GE Free New Zealand

In Food And Environment Inc.

[redacted]

Tel: [redacted]

17.9.2020

Re: 2nd call for submissions

A1186 – Soy Leghemoglobin in meat analogue products.

Tēnā koutou katoa,

We ask that you fully assess and consider our submission. We would like to be heard, we are happy to have the hearing in Wellington.

It is of great concern that the second call for submission has altered the original basis for approval to enter the food chain. The second call has added a health claim relating to its iron levels, meaning that it is now a high level nutritional claim under subdivision G as well as a product from gene technology.

This now requires further scientific evaluation under the high-level claims committee; however we have found it difficult to access their report.

We have many other concerns with the outlined approval. We fully support the previous issues raised in our original submission; Victorian Department of Health and Human Services and the Victorian Department of Jobs; Precincts and Regions and PrimeSafe, South Australia Health; The Queensland Health and New South Wales Health Departments submissions. We believe the issues raised have not been addressed in the second call summary, SD1 and 2 documents.

1. The applicant has asked that the permitted level of Soy leghemoglobin (SLH) is no higher than 0.8%. FSANZ has sought approval for these levels and stated

"Existing labeling requirements apply to enable consumers to make informed choice". [1]

This statement is incorrect, because it does not enable consumers to make informed choices or fulfill the requirement of the FSANZ Act for the protection of public health and safety. The FSANZ approval ensures that SLH is below the existing 0.9% threshold. There is no

requirement to label point of sale, unpackaged foods, and the Impossible Food website does not declare that its ingredients [2] are made and sourced from GM ingredients, so consumers will not be made aware that they are eating a GM product that has never been in the human diet before.

The Impossible Burger is made from a range of GM ingredients all escaping labeling requirements due to various exemptions. There is also a gap in legislation in that it is not clear whether a food that contains 100% GM ingredients but each ingredient is below the level of labeling is considered "adventitious" or required to be labeled.

It is misleading for consumers if they are not told of the nature of the product. Serious health reactions, allergy, and irritable bowel conditions could occur in susceptible people, as the food ingredient has never been in the food chain before. If they do have a negative reaction there is no way to prove it is related to the GM product.

There are no medical diagnostic tests to detect such allergens, and there is no proof to support claims of there being no potential allergens. Nor do health professionals have the expertise to specifically ask for confirmation tests when allergies present themselves.

Requirement: Soy leghemoglobin must be clearly labeled GM at all fast food outlets and on packaging. Post monitoring and diagnostic tests must also be developed and available for health professionals before SLH is available for sale.

2. FSANZ has been provided with data from a different strain of *P.pastoris* vector.

"Some of the data provided to FSANZ for the risk assessment analyses was obtained from a predecessor of MXY0541, designated MXY0291. The major differences between these two strains is the copy number of the leghemoglobin gene (MXY0291 contains fewer copies) and MXY0541 contains extra DNA sequences associated with one of the haem-synthesis enzyme genes".

This is not fully correct as the protein purity of SLH product is only 76% with MYX0541 as opposed to 80%. The fat, ash and carbohydrate levels are also altered.

It is dangerous to assume the safety of SLH because pharmaceuticals and industrial have used *P.pastoris* in their products. It is specious and deceptive to say that no adverse effects have been found when there is an absence of in vivo data as mainly the applicant has provided short-term ingestion or literature search.

FSANZ final assessment states

"While there is limited evidence that P. pastoris has been consumed by humans, this organism does have a long history of safe use for the production of pharmaceuticals and industrial chemicals, including a number of enzyme processing aids approved by EFSA, US FDA and FSANZ… Furthermore, a search of the literature did not identify any potential safety concerns associated with P. pastoris, K. phaffi or K. pastoris and no reports of adverse effects from products produced from P. pastoris strains were identified."

FSANZ statement is disingenuous and deliberately misleading about the potential differences of production and use between the yeast and the SLH. It is dangerous to assume the safety of SLH because pharmaceuticals and food industries have used *P.pastoris* as an expression vector for the production of recombinant proteins for clinical and industrial use.

It is specious and deceptive to assess the safety of *P.pastoris* instead of the final purified isolate of SLH. FSANZ's deduction that there are "no adverse effects" is deliberately misleading as the wrong product has been evaluated and there is no information or data to show the safety of GM SLH. Jin Y. et al (2018) [3] literature search found soybean is a relatively common food allergy among children, related to the proteins in the beans. There is no safety data on the roots as they are neither eaten nor are they safety-tested as genetically modified.

We are not being asked to submit on the introduction of *P.pastoris,* which has no history of safe use, into the human food chain. (FSANZ Supporting Document 1, p.8). The application is for approval for the isolated soy leghemoglobin [4] made through genetically engineered *P.pastoris.* There are few SLH safety studies, and has SLH has never been commercialized in Australia or New Zealand so has not been part of the food chain and has no history of safe use.

The 14 day study by Fraser et al (2018) on Sprague Dawley rats (FSANZ SD1, p.13) [5] by found that numbers of white blood cells, neutrophils and lymphocytes in males were >25% lower than those of controls. The 28 day study confirmed the statistically significant changes in haematology, liver and clinical chemistry values as well as oestrus cycles. (FSANZ SD1, p.14).

These changes have been ignored as not treatment related and were not fully addressed by the assessment. It is unacceptable that FSANZ chooses to constantly disregard, minimise, and ignore scientific research findings that show harm to the general public, especially those who are immune compromised.

It is a serious dereliction of FSANZ "duty of care" to assess the yeast instead of the SLH meat analogue product. Due to the lack of safety studies on SLH there remains potential for harm from allowing the product to be marketed, especially without notice to shoppers. This unrecognized exposure to risk is unreasonable, especially when there is a range of vegetarian products on the market that are established as safe for consumers. It appears that FSANZ is set to approve a gimmick fast food with no evidence of safety for consumers.

Requirement: Further comprehensive safety testing carried out to address the unevaluated risks of SLH before approval is considered. Post monitoring and diagnostic tests must also be developed and deployed before it is available for sale.

3. FSANZ stated that the potential allergenicity or toxicity of the soy leghemoglobin and the *Pichia* proteins did not identify any significant similarities to known allergens or toxins. The proteins were shown to be susceptible to pepsin digestion in acidic conditions that mimic the stomach environment.

The applicant evaluated only in-vitro digestion tests on stomach acidity of pH2. *Therefore, in this study we only evaluated stability of the protein at pH 2.0.*Soy leghemoglobin tested at pH 2 found there was a slower rate of full-length protein and fragment degradation than at pH 1.5. As can be seen in the Beasley et al (2015) study there is a range of stomach pH levels throughout the digestive process that age plays a factor in stomach acidity [6]. Many people are on medications to suppress stomach acidity reducing acidity levels to ranges of pH 3.5 - 6. There is no information on the survival of the SLH at these reduced acidity levels of pH 2.5-6.6.

The applicant has estimated that there will be consumers from the ages of 2-65 yrs. old consuming their product. This is the most concerning outcome of FSANZ 's review as it completely ignores the children who have a lower gastric pH level of around pH4, the many people of all ages on medications, and those who have had stomach bypass operations that decrease the gastric pH to levels between 2.5-6pH [7]. It is highly possible that the GM protein will survive intact and resist degradation at these levels. Netherwood et al (2004) [7] detected full length DNA from soy survived stomach acids. As SLH is being marketed as a healthy dietary alternative to meat, the very people who are unwell and are looking for a dietary change to non-meat alternatives are increasingly susceptible to choosing such foods unknowingly exposing themselves to risks that FSANZ staff have failed to consider.

Requirement: Before approval for entry to the food chain, FSANZ requires ingestion studies in vivo on a range of human subjects of diverse ages and health status.

4. Impossible Foods has applied to use soy leghemoglobin only as a component within their meat analogue products, at levels of not more than 0.8% soy leghemoglobin in the raw product. However, FSANZ has signaled it will approve it for general use in non-Impossible Food products as well.

Soy leghemoglobin is permitted as a substance used as a nutritive substance only in meat analogue products to which subsection S17—4 applies, with a maximum permitted use level of 0.8% in raw product, in accordance with Standard 1.3.2, and as a permitted form of iron in the table to section S17—3.

This is another dereliction of duty as FSANZ has gone above its required responsibilities and scope. It has taken it upon itself to act unilaterally, beyond what it has been tasked to approve in the application to do with scant evidence of safety.

FSANZ's assessment ignores the submitters' concerns in round 1, further endangering the public, as the widespread approval for use without any quality control presents a danger, especially since the burgers have been evaluated at levels of 0.25% -0.45%. There is no evidence or data on the safety profile of SLH at double the levels will have.

We note that FSANZ is seriously compromised in its ability to reject the application. This is because the applicant has paid the assessment fee which, FSANZ is bound to refund if the approval is rejected. (FSANZ ACT, 110 (3)). This is not conducive to full and fair consideration and requirement of proof of safety. This compromise of its purpose also acts

as a disincentive for FSANZ to follow through the regulatory science strategy, which give the public a guarantee under the law and also stated on the FSANZ website [9].

Summary

1. This application be placed on stop clock or rejected until all points 2-5 below are addressed...
2. Required ingestion studies in vivo on a range of human subjects of all ages and health status are published.
3. Further safety testing is carried out with volunteers who are fully informed of the research and its objectives.
4. Soy leghemoglobin must be clearly labeled as genetically modified, not just "contains soy", in all point of sale outlets, fast food chains, on packaging and in all advertising.
5. Post monitoring and diagnostic tests must be developed and deployed before the ingredient, SLH, is allowed into the food chain and made available for sale.

Nga mihi,

[redacted]

Secretary GE Free NZ.

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[1] 2nd Call for submissions – Application A1186 (p.4).

[2] https://faq.impossiblefoods.com/hc/en-us/articles/360018937494-What-are-the-ingredients-

[3] Jin Y, He X, Andoh-Kumi K, et al. Evaluating Potential Risks of Food Allergy and Toxicity of Soy Leghemoglobin Expressed in Pichia pastoris. (2018) *Molecular Nutrition & Food Research*. 62 (1). DOI: 10.1002/mnfr.201700297.

[4] https://faq.impossiblefoods.com/hc/en-us/articles/360034767354-How-do-you-make-heme-

[5] Fraser, R. Z., 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. *International journal of toxicology*, *37*(3), 241–262. https://doi.org/10.1177/1091581818766318

[6] Beasley DA, Koltz AM., Lambert JE., Fierer N, Dunn RR. The Evolution of Stomach Acidity and Its Relevance to the Human Microbiome (2015) *PLoS One.* 10(7): e0134116. Published online 2015 Jul 29. doi: 10.1371/journal.pone.0134116

[7] Feldman M. (1996) Comparison of the effects of over-the-counter famotidine and calcium carbonate antacid on postprandial gastric acid. A randomized controlled trial. *JAMA*. 275(18): 1428-1431. https://pubmed.ncbi.nlm.nih.gov/8618369/

[8] Netherwood, T., Martín-Orúe, S., O'Donnell, A., Gockling, S., Graham, J., Mathers, J., & Gilbert, H. (2004). Assessing the survival of transgenic plant DNA in the human gastrointestinal tract. *Nature Biotechnology*, *22*(2), 204-209. https://doi.org/10.1038/nbt934

[9] Purpose of the FSANZ Regulatory Science Strategy https://www.foodstandards.gov.au/publications/RegulatoryScienceStrategy201923/Pages/Purpose-of-the-FSANZ-Regulatory-Science-Strategy.aspx