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Re: A1199 SPS V11 and Z6 GM potato lines

Thank you for the opportunity to make a submission on A1199, the Innate potato lines V11 and Z6.

I ask that FSANZ decline the Application. I submit FSANZ cannot approve the A1199 potato lines in the Application without a serious breach of its duty of care as well as the principles of its own mission statement.

I ask that FSANZ return A1199 to the applicant to provide the data on safety on ingestion, as there is a total absence of information and health data on the long-term effects on ingestion.

I note that FSANZ's legal requirements as stated in its mission statement are:

- To protect, in collaboration with others, the health and safety of people in Australia and New Zealand through the maintenance of a safe food supply.

FSANZ Values are:

- To be impartial, open and accountable;
- To use the best available sciences and evidence to guide decision-making; and
- To seek, respect and be responsive to the issues raised by others.

FSANZ Responsibilities are:

- Provide information to consumers to enable better consumer choice;
- Undertake dietary exposure modeling and scientific risk assessments; and
- Provide risk assessment advice on imported food.

I have read the assessments for this Application and consider that FSANZ has not required the relevant information to stake holders that would fulfill FSANZ mission requirements

Potatoes are a staple diet for a majority of people. Potatoes are eaten by 97% of New Zealanders, and 53% consume potatoes 4 times a week and 21% eat them daily.[1] Yet, FSANZ has not taken this into account when assessing the A1199. There is no scientific data to verify or confirm the FSANZ claim that, "Based on the data provided and other information, food derived from V11 and Z6 is considered to be as safe for human consumption as food derived from conventional potato cultivars."

I outline my concerns below.

1. Compositional Assessment of V11 & Z6 Compared to Snowden

The executive summary of the FSANZ evaluation reads:

"Analysis of the event Z6 has not revealed any biologically relevant differences compared to the conventional variety, except for the intended late blight protection, low free asparagine, low reducing sugars, and low polyphenol oxidase activity".

[1] https://www.5aday.co.nz/facts-and-tips/fruit-vegetable-info/potatoes/

There are concerns over the meaning of "biological relevant differences" as stated in the summary document. This statement is repeated in every application and shows a lack of rigor and understanding of the gene editing and transgene actions. It is misleading and has not been made with the best scientific risk assessment data. In fact FSANZ has not even required information that would fulfil their obligations to public health. It is not backed up by any biological data to confirm safety. The traits for blight protection, low asparagine, low reducing sugars and polyphenol oxidase activity show that these could have serious off/on target effects and mutations that have not been assessed, as seen in the significant differences in 20/22 amino acid profiles. I take that "biologically relevant differences" translates as food safety, there are no feeding studies to back up this statement, and so such assumptions are unable to be made.

2. Changes in the amino acids, free or otherwise, potentially affects the levels of all other compounds present in the GE potatoes. Any changes to amino acid balance may cause alterations to the assimilation of other amino acids.

   The changes in concentrations of glutamine and asparagine in the GE potato lines may be of some concern.

   The amino acid glutamine, for example, plays an important role in maintaining a healthy immune system, digestive tract and muscle cells. Studies have shown glutamine to reduce morbidity and mortality in periods of critical illness. This demonstrates that any changes to endogenous amino acid levels should not be ignored.

   Altered levels of asparagine[2] can result in complications in fetal development, causing brain and neurological problems.

   Published research on GE potatoes has shown unexpected harmful effects on animals fed with these crops. A 1999 study conducted on rats fed with transgenic potatoes found that abnormalities occurred in the gastrointestinal tract (small intestine and caecum) within a short time. The Ewan & Pusztai (1999) study found that the GE potatoes caused gut abnormalities with or without the lectin gene. Lectin is a harmless insecticidal compound produced by a number of plants. The authors concluded that:

   > *"because caecal thickness was similar in rats given boiled parent potatoes in the presence or absence of spiked GNA (a harmless lectin from the plant species Galanthus nivalis), we suggest that the decrease in caecal mucosal thickness seen in rats fed boiled GM-potato diets was the consequence of the transfer of the GNA gene into the potato."*
   >
   > (Ewen and Puzstai)[3]

   Similar results were obtained in feeding experiments using GE potatoes by Fares et al. who found that there were changes to the mucosal lining and other cells of the ileum of mice. They called for comprehensive feeding tests to avoid any potential risks:

   > *"Although transgenic crop plants used in food and feed production carry different beneficial transgenes… before releasing for marketing thorough tests and all possible consequences of these new types of heredity and new genetic structures must be*

[2] Ruzzo,E., Capo-Chichi, J., Ben-Zeev., Chitayat, D., Mao, H., & Pappas,A. et al. (2013). Deficiency Asparagine Synthetase Causes Congenital Microcephaly and a Progressive Form of Encephalopathy. Neuron, 80(2), 429-441.

[3] Ewen, S., & Pusztai, A. (1999). Effect of diets containing genetically modified potatoes expressing *Galanthus nivalis* lectin on rat small intestine. The Lancet, 354(9187), 1353-1354.

evaluated to avoid any potential risks."[4]

A study by Tacket (2007) showed that the consumption of GE potatoes has been observed to cause an increase in immunoglobulin (Ig) levels in human participants.[5]

This is cause for concern, as V11 and Z6 may increase antibody levels result of novel proteins trait expression. Law requires that FSANZ undertake dietary exposure modeling and scientific risk assessments to ensure that consumers are not affected adversely.

3. Whilst toxin and allergen database comparisons have been made there is no assessment of the data showing significant changes to the essential amino acid profiles in the Z6 and V11 potatoes namely alanine, arginine, cystine (including cysteine), glutamine, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tyrosine, and valine. A metabolite from Lysine metabolism is alpha-aminoadipic acid, not mentioned in the applicant data. It has been shown that PPO silencing causes a significant increase in levels of Lysine leading to increased levels of Alpha-aminoadipic acid and a more modest increase in the levels of chaconine-melanyl. Banasr and Duman research found that high levels of alpha-aminoadipic acid (AAA) lead to loss of glial cells in the frontal cortex, in rats, leading to neurological and depressive symptoms.

   "L-AAA enters cells via a Na^+-dependent transporter and blocks essential cellular functions involving glutamate, including protein synthesis and energetic metabolism thereby inducing glial death" (Bansar & Duman 2008).[6]

   Yet, as no studies have been conducted to see if the detrimental effects of this toxic compound alpha-aminoadipic acid (L-AAA) will have risks to consumers.

   These potatoes could also lead to lifethreatening misdiagnosis of illnesses as there is no ability for Health Care professionals to be able to diagnose or have an understanding of the clinical symptoms that might arise from the ingestion of these potatoes.

4. As there have been no studies completed on either animal or human ingestion it is difficult to know what the effects of increased levels of any toxic metabolites will occur when ingested. It is important for FSANZ to require ingestion studies on the target consumer population as the potential for increased harm is very high as potatoes are part of a staple diet and common everyday food for a majority of the population.

Summary

- The FSANZ assessment of A1199 does not protect, the health and safety of people in Australia and New Zealand through the maintenance of a safe food supply.

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[4] Fares, N., & El- Sayed, A. (1998). Fine Structural Changes in the Ileum of Mice Fed on δ- Endotoxin-Treated Potatoes and Transgenic Potatoes. Natural Toxins , 6 (6), 219- 233.
[5] Tacket, C. O. (2007). Plant-Based Vaccines Against Diarrheal Diseases. Transactions of the American Clinical and Climatological Association , 118 , 79–87
[6] Banasr, M., & Duman, R. S. (2008). Glial loss in the prefrontal cortex is sufficient to induce depressive-like behaviors. *Biological psychiatry*, *64*(10), 863–870. https://doi.org/10.1016/j.biopsych.2008.06.008

- The potential toxins and significant changes to the compositional profiles in the V11 and Z6 potato lines have serious health effects for consumers.

- The absence of scientific studies on ingestion does not support the FSANZ conclusion on safety.

- A required by the FSANZ Act FSANZ must undertake dietary exposure modeling and scientific risk assessments to ensure that consumers are not affected adversely.

Recommendation: This application is deficient in any safety for ingestion. FSANZ must return the A1199 to the applicant and require evidence of safety through target studies on the target populations who are going to eat these potatoes.

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