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A Public Consultation on Plant Molecular Farming

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Plant molecular farming (PMF) is another phase in the ongoing research and development of transgenic plants, offering possibilities of producing therapeutic and industrial proteins. However, this technology poses important social and policy challenges. A public consultation was held in four regions in Canada using a modified focus group approach. Respondents received a background document on the technology prior to discussions. Five specific applications were discussed to investigate views on food versus nonfood crops, medical versus industrial applications, and containment approaches. Public assessments were on a case-by-case basis but were also clearly based on balancing benefits and risks as well as considerations of environmental impacts and regulatory oversight.

Key words: molecular farming, public consultation, plant-made pharmaceuticals, policy and regulation, risk assessment, technology assessment.

Introduction

Plant molecular farming (PMF) is another phase in the ongoing research and development of transgenic plants, offering possibilities of producing therapeutic and industrial proteins. Molecular farming involves the use of genetically enhanced plants to produce pharmaceuticals and industrial products. The first pharmaceutical protein made in plants—in this case, the tobacco plant—was human growth hormone (Barta et al., 1986). Since 1986, when this experiment was publicized, other proteins have been produced, from experimental vaccines to antibodies to industrial proteins (Breithaupt, 2004; Fischer, Stoger, Schillberg, Christou, & Twyman, 2004; Ma, Drake, & Christou, 2003).

At the same time, plant molecular farming raises social, environmental, and regulatory challenges that need to be addressed when considering how these products might be successfully and responsibly commercialized. Recent changes to regulatory processes have taken place in response to concerns about the efficacy of seed production and commodity handling systems (Office of Science and Technology Policy, 2002), environmental safety issues, and contamination of the food supply (United States Department of Agriculture, 2004). In the face of these concerns, calls have been made for ongoing risk assessment (Peterson & Arntzen, 2004), regulatory assessment and reform, greater transparency, and enhanced public and stakeholder participation, with some arguing that "it is social support for the technology and trust in regulatory institutions that matter most" (Stewart & Knight, 2005, p. 521).

We began a major initiative to investigate various commercialization aspects of PMF in late 2003. The purpose of this larger PMF project is to investigate the policy and regulatory developments in this area and to explore stakeholder views and perceptions.[1] Although calls have been made to assess public views on this issue, there is very little published research in this area. One report in the United States (Nevitt et al., 2003) focused only on the use of tobacco as the PMF model crop, with data obtained via interviews by phone, face-to-face, email, and small-group discussion with a range of stakeholders (tobacco producers, policymakers, nongovernmental organizations [NGOs], and agricultural biotechnology company representatives). Although most were supportive of this technology (with the exception of those from the NGO sector), concerns were expressed about environmental impacts and regulatory capacity. The Canadian Biotechnology Secretariat (an arm of the Canadian federal government) addressed PMF in its semiannual survey work on biotechnology with two questions investigating yes/no support for two PMF applications: the production of interleukin, an enzyme for health treatments (80% supported this application), and the production of biodegradable plastics (78% supported this application). No other study has

1. *This larger study is being carried out by the genomics, ethics, economic, environmental, legal, and social studies project supported by the Genome Canada program. This public consultation is part of this larger study and was supported by funds from Agriculture and Agri-Food Canada and Genome Canada.*

been published on public and stakeholder perceptions of PMF. By uniting medical, industrial, and agricultural practices, PMF becomes a more complex technology in its social aspects. Although publics have generally been more supportive of "red" biotechnologies (i.e., medical applications) than "green" biotechnologies (i.e., agricultural applications; Gaskell et al., 2001; Nielsen et al., 2002), this study investigates how hybrid red-green technologies will be perceived and allows for elucidation from participants on the reasons for their choices (beyond the scope of the quantitative survey referenced above).

In 2004, we carried out a series of modified focus groups in four regions in Canada, designed as an early-stage public consultation with lay Canadians on PMF. There are many approaches to public consultation, from town hall meetings to deliberative forums (Rowe & Frewer, 2005). In comparison to quantitative surveys, focus groups are not designed to provide a representative picture of the general population. Instead, focus groups allow more extended discussions and uncover more detailed and nuanced explanations for people's positions. Discussions were structured around awareness of PMF, identification of key issues from the perspective of the layperson, reactions to specific PMF applications (i.e., using food vs. nonfood crops and producing medical vs. industrial products), and perceptions of various containment scenarios. These consultations were intended to understand early-stage consumer perceptions and policy preferences that could contribute to ongoing policy development as well as provide a base for a larger-scale consumer study to be carried out in 2005. Initiated at the behest of the Agriculture ministry, this study was designed and carried out independently.

Methodology

Approach

The consultation process was designed by the authors, and focus group field work was carried out by a commercial firm. Participants were recruited randomly from the general population. Final selection was based on fulfilling a set of demographic criteria so that the panel would be balanced in terms of age, gender, education, and occupation. Because this technological application was quite new, the traditional focus group approach was modified in two ways: (a) by providing background information to participants so the discussion to be undertaken would be based on some understanding of the basics of PMF (discussed in detail below) and (b) by providing more time for deliberation (each group was 2.5 hours in length). The consultation process was conducted by a research company in Vancouver, Toronto, Halifax, and Montreal between April 12–21, 2004.[2] Regional representation is a critical dimension in Canada; these highly urban sites are typically selected for this type of research.

Briefing Document

Each respondent was sent a discussion paper in advance of the meeting. The paper was a 10-page document developed by the authors that provided an explanation of the technology, some typical applications, a regulatory overview, and a discussion of the benefits and risks involved with the technology. To ensure scientific and factual validity, the document was given to a PMF expert with extensive experience in the field. The briefing document was then tested on volunteers from various education levels (from less than high school education to university graduates) to ensure clarity, understanding, and balance. The finished product was a detailed overview of the technology in a question-and-answer format (e.g., "What are PMFs?" "Why use plants?"). The objective of this discussion paper was to provide background information on the topic of PMFs to encourage a more informed discussion of the issues raised by the technology.

Procedure

During the recruitment process, volunteer participants were invited to read the discussion paper and to bring with them to the focus groups three key issue areas or concerns they had about PMF, and which they felt needed to be addressed before decisions could be made about applications and research in this area.

The facilitator first explored levels of awareness among the participants prior to their having read the briefing document. This was followed by a discussion of each participant's key issue areas—the questions and concerns that participants considered important to address in the development of the technology. A series of five PMF applications were then discussed in turn, focusing on different products (industrial and pharma-

2. *There were 25 males and 23 females in the final sample; 14 respondents were under 35 years of age, 20 were between 35 and 54 years old, and 14 were over 54 years old. The education distribution showed that 13 had a high school degree or less, 17 had a college degree or some university, and 18 were university graduates.*

ceutical) and different host crops (food and nonfood). Finally, responses to different containment strategies were explored as well as perceptions of regulatory capacities.

PMF Applications

We selected applications of plant molecular farming that are currently in (or within five years of) commercial production to be used in the focus group discussion. Each application was described by the moderator, and the participants were then invited to express their views on each one. The applications are described below.

- The enzyme trypsin, traditionally isolated from cow or pig pancreatic sources and used in large volumes in the detergent and leather industries as a catalyst, has been produced in genetically modified corn. It is thought to be the first large-scale protein product from transgenic plant technology (Horn, Woodard, & Howard, 2004).
- Tobacco plants have been genetically modified to produce interleukin, an enzyme used in treatments for diseases such as Crohn's disease. This application has been tested in field trials in Canada (Canadian Food Inspection Agency [CFIA], 2005).
- Transgenic potatoes have produced a vaccine against the Norwalk virus. Norwalk virus capsid protein (NVCP) was used as a test antigen and was able to trigger immune responses in healthy volunteers who ingested the transgenic potatoes (Tacket et al., 2000).
- Gastric lipase, an enzyme used to treat cystic fibrosis, has been produced using corn. This application is currently advancing through clinical trials (Horn et al., 2004; Ma et al., 2003).
- Corn plants have been modified to produce bioplastics. Still in the experimental stage, biodegradable molecules have been derived from modified corn to produce bioplastics (CFIA, 2005).

The discussion around these cases acted as a catalyst for deconstructing the factors relating to how judgments are made about specific applications (which have real-world implications) and to move beyond the initial conversation about the topic in general (which tended to be more of a theoretical discussion).

Acceptability Spectrum

After discussing the applications, participants rated each on a four-point acceptability spectrum: *fully acceptable*, *more acceptable*, *less acceptable*, and *unacceptable*. In addition, participants were asked to comment on each of their ratings in writing. They were also asked to give a rating of and comments on the technology of PMF as a whole.

Results

Awareness and Initial Reactions

Only two of the 48 participants had heard of the concept of PMF before being contacted for the focus group; none were aware of any specific applications of PMF. First impressions of the technology were mixed but leaned towards the positive. As a concept, PMF is a field of research that was described by most as being fascinating, promising, and exciting but also potentially very risky. It was initially viewed as positive because of the perceived potential for developing new treatments for diseases and/or cheaper and simpler drugs. Most of the participants viewed plant-made pharmaceuticals as a "cousin" of genetically modified (GM) foods under the general umbrella of biotechnology, and, like its relative, viewed this application with some trepidation.

Key Issue Areas

Respondents tabled a wide range of key issues and questions they considered were important for decision makers to take into account, many of which revolved around the following themes:

The potential for cross-pollination and contamination of food crops. This was the most dominant issue that was raised. Many participants (particularly women) felt that contamination of food crops could happen relatively easily. These concerns were fueled by several underlying factors: First, participants thought that the modified product would get into the food chain through direct cross-pollination, or through wind, animals, insects, or birds. Many made direct reference to the *Monsanto v. Schmeiser* case as evidence of this possibility.[3] Some expressed skepticism about the idea that the PMF versions of plants and crops or other agricultural versions of plants would be separated entirely from each other. Second, participants were concerned that humans might contaminate food crops either by error (for exam-

3. A Canadian farmer, Percy Schmeiser, claimed that his field had been accidentally contaminated by Roundup Ready canola from his neighbors' fields. The Canadian Supreme Court found Schmeiser in violation of Monsanto's intellectual property. Monsanto Canada Inc. v. Schmeiser. Supreme Court of Canada. Judgment of 21 May 2004. SCC 34.

ple, by accidentally taking plant material from a greenhouse and dropping it onto a field) or malicious intent (for example, bioterrorism, or modifying a food crop to produce a toxic substance and introducing that plant into the food supply). Third, participants thought that the methods of disposal of waste material would not eliminate sufficiently any chance of modified plants entering the ecosystem.

Common to these factors was the idea of some of these technologies "running wild" and taking over food crops. A few mentioned evidence of this type of event occurring with foreign species (zebra mussels and Asian ladybugs were mentioned).

Issues of safety, regulations, and policing. Participants had concerns about the ability of regulators to adequately monitor these technologies. There was a fairly widespread perception that regulators were hampered by a lack of resources or lack of sufficient expertise to appropriately oversee the research to ensure that all safety measures were being fully met. Participants also cited concerns about the scope of the existing rules and regulations; some suggested that there might not be appropriate guidelines and standards in place. However, the concern about adequate policing capacity tended to be greater than the concern about insufficient standards/regulations. For most, the issue was not about achieving zero risk, but rather minimizing risk, ensuring transparency about regulatory approaches, and factoring in uncertainties.

The potential long-term side effects, specifically impacts on human health or the environment. These considerations were of significant concern, particularly among those who expressed the strongest trepidation about the technology at the outset of the discussion. Participants suggested that these technologies might reveal impacts that will not be detectable for years after they are introduced.

The interests of those growing, farming, or researching these applications not being consonant with the public interest. There were a number of questions raised about the role of commercial interests in developing these applications and the potential of the profit motive to ultimately supersede the public interest in terms of safety. For example, participants felt that even if the rules and regulations were stringent, growers/farmers would not necessarily follow these rules carefully. Similarly, the discussion showed little faith in companies having concerns for the public interest as they develop these technologies.

Table 1. Acceptability of PMF applications.

Application	Fully acceptable	More acceptable	Less acceptable	Unacceptable
Interleukin in tobacco	8	25	13	2
Edible vaccines (Norwalk in potatoes)	10	25	11	2
Gastric lipase in corn for cystic fibrosis	6	26	15	1
Trypsin grown in corn for industrial uses	1	14	21	11
Bioplastics grown from corn	6	21	14	6
Overall impression of PMF	3	29	10	6

Acceptability of PMF Applications

Overall, participants tended toward the middle two points on the spectrum—either *more acceptable* or *less acceptable* than at the poles of outright acceptability or unacceptability (see Table 1 for results of all applications). The focus groups revealed that most people held a mix of views on these applications and tended to lean toward acceptability or unacceptability on a case-by-case basis, depending on the purpose of the application and how they weighed the benefits and risks involved. Below is a summary of the reactions to each of the applications, followed by a broader discussion of how participants made their judgements across applications.

Application 1: Interleukin in Tobacco

Some respondents suggested that this was an interesting and potentially beneficial application, especially if interleukin were a relatively scarce enzyme that might enable more people to have access to treatment. The idea of using tobacco as the medium to produce interleukin (instead of corn) also gave some people greater comfort about reducing potential food-crop contamination risks and finding a socially beneficial use for tobacco. However, uncertainty was also expressed about production costs and potential risks, particularly possible contamination between tobacco and food crops

Application 2: Bioplastics in Corn

This application also generated a fairly clear split in opinion. Most people found the principle behind this application to be compelling and appealing, primarily

because the idea that synthetic plastics could be reduced or eliminated was seen to be an important step in reducing waste and pressure on landfill sites. However, there were clearly and widely articulated concerns about the contamination risks of growing these PMF crops in corn plants. Participants were very concerned about the impact on health or the environment if this type of application made its way into the food system. Ultimately the environmental goals were not universally lauded, as several people in each group suggested that taking a measure like this is like a band-aid and that encouraging people to reduce waste was a more appropriate step. As a result, for the majority, the benefits side of the equation was not compelling enough to overcome concerns about the risks.

Application 3: Edible Vaccines

This was the most widely acceptable of the applications tested, for a number of important reasons on both the benefit and risk sides of the ledger. First, most saw it as an effective way to administer a vaccine, and participants imagined that there would be demonstrable benefits to being able to deliver vaccines in this form to developing countries in particular. In that sense, the application was seen as providing a new benefit to health treatment, over and above cost savings. However, cost savings was also seen to be of particular benefit in this case in terms of being able to distribute treatments in developing countries. The other compelling element of this application was that it would or could be utilized as a preventative measure as well as a treatment. The risks of contamination were viewed to be significant on this application, but they tended not to weigh as heavily in assessments. The idea that in some instances the product might be produced in powder form was seen as posing less risk of contamination than utilizing the product in its natural form. Thus, despite the fact that this application involved a food crop, respondents appeared to weigh the benefits from this application as being greater than the risks.

Application 4: Trypsin in Corn

Most participants did not view this as a beneficial application overall. Rather, they tended to view the benefits as accruing mainly to companies in the form of higher profits. Two respondents suggested that by introducing lower cost inputs, consumers would benefit by lower prices, but this was not a widely held view. Many others did not believe that money would be saved because of all the safety measures that would be required to use the PMF version of trypsin. Even if there were cost savings, there was skepticism that consumers would actually benefit and that whatever cost savings might be achieved would not be worth the risks. A number of people suggested that because there were conventional alternatives, the benefits of going forward with this application were not as great, especially when the risks were taken into account. Overall, there were few reasons that were seen to warrant engaging in research for this type of PMF technology.

Application 5: Gastric Lipase in Corn

This application generated mixed reviews. The drivers of acceptability tended to revolve around a couple of factors. First among these was the potential to treat the 15% of patients who do not have effective treatment options—here, the principle of the application being "new" was compelling to many people. The secondary driver of acceptability was the idea that this treatment will be safer for patients—participants suggested that more proof that treatment is truly safer would be required; if so, this would contribute to acceptability. The factors contributing to unacceptability again revolved around the idea of contamination of food crops and concerns that the benefits would primarily be about cost savings for companies that may not be passed on to consumers.

Determining Acceptability

The purpose (or benefit) of the application was the most important factor in determining whether an application was acceptable. From their comments, it was clear that participants tended to assign widely differing values to the benefit factor, depending on the application involved. Health and medical applications were consistently seen as being more acceptable than industrial applications. This was arguably one of the most important areas of consensus about PMF. Furthermore, if the purpose was seen to provide a significant potential benefit to human health or the environment that was greater than existing products or applications, people tended to be more supportive of it, assigning a higher value to the application. In addition, if an application was viewed as providing economic benefits (e.g., lower cost) but not significant new benefits to human health (i.e., not a new treatment, but a better way of producing an existing treatment), the weight that people assigned to the perceived benefit was lower. If the benefits were entirely economic (e.g., lower cost and an industrial product), the benefit value people assigned to it was quite low.

In the discussions, the risk side of the equation tended to be relatively constant (and relatively high) for all applications, whereas the benefit side tended to vary significantly. In cases where the benefits were seen to be substantial, they could overcome concerns about risk, but if the benefits were viewed as minimal, the overall assessment tended to move towards the less acceptable side of the spectrum. Our overall assessment is that people tend to engage in a risk-benefit analysis about each application, assigning weight to a number of factors associated with both benefits and risks.

In virtually every case, acceptability is predicated on the idea that there are stringent approval processes and long-term measures in place to ensure safety. This is essentially a quid pro quo for willingness to go forward with any PMF application.

The perceived level of risk was the first factor that people employed when considering acceptability. Risk of contamination and risk of impacts on humans, the environment, or wildlife were the major elements that were considered. The results showed that people tended to assign a level of risk to PMF applications which were dependent on a number of factors.

If the PMF application is grown in a food crop, it was likely to be assigned a higher level of risk than if grown in a nonfood crop. However, for some, the risks with nonfood crops would not necessarily be mitigated, because pollen dispersal could occur with insects or birds. When benefits were seen to be much greater (i.e., benefiting large numbers who had little or no alternatives), this modified the risk-benefit equation, as was the case with edible vaccines.

If the PMF application is grown in an outdoor context, it was likely to be assigned a higher level of risk than if it is grown in an indoor context. There was general agreement that growing these products in enclosed settings (such as greenhouses) would reduce the risks to a point where most applications would be acceptable (again assuming that appropriate regulatory provisions were in place).

If the PMF application retains properties of being able to seed or flower, it was likely to be assigned a higher level of risk than if it is unable to seed/flower. Flowing from the discussion of risks associated with food and nonfood crops, people in a number of the groups discussed the prospect of developing nonflowering versions of the plants that would be used for PMF. The idea of producing nonflowering plants as PMF-designated plants was appealing as a counter to contamination of food crops.

Conclusions and Policy Implications

This modified consultation yielded a number of important findings. Participants weighed in thoughtfully on plant molecular farming and discussed policy options; they also clearly articulated the nature of their expectations and concerns.

Although initial awareness of the technology was very low prior to this consultation, background information provided a sufficient basis for informed discussion. The key concern most often identified by participants was the potential for contamination of food crops (whether the product was grown in a food or a nonfood crop). Other concerns included issues of safety, regulation, adequate monitoring, and the possible long-term human health and environmental side effects. Distinctions in risk determinations were made in the following areas:

- PMF products grown in food crops were seen as riskier than nonfood crops;
- PMF products grown in the outdoors were perceived as riskier than those grown indoors; and
- if the plant host is able to go to seed or flower, it was seen as riskier.

These concerns weighed heavily in evaluating the various PMF applications. However, it was the nature of the perceived benefits that ultimately determined the level of acceptability of each application: Are the benefits sufficient to warrant taking a substantial risk? The purpose of the product being made via PMF was a major factor in answering this question. This *purpose test* essentially responded to two questions: What is the application for? Who is it going to benefit? Medical applications were preferred over industrial applications, and within the industrial realm, producing environmentally friendly products was preferred over the ability to produce products at a lower cost. Although food crops were essentially rejected as a production mechanism, edible vaccines proved to be an exception in this case, with the benefit for developing countries seen as a positive outweighing the perceived risk.

What these results suggest is that the conditions under which PMF is carried out are important to public assessments of the technology, but in addition, the nature of regulatory oversight is equally critical. Such conditions could warrant greater confidence in the technology. Ultimately, the purpose test was really a surrogate for assessing the benefits of an application, which proved to be the most important arbiter of how respondents viewed the specific applications that were discussed in the group. Indeed, in several cases, this test

trumped the various other risk considerations that were tabled in the discussion.

For policy makers, these findings suggest that attention to a number of areas is critical. First, the issues around impacts to human health and to the environment, biosafety, and risk assessment and risk management processes are clearly important for publics, in much the same way they remain important challenges for those involved in research and production of plant-made pharmaceuticals (Twyman, Stoger, Schillberg, Christou, & Fischer, 2003). The issue of potential contamination, from the perspective of publics, also raises the importance of comprehensive liability frameworks as a priority (Agriculture and Environment Biotechnology Commission, 2003). Some countries with biosafety frameworks have made clear that the entity marketing the GMO is solely liable for all consequences.

Second, the importance of access to information and transparency in the regulatory process are going to be priorities for publics. Our study demonstrated that publics who were consulted in this initial stage had a very good grasp of important elements about this technology to make considered judgments—judgments which were sufficiently nuanced when participants were provided with a reasonable information base.

Finally, early considerations of full life-cycle dimensions of the technology will be critical. These include upstream considerations of choices of plant vehicles, downstream elements including cost-benefit assessments, full risk-assessment plans that include disposal at the production end, and post-market monitoring of impacts of plant-derived pharmaceutical and industrial products.

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