Comment for Health Canada's Consultation:
Proposed new guidance for Novel Food Regulations focused on plant breeding

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Key points

1. Canada is a leading global agri-food exporter and requires timely access to the latest technological innovations to remain competitive.
2. Regulatory processes across the economy undercut innovation and industrial competitiveness.
3. Global agri-food R&D is fluid, and inefficient regulatory processes drive investment to countries with more responsive regulatory systems (at no added risk to the food system).
4. Both in Canada and abroad, regulatory uncertainty is leading to suboptimal use of new technologies.
5. Canada's PNT system, used reasonably efficiently for GM foods, is not proportionate to the risks arising from new breeding technologies, such as gene-edited crops.
6. We support Health Canada's move to establish new guidelines to clarify the concept of novelty, to introduce tiers, and to address retransformants. We also suggest this is an opportunity to drive out inefficiencies that delay decisions.

1. The context

Canada is a global leader in many aspects of innovation, but its position is neither dominant, nor secure in a world of fluid global research.

Nationally, in 2020, Canada was ranked in 17th position for innovative inputs (Global Innovation Index 2021), in a group with Ireland, Japan, Luxembourg and Austria. But in terms of innovation outputs, Canada slips to 22nd position, only marginally ahead of Austria and Italy, but

trailing Estonia and Malta. Offsetting this is that Canada is exceptionally well positioned in terms of market sophistication, ranked in 3rd position, trailing only Hong Kong and the USA, while Canada has four of the top 100 innovation clusters globally: Toronto (39th); Montreal (52nd); Vancouver (74th); and Ottawa (81st). Using the World Economic Forum competitiveness index, Canada places 14th in terms of both our competitive economy and innovation capacity (World Economic Forum 2019).

The main weakness in both measures of competitiveness is in the category 'burden of government regulation', where Canada places 38th. While our policy and market systems are able to generate new good ideas, our regulations work to slow the innovation process, creating added cost in the R&D process and leading to fewer commercialized products for Canadian consumers. The gap between innovation capability and commercialization is illustrated by the Global Innovation Index (2018) ranking Canada 61st in terms of innovation efficiency, comparing innovation outputs relative to innovation investments. This positions Canada the second lowest of the G20 countries in terms of innovation efficiency.

This is especially important for our globally competitive agri-food sector. Canada is currently one of the top 5 agri-food exporters globally, and one of a handful of countries that is a net exporter of nutrition products, we are a leading country that will need to sustain and accelerate production of secure global food supplies to match the growing demand.

Canada is not alone facing this challenge. Researchers have found that fewer than 1% of agri-food innovations succeed (Graff et al. 2009) and that the cost and time to get to market are rising and becoming less certain in Canada and abroad (Phillips McDougall 2011). These are general problems compounded by our slow, and at times, overly cautious and costly regulatory processes. This has been exemplified by our approach to genetically modified (GM) crops and foods. Our processes have been slower and more cautious than many of the countries competing for those technologies. While we usually get to a comparable decision, the delays and costs mean that these technologies are developed first in other countries, which lowers the returns and puts our producers behind the competition. We are forced into playing catch-up, in an industry in which we are, and should be, a leading innovator.

Now countries everywhere are forced to decide how to handle the next generation of new plant breeding technologies (NBTs), including gene editing. Some countries, such as the EU, have extended their GM regulations to govern these technologies while others, like the US, have decided that as long as the resulting products do not have any transgenes that they will be regulated through as non-GMO and will have lighter oversight.

The proposed new guidance for novel food regulations issued by Health Canada lays out rules that would put us closer to the US than the EU model, which we believe is justified and appropriate for the nature of the risks and our position in the global food industry.

2. Impacts of regulatory uncertainty

Globally, it is now estimated that approximately US$40 billion is invested per year in plant breeding—roughly 80% by public entities and 20% by agri-food conglomerates (Beintema et al. 2012). Many of these investments can be, and are, shifted from one jurisdiction to another to optimize returns. Evidence indicates that a large driver of innovation investments is the reduction in regulatory uncertainty (Smyth et al. 2014). A two-year regulatory delay for public crop breeding was found to drive returns on the investment negative, while private technology

developers would experience negative investment returns after a six-year delay. Crops have been delayed somewhere between two to six years in our regulatory system.

The impacts of such delays can be seen in the EU. In the mid-1990s the EU accounted for one-third of global agricultural research and development (R&D) investments. Since the EU adopted its precautionary regulatory framework for GM crops, agricultural R&D investments have moved out of the EU to countries with regulatory systems for GM crops that offered more predictable pathways to market (Smyth and Lassoued 2019). Between 1995 and 2015, the EU annually lost 1% of global agricultural R&D investment, a cumulative estimated loss of US$20 billion. By 2015, the EU accounted for 8% of global agricultural R&D investment. The EU has extended this period of uncertainty with the decision to extend GM regulations to most if not all NBTs.

In contrast, Argentina adopted a progressive regulatory system for new gene-edited crop varieties. Research by Whelan et al. (2020) shows that this has led to an increase in R&D and variety commercialization by domestic companies and public research institutions when compared with the development of GM crop varieties. Not only has there been an expansion in the number of stakeholders engaged in gene editing plant research, but the research has additionally expanded to animals and microorganisms.

Our research team has undertaken a multi-year research project on the regulation and management of NBTs. These surveys have focused on regulatory and social barriers pertaining to NBTs (Lassoued et al. 2018, Smyth and Lassoued 2018), perceived benefits (Lassoued et al. 2019a), related potential risks (Lassoued et al. 2019b), the costs of regulating NBT developed crops (Lassoued et al. 2019c) and how policies could change in response to NBTs and their resulting products (Lassoued et al. 2020). Our research on the regulation of NBTs found that if gene-edited varieties were regulated as equivalent to GM crops, the time and cost for variety development rise significantly (Lassoued et al. 2019c). Table 1 highlights that jurisdictions that chose to regulate a gene-edited crop variety within the regulatory framework designed for GM crops, result in a variety requiring an additional 9 years to receive approval, costing an additional US$10 million.

Table 1: Estimated cost and time involved in getting gene-edited crops to market

	Case 1: Not likely regulated				**Case 2: Likely regulated**			
	Cost		**Time**		**Cost**		**Time**	
R&D stages	**US$ M**	**%**	**Years**	**%**	**US$ M**	**%**	**Years**	**%**
Research/Discovery/ Conception	3	29	1.5	30	4	17	2	14
Development/ Implementation	3.5	33	1.5	30	6.5	27	4	29
Regulatory activity/ Authorization	2	19	1	20	9	37	5	36
Launch/1st commercial sale	2	19	1	20	5	20	3	21
Total	**10.5**	100	**5**	100	**24.5**	100	**14**	100

Source: Lassoued et al. 2019c.

In 2018, we undertook a survey of Canadian plant breeders to gain insights into how the Canadian PNT regulations were impacting current R&D initiatives. It is estimated there are somewhere between 400 and 450 plant breeders in Canada. Our survey had nearly 100

responses, a rate of 22% based on the number of invitations that were sent (Smyth et al. 2020). One positive result we found was that plant breeders strongly support the science-based regulatory system, with 32% of respondents expressing the belief this provides a competitive advantage for Canada. This is compared to 41% that indicated the regulatory system is the same as other jurisdictions and 21% who felt it is not an advantage.

While support for science-based regulations is strong, the survey results indicated that plant breeders strongly believed the existing PNT regulations act as a barrier to innovation. The strongest indication of this was that 77% of respondents indicated that Canada's PNT regulatory framework needs to be updated to reflect current levels of knowledge and the advancements in plant breeding technologies. We explored the impact of regulatory uncertainty on research design and learned that 22% of plant breeders (14% public and 8% private) had at least one project proposal turned down due to uncertainty about whether the resulting variety might trigger PNT oversight. The key concerns seemed to be the anticipated regulatory costs (29%) and possible adverse public acceptance (25%).

Table 2: PNT regulation impacts on research proposals (N=93)

At least one of my research proposals has been turned down…	**Public *sector***				**Private *sector***			
	Agree	Disagree	Don't know	No response	Agree	Disagree	Don't know	No response
…due to uncertainty about the product's potential novelty during the development and evaluation phase.	14%	24%	12%	9%	8%	10%	15%	10%
…due to uncertainty about the regulatory costs in commercialization and marketing.	18%	22%	12%	6%	11%	8%	14%	10%
… due to uncertainty about the public acceptance of a GM product.	19%	19%	11%	9%	6%	11%	14%	11%

Source: Smyth et al. 2020.

We then asked breeders what they did in response to the uncertainty about how their breeding products might be regulated. About 34% of breeders reported that they ended research when they determined that the resulting products would trigger PNT rules. We also found that 19% altered their research plans to ensure the variety was not deemed to be a PNT, that 18% experienced a delay once PNT status was applied; and that 26% believed PNT regulations discouraged investment. This regulatory lag serves as a disadvantage for the Canadian agricultural sector, especially with the need for greater innovation as climate change impacts Canadian production.

Table 3: Impacts on extend research due to Canadian regulatory barriers (N=93)

	Public sector			Private sector		
	Agree	Disagree	No response	Agree	Disagree	No response
I decided not to undertake a research proposal or develop an innovation because I self-determined the innovation would be considered novel.	22%	31%	5%	12%	17%	13%
I altered my/our breeding objective to avoid having a product reviewed as novel in Canada.	15%	32%	11%	4%	20%	17%
I had a product in a pathway to commercialization in Canada, but I did not proceed as I found out the product would be considered novel.	3%	38%	17%	3%	22%	17%
I conducted extra research to provide evidence to Canadian regulators that our innovation should not be considered novel.	8%	31%	19%	13%	15%	14%
I experienced delays introducing a new variety in Canada compared to other markets due to the novelty trigger.	9%	27%	23%	9%	16%	17%

Source: Smyth et al. (2020).

Of particular concern is that the negative impacts of PNT regulations affect public sector plant breeders more than private sector breeders. Tables 2 and 3 illustrate the variation in impact between public and private breeders. In the responses to most questions, public breeders signaled PNT regulations pose a barrier. Most public sector plant breeders are unable to develop PNT varieties due to the inability to have adequate development infrastructure (phytotrons, greenhouses and land for field trials), due to space, time and cost.

While it was not possible to quantify the fiscal costs of these stranded research projects, based on the amount of plant science funding in Canada, a conservative estimate would place this cost in the millions of dollars annually.

Our 2018 survey then asked breeders whether they planned to use gene editing tools, such as CRISPR, within the next 3 years. About two-thirds indicated they planned to do so (Gleim et al. 2020). With agricultural R&D investments fleeing Europe, Canada's strong history of R&D and science-based regulations, provides an attractive market. Securing this work in Canada will require the products of NBTs are not regulated using the existing PNT regulatory framework used for GM varieties.

3. Possible improvements in regulatory treatment of NBTs

As part of the survey work that was undertaken in 2018, follow-up interviews were done with 35 plant breeders, to gain further insights into how the PNT regulatory framework definition of novelty acted as a barrier to their research. Most breeders say the PNT system does a decent job of assessing GMOs, and that it is preferred over the systems operating in most other

countries. In addition, virtually all the interviewees were highly complementary of their personal interactions with Health Canada and CFIA regulators. They congratulated them on their help in clarifying and addressing specific concerns about their dockets.

Our judgment is that the proposed changes by Health Canada address the leading concerns raised by breeders, but that that there are some other ways the system might be improved:

a. **Application of novelty**: One observation shared by numerous interviewees was that the novelty trigger was used inconsistently. Breeders indicated that a targeted breeding change that delivers a new level of a nutrient that is within the range of commercial products in the market, should not be a novel product. But under current rules, the nutritional change is regulated because it was achieved through genetic modification. This is not the intent of the PNT regulations, which are not supposed to be regulating process, but rather supposed to be regulating the novelty of the resulting products. Some respondents indicated that novelty is at times assessed differently by regulators within Health Canada and the CFIA, and between the seed assessment and feed assessment divisions. Breeders expressed support for greater clarity of what is novel. It was suggested that the concept of novelty could be redefined by expanding the sphere of what would be considered 'non-material changes'. This could also involve redefining the notion of 'change' to more specifically target 'a material change'. A material change is most importantly a nutritional, compositional or functional change or change in allergenicity that affects the biology of the organism or the performance of the final food or feed product.

b. **Tiered approach to novelty**: Respondents were also of the view that if Canada is going to have a novelty trigger, there should be a tiered approach, based on the process used and the risk associated with that process and the resulting product. The risk associated with the product should then be determined by a variety of factors. Most important, familiarity with the trait and product needs to be the same across all regulatory agencies.

c. **Retransformants:** Breeders concurred with the proposed guidelines for retransformants. They asserted that if gene editing is applied to varieties and traits that have already been regulated and approved as a PNT, then any subsequent gene editing that simply works with the same variety and trait, should be not be regulated as a PNT, but rather should be reviewed as a conventional crop variety. In effect, breeders are pushing for de facto deregistration of well characterized novel traits where extensive evidence of their safe production and use exists. This policy should be common across both Health Canada and the CFIA. The proposed changes and tiering regarding retransformants aligns with the comments provided by breeders.

d. **Timeliness of reviews:** Some breeders suggested this review might be an opportunity speed up reviews. Canada tends to be slower to do its reviews than competing countries. Time is not a proxy for the quality or rigour of the review. Many of the steps can and should be expedited. Some asserted that as much as 3-4 years could be removed from the breeding process if the regulatory system was streamlined.

At the end of the day, clarity about the use of the novelty system for gene editing was the key concern.

4. Summary

The level of regulatory uncertainty is directly connected to innovative R&D investments. Research has shown that in Canada the level of uncertainty regarding what is novel has been significant enough to reduce investment. While there is no definitive quantification of the scale of reduced investments, it can conservatively be estimated these would be in the millions of dollars per year.

Given that countries that Canada competes with for international commodity sales, such as Argentina, Australia, Brazil and the US, have already indicated that most gene editing technologies will not require additional regulatory oversight, it is essential that Canada have a similar regulatory framework to ensure Canadian producers remain competitive. If it takes longer for a gene-edited variety to be approved in Canada than in other countries, Canada's competitiveness will decline, which can signal investors to seek alternative markets for new crop variety development investments.

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