



# Ag-Biotech: It's Not Just What's for Dinner Anymore, but the Future Contents of our Medicine Cabinets

by Jennifer Medlock and Edna Einsiedel

Forget about farm-to-fork when it comes to genetically modified (GM) crops. Think farm-to-pharmacy, or farm-to-factory. Produced through plant molecular farming (PMF), this new set of transgenic crops is being grown not for food, but to produce medicines and industrial products. For example, potatoes have been modified to produce a vaccine against the Norwalk virus, research that is currently in human clinical trials to determine efficacy (Tacket et al., 2000). On the industrial side, corn plants have been modified to produce trypsin, an enzyme used in the manufacturing process of insulin and vaccines, an application already on the market in the United States under the name TrypZean™ ([www.prodigene.com](http://www.prodigene.com)).

GM food production and PMF differ in one very significant way. In GM food, the product is the plant (to be consumed by humans or animals). In PMF, the product is the medical or industrial compound (the plant is not destined for the food chain). For GM food, the idea is to make crops easier to grow, for example through insect or herbicide resistance, or to enhance a crop's nutritional value, as in vitamin A enriched "Golden Rice." In PMF, the crop is used as a production vehicle or factory (Ma, Drake, & Christou, 2003). It is the ultimate product, the medical or industrial compound that is of interest, not the plant itself, which is considered a waste product after the compound is removed. PMF products can be grown in both food crops and nonfood crops (corn and tobacco are the most common platforms).

By uniting agricultural biotechnologies with medicinal and industrial processes, PMF has already aroused controversy. Those with a stake in this technology include conventional farmers, PMF companies, food processors and exporters, academic scientists, patient groups, policymakers, as well as members of the general public. And just as

the number of stakeholders is large, so is the disparity in opinion. Prodigene, an early industry player in PMF, has this outlook for the technology on its website ([www.prodigene.com](http://www.prodigene.com)):

Imagine a day when taking children in for vaccinations will not involve a single tear being shed. Imagine that, in the place of a shot, the doctor gives your child a small bag of edible treats. This bag of treats will not be any ordinary snack—it will be an edible vaccine grown in corn and then made into an appealing snack.

Meanwhile, from the NGO perspective, a spokesperson from Friends of the Earth forecasts a very different future, saying that with "just one mistake by a biotech company, we'll be eating other people's prescription drugs in our cornflakes" ([www.foe.org](http://www.foe.org)).

The diversity of stakeholders demonstrates the challenges for policy development around this emerging technology. In Canada, no commercial applications of PMF have yet been approved. Policy is still in the early stages of development, which provides a useful entry point for stakeholder and public assessment of the technology to be incorporated into policy development. Two studies conducted by the Genome Prairie GE<sup>3</sup>LS (Genomics, Ethics, Environment, Economics, Law, and Society) research team, one on focus group discussions with the general public (Einsiedel & Medlock, 2005) and one on stakeholder interviews (Mistry, Einsiedel, Medlock, & Perraton, 2005), will be discussed in this article (along with their consequent policy implications), but first we will provide context on the regulatory situation in Canada.

While the Canadian government conducts its policy review (involving a number of departments including

Agriculture and Agri-Food Canada, Health Canada, and Industry Canada), the crops involved in PMF are regulated under the authority of the Canadian Food Inspection Agency (CFIA). Plants used for plant molecular farming are labelled as 'plants with novel traits' or PNTs, and broadly PNTs are defined as plants that have had a specific trait added to them through genetic engineering or other methods. PNTs can be developed using conventional breeding or through transgenic techniques. It is the resulting product that defines it as a PNT, and not the process of development.

The following appears on the CFIA's molecular farming web page: "**All PNTs in Canada are subject to the same strict science-based regulations.** However, since PNTs for molecular farming may present greater potential for environmental or human health risks, the Government of Canada may put even more stringent restrictions on the use of these novel plants than for other PNTs" (bold in original) (CFIA, 2005).

In the meantime, the CFIA has indicated that it is currently involved in a broad policy review of plant molecular farming. Until this consultation and analysis are complete, applications for confined research field trials for PNTs intended for plant molecular farming will be addressed on a **case-by-case** basis. The amendment lists a number of "interim recommendations" for PMF developers, the major one suggesting that use of major food or feed crop species for PMF is **not** recommended. Other recommendations include choosing host species that are "as amenable to confinement as possible" and encouragement to consider fibre crops, small-acreage specialty

food or feed crops, or new crops as production platforms.

As policy development moves beyond the bounds of the CFIA's science-based safety assessments, assessments by stakeholder groups and the public are integral to developing socially sustainable policy.

### Public Views

Focus groups were conducted in four cities across Canada (Toronto, Halifax, Vancouver and Montreal) (see Einsiedel & Medlock, 2005). Because of the unfamiliarity of PMF, participants received a 10-page briefing document in advance of the session that outlined the technology, its potential applications, and how it might be treated by the Canadian regulatory system. They were asked to read the document and bring with them three key questions and/or concerns with regards to the development of the technology.

Not surprisingly, awareness of PMF before being contacted for the study was very low, with only two of the 48 participants ever having heard of the technology, but none knowing of any specific applications. In contrast, participants revealed a high level of awareness of GM food and evaluated PMF within that reference, calling PMF a "cousin" of GM food.

Focus group participants discussed their concerns around four main themes: potential contamination of food crops; safety issues; appropriate regulation; and, long-term impacts.

The potential contamination of food crops was the most dominant issue raised. The main concern was that the 'modified' product would get into the food chain through direct cross-pollination, animals, or wind. As well, concern was raised that humans might contaminate food

crops either by mistake (accidentally moving plant material from a greenhouse to a field) or by malicious intent (for example, through bioterrorism).

On the issues of safety and regulation, while participants were willing to accept a certain level of uncertainty with PMF, they were also concerned about the abilities of regulators to adequately manage the technology because resources to do so were seen to be inadequate. Concern was also expressed about the adequacy of standards to monitor longer-term impacts.

Concern over long-term side effects for human health and the environment was raised by those respondents with the highest level of trepidation about PMF. They wondered about whether enough time had been or would be allowed to effectively study these effects. Concern about proper balancing of commercial versus public interests was also expressed.

Ultimately, acceptance or rejection of PMF was dependent on the perceived "purpose" of the application. Whether a particular application had a "useful" or worthwhile purpose had a substantial influence on participants' perceptions. This purpose dimension was explored in more detail in the next stage of the session, where reactions to five specific applications of PMF (that are currently in or close to commercial production) were elicited from participants. The different applications were chosen strategically to incorporate different streams of PMF work; for example, are reactions different for products made in food crops versus nonfood crops? Or for industrial compounds versus medical compounds? After discussing the applications, participants rated each of them on a four-point "acceptability spec-

trum” (Fully Acceptable, More Acceptable, Less Acceptable, and Unacceptable). The five applications that were used in the discussion are:

1. *Trypsin in corn*: Trypsin, a protein derived from corn, is used in a variety of commercial applications including the processing of some biopharmaceuticals;
2. *Interleukin in tobacco*: Interleukin, a potential treatment for Crohn’s disease, has been tested in field trials in Canada using tobacco as a platform;
3. *Norwalk virus vaccine in potatoes*: Norwalk virus capsid protein (NVCP), used as a test antigen, was able to trigger immune responses in healthy volunteers who ingested transgenic potatoes;
4. *Gastric lipase in corn*: Gastric lipase, used to treat cystic fibrosis, has been produced using corn as a production vehicle and is currently advancing through clinical trials; and
5. *Bioplastics in corn*: Still in the experimental stage, biodegradable molecules are derived from corn to produce bioplastics.

When judging the various applications, people assigned a higher level of acceptability if the purpose was seen to provide a significant benefit to human health (Norwalk virus vaccine in potatoes and gastric lipase in corn applications). If the purpose was seen to provide economic benefits, but not significant new benefits to human health (i.e., a new way of producing an existing treatment as in the Interleukin example), then the application was rated less highly. Finally, if the benefits were perceived to be entirely economic (i.e., lower cost industrial products), the value assigned was even lower.

In general, while medical applications were consistently preferred over industrial applications, members of the public appear to judge PMF on a

case-by-case basis, assigning different levels of acceptability depending on context of the application. Distinctions were made also between producing compounds in food crops and nonfood crops, with food crops assigned a lower level of acceptability overall, though a significant level of risk was perceived in all applications.

### PMF Stakeholder Views

To complement the public focus group work, the GE<sup>3</sup>LS team conducted a set of surveys with other groups with an interest in PMF (farmers, academic and government scientists, and representatives from the food industry, PMF industry, patient groups and social/environmental groups) (see Mistry et al., 2005). The specific objectives of this work were: 1) To obtain a general assessment of plant molecular farming in terms of risk, benefits, and challenges; 2) To examine perceived risk, benefit, and acceptability of four PMF applications currently in development; and 3) To elicit views on how PMF should be regulated.

An interim report has been completed on this work. The applications tested were similar to those in the public focus groups (Interleukin in tomato, bioplastics in plants, trypsin in corn, and vaccine in tomato). An interim report has been completed on this work. In the study, there was conditional acceptance of PMF across all sectors, except for the social and environment groups who did not support going ahead with any applications.

A major caveat for support of PMF was the lack of a regulatory framework. This gap was mentioned by all sectors, but for different reasons. From the industry perspective, not having a regulatory framework was seen as a threat to investment in

a burgeoning field. For social and environmental groups, if PMF were to proceed, a strong regulatory framework needed to be in place to control it. However, like members of the public, this group had doubts about the capacity of the government to adequately monitor the industry.

Also echoing the public groups, both food and nonfood crops were considered acceptable for PMF development (again across all sectors except for the social/environmental groups who did not support any applications), but there was a strong preference for nonfood crops as there was a sense of inevitability that contamination would occur at some point in the future (all sectors raised the risk of contamination to the food supply). A representative from the PMF industry preferred nonfood crops due to a perceptions issue, saying that “if it happens once, the industry is dead.”

Another finding common across all sectors was support for regulation on a case-by-case basis. There is a recognition that the vast variety of protein products that can be produced from PMF should not be dealt with using blanket regulation. How an application should be regulated was dependent on a combination of the product (toxicity/stability, location of accumulation), production platform (i.e., food/non-food) and scale (how many acres?). Preferences for containment/confinement strategies were also application-specific, but generally followed a ‘better safe-than-sorry’ attitude where more containment is better.

Where the stakeholder groups diverged from the public sample was in the comparison between medical and industrial applications. The opinions of stakeholder interviewees were more nuanced, and there was cautious support of both as respon-

dents could see benefits and concerns raised in both cases. For example, concern was raised in the medical arena regarding whether there would be pharmacologically active drugs in the plants or whether they would be benign until purified and then combined with other elements. In the industrial arena, concerns were voiced about the potentially large acreages to be used to be profitable.

The issue of public involvement and public awareness was raised many times in the stakeholder interviews. Those in the PMF industry fear the “drugs in my cornflakes” view will take hold. An agriculture industry representative suggested that “the biggest risk (of PMF) is public perception of risk.” Overall, there was general belief that public views on this technology will ultimately determine its future.

However, how to respond to the public perception issue differed among sectors, and fell into general spheres of thinking. Those in academia and the PMF and food industries felt that the public just needs objective information — educate them and they will understand and they will accept. Those in the government, social/environmental, and agricultural industry sector felt that yes, members of the public should receive information, but should also be engaged in discussion and their

voices need to be heard in shaping policy.

### **Lessons from These Early Conversations**

The importance of early understanding of public and stakeholder views is evident. This has been a major lesson from the experiences of the GM food debates. Public concerns revolve not just over why products are being made from a technology, but how they are produced and introduced into the marketplace. This involves the accompanying regulatory framework that can encourage confidence in their introduction and use.

Members of the public and stakeholders are clearly making trade-offs in their initial assessments. For members of the public, these include considerations of long-term impacts, not just to human health, but also to the environment. Expectations that regulatory systems similarly weigh different considerations, from economic and commercial gain to public interest considerations, are also evident. Members of the public, stakeholders, and regulators clearly have much to learn from each other.

### **For More Information**

Canadian Food Inspection Agency (CFIA). (2005). Plant Molecular Farming. Available online: [\[biotech/reg/pmfamve.shtml\]\(http://biotech/reg/pmfamve.shtml\) \(Accessed November 8, 2005\).](http://www.inspection.gc.ca/english/sci/</a></p></div><div data-bbox=)

Einsiedel, E.F., & Medlock, J.E. (2005). A public consultation on plant made pharmaceuticals.

*AgBioForum*, 8(1).

Ma, J.K., Drake, P.M., & Christou, P. (October 2003). The production of recombinant pharmaceutical proteins in plants. *Nature Reviews Genetics*, 4, 794-805.

Mistry, J., Einsiedel, E., Medlock, J., & Perraton, K. (July 2005).

*Stakeholder and public views on plant molecular farming*. Paper presented to the International Consortium of Agricultural Biotechnology Research (ICABR), Ravello, Italy.

Tacket, C.O., Mason, H.S., Losonsky, G., Estes, M.K., Levine, M.M., & Arntzen, C.J. (July 2000). Human immune responses to a novel norwalk virus vaccine delivered in transgenic potatoes. *Journal of Infectious Diseases*, 182(1),302-305. Epub 2000 Jul 06.

*Jennifer Medlock (jemedloc@ucalgary.ca) is a PhD student and Edna Einsiedel is Professor, respectively, Faculty of Communication and Culture, University of Calgary, Alberta, Canada. Support for this study from Genome Canada and Agriculture and Agri-Food Canada is gratefully acknowledged.*