

**Centre for Integrated Research
in Biosafety**

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Submission on the DAR for **APPLICATION A549 FOOD**

Non-technical summary of key points in this submission

According to the Authority's Draft Assessment Report (section 5.4.2.1), "LY038 corn must be shown to be as safe as other varieties of corn currently available if it is to

saying that “[t]he levels of saccharopine found in LY038 corn grain (499 – 818 µg/g dwt, mean 650 µg/g) are substantially higher than those found in broccoli or cauliflower, but similar to the level in button mushrooms” (DAR, p. 48). Button mushrooms are not a conventional food *of the same type as corn*.

- d. High levels of the lysine catabolite ϵ -amino adipic acid, which has a known neurotoxic activity (Rozan et al., 2001), were dismissed as a human food hazard because “[c]ompared to the levels found in other common plant foods, [e.g. lentils, mushrooms, cauliflower, green beans and broccoli] this level is not a cause for concern” (DAR, p. 48). These plants are not a conventional food *of the same type as corn*.

The foods used as a comparison to LY038 differ from corn in the varieties of ways they are prepared, the types of processed foods in which they are found, and in the quantities in which they are consumed. Kiwis and Aussies eat corn chips, but probably do not eat mushroom chips.

2. LY038 has a substantially different potential to create food hazards during cooking

LY038 has high concentrations of compounds that are known to produce food hazards when heated with the sugars found in corn. The modification results in highly elevated concentrations of lysine (total), free lysine (not in protein), saccharopine, ϵ -amino adipic acid, cadaverine and pipercolic acid, all of which may be converted into advanced glycoxidation endproducts (AGEs) during cooking and processing.

AGEs are strongly implicated in causing a variety of dietary-related diseases including diabetes and Alzheimer’s and their sequela (Goldberg et al., 2004, Peppia et al., 2003a, Peppia et al., 2003b, Vlassara et al., 2002), as well as cancer (Heijst et al., 2005). AGE content in food increases with cooking and food processing temperatures and pressures (Elliott, in press, Goldberg et al., 2004).

<u>Compound</u>	<u>Concentration in LY038</u>	<u>Potential Hazard</u>
Lysine	50% higher	AGEs
Free Lysine	50 times higher	AGEs
Saccharopine	110 times higher	AGEs
ϵ -amino adipic acid	at least 10 times higher	AGEs, neurotoxic
Cadaverine	unknown but expected to be higher	AGEs, accentuates reactions to histamine, evidence of further toxic properties
Pipercolic acid	100% higher*	AGEs, chronic hepatic encephalopathy

*Applicant only reports L-pipercolic acid levels. Because D-pipercolic acid can be created from L-pipercolic acid by conversion of either pipercolic acid or lysine to the D-isoform during cooking or in the gut by bacteria, the Authority has likely underestimated pipercolic acid exposure levels derived from high lysine corn or produced by gut bacteria receiving higher levels.

composition of food has been significantly changed, *as is the case with high-lysine corn, feeding studies with suitable livestock species may be useful to confirm the wholesomeness of the food*” [emphasis ours]. Only feeding studies, using whole plant material in food that has been cooked and processed in ways that humans would consume it, can provide the proper basis for a safety review. No such studies were provided for public review in A549, and from the DAR we have no reason to suspect that such studies were ever provided to the Authority. *We are particularly concerned that the Authority sight, or provide the people of Australia and New Zealand with, reliable data demonstrating that processing and cooking temperatures normal to products that could contain this corn are as safe as products that do contain conventional corn.*

3. Hybrids with LY038 could create significant additional food hazards

The Applicant has assured the Authority that corn derived from LY038 and hybrids will have total lysine in the range of 3500 to 5300 ppm, and free lysine in the range of 1000 to 2500 ppm. However, it is known that research hybrids with parents similar or identical to LY038 could have much higher levels of lysine and free lysine. Free lysine and lysine catabolites were higher in crosses with other GM varieties of corn (Monsanto study published under Huang et al.,

Should the Authority recommend a change in the Australia New Zealand Food Code to allow LY038 and its derivatives, it does so in the knowledge that total free lysine and lysine catabolite levels could reach significantly higher levels in LY038 hybrid corn varieties that do not require a safety assessment.

4. Recombinant protein has no history of safe use

The Authority should have undertaken work aimed at establishing that

“Although LY038 will be grown as a high value animal feed, a small percentage of this corn may enter the food supply”	DAR p. 20
“because LY038 corn is not intended for food, human consumption is expected to be extremely low”	DAR p. 23
“Further, it is expected that the amount of LY038 grain entering the food supply will be small”	DAR p. 31
“It is less likely that food industry would pay premium price for high-lysine corn and therefore likely that the levels of high-lysine corn entering the food supply would be small”	DAR p. 72

6. The Authority has accepted a standard of evidence of safety that is below what it could request under international guidelines

International bodies have set higher standards for the description and testing of genetically modified food organisms, such as LY038, that are significantly different from their conventional counterparts. According to CAC, the Authority could ask for:

- a. feeding studies using LY038 grains cooked and processed in ways that humans prepare corn for food to identify food hazards that derive from, for example, unusually high concentrations of AGEs. “The potential effects of food processing, including home preparation, on foods derived from recombinant-DNA plants should also be considered.”
- b. feeding studies using cooked and processed LY038 grains to determine the potential for cDHDPS to form toxic aggregates or sugar-protein derived allergens (another AGE product). “The absolute exposure to the newly expressed protein [cDHDPS] and the effects of relevant food processing will contribute toward an overall conclusion about the potential for human health risk.”
- c. a compositional analysis using a comparator that was “the near isogenic parental line”, and only if this were not feasible should the Authority consider another line that was “as close as possible”. In this particular case, the Authority does not have to accept the use of LYo

7. A recommendation to amend the Food Code does not follow from a case-by-case assessment

The Authority has expressed its commitment to case-by-case assessment. “The safety of GM foods cannot be assessed as a single class because the safety concerns depend on the type of food and the nature of the genetic modification. For this reason, safety assessments are performed

made for a benefit to Australians or New Zealanders to have LY038 in their food. There is considerable evidence of probable harm in comparison to conventional corn.

In our view, the Authority is making a recommendation that is also inconsistent with Codex Alimentarius. At the very least, the Authority should commission the following:

- a compositional study using H99 as the control in five sites over at least two years because H99 is the closest relative of LY038 and is the non-GM parental;
- a compositional study describing the compound

References for the non-technical summary

1. Blickling, S., Beisel, H.-G., Bozic, D., Knablein, J., Laber, B. and Huber, R. (1997). Structure of dihydrodipicolinate synthase of *Nicotiana sylvestris* reveals novel quaternary structure. *J. Mol. Biol.* 274, 608-621.
2. Elliott, R. B. (in press). Diabetes - A man made disease. *Med. Hypoth. In Press, Corrected Proof.*
3. Goldberg, T., Cai, W., Peppas, M., Dardaine, V., Baliga, B. S.,