GRAS panel reviewed publicly available data on the toxicology of carbon monoxide, including the currently effective GRAS Notices (GRASN 43, 83 and 167) and concluded that:

> addition of carbon monoxide at levels intended not to exceed 5.5 mg per pound ... to MAP packaging systems ... is safe for addition to fresh muscle cuts of beef and pork and fresh ground beef. Further, based on

[1] As shown In GRASN 167, 0.4% by weight is equivalent to 2.2 mg/pound of packaged meat. Therefore, 1.0% by weight will be equivalent to 5.5 mg/pound or 12 mg/kg.

current good manufacturing practices, the addition of carbon monoxide to MAP as presented in this notification, presents no significant risk of pathogenic growth or spoilage masking to the consumer when properly labeled with open code or "use or freeze by" dating with expiration dates as specified for the meat types.

The full report of the GRAS Panel is attached in Appendix I.

E. **Data Availability Statement:**

The data and information that are the basis for the Notifier's GRAS is attached in Appendix I.

Respectfully submitted,

Mark L. Itzkoff
Counsel for Tyson Foods, Inc.

Section II

Identity of the Notified Substance

The substance that is the subject of this Notice is Carbon Monoxide (CO), a colorless, odorless gas, with the CASRN 630-08-0. A Material Safety Data Sheet for this material is attached in Appendix II.

The specific CO used in this process will be commercial, "food grade" CO. The purity specifications will be the same as those set forth for CO in GRASN 167, *i.e.*, the minimum purity will be 98 percent carbon monoxide while the other 2 percent will be residual atmospheric gases (nitrogen, oxygen, carbon dioxide, argon, water, hydrogen, methane, etc). Thus, the use of carbon monoxide set forth herein will not result in the introduction into processed red meat of any materials not previously considered under GRASN's 83, 143 and 167.

Section III

INFORMATION ON SELF-LIMITING LEVELS OF USE

As discussed in the GRAS panel report, the function of carbon monoxide in the MAP is to help maintain the appearance of the packaged meat. More specifically, the CO reacts with myoglobin in the muscle, similar to oxygen to form carboxy-myoglobin. The CO-myoglobin complex fixes the red color in the packaged meats that is also imparted by oxymyoglobin. Since the CO must react with myoglobin to produce the desired effect, the effectiveness of additional CO in the MAP is limited by the concentration of myoglobin in the processed meats.

Data in the public literature shows that the use of CO in concentrations between 1.0 and 10% by weight in MAP packaging result in the optimum product appearance.[2] As noted in Table 1, attached, 1.0% by weight in MAP packaging is equivalent to 5.5 mg per pound of meat assuming a standard packaging configuration. In this Notice, we have opted to limit the concentration of CO to the lowest level that will produce the optimum appearance, 5.5 mg per pound of meat.

While this Notice will increase the level of CO in MAP packaging from 2.2 mg/ lb to 5.5 mg/ lb, it should be emphasized that this increase will not affect consumer safety. The GRAS Panel has fully evaluated the safety of the exposure to carbon monoxide and, as noted above, has concluded that such use is safe.

Further, this use will not pose any additional risk from pathogenic growth or spoilage organisms. All meat products packaged will be labeled with a "use-or-freeze-by" date. There is no incentive for meat packagers to add additional CO, since such addition would not extend the period of optimum color. Therefore, there is an economic incentive to limit the quantity of CO used in modified atmosphere.

The increase in CO concentration over GRASN 167 is intended to allow for reduced package size which requires a corresponding reduction in package headspace. Consumers desire this type of package and a .40% CO gas blend will not produce this type of package.

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[2] Clark et. al., *Use of Carbon Monoxide for Extending Shelf-life of Prepackaged Fresh Beef*, 9 J. Inst of Food Science Technology, 114-118 (1976)

Section IV

Basis for Notifier's Claim

The basis for the Notifier's claim is set forth in detail in the attached Expert Panel ("GRAS Panel") Statement, "Determination of the GRAS Status of Carbon Monoxide as a Component of a Modified Atmosphere Packaging System for Use with Fresh Beef and Pork." The Statement and supporting documents are attached in Appendix I.

In brief, the GRAS Panel estimated that the potential exposure to CO from the proposed use in the modified atmosphere packaging will be about 0.14 mg/meal with a "worse case" exposure of 3 mg CO per meal. The Panel compared this exposure to the available literature, including the Environmental Protection Agency's National Ambient Air Quality Standard (NAAQS) for carbon monoxide and concluded that the negligible increased contributions from the intake or inhalation of CO packaging containing MAP gases, the proposed increase in allowable CO concentrations to 5.5 mg per pound of meat or a maximum of 6.6 mg per pound allowing for process variants, from prior approved levels of 2.2 mg per pound poses no health concerns.

As noted in the Expert Panel Statement, the Panel addressed only the potential toxicological affect of CO exposure. The Expert Panel did not address the potential for masking the presence of spoilage organisms on the packaged beef. As discussed above, all products packaged using this system will be labeled with a "use-or-freeze-by" date. The same dating system is used by Tyson in accordance with meat packaged under GRAS No. 167. The only difference between the earlier GRAS Notice and the current Notice is the higher CO concentration.

Under this notification, the quantity of CO present in the food package will be no more than 5.5 mg per pound of meat. In GRN 143, Precept Foods estimated that 30% of the CO present in the MAP package will be absorbed by the meat. Using this same estimate, we calculate that the amount of CO that may be present in package meat from the use of the MAP packaging will not exceed 1.65 milligrams per pound.[3] Published studies indicate that the concentration of CO in the meat is reduced by 85% during cooking.[4] Thus, the final concentration in the cooked meat product should be no more than 0.25 mg/lb.[5]

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[3] (5.5 mg/lb)(0.30) = 1.65 mg/lb.

[4] The studies are discussed in detail in the attached Expert Panel Statement.

[5] (1.65 mg/lb)(0.15) = 0.25 mg/lb

Finally, it is estimated that a typical serving of the package meat consists of an 8.8 ounce portion. Thus, the quantity of CO that may be consumed as a result of this notice will not exceed 0.14 milligrams per meal.[6]

As discussed in the GRAS Panel Statement, the literature shows that the use of 5.5 mg carbon monoxide per lb of meat in the MAP will not result in increased microbial growth. Thus the rate of microbial growth will not exceed the rate in systems where FDA and USDA have already determined that the "use-or-freeze-by" dating system provides proper protection from spoilage organisms. Therefore, the "use-or-freeze-by" dating system currently in place under GRAS No. 167 will also ensure the suitability of meat packaged with the prior CO concentration.

[6] ((8.8 ounces/meal)/(16 ounces/lb.))(0.25 mg/lb) = 0.14 mg/meal

EXPERT PANEL STATEMENT

DETERMINATION OF THE GRAS STATUS OF CARBON MONOXIDE AS A COMPONENT OF A MODIFIED ATMOSPHERE PACKAGING SYSTEM FOR USE WITH FRESH BEEF AND PORK

The undersigned, an independent panel of recognized experts, qualified by scientific training and relevant national and international experience to evaluate the safety of food and food ingredients, was requested by Tyson Foods, Inc. to determine the Generally Recognized As Safe (GRAS) status of carbon monoxide as a component of a modified atmosphere packaging system (MAP) for use with case-ready fresh beef (muscle cuts and ground beef) and fresh pork muscle cuts. Carbon monoxide (CO) will be added at varying concentrations of CO in the MAP gases so as not to exceed 12.0 mg/kg (5.5 mg/lb) in the packaged meats. Three prior GRAS notices to FDA on carbon monoxide as a component of modified atmosphere packaging systems (MAP) for use with case-ready fresh meats were also utilized for this review. The Expert Panel independently evaluated this information and other materials deemed necessary or appropriate. Following independent, critical evaluation, the Expert Panel conferred and unanimously agreed to the decision described herein.

INTRODUCTION

Case-ready packaging systems offer advantages of product quality, presentation and convenience to both retailers and consumers. Significantly, case-ready meat programs allow for less handling of products prior to retail purchase, enhancing not just convenience and efficiency, but product safety and quality as well. In addition, case-ready meat packaging minimizes the amount of effort and involvement expended at retail in the preparation of fresh meat products for display. Not all systems commonly described as "case-ready" employ packaging that is ready for immediate display upon delivery to the retailer. Many of the programs available require some intermediate preparation at the retail level, and thus are not fully case-ready." For instance, primary

packages of meat may be provided to retailers in either a master container or secondary packaging that is flushed with a mixture of gases, including 0_2, C0, $C0_2$ and N_2. Retailers are advised to remove these products from the MAP environment within a fixed or stated distribution shelf life, and then offer products for retail display for a defined period of time. A drawback is that products cannot be open code dated in such systems, as it is not known when in the distribution life the products will be placed in the retail case for display. Thus, the retailer remains responsible for applying the consumer code date on the product.

In the proposed MAP system, fresh meat, either beef or pork, will be placed on a tray within a chamber. Once the desired atmosphere is achieved, a barrier film will be affixed to the tray to ensure that the atmosphere is maintained throughout the product's distribution. The packages will be prepared and labeled with a validated open date code at a central location and will be subject to no further processing or manipulation at retail. Thus, the product will be ready for retail display and delivery to consumers upon packaging, and the product label will not be altered following application of the mark of inspection by the U.S. Department of Agriculture. Food Safety and Inspection Service (FSIS). The open date code or "use or freeze by" dates established for products packed in the MAP system will not exceed 35 days following the date of pack for intact muscle cuts, and 28 days for ground beef. The use of a centralized packing facility for the finished retail package will eliminate all retailer discretion in the process, adding the consumer benefit of an open dating system that is scientifically established, validated and controlled. In addition to minimizing any risk of cross -contamination that can occur in a retail establishment, the use of such a system substantially reduces any risk that the shelf life will be manipulated inappropriately at the retail level.

CO is included in the modified atmosphere to help maintain the characteristic color of fresh meat. Like 0_2, CO has long been known to have a color-stabilizing effect on fresh meat. The desirable red color of fresh beef, in particular, is attributed to oxymyoglobin, which is formed when myoglobin in meat muscle fibers is exposed to oxygen. When CO comes into direct contact with meat, myoglobin is converted to carboxymyoglobin,

resulting in a color that is substantially indistinguishable from that of oxymyoglobin. In the absence of a modified atmosphere, oxymyoglobin is eventually converted to metmyoglobin, which has an unappealing, brown color. This conversion can occur before microbial spoilage renders the product unfit for human consumption. Odor, gas formation and/or slime formation are also indicators of spoilage. Indeed, although the use of CO will stabilize the characteristic color of meat, CO is not intended to affect microbial growth. Microbial shelf life will continue to be determined, as it always has been, on such considerations as anticipated microbial growth, product composition, and distribution conditions, including storage temperatures. Significantly, the proposed system is not intended to extend the shelf life of products in excess of what has been implemented with CO in similar systems.

The proposed use, types of foods and MAP system described herein is the same as described in GRN No. 000167 to Tyson Foods effective September 29, 2005 other than increasing the delivery of carbon monoxide to achieve a meat concentration from 2.2 mg/lb to 5.5 mg/lb of meat. For the current GRAS notification, carbon monoxide is also intended for use as a component of a modified atmosphere packaging (MAP) system for case-ready fresh beef and pork. The carbon monoxide will be used at varying concentrations, depending on the headspace volume and amount of meat in the container to achieve a final meat CO concentration of 5.5 mg/lb or less (6.6 mg/lb maximum with a process tolerance of 20% in the modified environment). As noted in GRN 000167, a 620 cubic centimeter (cc) package containing 1 lb of ground beef would require a 0.89 percent concentration of CO to achieve the required concentration of 2.2 mg/lb CO; a 3000 cc package containing 5 lbs of meat would require 1.19 percent concentration of CO to achieve the required concentration of CO. To achieve 5.5 mg/lb of CO in meat for this notification, comparable CO levels in the MAP would be 2.23% and 2.98% CO for the first and second examples above, respectively. By delivering the CO concentration as a function of headspace volume and contained meat volume, it is possible to better define the meat concentrations of CO than just specifying the CO content of the MAP without consideration of the ratio of meat to headspace volume.

REGULATORY STATUS

There have been three prior GRAS notice submissions to the agency on the use of carbon monoxide in MAP systems that are summarized briefly below. In each case, FDA responded that they had no questions on the proposed use and did not object to the GRAS notice. Further, in each case, USDA has concluded that the use of carbon monoxide as described in these notices in the MAP systems and the notified conditions of use with fresh beef and pork muscle and ground beef were acceptable.

1. GRAS Notice No. GRN 000083: Response dated February 21, 2002 from FDA to a submission from Pactiv Corporation. (Pactiv)

The subject of the notice is carbon monoxide (CO). The notice informs FDA of the view of Pactiv Corporation (Pactiv) that CO is GRAS, through scientific procedures, for use as a component of a gas mixture in a modified atmosphere packaging (MAP) system. The level of CO in this MAP system is 0.4%. The other components of the MAP system are carbon dioxide (30%) and nitrogen (69.6%). The MAP system would be used for packaging fresh cuts of case ready muscle meat and ground case ready meat to maintain wholesomeness, provide flexibility in distribution, and reduce shrinkage of the meat. The case ready meats would be removed from the MAP system prior to retail display. In the ActivTech MAP system, CO is used at a target level of 0.4% in a mixture of N_2 (70%) and CO_2 (30%). The gases are flushed into a "pillow pack" that contains an inner tray upon which the meat is wrapped in a hermetically sealed permeable film. Prior to retail display, the inner tray is removed, exposing the package to normal atmospheric conditions and allowing the CO to escape.

The notice describes the estimated consumption of CO per meal as a consequence of its intended use as a component in a MAP system for storing meat. Assuming that 30% of the CO present in the MAP is absorbed into the meat, and that there is an 85% reduction of CO due to cooking the meat, Pactiv calculates a realistic intake estimate to be 0.084 milligrams (mg) CO per meal. Pactiv also calculates a worst case intake estimate to be 1.88 mg CO per meal, assuming that 100% of the CO present in the MAP is absorbed into the meat and that there is no reduction in CO during cooking. Pactiv cites published

articles to support the assumptions used in the realistic exposure estimate and to support the conclusion that exposure to CO is safe at this level.

Based on the information provided by Pactiv, FDA had no questions at that time regarding Pactiv's conclusion that CO is GRAS under the intended conditions of use. During its evaluation of GRN 000083, OFAS consulted with the Labeling and Consumer Protection Staff of the Food Safety and Inspection Service (FSIS) of the United States Department of Agriculture regarding the use of CO in meat products. Based on the information submitted by Pactiv, USDA FSIS has concluded that the MAP system ActiveTech™ 2001) as described in Pactiv's notice, and used under the conditions stated in Pactiv's notice, would be acceptable for packaging red meat cuts and ground meat. In FSIS's view, Pactiv has demonstrated that this MAP system complies with FDA's definition of a processing aid that appears in labeling regulations (21 CFR 101.100(a)(3)). 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. As such, for similar uses of other MAP gases (e.g., nitrogen), there are no labeling issues in regard to meat cuts and ground meat packaged using this MAP. Additionally, when considering the use of a food ingredient or additive in a meat product, FSIS historically has treated each livestock species separately. However, in this case, the data submitted by Pactiv can be extrapolated to all species of livestock.

2. GRAS Notice No. GRN 000143: Response on July 29, 2004 from FDA to a submission from Precept Foods, LLC (Precept)

The subject of the notice is carbon monoxide (CO). The notice informs FDA of the view of Precept that CO is GRAS, through scientific procedures, for use as a component of a modified atmosphere packaging (MAP) system for case-ready fresh beef and pork. The level of CO in this MAP system is 0.4%. The other components of the MAP system are carbon dioxide (20-100%) and nitrogen (0-80%). Precept states that the CO is included in the modified atmosphere to help maintain the characteristic color of fresh meat. Precept states that the CO is not intended to affect microbial growth and will not extend the shelf life of the product.

Precept estimates that the exposure to CO would be 0.054 mg CO per meal of cooked meat. Precept first assumes a scenario where the meat absorbs 30% of the CO in the package and 100% of the CO present in the meat is absorbed by the consumer. A dietary intake of 0.36 mg of CO per meal would occur when 8.8 ounces (250 g) of meat is consumed. Precept considers that this estimated intake of CO from its use 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). Precept then accounts for the fact that meat packaged with CO will be cooked prior to consumption and assumes an 85% reduction in CO exposure due to cooking of the meat. This 85% reduction decreases the maximum exposure from 0.36 mg to 0.054 mg CO per meal.

Precept makes two additional exposure estimates. First, if 100% of the CO in the package is absorbed, and 100% of the CO is consumed, an 8.8 ounce serving would expose the consumer to 1.2 mg of CO. Second, Precept states that a consumer exposed to 100% of the CO in the package would only be exposed to 2.18 mg CO, which is well below the safety limit set by the EPA and OSHA.

In Precept's packaging system, meat is placed on a tray within a chamber, the chamber is then filled with the desired atmosphere, and finally, a barrier film is affixed to the package. The packages are then labeled with a validated open date code at a central location and will be subject to no further processing or manipulation at retail. The open date code established for products packed in the MAP system will not exceed 35 days following the date of packaging for intact muscle cuts and 28 days for ground beef.

Based on the information provided, FDA had no questions at that time regarding Precept's conclusion that CO is GRAS under the intended conditions of use. During its evaluation of GRN 000143, FDA's Office of Food Additive Safety (OFAS) consulted with the Labeling and Consumer Protection Staff of FSIS regarding the use of CO in meat products. Based on the information submitted by Precept, FSIS concluded that the MAP system as described in Precept's notice, and used under the conditions stated in Precept's notice, would be acceptable for packaging red meat cuts and ground meat.

3. GRAS Notice No. GRN 000167: Response on September 29, 2004 from FDA to a submission from Tyson Foods, Inc. (Tyson)

The subject of the notice is carbon monoxide (CO). The notice informs FDA of the view of Tyson that CO is GRAS, through scientific procedures, for use as a component of a modified atmosphere packaging (MAP) system for case-ready fresh beef and pork. The level of CO in this MAP system is 2.2 milligrams (mg) CO per pound (lb) of meat. The other components of the MAP system are carbon dioxide and nitrogen. This packaging system is used for packaging fresh cuts of muscle meat and ground meat to maintain wholesomeness, provide flexibility in distribution, and reduce shrinkage of the meat.

As compared to Pactiv's and Precept's packaging system, Tyson's packaging system is a reduced head space system, and therefore to achieve the same ratio of CO to meat, they use a higher concentration of CO per unit volume. To achieve this end, Tyson states that they will use the concentration of CO necessary to achieve the same ratio of CO to meat (2.2 mg CO per lb of meat) as is used in the Precept and Pactiv systems. For example, a 620 cubic centimeter (cc) package containing 1 lb of ground beef would require a 0.89 percent concentration of CO to achieve the required concentration of CO; a 3000 cc package containing 5 lbs of meat would require 1.19 percent concentration of CO to achieve the required concentration of CO.

Meat is placed on a tray within a chamber, the chamber is then filled with the desired atmosphere, and finally, a barrier film is affixed to the package. The packages are then labeled with a validated open date code at a central location and will be subject to no further processing or manipulation at retail. The open date code established for products packed in the MAP system will not exceed 35 days following the date of packaging for intact muscle cuts and 28 days for ground beef.

Tyson states that the CO is included in the modified atmosphere to help maintain the characteristic color of fresh meat. Tyson states that the CO is not intended to affect microbial growth and will not extend the shelf life of the product.

Tyson estimates that the exposure to CO would be 0.054 mg CO per meal of cooked meat. Tyson first assumes a scenario where the meat absorbs 30 percent of the CO in the package and 100 percent of the CO present in the meat is absorbed by the consumer. A dietary intake of 0.36 mg of CO per meal would occur when 8.8 ounces (250 grams) of meat is consumed. Tyson considers that this estimated intake of CO from its use 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). Tyson then accounts for the fact that meat packaged with CO will be cooked prior to consumption and assumes an 85 percent reduction in CO exposure due to cooking of the meat. This 85 percent reduction decreases the maximum exposure from 0.36 mg to 0.054 mg CO per meal. If 100 percent of the CO in the package is absorbed, and 100 percent of the CO is consumed, an 8.8 ounce serving would expose the consumer to 1.2 mg of CO.

Based on the information that provided, as well as other information available to FDA, the agency has no questions at this time regarding Tyson's conclusion that CO is GRAS under the intended conditions of use. During its evaluation of GRN 000167, OFAS consulted with the Labeling and Consumer Protection Staff of FSIS regarding the use of CO in meat products. Based on the information submitted by Tyson, FSIS has concluded that the MAP system as described in Tyson's notice, and used under the conditions stated in Tyson's notice, would be acceptable for packaging red meat cuts and ground meat

IDENTITY AND SPECIFICATIONS

The physical properties of carbon monoxide are presented in Table 1 below. The Chemical Abstracts Service (CAS) number for carbon monoxide is 630-08-0.

Table 1. Physical Properties	**Value**
Empirical formula	C=0
Relative molecule mass	28.01
Critical point	-140.2 °C at 34.5 atm (3.5 MPa)
Melting point	-205.1 °C
Boiling point	-191.5 °C
Density, at 0°C, 1 atm	1.250 g/litre

Table 1. Physical Properties	Value
Density, at 25°C, 1 atm	1.145 g/litre
Specific gravity relative to air	0.967
Solubility in water at 0°C, 1 atm	3.54 mL/l00mL
Solubility in water at 25°C, 1 atm	2.14 mL/100mL
Solubility in water at 37CC, 1 atm	1.83 mL/ 100mL

The carbon monoxide will be of a purity suitable for use in contact with food. The specification will require a minimum CO content of 98%. The impurities anticipated to be present in the remaining 2% of the CO gas product consist of components that are found naturally in the atmosphere, such as nitrogen, carbon dioxide, argon, hydrogen, methane and water.

MANUFACTURING PROCESS

Carbon monoxide is typically produced in a steam methane reformer, a single reactor that is used to produce a synthesis gas of hydrogen and carbon oxides. In the reactor, sulfur-free hydrocarbons such as methane and superheated steam are passed over a refractory-supported nickel catalyst (or nickel and lanthanum catalyst) placed in Ni-Cr alloy tubes. When passing the nickel-based catalyst, the feed hydrocarbon/steam mixture converts to hydrogen and carbon oxides. The conversion is used to produce a mixture of hydrogen, carbon dioxide, carbon monoxide, methane and steam. The component gases are separated from each other via such techniques as cryogenic separation.

CONDITIONS OF USE

By this notification, the applicant proposes to increase the CO content in the meat product to 5.5 mg/lb (with a process tolerance of 20% in the modified environment), as compared to the 2.2 mg/lb previously accepted in prior GRAS notices. The proposed MAP system and subsequent distribution to the consumer is the same as described in GRN 000167. CO will be used in a mixture of nitrogen (N_2) (0-80%) and carbon dioxide ($C0_2$) (20%-100%).

In prior notices, no mention was made of the volume of gas-to-beef mass in the MAP systems. A calculation of the volume is presented below for the estimated volume of MAP gas/kg beef added to the packaging.

According to GRN 000143, "if 100% of the CO in the package is absorbed, and 100% of the CO is consumed, an 8.8 ounce serving would expose the consumer to 1.2 mg of CO." Because the notification response does not specify the dimensions of the package or volume of MAP gas used, we will use this information to back-calculate the volume of MAP gas to meat ratio.

Using the standard gas volume as 1 mole = 22.4 liter (l) at STP, and since 1 mole of CO is 28 grams (g), we calculate the density of CO gas as:
(28 g)/(22.4 l) = 1.25 g/l = 1.25 mg/ml

If the package contains 1.2 mg CO per 8.8 ounce serving, then a one kg package will contain:
(1.25 mg/8.8 oz)(16 oz/lb)(2.2 lb/kg) = 5.0 mg/kg.

Further, the volume of CO gas will be:
(5.0 mg/kg)/(1.25 mg/ml) = 4.0 ml CO /kg meat

Since the CO will be only 0.04% of the MAP gas, the total quantity of gas will be:
(4.0 ml)/(0.004) = 1000 ml MAP gas/kg meat or 1 ml MAP gas/g meat.

In the proposed MAP system, fresh meat, either beef or pork muscle meats or ground beef, will be placed on a tray within a chamber. Once the desired atmosphere is achieved that will deliver 5.5 mg/lb, a barrier film will be affixed to the tray to ensure that the atmosphere is maintained throughout the product's distribution. The packages will be prepared and labeled with a validated open date code at a central location and will be case-ready, with no further processing or manipulation at retail. Thus, the product will be ready for retail display and delivery to consumers upon packaging, and the product label will not be altered following application of the mark of inspection by the U.S. Department of Agriculture. Food Safety and Inspection Service (FSIS). The open date code or "use or freeze by" date established for products packed in the proposed MAP

system will not exceed 35 days following the date of pack for intact muscle cuts, and 28 days for ground beef.

Safety Assessment

Regulatory Exposure Standards for Carbon Monoxide

Detailed information establishing the GRAS status of CO intended for use in MAP systems for fresh meat are set forth in GRN 000083, 000143, and 000167 which are incorporated by reference as described herein. Consistent with previous GRAS determinations, an acceptable daily intake (ADI) has not been identified for CO. As described in GRN 000083 and GRN 000143 and summarized below, typical background levels of CO and national air quality standards provide a reference by which the safety of CO in MAP systems may be assessed.

Specifically, as described in GRN 000083 and GRN 000143, typical "background" levels of CO in the atmosphere are <20 mg/m^3 measured as an 8-hour mean. These background levels may result in typical serum CO levels (in the form of carboxyhemoglobin) of approximately 1.2 to 1.5%. Healthy adults are expected to experience no ill health effects at levels of 4 to 5%; compromised or sensitive individuals may experience adverse health effects at levels of 2 to 3%. Background levels may be higher in urban areas or areas with significant traffic congestion. At levels that substantially exceed background, CO is viewed as a significant air pollutant. The health-based national air quality standard for CO, as promulgated by EPA, is 9 ppm (10 mg/m^3), measured as an annual maximum 8-hour average concentration. This level would be expected to result in an exposure of 50 mg CO per 8 hours, based on the amount of air breathed by a typical person (15 m^3 per day or approximately 5 m^3 per 8 hours). The federal safety standard for occupational exposure to CO, as promulgated by OSHA, is 50 ppm (58 mg/m^3), measured as an 8-hour time weighted average and assuming a 5 m^3 per 8 hours breathing rate for workers. This level would be expected to result in an exposure of 290 mg CO per 8 hours, based on the amount of air breathed by a typical worker.

Estimated Carbon Monoxide Intake

The volume of the gas mixture and CO concentration in a package will vary depending upon tray size and product volume. For example, assuming a fresh meat portion of 500 grams and an anticipated meat weight to gas volume ratio of approximately 1.0 as calculated above in conditions of use, the gas volume would be 0.5 liter. As the meat weight to gas ratio is decreased, the CO concentration will increase proportionately to achieve 5.5 mg/lb CO.

Using a concentration of 1.0% CO in this example of a modified atmosphere, CO is estimated to account for approximately 5 ml CO gas per 500 g meat package. The mass of CO per unit volume is 1.25 mg/ml: Therefore, 5 ml of CO gas in the MAP system would be 6 mg CO in contact with 500 g or approximately 12 mg/kg (5.5 mg/lb).

It has been reported (Watts *et al.,* 1978) that 30% of the CO present in a modified atmosphere may be absorbed into packaged meat. Assuming that 30% of the CO is taken up by the meat, the amount of CO absorbed into meat packaged in the proposed MAP system is calculated as follows:

0.3 x (5ml/package) x 1.25 mg/ml / 0.500 kg meat/package = 3.75 mg CO/kg meat.

If it is assumed that the CO content is reduced 85% during cooking (Sørheim *et al.*, 1997) that a person consumes an 8.8 ounce serving portion of meat (250 g = 0.25 kg) at a meal, and that 100% of the ingested CO is absorbed, the estimated intake of CO is calculated as follows:

0.15 x 3.75 mg CO/kg meat x 0.25 kg meat/meal = 0.141 mg CO/meal.

Using "worst case" assumptions, if it is assumed that 100% of CO is taken up by the meat and no reduction occurs during cooking, the maximum theoretical CO content and intake per 8.8 ounce (250 gram) serving portion of the meat is estimated as follows:

12 mg CO/kg meat x 0.25 kg meat/meal = 3 mg CO/meal.

Similarly, if it is conservatively assumed as a worst case scenario that all of the CO in the package was respired by the consumer, it would result in the following exposure:

(5 ml/package) x 1.25 mg/mL = 6 mg CO in package released to air.

As described below, these estimated exposures to CO are negligible as compared to health-based standards for CO intake, are not expected to significantly alter environmental exposure to CO, and therefore present no toxicological concern.

Comparison of Potential Exposure to Regulatory Standards for Carbon Monoxide

The exposure to CO that is estimated to result from the proposed MAP system is a negligible fraction of the exposures considered acceptable under health-based standards for CO. Under realistic conditions of use, inclusion of CO in the planned MAP system is expected to result in an intake of 0.141 mg CO from meat intake. This level of intake corresponds to just 0.28% of the 8 hour exposure expected to result from air in compliance with EPA's health-based National Ambient Air Quality Standard (NAAQS) for CO of 9 ppm (10 mg/m^3) or 50 mg/8 hr period. Even the "worst case" intake exposure of 3 mg that may result from intake of a meal from meat packaged in the MAP system corresponds to only 6% of the likely exposure from air meeting EPA's NAAQS for CO.

In the very worst case that all CO in the package is respired by the consumer, the exposure is similarly negligible as compared to the conservative EPA NAAQS. Assuming a relatively small room of approximately 30 m^3, opening of one bag with 5 ml CO would contribute 0.2 mg/m^3 to the CO concentration in the air, or approximately 2% of the EPA NAAQS of 10 mg/m^3. At this rate, approximately 50 bags would need to be opened in order for the ambient air in the room to approach the EPA standard. This conservative estimate assumes that there is no exchange of air between the room where the package is opened and other rooms or the outdoors.

Similarly, these realistic and "worst case estimates" of intake are nearly a six-fold lesser fraction of the OSHA standard for CO of 58 mg/m^3 that is acceptably safe in the workforce as compared to the EPA NAAQS standard for the public of 10 mg/ m^3.

Accordingly, based on national, health-based standards for CO exposure, it may be persuasively concluded that the use of CO in a MAP system delivering 5.5 mg/lb CO for fresh meats poses no health or safety concern and is not reasonably expected to result in any measurable levels of carboxymyoglobin in the blood of those who consume treated meat or who are nearby when one or more packages of case-ready meat are opened. This conclusion is consistent with the conclusion of Sorheim *et al.* (1997) in the published literature that it is highly improbable that CO exposure from meat packaged in an atmosphere containing up to 0.5% will represent a toxic threat to consumers through the formation of COHb." It is also consistent with GRN 000083, GRN 000143 and GRN 000167 GRAS determinations for CO. Thus, on the basis of the above assessment and the negligible increased contributions from meat intake or inhalation of sealed packaging containing MAP gases, the proposed increase in allowable CO concentrations to 5.5 mg/lb (6.6 mg/lb CO allowing for process variance), from prior approved levels of 2.2 mg/lb, poses no health concerns.

Safety of Proposed MAP System Regarding Food Spoilage and Appearance

The finished MAP system does not pose a safety concern under the intended conditions of use. The finished system will utilize an environment with CO metered at desired concentrations dependent on headspace and meat volume in a mixture of CO_2 and N_2. The CO-containing environment will allow meat to maintain a desirable color, but will neither preclude microbial growth nor affect the characteristic odor or other indicators (e.g., gas or slime formation) of meat spoilage. In other words, the system does not mask spoilage.

In the literature addressing the use of CO in packaging of meat products, it has been observed that objections are sometimes raised because the color stability made possible by CO may exceed the microbiological shelf life. The specific concern that is cited in this regard is that color stability in such circumstances may mask spoilage of the CO-treated meat. Because CO does not inhibit the growth of spoilage microorganisms, it has no effect on characteristic signs of spoilage such as odor, gas formation, and/or slime formation. Indeed, the odor of spoiled meat will be immediately apparent, conveying to

consumers any spoilage that has occurred. The ability of meat packaged in CO to spoil and to emanate off-odors has been reported in the published literature (Sørheim *et al.*, 1999). Low concentrations of 0.4 and 1% CO did not affect microbiological loads of meat when applied in combination with atmospheres containing CO_2.

The effects of CO, O_2 and CO_2 on the microbiological spoilage of MAP packaged meat has been reviewed by Sørheim *et al.*, 2001. In MAP of meat, the effects of low concentrations of CO on microorganisms seem to be of either no or minor importance. Clark *et al.* (1976) found that by adding 0.5 – 10 % CO to N_2 atmospheres, the shelf life based on odor was extended and the growth of psychrotrophic bacteria was reduced at 0.5 and 10°C. In the evaluation of antimicrobiological effects of CO, considerations to other gases in the gas mixtures must be made. In most MAP of meat, bacteriostatic CO_2 at levels of 20–100% are usually present. Low concentrations of 0.4 and 1 % CO did not affect microbiological loads of meat when applied in combination with atmospheres containing CO_2 (Sørheim *et al.*, 1999; Luño *et al.*, 1998). Therefore, in gas mixtures containing high levels of CO_2, the possible antimicrobiological effect of low CO concentrations is likely to be overshadowed by CO_2.

The microbiological benefits of using CO for MAP of meat is two-fold: O_2 can be omitted from the atmosphere, and concentrations of CO_2 can be high, from 60 to near 100%. The absence of O_2 inhibits the growth of aerobic spoilage bacteria. In storage experiments of beef steaks, ground beef and pork chops in a 0.4% CO/ 60% CO_2 / 40% N_2 gas mixture, the shelf life, as evaluated by off-odor, increased with 2 to 7 days compared to storage in a 70% O_2 / 30% CO_2 mixture at 4 and 8°C (Sørheim *et al.*, 1999). The microflora of the meat in the CO gas mixture was dominated by lactic acid bacteria, and this gas mixture reduced the growth of spoilage flora of *Brochothrix thermosphacta* and pseudomonads. Nissen *et al.* (2000) studied the growth of pathogens in ground beef stored in 0.4% CO/ 60% CO_2 / 40% N_2 at 4 and 10°C. The CO mixture reduced the growth of *Yersinia enterocolitica* and *Listeria monocytogenes* compared to a 70% O_2 / 30% CO_2 atmosphere and chub packages. *Escherichia coli* O157:H7 was inhibited at 10°C. However, growth of *Salmonella* spp. was not reduced in meat in the CO mixture at

10°C, which emphasizes the importance of low storage temperatures for inhibiting these pathogenic bacteria.

Exposure of pure bacterial cultures to high CO concentrations of 5–30% in air, inhibited the growth of *E. coli*, *Achromobacter* and *Pseudomonas fluorescens*, but *Pseudomonas aeruginosa* was not affected (Gee and Brown, 1980). In another study, continuous storage of meat in 100 % CO reduced the development of off-odor and bacteria (Tsemakhovich and Shaklai, 2000). Pretreatment of beef steaks with 100 % CO for 30 minutes lowered aerobic plate counts by 1 log after 8 weeks of vacuum storage, compared to no CO pretreatment (Brewer at al., 1994).

These data demonstrate that at low CO concentrations of 0.4-1% in a MAP system with CO_2 and N_2 did not markedly affect microbial growth of spoilage organisms. The presence of CO_2 as an O_2 replacement appears to have a greater overall effect on retardation of spoilage than the CO addition up to 1%.

Other Safety Considerations

As noted in GRN 000143, Precept Foods has also commented on whether the planned system presents any unique or unusual risk of pathogenic growth or other harm to consumers. Significantly, application of a consistent "freeze by" date offers considerable consumer benefit, including enhanced safety, because the product will be subject to less handling than retailer-packed products and an appropriate shelf life will be objectively established and communicated via a validated open date code. Indeed, reliance on a centrally applied open code or "use or freeze by" date offers a far more objective means of assessing product age and quality than highly subjective measures such as color.

With regard to the theoretical risk of pathogenic growth, Precept Foods concluded that a risk of pathogenic growth exists with any packaging system that is subject to temperature abuse or other mishandling, and that the planned system presents no particular vulnerabilities in this regard. Psychrotropic pathogens of theoretical concern for an anaerobically packaged product, such as non-proteolytic *Clostridium botulinum,* are not typically associated with fresh meats, so such organisms are not reasonably expected to

be present in the first place. Moreover, the total time that product will spend in the modified atmosphere, as determined by the anticipated shelf life of 35 days for muscle cuts and 28 days for ground beef, is comparable to time that may be spent in similar anaerobic atmospheres in systems judged to be safe. Such systems include vacuum packaging and the Pactiv master bag system that was asserted to be GRAS in GRN 000083. In the unlikely event that product is mishandled prior to purchase, microbial spoilage can and will occur, and the fact of spoilage will be apparent through off odors or other indicators of spoilage. Thus, in addition to the certainty provided by the open date or "us or freeze by" code, natural spoilage processes provide additional safeguards that will prevent consumption of spoiled meat that may contain food-borne pathogens. The fact that the system will be used to package only raw products that require safe handling instructions and cooking to appropriate temperatures offers an additional assurance of safety.

It is our understanding that the microbiological issues regarding spoilage are of no concern to FDA and USDA, providing the meat products are properly labeled with "use or freeze by" date periods agreeable to these governmental bodies. Consequently, the Expert Panel, in keeping with this understanding, has not pursued the matter of potential for spoilage masking further by requesting additional studies for purposes of safety assessment.

Discussion and Summary

In this GRAS notification, carbon monoxide is intended for use as a component of a modified atmosphere packaging (MAP) system for case-ready fresh beef and pork. The carbon monoxide will be used at a target concentration intended to deliver 5.5 mg/lb CO as a function of headspace and meaty volume (with a process tolerance of 20% in the modified environment). The proposed MAP system and subsequent distribution to the consumer is the same as described in GRN 000143, with CO used in a mixture of nitrogen (N_2) (0-80%) and carbon dioxide ($C0_2$) (20%-100%). Typical concentrations used by meat processors are nitrogen (30-40%) and carbon dioxide (60%-70%).The

presence of 2.2-5.5 mg/lb CO is sufficient to impart the desirable and stable red meat coloration.

The volume of MAP gas to meat volume will be used to determine the concentration of CO. With a ratio of 1 ml MAP gas/g meat, the calculated concentration of CO in the modified atmosphere is 1%. CO is estimated to account for approximately 5 ml CO gas per 500 g meat package at retail. The mass of CO per unit volume is 1.25 mg/ml: Therefore, 5 ml of CO gas in the MAP system would be 6 mg CO in contact with 500 g or approximately 12 mg/kg or 5.5 mg/lb CO.

Using "worst case" assumptions, if it is assumed that 100% of CO is taken up by the meat and no reduction occurs during cooking, the maximum theoretical CO content and intake per 8.8 ounce (250 gram) serving portion of the meat is estimated as 3 mg CO/meal. More realistically, based on literature regarding absorption on CO into meat and loss during cooking, 30% of the CO present in a modified atmosphere is likely to be absorbed into packaged meat and CO content is reduced 85% during cooking, a person consuming an 8.8 ounce serving portion of meat (0.25 kg) at a meal, and that 100% of the ingested CO is absorbed, the estimated intake of CO is approximately 0.14 mg CO/meal.

As noted before, under realistic conditions of use, inclusion of CO in the planned MAP system is expected to result in an intake of 0.14 mg CO from meat intake per serving, an intake corresponding to just 0.28% of the 8 hour exposure expected to result from air in compliance with EPA's health based NAAQS for CO of 9 ppm (10 mg/m^3) or 50 mg/8 hr period. Even the "worst case" intake exposure that may result from ingestion of meat packaged in the MAP system of 3 mg corresponds to only 6% of the likely exposure from air meeting EPA's NAAQS for CO. Similarly, in the worst case estimation of inhalation exposure to CO in a small room from opening a MAP container, the exposure is also negligible when compared to the conservative EPA NAAQS, with worst case exposure to approximately 2% of the EPA NAAQS of 10 mg/ m^3. Thus, even with 1-2 beef or pork meals/day and possible exposure by inhalation of released gas, these CO intakes and exposures are considered unlikely to cause any measurable increase in normal COHb concentration in the blood (typically ~0.5%) above that associated with breakdown of

heme protein or ambient CO levels in the atmosphere or pose any associated health risk to the consumer.

Further, the literature reviewed and studies that have been conducted with MAP containing 0.4-1% CO have demonstrated that addition of a higher level of CO will not result in growth retardation of spoilage microorganisms or mask spoilage of the CO-treated meat as normally indicated by characteristic signs of spoilage such as odor, gas formation, and/or slime formation. It is our understanding that there are no issues regarding spoilage for FDA and USDA, providing the meat products are properly labeled with "use or freeze by" date periods.

CONCLUSION

Based on a critical evaluation of the publicly available data and information summarized above, the Expert Panel members whose signatures appear below, have individually and collectively concluded that addition of carbon monoxide at levels intended to not exceed 5.5 mg/lb (maximum6.6 mg/lb to allow for process variation) to MAP packaging systems meeting the specifications cited above, is safe for addition to fresh muscle cuts of beef and pork and fresh ground beef. Further, based on current good manufacturing practices, the addition of carbon monoxide to MAP as presented in this notification, presents no significant risk of pathogenic growth or spoilage masking to the consumer when properly labeled with open code or "use or freeze by" dating with expiration dates as specified for the meat types.

It is also our opinion that other qualified and competent scientists reviewing the same publicly available toxicological and safety information would reach the same conclusion. Therefore, we have also concluded that carbon monoxide in MAP systems delivering up to 5.5 mg/lb fresh meat, when used as described, are GRAS based on scientific procedures.

James W. Barnett, Jr., Ph.D., DABT	12/16/05 Date
W. Gary Flamm, Ph.D., FACT, FATS	12/12/05 Date
Stanley M. Tarka, Jr., Ph.D.	12/9/05 Date

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