GE Free New Zealand

In Food And Environment Inc.

PO Box 13402, Wellington, NZ

Tel: 027 479 4195

11 February 2020
Re: A1186

Dear FSANZ,

GE Free NZ has concerns over the assurance of safety that this product has.

The Application A1186 says "FSANZ has undertaken a risk and technical assessment which found no public health and safety concerns associated with its intended use".

FSANZ admits that there is no evidence or data to back the statement up. However, under Standard 1.5.2 and the Food Standards Australia New Zealand (FSANZ)Act 1991 section 3 – there is no evidence that regulatory safety assessments have provided adequate information and high degree of consumer confidence in the quality and safety of Soy LegHemoglobin (SLH) if it enters the food chain.

GE Free NZ asked under the FOIA for

1. *All reports on the long term animal feeding studies that was conducted on the soy leghemoglobin,*
    a. *On animals*
    b. *On humans*
2. *The journal they were published in?*
3. *Levels of microbiological contaminants in the liquid?*
4. *Levels of fermentation substrates, production strain, and processing aids in the liquid*
5. *Levels of Heavy metals in the liquid?*
6. *DNA fragments from the process?*

As soy hemoglobin has not been in the animals or human food chain before as a GE or natural product, Please can we have the

7. *Allergen feeding studies and*
8. *Any studies to show if GE DNA fragments are absorbed into the blood stream?*
9. *Safety studies on children eating it?*
10. *Safety studies on elderly, sick eating it.*
11. *Evidence that the denatured protein will not harm consumers?*

In the FSANZ reply from Mary Jordan and Glen Neal (28.1.2020) under section 24 A

(attachment 1) they refused the FOIA request due to the absence of data as requested points 1,2,7,8,9,10 had no information generated. Neither did FSANZ seek or was provided with the information, however a short term (28 day) study summary could be found in the application.

It is then very difficult for the citizens of our Country to understand how FSANZ reached the conclusion that "FSANZ has undertaken a risk and technical assessment which found no public health and safety concerns associated with its intended use".

FSANZ approach to science shows that they do not have the appropriate skills able to evaluate the safety of any unknown GM SLH proteins and their effects.

This puts all consumers at risk and shows that FSANZ is not carrying out its due diligence in relation to the Act and the expectation of the public it serves.

The Soy Leghemoglobin (SLH) was separated from the yeast fermentation, 73% was SLH and there were 46 other new proteins were also found. As SLH has never been in the food supply before and these new proteins were detected it is extremely concerning that further data as not called for by FSANZ. The product contains DNA from these sources and there is no data showing safety of these products there is a requirement for it to be labeled at all point of sale both in packaged and unpackaged form. (Food Code 1.5.2 – 4 (3))

It is a serious omission if any reliance is made on the FDA approval that was made on the understanding that the applicant/manufacturer gave them the assurance it was safe. Mr. Keefe stated for the GRAS approval –

"This letter is not an affirmation that soy leghemoglobin preparation 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.

However, the FDA did not evaluate it as safe. This is because the laws in the US allow of consumer protection through the courts, this is not allowed in NZ.

Where it has been sold in the United States (US) reports also note some people have had unpleasant digestive reactions to eating Impossible burger - nausea, diarrhoea, bloating, and lots of intestinal gas.

- What is FSANZ assessment of these impacts on people who ingest them, in the short and long term?

Summary:

1. There is an absence of data on any allergies, anaphylaxis reaction that might occur.
2. There is an absence of data on the type and long-term effects of SLH and the new proteins formed in the SLH process.
3. FSANZ has not carried out its requirement under the Act to ensure consumer safety.

4. We do not believe that you have guaranteed a high degree of consumer confidence in the quality and safety of Soy Leghemoglobin that is going to be sold in Australia and New Zealand;
5. We do not believe that the provision of adequate information relating to food to enable consumers to make informed choices;
6. We do not believe that there will be protection of public health and safety;
7. We do not believe that the assessment and provision of adequate information relating to Soy Leghemoglobin will enable consumers to make informed choices;
8. We do not believe that there has been an effective, transparent and accountable regulatory framework which reduces the safeguards applying to public health and consumer protection.

Recommendation:

1. Decline the application

2. FSANZ conduct more research into the effects of the new proteins before release

3. If there is proof of consumer safety then if SLG is released into the food chain labels must contain warnings about possible adverse effects.

4. Full GM labelling must be on all products containing Soy Leghemoglobin on foods made and sold from food premises and vending vehicles, e.g. restaurants, junk food outlets, caterers, or self-caterers.

5. Post marketing survey must be conducted and product withdrawn if any adverse reaction occur.

Yours sincerely,

Attachments
GE Free NZ decision (FOIA) 28.1.2020
GRAS notice GRN 737 response letter

FOOD STANDARDS
Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

PO Box 5423
KINGSTON ACT 2604
Australia
Tel + 61 2 6271 2222
www.foodstandards.gov.au

PO Box 10559
The Terrace
Wellington 6143
New Zealand
Tel + 64 4 978 5630
www.foodstandards.govt.nz

Dear

I refer to your request, dated 24 December 2019 under the *Freedom of Information Act 1982* (FOI Act) to Food Standards Australia New Zealand (FSANZ) seeking documents and information regarding Application A1186.

Your request

Your request sought the following in relation to Application A1186.

1. All report on the long term animal feeding studies that was conducted on the soy leghemoglobin,
    a. On animals
    b. On humans
2. The journal they were published in?
3. Levels of microbiological contaminants in the liquid?
4. Levels of fermentation substrates, production strain, and processing aids in the liquid
5. Levels of Heavy metals in the liquid?
6. DNA fragments from the process?
7. Allergen feeding studies and
8. Any studies to show if GE DNA fragments are absorbed into the blood stream?
9. Safety studies on children eating it?
10. Safety studies on elderly, sick eating it.
11. Evidence that the denatured protein will not harm consumers?
12. Confirmation that the imported liquid and the end product containing the Soy leghemoglobin protein will be labelled?

Application A1186 seeks an amendment to the *Australia New Zealand Food Standards Code* (the Code) to permit a specific soy leghemoglobin (which is in the form a liquid concentrate). FSANZ is proceeding with your request on the basis that it relates specifically to Application A1186 and to the specific soy leghemoglobin (or 'the liquid') which is the subject of that Application.

I note your advice that you have received the A1186 Call for Submission, which was released publically on 20 December 2019.

In terms of part 12 of your FOI request, I understand that you advised that, after receiving and reviewing the A1186 Call for Submissions and its supporting document, you are now satisfied that the information sought under Part 12 is provided in the Call for Submission.

You consider that this part of the request has been addressed. FSANZ therefore is also proceeding on the basis that part 12 of your FOI request is withdrawn.

Timeframe for a decision

Your FOI request must be decided by close of business on 23 January 2020. Thank you for agreeing under section 15AA of the FOI Act to the extension to 28 January 2020 to enable us to process your FOI request. As discussed, we were closed for the Christmas holiday period and many of the relevant staff were also absent on annual holidays.

FOI decision maker

I am an officer authorised under subsection 23(1) of the FOI Act to make decisions in relation to your FOI request.

Documents identified

No documents were identified that matched parts 1, 7, 8, 9, and 10 of the FOI request.

As FSANZ does not hold any documents that match part 1 of the FOI request, it also does not hold any documents that match part 2 of that request.

As explained below, parts 3, 4, 5, 6 and 11 of the FOI request sought the provision of information, not documents. The FOI Act only provides a right of access to existing documents.

Decision

I have decided to refuse your request for access to documents relating to parts 1, 7, 8, 9 and 10 of the FOI request under section 24A of the FOI Act.

Parts 2, 3, 4 5, 6 and 11 of your FOI request did not seek access to documents and therefore is out of scope for the purposes of the FOI Act.

Please note that most of the information sought in Parts 2, 3, 4 5, 6 and 11 of your FOI request is publically available. Please see the attachment to this letter which explains where and how you can access this information quickly to enable you to prepare a submission in relation to Application A1186.

Material taken into account

In making my decision, I had regard to:

a. the terms of the FOI request;

b. relevant provisions in the FOI Act;

c. the Guidelines published by the Office of the Australian Information Commissioner under section 93A of the FOI Act (the Guidelines); and

d. advice received from FSANZ officers responsible for processing and assessing Application A1186 and from FSANZ staff responsible for managing FOI requests received by FSANZ.

Reasons for decision

Section 24A – Refusal if documents cannot be found

Subsection 24A(1)(b)(i) of the FOI Act allows refusal of an FOI request if the agency is satisfied the requested document cannot be found or does not exist or has not been received.

An email was sent to all FSANZ staff on 8 January 2020 advising them of the request and asking them to identify and locate all relevant documents. Advice was also sought from the FSANZ officers responsible for processing and assessing Application A1186. These checks confirmed that FSANZ does not hold any documents that match the description of parts 1, 7, 8, 9, and 10 to your request.

In terms of part 1 to the request, it is noted that Application A1186 states that 28-day feeding studies in rats were undertaken for the purposes of preclinical toxicological testing and to corroborate safety. The results of these studies, which are not long term studies, are summarised in Application A1186. Reports of these feeding studies were not requested by or provided to FSANZ.

No long term animal or human feeding studies were sought by or provided to FSANZ for the purposes of Application A1186.

Similarly, none of the studies listed in parts 7, 8, 9 and 10 of your FOI request were sought by or provided to FSANZ for the purposes of Application A1186.

Nor have any such studies been generated by FSANZ.

As FSANZ does not hold any documents that match part 1 of the FOI request, it also does not hold any documents that match part 2 of your request.

Based on the above, I am satisfied that no documents could reasonably be found as matching parts 1, 2, 7, 8, 9, and 10 of the FOI request. Accordingly, I have decided to refuse access under section 24A of the FOI Act.

Request for information, advice or an opinion – out of scope

Parts 2, 3, 4, 5, 6, 11 and 12 of your request asked to be provided with advice or information, not documents held by FSANZ.

The FOI Act only provides a right of access to documents (see, for example, section 11 of that Act). This right is limited to documents that already exist. The Act does not require an agency such as FSANZ to create a new document to satisfy an FOI request (see Guideline 2.33 of the Guidelines). This means that the FOI Act does not provide a general right to request, and be provided with information, advice or an opinion. The right is also limited to documents that exist at the time the FOI request was made (see Guideline 2.34 of the Guidelines).

Part 12 of the request has been withdrawn (see above) as your query has been addressed to your satisfaction in the Call for Submission.

Part 2 of the request has been considered above.

The information sought in parts 3, 4 (with the exception of "levels of processing aids in the liquid;), 5, 6 and 11 of the FOI request is publically available. It is detailed in the Application A1186 Call for Submissions and/or Supporting Document 1 – the risk and technical assessment report – which are available on the FSANZ website. Please see the attachment to this letter which explains how and where you can access this information.

No information was sought by or provided to FSANZ for the purpose of Application A1186 in relation to the 'levels of processing aids in the liquid' (part 4 of the request).

Providing the requested information to you administratively

I understand that your FOI request was made for the purposes of assisting you to prepare a submission in response to the A1186 Call for Submissions. Therefore, to assist you prepare your submission, FSANZ staff have prepared the attachment to this letter which sets out where and how you can access the information sought in your FOI request.

Your review rights

If you are dissatisfied with my decision or the searches we did to locate any documents related to your request, you may apply for internal review or Information Commissioner review of the decision. We encourage you to seek internal review as a first step as it may provide a more rapid resolution of your concerns.

Internal review

Under section 54 of the FOI Act, you may apply in writing to the CEO, Food Standards Australia New Zealand for an internal review of my decision. You should send your request by email to FOI@foodstandards.gov.au . The internal review application must be made within 30 days of the date of this letter.

Where possible please attach reasons why you believe review of the decision is necessary. The internal review will be carried out by another officer within 30 days.

Information Commissioner review

Under section 54L of the FOI Act, you may apply to the Australian Information Commissioner to review my decision. An application for review by the Information Commissioner must be made in writing within 60 days of the date of this letter, and be lodged in one of the following ways:

online:	https://forms.business.gov.au/aba/oaic/foi-review-/
email:	enquiries@oaic.gov.au
post:	GPO Box 2999, Canberra ACT 2601
in person:	Level 3, 175 Pitt Street, Sydney NSW

More information about Information Commissioner review is available on the Office of the Australian Information Commissioner website. Go to www.oaic.gov.au/freedom-of-information/foi-reviews.

Further information

The contact officer for this matter is:

Ph: +61 2 6271 2222
Email: FOI@foodstandards.gov.au

Please contact if you require further information.

Yours sincerely

28 January 2020

Incl/ Attachment

ATTACHMENT - FOI GE FREE NZ A1186 – WHERE TO FIND THE REQUESTED INFORMATION TO ASSIST YOUR SUBMISSION

1. ***All report on the long term animal feeding studies that were conducted on the soy leghemoglobin,***

    a. ***On animals***
    b. ***On humans***

Details of feeding studies are provided as part of the main A1186 Application document (see Section C.4 *Toxicology data*). An assessment of this information is provided in the SD1 (see Section 2.4 *Toxicological assessment of LegH Prep*).

2. ***The journal they were published in?***

The feeding studies we have been provided and have assessed are published. They are publically available. You may access them from the websites noted below.

- Fraser RZ, Shitut M, Agrawal P, Mendes O, Klapholz S (2018) Safety Evaluation of Soy Leghemoglobin Protein Preparation Derived From *Pichia pastoris*, Intended for Use as a Flavor Catalyst in Plant-Based Meat. Int J Toxicol 37: 241-262 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5956568/)

- Jin Y, He X, Andoh-Kumi K, Fraser RZ, Lu M, Goodman RE (2018) Evaluating potential risks of food allergy and toxicity of soy leghemoglobin expressed in *Pichia pastoris.* Mol Nutr Fod Res 62:e1700297 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5813221/)

3. ***Levels of microbiological contaminants in the liquid?***

FSANZ is assuming that, by "the liquid", you are referring to the LegH preparation. Details of microbiological contaminants in this preparation is presented in the main A1186 Application document (see Section B.6 *Specifications*). A summary is also provided in the SD1 (see Section 2.1.3 *LegH Prep specifications*).

4. ***Levels of fermentation substrates, production strain, and processing aids in the liquid***

An outline of the manufacturing process, including the raw materials and processing aids, is provided in the main A1186 Application document (see Section B.4 *Manufacturing Process*).

Levels of the production strain in the LegH preparation is discussed in the main A1186 Application document (see Section B.4.4 *Fermentation and Recovery Processes* and Section B.5 *Information on the Impurity Profile*).

A summary of the FSANZ assessment of the manufacturing process is provided in the SD1 (see Section 2.7 *Manufacturing process*).

5. ***Levels of Heavy metals in the liquid?***

Details of heavy metal contaminants in the LegH preparation are presented in the main main A1186 Application document (see Section B.6 *Specifications*). You may also access this information from the summary which is provided in the SD1 (Section 2.1.3 *LegH Prep specifications*).

6. DNA fragments from the process?

FSANZ assumes this question refers to the presence of DNA in the LegH preparation.

Details are provided in the main A1186 Application document in Section B.4.2.4 *History of Use* and Section C.5.1 *Origins and History of Use.*

Please also note the summary of information provided in the SD1 (Section 2.7 *Manufacturing Process – Presence of novel DNA in the final product*).

7 to 10 – Studies and Evidence

You asked for the following 'as soy hemoglobin has not been in the animals or human food chain before as a GE or natural product':

7. *Allergen feeding studies and*
8. *Any studies to show if GE DNA fragments are absorbed into the blood stream?*
9. *Safety studies on children eating it?*
10. *Safety studies on elderly, sick eating it.*
11. *Evidence that the denatured protein will not harm consumers?*

Please see:

- the main A1186 Application document in Section C.4 *Toxicological Data,* and Section C.6 *Allergenicity*;
- the following Appendices of the A1186 Application:

  - Appendix VI *Structural comparison of plant hemoglobins and animal myoglobins*
  - Appendix VIII *Expert opinions on the safety of soy leghemoglobin and Pichia pastoris*
  - Appendix X *In vitro pepsin digestibility study/*

  These Appendices are available in the A1186 Call for submissions section of the FSANZ website and as listed separately above for ease of reference.

- SD1 – the technical and risk assessment, in particular:

  - Section 2.3 *Characterisation of the novel proteins*,
  - Section 2.4 *Toxicological assessment*,
  - Section 2.5 *Nutritional assessment* and
  - Section 2.6 *Dietary assessment*

Labelling

You requested confirmation that the imported liquid and the end product containing the Soy leghemoglobin protein will be labeled. Please see Section 3.2 *Labelling requirements* of the A1186 Call for Submissions for details regarding labelling.

Re: GRAS Notice No. GRN 000737

Dear

The Food and Drug Administration (FDA, we) completed our evaluation of GRN 000737. We received the notice that you submitted on behalf of Impossible Foods Inc. on October 3, 2017,[1] and filed it on October 26, 2017. Impossible Foods submitted amendments to the notice on November 29 and December 5, 2017; and February 27, March 6, June 29, and July 10, 2018. In the amendments, the notifier informs FDA of the publication status of two scientific articles and clarifies the intended conditions of use of soy leghemoglobin preparation.

The subject of the notice is soy leghemoglobin preparation from a strain of *Pichia pastoris* (soy leghemoglobin preparation) for use at a level up to 0.8% soybean leghemoglobin protein to optimize flavor in ground beef analogue products intended to be cooked. The notice informs us of Impossible Foods' view that this use of soy leghemoglobin preparation is GRAS through scientific procedures.

Our use of the term, "soy leghemoglobin preparation," in this letter is not our recommendation of that term as an appropriate common or usual name for declaring the substance in accordance with FDA's labeling requirements. Under 21 CFR 101.4, each ingredient must be declared by its common or usual name. In addition, 21 CFR 102.5 outlines general principles to use when establishing common or usual names for nonstandardized foods. Issues associated with labeling and the common or usual name of a food ingredient are under the purview of the Office of Nutrition and Food Labeling (ONFL) in the Center for Food Safety and Applied Nutrition. The Office of Food Additive Safety (OFAS) did not consult with ONFL regarding the appropriate common or usual name for "soy leghemoglobin preparation."

Impossible Foods describes soy leghemoglobin preparation as a mixture containing soy leghemoglobin protein, *P. pastoris* proteins, sodium chloride, and sodium ascorbate. The soy leghemoglobin preparation is red/brown. The preparation is produced using

[1] Impossible Foods provided an update to its notice on October 18, 2017. The update includes information about the intended use of soy leghemoglobin preparation.

U.S. Food and Drug Administration
Center for Food Safety & Applied Nutrition
5001 Campus Drive
College Park, MD 20740
www.fda.gov

P. pastoris production strain MXY0291, which was constructed from the commercially available *P. pastoris* Bg11 strain. Impossible Foods describes *P. pastoris* as a non-pathogenic, non-toxigenic, and well-characterized yeast with a history of safe use in the food industry.

Impossible Foods describes the construction of the production strain through transformation of the recipient Bg11 strain using (1) multiple copies of a codon-optimized gene encoding the leghemoglobin LGB2 apoprotein from soybean (*Glycine max*), (2) additional copies of eight *P. pastoris* genes encoding enzymes catalyzing heme B biosynthesis, and (3) transcriptional regulatory elements to improve protein production. The expression of these genes results in overexpression of the soy leghemoglobin apoprotein and the yeast heme B prosthetic group, which combine to form soy leghemoglobin protein. Impossible Foods has sequenced the *P. pastoris* production strain genome, verifying the sequence of the inserted DNA and confirming the production strain does not contain antibiotic resistance genes. Impossible Foods also states that the transformed DNA is stably integrated in the production strain.

Impossible Foods states that soy leghemoglobin preparation is manufactured by submerged batch fed fermentation of the *P. pastoris* production strain under controlled conditions. The culture is periodically tested to ensure production strain identity, purity, and protein generating ability. Following fermentation, the *P. pastoris* cells are lysed by mechanical shearing and the insoluble content is removed by centrifugation and microfiltration. The resulting lysate is concentrated by ultrafiltration, stabilized with sodium chloride and sodium ascorbate, and stored as a frozen liquid concentrate. The frozen concentrate is standardized to a final concentration of 6-9% of soy leghemoglobin protein. Impossible Foods states that the raw materials used in the production of soy leghemoglobin preparation are food grade, that the manufacturing process is performed in accordance with current good manufacturing practices, and that the components of the fermentation media are not derived from major food allergens.

Impossible Foods provides specifications for soy leghemoglobin preparation; these include solids (≤ 24% w/w), which includes soy leghemoglobin protein content (6-9 %) at a purity of ≥ 65%, fat (≤ 2%), carbohydrates (≤ 4%), ash (≤ 4%), pH (6.5-8.5), and lead (< 0.4 mg/kg), as well as limits for microorganisms. Impossible Foods also provides results from batch analyses that demonstrate soy leghemoglobin preparation can be manufactured to meet these specifications. Impossible Foods states that soy leghemoglobin preparation can be stored at -20 °C as a frozen liquid for at least 12 months with no observable change in soy leghemoglobin protein stability.

Impossible Foods estimates dietary exposure to the soy leghemoglobin protein and the soy leghemoglobin preparation at the maximum use level of 0.8% soy leghemoglobin protein. Impossible Foods estimates mean and 90th percentile dietary exposures for the general population based on the conservative assumption that consumers will substitute ground beef analogue products containing soy leghemoglobin preparation for traditional meat products on a 1:1 basis. Impossible Foods used food consumption data from “Retail Commodity Intakes: Mean Amounts of Retail Commodities per Individual” (USDA, 2007-2008). Impossible Foods estimates mean and 90th percentile intake of soy leghemoglobin protein to be 3.3 mg/kg bw/d, and 6.7 mg/kg bw/d respectively.

Impossible Foods also estimates 90th percentile intake of soy leghemoglobin preparation to be 8.9 mg/kg bw/d, accounting for the *P. pastoris* proteins present in the final soy leghemoglobin preparation.

Impossible Foods uses several lines of evidence to develop a weight-of-evidence approach to assess the safety of soy leghemoglobin preparation for use in food. In addition to considering the safety of *P. pastoris* for use as the production microorganism, Impossible Foods considers (1) the history of consumption of hemoglobin proteins in food, (2) the results of bioinformatic analyses comparing soy leghemoglobin and *P. pastoris* proteins to known toxins and allergens, (3) the digestibility of soy leghemoglobin preparation proteins in simulated gastric fluid, and (4) publicly available scientific literature. Impossible Foods also describes publicly available experimental evidence from toxicity studies, along with a detailed discussion of the evidence and its relevance to their safety assessment.

Impossible Foods discusses the prevalence and function of hemoglobin proteins, which are found in the tissues of plants and animals commonly consumed in the human diet. These proteins are involved in selective transport, storage, or buffering of oxygen levels in cells and tissues. Examples of dietary sources of plant-derived hemoglobins include malted grain products and sprouted seeds, grains, rice, and beans.

Impossible Foods assesses the potential for soy leghemoglobin and *P. pastoris* proteins to be toxic or allergenic. Bioinformatic analyses of soy leghemoglobin protein were conducted using both sequence alignment- and Support Vector Machine (SVM)-based methods, while analyses of the 17 most abundant *P. pastoris* proteins were conducted using the sequence alignment-based method alone. Impossible Foods reports the sequence-alignment results demonstrate that neither soy leghemoglobin nor the 17 analyzed *P. pastoris* proteins contain significant amino acid sequence homology to known or putative allergens or toxins. Impossible Foods further reports that the combined results of multiple SVM analyses predict that soy leghemoglobin is not likely to be an allergen. Impossible Foods reports that the digestibility analysis shows that proteins in the soy leghemoglobin preparation are digested by pepsin in simulated gastric fluid. Impossible Foods concludes that soy leghemoglobin and the *P. pastoris* proteins within the preparation have little or no toxic or allergenic potential.

Impossible Foods reports that the published scientific literature was searched for reports of toxicity or allergenicity associated with soy leghemoglobin or with *P. pastoris*. Impossible Foods states that the literature search did not identify information that suggested allergic, toxic, or adverse health effects related to consumption of soy leghemoglobin or *P. pastoris* proteins.

Impossible Foods describes a published study that it conducted. This study includes a bacterial reverse mutation assay and a chromosomal aberration assay in human peripheral blood lymphocytes; these demonstrate soy leghemoglobin preparation is non-mutagenic and non-clastogenic. The published study also includes 14- and 28-day oral toxicity studies in rats; Impossible Foods reports that there were no treatment-related, toxicologically relevant effects up to 1536 mg/kg/day, the highest dose of the soy leghemoglobin preparation tested.

Impossible Foods includes the report of a panel of individuals (Impossible Foods' GRAS panel). Based on its review, Impossible Foods' GRAS panel concluded that soy leghemoglobin preparation is safe under the conditions of its intended use.

Based on the publicly available scientific data assembled and presented in its GRAS notice, Impossible Foods' concludes that soy leghemoglobin preparation is generally recognized as safe for use to optimize flavor in ground beef analogue products intended to be cooked.

Potential Labeling Issues

Under section 403(a) of the Federal Food, Drug, and Cosmetic Act (FD&C Act), a food is misbranded if its labeling is false or misleading in any way. Section 403(r) of the FD&C Act lays out the statutory framework for labeling claims characterizing a nutrient level in a food or the relationship of a nutrient to a disease or health-related condition (also referred to as nutrient content claims and health claims). The notice raises a potential issue under these labeling provisions. In the notice, Impossible Foods states that soy leghemoglobin preparation has nutritive value as a source of iron. If products containing soy leghemoglobin preparation bear any nutrient content or health claims on the label or in labeling, such claims are subject to the applicable requirements and are under the purview of ONFL. OFAS did not consult with ONFL on this issue or evaluate any information in terms of labeling claims. Questions related to food labeling should be directed to ONFL.

Allergen Labeling

The FD&C Act requires that the label of a food that is or contains an ingredient that contains a "major food allergen" declare the allergen's presence (section 403(w)). The FD&C Act defines a "major food allergen" as one of eight foods or food groups (i.e., milk, eggs, fish, Crustacean shellfish, tree nuts, peanuts, wheat, and soybeans) or a food ingredient that contains protein derived from one of those foods. Soy leghemoglobin preparation requires labeling under the FD&C Act because it contains protein derived from soybean.

Potential Requirement for a Color Additive Petition

There is no GRAS provision for color additives. In Impossible Foods' notice, soy leghemoglobin preparation is described as red/brown. As such, the use of soy leghemoglobin preparation in food products (other than ground beef analogue products intended to be cooked) may constitute a color additive use under section 201(t)(1) of the FD&C Act and FDA's implementing regulations in 21 CFR Part 70. Under section 201(t)(1) and 21 CFR 70.3(f), a color additive is a material that is a dye, pigment, or other substance made by a synthetic process or similar artifice, or is extracted, isolated, or otherwise derived from a vegetable, animal, mineral, or other source. Under 21 CFR 70.3(g), a material that otherwise meets the definition of a color additive can be exempt from that definition if it is used (or is intended to be used) solely for a purpose or purposes other than coloring. Our response to GRN 000737 is not an approval for use as

a color additive nor is it a finding of the Secretary of the Department of Health and Human Services within the meaning of section 721(b)(4) of the FD&C Act. Questions about color additives should be directed to the Division of Petition Review in OFAS.

Section 301(ll) of the 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 Impossible Foods' notice concluding that soy leghemoglobin preparation 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 soy leghemoglobin preparation. Accordingly, our response should not be construed to be a statement that foods containing soy leghemoglobin preparation, if introduced or delivered for introduction into interstate commerce, would not violate section 301(ll).

Conclusions

Based on the information that Impossible Foods provided, as well as other information available to FDA, we have no questions at this time regarding Impossible Foods' conclusion that soy leghemoglobin preparation is GRAS under its intended conditions of use to optimize flavor in ground beef analogue products intended to be cooked. This letter is not an affirmation that soy leghemoglobin preparation 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 000737 is accessible to the public at www.fda.gov/grasnoticeinventory.

Office of Food Additive Safety
Center for Food Safety
and Applied Nutrition