GE Free New Zealand

In Food and Environment Inc.

PO Box 13402, Wellington, NZ

6 November 2023

Re: A1274: Food derived from disease-resistant banana line QCAV-4.

Tēnā koutou FSANZ chair and committee members,

GE-Free New Zealand in food & environment Inc. is a non-profit voluntary organisation. We regularly contact our members updating them on the current submissions and information on genetic engineering.

We ask FSANZ to "Stop the Clock" due to a lack of vital safety information. Once the comprehensive scientific data on the long-term safety on public health has been conducted, the application (A1274) must be then re submitted.

1. **Safety Issues**: The FSANZ Act guarantees that consumers have confidence in the safety and quality of the food they buy. This is through adequate information relating to food safety that enables consumers to make a choice. The information and safety must be through an effective, transparent, and accountable regulatory framework (Sect: 3 FSANZ Act 1991).

   This responsibility by the FSANZ assessment team for Application A1274 has not been carried out. The precautionary approach has been ignored and every GM application that FSANZ has evaluated in its summary assessment receives the same statement of acceptance-

   > *"No potential public health and safety concerns have been identified in the assessment of disease-resistant banana line QCAV-4. On the basis of the data provided in the present application and other available information, food derived from QCAV-4 is considered to be as safe for human consumption as food derived from non-GM banana cultivars"*[1]

   This statement is deceptive and misleading as it implies that FSANZ has either seen safety studies or conducted them.

   The statement does not adequately address the safety issues for consumption as there is an absence of scientific data to support the statement. There is no available evidence on safety of consumption of the GM banana and no studies into the health effects the transgene could cause for infants, children, sick, elderly or the public.

   The Impact Statement that has not been done, should have addressed the cost benefit analysis on the consumer if ill health is a consequence of eating this banana.

   To ensure that FSANZ meets its legal responsibility it must ensure that safety to the consumer is confirmed, not assumed without supporting g data.

   In replying to correspondence to GE Free NZ regarding the absence of scientific proof of safety. FSANZ (25.10.23) response was -

[1] https://www.foodstandards.gov.au/code/applications/Documents/01_A1274_SD1.pdf

"Human and animal consumption studies are not an Application Handbook requirement for the safety assessment of GM foods. As such, these studies were not provided for the banana line QCAV-4… FSANZ did not identify any new or altered hazards as a result of the genetic modification to the banana. In the absence of any new or altered hazards, additional studies such as animal or human studies are not warranted.[2]

This statement directly contradicts the Object of the FSANZ Act (sec:3) and disregards the guidance documents on Science Based Risk analysis[3] and ignores that guidance document on the Safety Assessment Of Genetically Modified Foods [4] that clearly states that consideration of unintended effects of the genetic modification must be considered in detail.

FSANZ has the responsibility to ensure consumer safety in the approval of foods into the food chain. This application has not included the scientific data that is relevant to human ingestion and due to the insufficient scientific safety information, that is needed to guarantee consumer health protection, consumers cannot to be assured that the food is safe.

FSANZ Act 18 clearly states in Section 4 [5]

(4) Where the Authority considers that the best available scientific evidence … is insufficient, the Authority may provisionally adopt sanitary or phytosanitary measures on the basis of available pertinent scientific information. In such cases, the Authority must take all reasonable steps to obtain the information necessary for a more objective risk analysis and a review of the sanitary or phytosanitary measures, to be undertaken within a reasonable period of time.

FSANZ, in order to protect the public and assure the public has adequate information, is charged with obtaining scientific data that may come from

"laboratory based studies; toxicological studies; microbiological studies; relevant human studies such as volunteer studies; occupational exposure studies; poisoning case reports and epidemiology studies; and consumer and social research using survey, experimental and qualitative studies."

"The goal of the safety assessment is to identify the differences (either intended or unintended) which become the focus of further scrutiny and to the undertaking of traditional nutritional, toxicological or immunological testing".

'Traditional testing' infers oral consumption or skin prick studies, but no scrutiny has been undertaken in evaluating the differences in the new and unintended proteins (ORFS.)

Because of this lack of high quality, relevant, credible, and objective information on toxicological, oral exposure and relevant human impacts , FSANZ cannot meet its duty of care, and is not able to provide scientific proof of safety to the public/consumer.

FSANZ has ignored that this GM banana, that has no history of safe use, and is different to the conventional counterpart. FSANZ have chosen to assume safety by not evaluating the

[2] RE: Application A1274 [SEC=OFFICIAL] email to Claire Bleakley 25.10.2023 at 5:48pm
[3] https://www.foodstandards.gov.au/science/riskanalysis/Pages/default.aspx
[4] https://www.foodstandards.gov.au/consumer/gmfood/safety/documents/GM%20FINAL%20Sept%2007L%20_2_.pdf
[5] https://www.legislation.gov.au/Details/C2018C00243

survival of the transgenes in the digestive system that has potential immunological and organ effects from fresh raw GM banana, on infants, children, elderly, or people on medication.

This GM banana is not comparable or similar to its conventional counterpart. The insertion of infection by Agrobacterium-mediated plant transformation of the synthetic bacterial genes from E. coli K12 creating new genetic constructs in the GM banana cannot be considered as safe as its conventional counterpart and the differences left unstudied.

The GM banana has not undergone any allergen or oral consumption studies. This banana will be eaten fresh, and the existence of new and unintended proteins sourced from the engineering process have not been scientifically tested to prove consumer safety.

The unsubstantiated statement "*no potential public health and safety concerns …*" shows that regardless of the absence of information on the consumption of GM bananas provided by the applicant, the FSANZ assessment team either does not have the expertise or is deliberately overlooking serious findings reported in Studies submitted in Support of the Food Safety Assessment of Fusarium Wilt Tropical Race 4 Resistant Banana Event QCAV-4.[6]

2. **New Proteins**:
   The Safety Assessment of Genetically Modified Foods summary Information required by FSANZ for the safety assessment of a GM food[7] requires that the *"impacts on human health from potential transfer of new genetic material to cells in the human digestive tract in undertaken."* (Table 15.1, p.36).

   GE Free NZ asked in May 2023 for the consumption studies, but these have not been provided, so it is unscientific and does not have the necessary scientific information to assure the consumer of the food's safety. There is no data on the fate of the gene constructs to transfer to gut flora and the ability to transfer over the barrier into the blood and their effects.

   GE Free NZ did receive 5 documents under the FOI. These are more detailed than the documents provided on their website for the public.

   The most detailed is Document 3: Compilation of Study Reports[8] These were the studies submitted in support of the Food Safety Assessment of the Race4 Resistant Banana Event QCAV-4.

   FSANZ's assessment team has evaluated the new intended proteins MamRGA2 and NPTII.

   However, they have overlooked the 7 new and unidentified synthetic proteins.

   These appear to be related to the plasmids engineered into the bananas. The 7 unidentified genes had open reading frames (ORFS) meaning they could produce new and deleterious proteins that FSANZ staff have decided are of no biological significance. This is assumption with no scientific data to support the comment but simply reflects the applicant's opinion.

   The Centre for Agriculture and the Bioeconomy section A.3 reports –

   > *"Sequence analysis of the insert and it 5 'and 3 'flanking regions revealed the presence of three identical copies of the pSAN3 T-DNA, a 6,668 bp hybrid fragment of the MamRGA2 expression cassette recombined in opposite directions and several minor rearrangements at T-DNA/T-DNA and TDNA/genome junctions. Seven new and unintended ORFs resulted from the presence of the insert ...*" (study report QUT2023-4, p.30)

[6] https://www.gefree.org.nz/assets/Uploads/3-Event-QCAV-4-Compilation-of-Study-Reports-Redacted.pdf
[7] https://www.foodstandards.govt.nz/consumer/gmfood/safety/documents/GM%20Foods_text_pp_final.pdf
[8] https://www.gefree.org.nz/assets/Uploads/3-Event-QCAV-4-Compilation-of-Study-Reports-Redacted.pdf

There are statistical differences between the QCAV-4 banana and non-GM control in the protein levels. The non-GM banana does not have the transgenic protein engineered into its DNA, so it is impossible to say that there are no differences between the QCAV-4 and non-GM control. So, what proteins were assessed?

The fact that the banana expresses 7 new unintended synthetic protein sequences as stated-

> *"While seven unintended open reading frames (ORFs) resulted from the insertion, none contained the required regulatory elements necessary for expression of mRNA and protein biosynthesis and this was confirmed by RNA-Seq. Analysis of the predicted amino acid sequences from these new ORFs showed that none had the potential to encode a protein with* ***any significant amino acid sequence*** *similarity to known toxins or allergens. Using Southern blot analysis, the introduced genetic material was shown to be* ***stably inherited over five generations*** *of plants" (FSANZ Executive summary, p.1)*[9]

The term *"significant"* infers that the proteins were detected and was "*stably inherited for over 5 generations"*. The suppositions and assumptions of safety of the 7 new and unintended proteins, in the provided studies data, cannot be established as safe for human consumption, as no scientific evidence on their allergen potential or toxicity. As they are new proteins the constructs are not in the database to be able to confirm safety.

This means that FSANZ must address the missing information, "stop the clock" and call for skin prick allergen and a 90-day ingestion study as outlined in the Safety Assessment of Genetically Modified Foods that assure the public that safety of the GM banana is scientifically confirmed.

3. **Effects of Pesticides:** The bananas have been grown in ground that has been sprayed heavily with herbicides. (Australian Pesticides and Veterinary Medicines Authority). Seralini *et al* (2014)[10] conducted a long-term study on rats and found that Roundup (a glyphosate-based herbicide), caused immune system, renal and hepatic changes and tumour progression. Ulrich J. *et al* [11] (2023) study of Sri Lankan people found an association with chronic kidney disease (CKDu), glyphosate and its metabolites in people who eat and drink hard water. Hard water is a complex of dissolved calcium and magnesium and the Grand Naine banana plant [12] is rich in calcium (140mg) and magnesium. We ask that the Australian Pesticides and Veterinary Medicines Authority (APVMA) report on the minerals and the effects from pesticides and their effects in the GM banana. The soils might alter the gene expression in the GM banana in adverse ways.

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[9] https://www.foodstandards.gov.au/code/applications/Pages/A1274---Food-derived-from-disease-resistant-banana-line-QCAV-4-.aspx

[10] Séralini GE, Clair E, Mesnage R, Gress S, Defarge N, Malatesta M, Hennequin D, de Vendômois JS. Republished study: long-term toxicity of a Roundup herbicide and a Roundup-tolerant genetically modified maize. Environ Sci Eur. 2014;26(1):14. doi: 10.1186/s12302-014-0014-5. Epub 2014 Jun 24. PMID: 27752412; PMCID: PMC5044955.

[11] Glyphosate and Fluoride in High-Hardness Drinking Water Are Positively Associated with Chronic Kidney Disease of Unknown Etiology (CKDu) in Sri Lanka. Ulrich J.C., Hoffman K., T., Gunasekara T.D. K., Sandamini P.M., Jackson B.P., Mangala P., De Silva C.S., Jayasundara P., Ferguson L. (2023) *Environmental Science and Technology Letters, Oct. 10, 2023.* DOI: 10.1021/acs.estlett.3c00504

[12] National Research Centre for Banana https://krishi.icar.gov.in/jspui/bitstream/123456789/1279/1/4%20-%20Banana%20fruit%20nutritive%20%28English%29.pdf

4. **Protein survival and gastric fluids:** The E. coli expressed MamRGA2 protein by pepsin, trypsin, and chymotrypsin in simulated gastric fluid (SGF) was tested. (QUT2023-9, p.76). The acid content of these digestive enzymes was between pH 1-3 ->2.

   Ott et al (2022) studies showed that in the rich microbiota of the small intestine there was horizontal gene transfer, the conventional pathway that bacteria conjugate, and the capacity to acquire DNA from the foods ingested. They concluded:

   > "*In vitro models do not incorporate the combination of microbial, and host secreted factors such as antimicrobial peptides, reactive oxygen species, immune mediates like IgA, or physiochemical factors such as pH and osmolarity. Thus in vivo models that approximate the human gut are desirable."* [13]

   The simulated gastric fluid tests were not conducted on human gastric fluids but porcine gastric mucosa pepsin, which may have a different outcome to the secretion factors in human gastric fluids.

5. **Pharmaceutical interactions:** The applicant has conducted simulation gastric studies on the stomach fluids of healthy people. FSANZ must call for *in-vitro* and *in-vivo* testing to ascertain the survival of the transgenes in people who are on medications that alter or suppress the stomach digestive fluids, like antacids or pepsin inhibitors.[14] These medications alter the pH or suppress the digestive enzymes therefore the transgenes may not be degraded, and the transgenes will enter the small bowel intact.

   It is of concern that the *nptII* marker gene has been overlooked and is deemed to be of no biological significance when the Study Identification report found that-

   The relative amounts of transcripts originating from the nptII selectable marker gene were high especially in the fruit of QCAV-4 consistent with the expected transgene controlled by the strong, constitutive CaMV35S promoter in banana. (study report QUT2023-5, p 39).

   The antibiotic marker gene has not undergone any testing to show how it might transfer if it survives the stomach fluids *in-vivo* from people on medicines that alter stomach digestive fluids.

6. **Diagnostic Tools**: It is important for medical laboratories to have diagnostic tests available for Health Professionals to be able to check any health problems associated with the consumption of genetically engineered foods. Tests must be required to be developed to be able to address the cause of any illness associated with GM ingestion.

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[13] Ott LC, Mellata M. Models for Gut-Mediated Horizontal Gene Transfer by Bacterial Plasmid Conjugation. *Front Microbiol.* 2022 Jun 30;13:891548. doi: 10.3389/fmicb.2022.891548. PMID: 35847067; PMCID: PMC9280185.

[14] Salisbury BH, Terrell JM. Antacids. [Updated 2023 Aug 8]. In: StatPearls [Internet]. Treasure Island (FL): *StatPearls Publishing;* https://www.ncbi.nlm.nih.gov/books/NBK526049/

7. **Transgene survival in the gut**: We recognize that there are a large range of differences in animal's and human digestive systems. Schubert et al (1997) [15] detected transgenes in the peripheral leukocytes, spleen, and liver via intestinal wall mucosa of test animals. Netherwood et al (2004) found that the intact transgenes survived digestion through the small bowel (duodenum, jejunum, and ileum) in human ileostomy subjects but was not detected in the stool of subjects with intact digestive systems.

   Nawaz M.A. *et al* (2019) research confirmed that there was strong evidence that plant food miRNA could survive digestion and enter the body affecting gene expression.[16]

   It is to be observed that the organs and microbial flora of the small intestine of the intact subjects have never undergone testing for detection so it cannot be dismissed that there was gene persistence in the small bowel nor that in all subjects there was no transfer to the organs. The Netherwood et al (2004) study appears to be the only human study to date on food transgenes and their fate in the digestive system, the small bowel to the end of the ileum.

   These studies show that there is a possibility of transgene survival and travel to the lymphatic and organ systems. As gut dysbiosis leads to inflammatory illnesses of the skin and respiratory systems any factor that could be a trigger needs to be investigated for safety before being discounted.

   Renz H., Brandtzaeg P et al [17](2011) detected that there was a rise in inflammatory disorders especially in the bowel and respiratory systems of neonates. These need to be better understood especially at a time when the microbial flora in the digestive system is developing. Their article concluded -

   > *"The pre-natal and neonatal time sets down the mucosal homeostasis that programme the immune system, this includes the gut and airways for the commensal microorganisms."*

   As bananas are one of the most common foods in an infant's diet, any effects of transgene on gut mucosal development must be properly investigated.

   Ewan and Puzstai [18](1999) found -

   > "Crypt length in the jejunum of rats fed on raw GM potato diets was significantly greater than in those given parent-line or parent-line plus GNA potato diets…With raw potato diets, the intraepithelial lymphocyte counts were again significantly different: 5·3 (2·0) and 9·3 (2·6) in parent and GM potatoes, respectively ($p<0·01$)."

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[15] Schubert R., Renz D., Schmitz B., Doerfler W., 1997 – Foreign DNA (M13) ingested by mice reaches peripheral leukocytes, spleen, and liver via intestinal wall mucosa and can be covalently linked to mouse DNA. *Proceedings of the National Academy of Sciences of the USA* 94, 961-966.

[16] Nawaz, M. A., Mesnage, R., Tsatsakis, A. M., Golokhvast, K. S., Yang, S. H., Antoniou, M. N., & Chung, G. (2019). Addressing concerns over the fate of DNA derived from genetically modified food in the human body: A review. *Food and Chemical Toxicology*, *124*, 423-430. https://doi.org/10.1016/j.fct.2018.12.030

[17] Renz, H., Brandtzaeg, P. & Hornef, M. The impact of perinatal immune development on mucosal homeostasis and chronic inflammation. *Nat Rev Immunol* **12**, 9–23 (2012). https://doi.org/10.1038/nri3112

[18] Ewen SW, Pusztai A. Effect of diets containing genetically modified potatoes expressing Galanthus nivalis lectin on rat small intestine. Lancet. 1999 Oct 16;354(9187):1353-4. doi: 10.1016/S0140-6736(98)05860-7. PMID: 10533866.

As bananas are eaten raw the transgene expression is more likely to persist and not be degraded to any extent by cooking. As there are no feeding studies, it is guess-work to assess whether the transgene expression will have an adverse effect on the stomach epithelium and villi. Until we receive the information on this it is impossible to ensure that the GM banana is safe to eat.

With the new omics tools that provide better detection and accuracy of findings, these omics should be a required safety test to be undertaken. It is especially concerning due to the many transgenic foods that FSANZ has approved for human consumption and if there is a buildup of transgenes that affect the health of people. There are no studies provided to show that genetic persistence of GM genes will not be dangerous to consumers.

FSANZ is treating consumers as guinea pigs without the transgenic constructs having laboratory diagnostic tests available to rule out any harm that the GM banana may cause. Until this is completed there can be no confidence in assumptions from the information regarding consumer safety.

Summary

We request that FSANZ impose a "Stop Clock" on application A1274 until robust scientific safety testing is conducted and provided to FSANZ for assessment. Until then we ask that A1274 is declined.

1. The FSANZ Authority must provide the public with adequate information relating to food safety.
2. The absence of safety information in the A1274 application does not allow the making of an informed submission to FSANZ nor allow informed health professional or consumer choice to protect public health.
3. The information provided does not give confidence that the FSANZ Authority has made an effective, transparent, and accountable regulatory framework assessment.
4. The applicant is required to produce long term scientific evidence on safety of consumption of the GM banana for infants, children, sick, elderly or the public.
5. The GM banana has seven new and unintended proteins that have no scientific information provided on their effects if eaten, and the safety of these need to be scientifically established.
6. Data confirmation on all the medications that will affect the survival of the GM constructs needs to be provided for FSANZ's assessment of safety.
7. Scientific data on the long-term studies on the transgene effects are necessary to see if there is an inflammatory response in small bowel flora, villi, and epithelium.
8. Before entry into the food chain, laboratory diagnostic tests for detection of the transgenes for health professionals must be available.
9. If this product enters the food chain the GM banana must have clear labelling as being GE.

Ngā mihi,

Jon Muller
Secretary GE Free NZ in Food and Environment

Cc: Jon Carapiet, Claire Bleakley, Kara Vandeleur