Centre for Integrated Research in Biosafety

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Dear Madeleine

Thank you for contacting me regarding the approval by Food Standards Australia New Zealand of "Smartstax" for use as human food.

There is no question whatsoever that the parents of Smartstax are products of modern (including gene) biotechnology and thus they and their descendants are subject to regulation in many countries including Australia and New Zealand. This is clearly stated in Standard 1.5.2 which states that any plant that has a transformation event regardless of whether that is through direct transformation or inheritance through subsequent breeding cannot be sold unless it is listed in the Table to the Standard. Smartstax is a direct descendant of multiple parents that are products of gene technology.

Smartstax itself is not listed in the Table. However, as I understand it, FSANZ claims that all parental lines that were products of gene technology are listed in the Table and thus Smartstax does not have to be reviewed separately. I would assume that any and all regulations that pertain to each of its parental lines would also apply to food derived from Smartstax.

Personally, as a genetic scientist with a professional interest in risk assessment and biosafety, I do not agree with the practice of not separately assessing the risks of Smartstax. I believe that when new combinations of GM plants are derived from parental GM lines, they should be subject to a separate and full risk assessment just like the parents. All other products of breeding, i.e. conventional x conventional parent, or conventional x approved GM parent, involve at least one parent that has a history of safe use. The approved GM parent was assessed as safe relative to a conventional parent with a history of safe use. When both parents are products of gene technology, neither has a history of safe use. According to international food safety guidelines, products of gene technology should not be used as comparators to establish the safety of another product of gene technology. When the safety of a cross between two GM lines is assumed by the regulator based on the safety of each GM parent, it is my view that the regulator is using the parents as comparators and that would be a practice that deviates from international food safety guidelines.[1]

[1] Footnote 5 of CAC/GL 44-2003.

I am joined in this feeling by the many expert risk assessors that were convened by mandate of the Parties of the Cartagena Protocol on Biosafety, an international agreement regulating living modified organisms (a subset of all genetically modified organisms). Australia is not a Party to the Protocol, and the use of Smartstax in processed food is generally not under the jurisdiction of the Protocol if the corn is not considered "living". Those issues not withstanding, the Ad Hoc Technical Expert Group was clear in its recommendation that stacked LMOs, specifically of the kind that includes Smartstax, should be subject to a separate risk assessment process from their parents and the reasons for such a separate assessment pertain regardless of whether or not the product is living, and that this assessment should be done because of potential adverse effects to human health:

1. "Although recombination, mutation and rearrangements are not limited to LMOs, the combination of transgenic traits via cross breeding may further change the molecular characteristics of the inserted genes/gene fragments at the insertion site and/or influence the regulation of the expression of the transgenes."

2. "The combination of two or more [transformation events] resulting in a [stacked product of gene technology] may influence the expression level of each of the transgenes and there may be interaction between the genes and the expressed products of the different transgenes. In addition, the stacked transgenes may alter the expression of endogenous genes. Therefore, in addition to information about the characteristics of the parental single-[transformation event] LMOs, specific information on potential for interactions between the altered or inserted genes, stacked proteins or modified traits and endogenous genes and their products in the [stacked product of gene technology] LMO should be considered and assessed. For example, it should be assessed whether the different transgenes affect the same biochemical pathways or physiological processes, or are expected to or may have any combinatorial effects that may result in potential for new or increased adverse effects relative to the parent LMOs."[2]

These potential changes may lead to unintended changes in the final descendant, Smartstax, that could not be detected or anticipated by a review of the parental lines. These changes may have relevance to food safety. For example, according to information available on the Biosafety Clearing House (of the Convention on Biodiversity), some of the various transgene events in Smartstax have a high degree of sequence similarity. This may promote two kinds of unintended changes, recombination between similar DNA sequences and/or gene silencing (of the transgene or other unintended genes).

Codex Alimentarius, an international body formed by the UN Food and Agriculture Organisation and the World Health Organisation, issues guidelines for risk assessment of GMOs, both living and processed. With regard to unintended changes that have the potential to cause adverse effects Codex says[3]:

> "In achieving the objective of conferring a specific target trait (intended effect) to a plant by the insertion of defined DNA sequences, additional traits could, in some cases, be acquired or existing traits could be lost or modified (unintended effects). The potential occurrence of

[2] Final report of the Ad Hoc Technical Expert Group on Risk Assessment and Risk Management under the Cartagena Protocol on Biosafety UNEP/CBD/BS/AHTEG-RA&RM/2/5
[3] Paragraph 14 of CAC/GL 45-2003

> unintended effects is not restricted to the use of *in vitro* nucleic acid techniques. Rather, it is an inherent and general phenomenon that can also occur in conventional breeding. Unintended effects may be deleterious, beneficial, or neutral with respect to the health of the plant or the safety of foods derived from the plant. Unintended effects in recombinant-DNA plants may also arise through the insertion of DNA sequences and/or they may arise through subsequent conventional breeding of the recombinant-DNA plant. *Safety assessment should include data and information to reduce the possibility that a food derived from a recombinant-DNA plant would have an unexpected, adverse effect on human health* [emphasis added]."

The first part of the Codex statement indicates that both breeding and gene technology can produce unintended effects. That is undoubtedly true. However, the second part of the statement makes perfectly clear to me that it is legitimate to describe and assess the unintended effects caused by gene technology and the potential for these changes to cause adverse effects even if those adverse effects are transmitted through breeding.

My recommendation would be that Smartstax should benefit from a risk assessment which, if it provides sufficient evidence of safety, would result in its listing in the Table to Standard 1.5.2. The informal nature of its approval for use in food provides me with no confidence that the regulator has identified and then considered unintended changes that have the potential to cause adverse effects.

With best wishes

Prof. Jack Heinemann
Director

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Jack Heinemann is a professor of genetics and molecular biology in the School of Biological Sciences at the University of Canterbury and is a senior adjunct scientist at GenØk – Centre for Biosafety in Tromsø, Norway. Jack was previously a staff fellow at the US National Institutes of Health Institute of Allergy and Infectious Diseases. He holds a double undergraduate honours degree in biochemistry and molecular biology from the University of Wisconsin – Madison and a PhD in molecular biology from the University of Oregon.

Jack has been a member of the American Society for Microbiology (ASM) his entire professional life and is also a member of the New Zealand Society of Microbiology. He received the ICAAC Young Investigator Award from the ASM in 1993 and was the recipient of the New Zealand Association of Scientists Research Medal in 2002. He was appointed to the UN Roster of Biosafety Experts in 2005. Jack and his research group publishes extensively in the internationally peer-reviewed scientific literature. He recently served the UN FAO as author of their study paper on transgene flow (approved by an intergovernmental panel) and a consortium of international agencies as a lead author and synthesis author on the International Assessment of Agriculture Science and Technology for Development Report (adopted by an intergovernmental panel).

His main research interests are microbial genetics with particular fascination with how genomes emerge from mobile collections of genes, as exhibited in rapidly evolving traits such as antibiotic

resistance, virulence and metabolic pathways. This interest has awakened him to human behaviours that can influence the evolution of such traits and the responsibility for academics to exercise their role as critic and conscience of society on these matters.