

9th ICABR International Conference on:

Agricultural Biotechnology: Ten Years Later

Ravello (Italy), July 6 to July 10, 2005

Plant Molecular Farming: Early Stakeholder Assessments

Edna Einsiedel, Jyoti Mistry, Jennifer Medlock, Kris Perraton

University of Calgary

Calgary Alberta T2N 1N4

Canada

ABSTRACT: Public consultations and stakeholder assessments were carried out in Canada to explore perceptions and assessments of different policy options on Plant Molecular Farming. The findings of this study suggest it is imperative to have a regulatory framework in place that instills confidence; one that ensures that the regulating body has the knowledge and capacity to handle this new technology. Secondly, procedures assuring that human safety and the environment are protected need to be in place and communicated to the public. The importance of communication was emphasized, as PMF should be regulated with input from all stakeholder groups and greater communication is required for better understanding of the technology on the part of publics and other stakeholders.

KEY WORDS: plant, molecular, farming, pharmaceutical, stakeholder, public, perceptions, policy, regulatory, risk, benefit

TABLE OF CONTENTS

INTRODUCTION	3
METHODOLOGY	4
<i>Stakeholder Assessment</i>	<i>5</i>
<i>Public Consultation</i>	<i>6</i>
RESULTS	8
STAKEHOLDER ASSESSMENT	8
General Assessment	8
PMF Applications in Development	9
PUBLIC CONSULTATION	12
General Assessment	12
PMF Applications in Development	12
DISCUSSION	17
Food vs Non-food	17
Medical vs Industrial Products.....	17
Containment/Confinement Strategies	18
Regulation	18
Other critical issues.....	19
Perception of risk	20
Limitations to Study.....	20
CONCLUSION	21
REFERENCES.....	22
Appendix 1: Value chain of PMF Stakeholders.....	24

INTRODUCTION

Plant molecular farming (PMF) involves the use of genetically enhanced plants to produce pharmaceuticals and industrial products. The first pharmaceutical protein made in plants was human growth hormone, made in the tobacco plant (Barta et.al., 1986). Since 1986 when this experiment was publicized, other proteins have been produced, from experimental vaccines to antibodies to industrial proteins (Ma, Drake and Christou, 2003).

Plant molecular farming is an emerging technology that promises many benefits, but also carries a number of risks. A primary rationale for pursuing this technology is to provide a cost-effective alternative method for producing pharmaceutical drugs and vaccines, compared to conventional mammalian cell culture systems. The production of industrial products through plant molecular farming has also been touted as potentially cheaper and more environmentally sustainable than conventional production methods. At the same time, this innovation raises social, environmental, and regulatory challenges which need to be addressed when considering how these products might be commercialized successfully and responsibly.

Recent changes to regulatory processes have taken place in response to concerns about the efficacy of seed production and commodity handling systems (OSTP, 2002), environmental safety issues, and concerns about contamination of the food supply (USDA, 2004). The Prodigene[∇] incident in the United States is frequently cited as an example of a breach of confinement (APHIS, 2002). In the face of these concerns, calls have been made for on-going 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 and Knight, 2004).

A major initiative to investigate various commercialization aspects of PMF commenced 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

[∇] The ProdiGene incident involved the inadequate clearing of a field of transgenic corn engineered to produce a swine vaccine. Soybeans were planted in that field the next spring, but volunteer transgenic corn also germinated, leading to commingling of transgenic corn and soybeans.

perceptions. While calls have been made to assess public views on this issue, there is very little published research in this area. One report in the US (Nevitt, et.al., 2003) focused on the use of tobacco as the PMF model crop, with data obtained via interviews by phone, face-to-face, e-mail and small-group discussion with a range of stakeholders (from tobacco producers to policymakers, non-government organizations, and agricultural biotechnology company representatives). While most, with the exception of those from the NGO sector, were supportive of this technology, concerns were expressed about environmental impacts and regulatory capacity.

In 2004, we initiated a study where the general public and stakeholder groups were solicited at this early stage of technology development to explore perceptions and assessments of different policy options on plant molecular farming in Canada. For the first part of the assessment, a series of consultations were held with members of the general public. These consultations were held in four regions in Canada, using modified focus groups and a scenario assessment approach. This was followed by a series of key informant interviews with representatives from the PMF industry, agriculture industry, food industry, scientists, regulators and NGOs. The respondents were individuals from across Canada and the interview also utilized a scenario assessment approach. The specific objectives of these two phases were:

- 1) To obtain a general assessment and awareness of plant molecular farming in terms of risks, benefits, key issues and challenges
- 2) To examine perceived risk, benefit and acceptability of PMF applications currently in development
- 3) To elicit views on how plant molecular farming should be regulated and to determine preferences among regulatory options.

METHODOLOGY

The first part of the PMF project involved a series of public consultations via modified focus groups. The second part of the project consisted of a stakeholder assessment obtained through the use of a survey administered through one-on-one interviews. For the purposes of this report the stakeholder assessment will be described first to provide a broad perspective of the perceptions across the various groups, followed by the data obtained from the public consultations. The methodologies are described below.

Stakeholder Assessment

Approach: A qualitative survey was developed and data was solicited from the various stakeholder groups having involvement or interest in plant molecular farming. Prior to initiating this study, ethics approval was obtained from The University of Calgary Conjoint Faculties Research Ethics Board.

Participants: To identify and select stakeholders groups, a value chain was created (Appendix 1). This series of value-generating activities relevant to PMF was used as a criterion to identify the appropriate groups. The aim was to represent various viewpoints along the production chain and to represent the distinct sectors. The stakeholder groups used in the survey included: 1) PMF industry, 2) Agriculture industry, 3) Food industry, 4) Academia (consisting of university scientists conducting PMF research and ecologists), 5) NGOs (including social and environmental groups), and 6) Government. The participant list from a recent PMF Workshop [The Bio-Based Molecular Production Systems Workshop (Ottawa, April 2004)] was used as a starting point to develop a contact list. Internet searches and referrals were also approaches used to identify appropriate participants. The questionnaire was limited to Canadian stakeholders. A total of 39 interviews were completed across the six stakeholder groups. The number of individuals interviewed from each sector include: PMF Industry (10), Academia (7), Social/Environmental (8), Government (6), Agriculture (5), and Food industry (3). PMF industry refers to companies engaged in commercialization ventures on PMF; “agriculture” includes representatives from this sector who might be involved in PMF production (e.g., farming organizations); the food industry consisted primarily of representatives from the food retail sector.

Instrument: The interview protocol consisted of 27 questions and was designed in an open-ended format to allow respondents to express their views more fully. Prior to initiating the survey, the survey was given to a few individuals with extensive knowledge of PMF to obtain their feedback with respect to the content and accuracy of the questions. Questions were developed based on the three objectives of the survey, including a general assessment of PMF, an analysis of four current PMF

projects and PMF regulation. The four PMF projects in development were Interleukin-10 in Tobacco, Vaccine in Tomato, Trypsin in Corn and Bioplastics in Plants. They were specifically selected to include a balance of food vs non-food crops, medical vs industrial products and different confinement/containment strategies. The resulting risk/benefit assessment of each scenario was captured on an acceptability spectrum ranging from “acceptable”, “acceptable with certain conditions”, “unacceptable at the present time” and “not acceptable under any circumstances”. Questions on PMF regulation helped to identify the role of the government and a discussion on specific challenges. The survey concluded with an opportunity to provide an overall assessment on PMF.

Procedure: Individuals representative of their sector were invited to participate in the survey through e-mail. Methods for answering the survey included, phone interviews, in-person interviews, or written surveys. The questionnaire was sent to the participants in advance to review the questions, prior to the interview. Interviews were recorded with the participant’s permission for transcription purposes. Respondents were also informed that their participation is entirely voluntary and they have the right to withdraw at any time. Should they do so, their data will not be utilized. The identity of the respondents will remain confidential and the results will be described in the aggregate. The interviews generally took 45 min-1 hour to complete.

Assessment: Comparisons of perceived risk and benefit will be assessed between food vs non-food crops, medical vs industrial uses and containment strategies across the various sectors. Policy recommendations and an overall assessment of the technology will be derived.

Public Consultation

Approach: The consultation process was designed by the authors and the discussions were implemented and facilitated by a research company in Vancouver, Toronto, Halifax, and Montreal. Since this technological application was quite new, the consultation employed a focus group approach that was modified in two ways: by providing background information to participants so the discussion to be undertaken

would be based on some understanding of the basics of PMF; and by providing more time for deliberation.

Participants: In each city, one discussion group took place, involving between 12-15 respondents. A total of 48 respondents participated, chosen at random from their respective communities. The participants in each of the four cities were recruited randomly from the general population and were broadly representative of the population by age, gender, and education level. The 48 participants included 23 Females, 25 Males; 14 were under 35 years old, 20 were between 35-54, and 14 were 55 or older. Thirteen had a high school education or less, 17 had a college degree or some university, and 18 were university graduates.

Briefing Document: Each respondent was sent a 10-page discussion paper in advance of the meeting, developed by the authors, which provided a brief overview of plant molecular farming, an explanation of the technology, some typical applications, a regulatory overview, and a discussion of the benefits and risks involved with the technology. The briefing document, in a question-and-answer format was geared to a layperson unfamiliar with the technology. The document was given to a PMF expert with extensive experience in the field to ensure scientific and factual validity but was also tested on volunteers from various education levels (from less than high school education to university graduates) to ensure clarity and understanding as well as balance. All facets of the PMF technology were included in the briefing document, both positive and negative.

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 questions they have about PMF, and which they feel need to be addressed before decisions can be made about applications and research in this area. Each of the discussion groups was about 2.5 hours long.

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 issues participants considered important. A series of PMF applications were then discussed in turn, focusing on different products (industrial and pharmaceutical) and different

host crops (food and non-food). Responses to different containment strategies were also explored. This was followed by a brief discussion on perceptions of regulatory capacities.

The discussion ended by providing participants with a sheet of paper which included the list of applications discussed and a rating scale labeled as an “acceptability spectrum”. The scale was on a continuum that ranged from “fully acceptable” to “acceptable with conditions”, “unacceptable unless conditions were met” to “totally unacceptable”. On the one-page rating sheets, participants were also asked to provide brief explanations for their ratings.

RESULTS

STAKEHOLDER ASSESSMENT

General Assessment

As expected, respondents from the PMF industry, academia and government indicated that they were very familiar and very involved with plant molecular farming. On the other hand, the social/environmental groups, the agricultural sector and food industry groups rated their familiarity and involvement with PMF as ranging from more familiar to less familiar and more involved to uninvolved. Generally, across all sectors except the social/environmental sector, participants were in favour of PMF and thought that it should be pursued or pursued with strict restrictions. However, participants representing social/environmental groups and an agriculture representative thought that it should not be pursued at the current time or that it should never be pursued. A social group representative felt the technology itself was great, however gave an overall negative assessment as a result of the corporate control over the technology. Most respondents indicated that the main benefits of PMF were its economic growth potential and the promised production of affordable drugs in sufficient quantities. The social/environmental sector indicated economic benefits likely to corporate players and worried that consumers may not see the cost-savings. When asked about potential risks of PMF, most respondents from all sectors except the social/environmental sector felt that the risks of PMF could be managed. In contrast, social/environmental groups along with an agriculture representative felt the risks of PMF are much too great and certainly outweigh any benefits. Major risks

identified include potential contamination of the food supply and environmental risks such as gene flow. However, across all the groups, the most significant challenges for PMF included public acceptance of the technology and education of the public.

PMF Applications in Development

Participants were asked about the risks, benefits and acceptability of four current applications of PMF. The use of individual scenarios provided insight on how judgments are made about specific applications rather than about the topic in general. The scenarios represented various combinations of products, plant platforms and containment/confinement[♦] strategies resulting in varying degrees of risk. Generally, across all four applications, the majority of respondents considered the applications acceptable with certain conditions (Table 1). The social/environmental group was the only group where most respondents found all PMF applications unacceptable.

TABLE 1: Stakeholder Assessment of the Acceptability of PMF Applications Currently in Development

APPLICATION	ACCEPTABLE	ACCEPTABLE WITH CERTAIN CONDITIONS	UNACCEPTABLE AT THE PRESENT TIME	NOT ACCEPTABLE UNDER ANY CIRCUMSTANCES
Interleukin-10 in tobacco	7	22	5	4
Cholera vaccine in tomato	8	20	7	3
Trypsin grown in corn for industrial uses	5	17	10	5
Bioplastics grown in plants	6	18	9	4
TOTAL	26	77	31	16

Scenario 1: Interleukin-10 in Tobacco

The genetic modification of tobacco plants to produce interleukin, an enzyme used in treatments for diseases such as Crohn’s disease in the field.

[♦] Containment refers to physical isolation of a plant with novel traits (PNT) from its environment (i.e secure greenhouses)
 Confinement refers to biological and genetic mechanisms that isolate a PNT from its environment (i.e isolation distances, male sterility) [CFIA, 2002]

Generally, the majority of respondents considered this application acceptable with certain conditions. Acceptability was based on the fact that the benefits outweighed the risks. It was seen as an economical alternative in the production of a high value product with health benefits. The risks were thought to be highly manageable through the use of a non-food crop and employment of the described confinement strategies. Respondents who found it unacceptable included representatives from the social/environmental groups, organic farming, and some from the PMF industry and academia. There was an aversion to producing pharmacologically active proteins in open field production, due to the possibility of unintended effects. Other reasons for not pursuing this application include: tobacco being a poor plant platform due to the low accumulation of protein, protein produced in leaf tissue is unstable and must be processed immediately and extensive purification costs. Other considerations included, determining the supply and demand of IL-10, the bioactivity of IL-10, the requirement for proper confinement and the potential for IL-10 to get into cigarettes.

Scenario 2: Cholera Vaccine in Tomato

The genetic modification of tomatoes to produce a vaccine against cholera that is grown in a greenhouse.

The majority of respondents rated this application acceptable with certain conditions. The low risk/high benefit ratio was supported by the fact that a large number of doses could be produced by few plants. In this way, a more economical production of vaccines was possible, supply would not be an issue and the risks could be managed due to the small crop size. The use of freeze-dried plant tissue for standardizing the dose and potential use in developing countries were also strongly favoured. This application was largely considered acceptable, given the condition that the use of an established food crop must be highly contained, to prevent contamination of the food supply. In contrast, social/environmental groups found this application unacceptable because the environmental risks are too great. Use of a food crop and the risk of exposure to wildlife were main concerns. The ingestion of a vaccine was thought to have major problems due to differences in physiology, genetics and diet. On a more global scale, the question was raised as to whether vaccinations a genuine solution to the problem in developing countries? Respondents indicated money would be better spent improving their standard of living. Other considerations included the burden of proof has yet to be established, improper administration could result in immune

suppression, the lack of clarity on greenhouse regulations and the lack of commercial interest were potential problems.

Scenario 3: Trypsin in Corn for Industrial Uses

An enzyme called trypsin, traditionally isolated from bovine sources is used in large quantities in the leather tanning and detergent industries is being produced in genetically modified corn.

Similarly, the majority of respondents found this application acceptable with certain conditions. This application was favoured since it could provide a better product in larger quantities at reduced cost. By increasing the value of a commodity crop, it was seen as an opportunity for farmers. Many respondents from the PMF sector were fairly confident that trypsin would not be harmful to humans since it is an animal protein we have been exposed to before through our diets. Again, appropriate confinement measures would have to be utilized to reduce risk of exposure to the environment and the need for secure segregation and handling strategies to ensure contamination of the food supply does not occur. Respondents from social/environmental groups, as well as some respondents from the PMF sector and academia found this application unacceptable. It was deemed unacceptable to be producing an industrial product on large acreages in corn, which is a major commodity food crop, especially in the corn belt. The risk of environmental exposure is too great. Contamination of the food supply was thought to be inevitable, especially considering the human factor. Furthermore, the Prodigene incident was used as an example of previous contamination. Other considerations include determining the current supply and demand of trypsin, the toxicity of trypsin, growing corn of different colour or outside typical growing season, and having appropriate IP systems.

Scenario 4: Bioplastics in Plants

The genetic modification of non-food crops (i.e switchgrass) to produce bioplastics which are biodegradable.

The majority of respondents across all stakeholder groups rated this application acceptable with certain conditions. Reasons for acceptability included the production of a biodegradable plastic from a renewable resource would be beneficial to the environment and it's a diversion away from petroleum sources. The use of a non-

food crop means there is less of a chance for outcrossing with crop species. Furthermore, it was observed as an opportunity for value-added agriculture. However, conditions for acceptance included demonstrating safety of the plant platform and product, as well as ensuring adequate confinement and containment measures. Individuals who found this application unacceptable were from the social/environmental, PMF industry and agriculture sectors. Some of the reasons for unacceptability included, if such a plant were grown on large acreages, the risk of exposure to the environment would increase and it would be difficult to prevent gene flow. Furthermore, the long term effects are unknown and potentially dangerous and we do not know enough about plant biology to know the impacts of this application. There was greater hesitation in accepting this application across all sectors since individuals were less familiar about the production of plastic and the use of switchgrass as a plant platform.

PUBLIC CONSULTATION

General Assessment

Of the 48 participants, only two had heard of plant molecular farming. After reading the briefing document, most of the participants viewed plant-made pharmaceuticals as a “cousin” of GM foods, falling under the general umbrella of biotechnology. First impressions of the technology were mixed, but leaning towards the positive. As a concept, PMF was described by most as being fascinating, promising, and exciting but also potentially very risky. The main reason why it was initially viewed as positive involved the potential for developing new treatments for diseases, and/or cheaper and simpler treatment of diseases.

PMF Applications in Development

The five different applications were chosen strategically to incorporate a number of different combinations of both medical/industrial use and food/non-food use. One of each medical and industrial product was combined with both a food crop and a non-food crop. This reads out as: (1) Medical product in a Food crop; (2) Medical product in a Non-Food crop; (3) Industrial product in a Food crop; and (4) Industrial product in a Non-Food crop.

TABLE 2: Public Assessment of Acceptability of PMF Applications Currently in Development

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

It was found that 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 (Table 2). Second, the group discussions showed that most people indeed hold a mix of views on these applications, and tend to lean toward acceptability or unacceptability on a case-by-case basis, depending on the application, and the benefits and risks involved. As a result, not all applications received the same level of acceptability – indeed there is some fairly wide variation in acceptability across PMF applications. Third, 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. Furthermore, 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/wildlife were the major elements that were considered. The results showed that people tend to assign a level of risk to PMF applications which are dependent on a number of factors (i.e use of a food crop, grown in greenhouse or field, ability to seed/flower). Finally, the purpose (or benefit) of the application was the most important factor in determining whether it was acceptable or not. From their comments, it was clear that people tended to assign differing values to the benefit factor, depending on the application involved.

Our overall assessment is that members of the general public tend to engage in a risk-benefit analysis about each application, assigning weight to a number of factors associated with both benefits and risks. Indeed, the analysis can be broken down into something of a mathematical equation, which has a benefits side and a risk side to the ledger, with weights assigned to variables within each category.

Application 1: Interleukin in Tobacco

The genetic modification of tobacco plants to produce interleukin, an enzyme used in treatments for diseases such as Crohn's disease.

This application created something of a divide among respondents. At first blush, several respondents suggested that this was an interesting and potentially beneficial application, especially if interleukin were a relatively scarce enzyme and this might enable more people to have access to treatment but uncertainty was also expressed about such access and production costs. In addition, some indicated that the idea of using tobacco for a socially useful purpose would be a good idea for consumers and tobacco farmers. 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.

Others were concerned about risks. There were a sizeable number of respondents that suggested that cross-contamination into the food supply was possible – indeed in some groups suggested that it was equally likely that contamination could occur between tobacco and food crops as it might be between two food products (conventional and GM corn)

Overall, because the purpose of the application was perceived to revolve around cost savings rather than other more compelling health benefits, there was a rough split between the “more acceptable” and “less acceptable” sides of the spectrum.

Application 2: Bioplastics in Corn

The genetic modification of corn plants to produce bioplastics, which are biodegradable plastic products that come from certain proteins in those plants.

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

Edible vaccines, for example the genetic modification of potatoes to produce a vaccine against the Norwalk virus.

This was the most widely acceptable of the applications tested, for a number of important reasons on both the benefit and risk side 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 greater than the risks.

Application 4: Trypsin in Corn

An enzyme called Trypsin, traditionally isolated from cow or pig pancreatic sources and used in large volumes in the detergent and leather industries as a catalyst, produced in genetically modified 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. While two respondents suggested that by introducing lower cost inputs that consumers would benefit by lower prices, 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 taking the risks.

A number of people suggested that since 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

The development of an enzyme used in the treatment of cystic fibrosis, called gastric lipase.

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 could potentially be safer for patients – people suggested that more proof that it is truly safer would be required, but if so, then 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 will primarily be about cost savings for companies which may not be passed on to consumers.

DISCUSSION

Food vs Non-food: Among the stakeholders who favoured PMF, there was a general sense that both food and non-food crops would be acceptable. This was particularly true among the scientists working in this area, since they were more familiar with the technical aspects of the risks entailed in PMF. However, across the larger group, if given the choice there was a general aversion to using food crops, since there was a greater perceived risk of contamination of the food supply in using these crops. Some individuals from the PMF industry indicated they would not use a food plant platform since they were not willing to take that risk. Interim regulations on the CFIA website recommend not using food crops (CFIA, 2003) Given the more limited information available on the biology of non-food crops as a production platform, some individuals from the stakeholder group recommended greater funding for research using non-food plant platforms. If food crops are to be used, some respondents felt they should be under strict containment, such as fully-contained greenhouses or underground mines. Suggestions were also made for the potential use of food crop varieties that we do not consume (i.e white dwarf varieties of tomato). Lastly, to keep this topic in perspective, another respondent from the PMF industry remarked that some potatoes are known to be poisonous and kiwi is highly allergenic, therefore suggesting that certain products we assume to be safe also carry risks.

In general, the level of risk assigned to growing PMF applications was believed by a majority of participants from the general public to be higher in the case of food crops (like corn) than non-food crops (like cotton). However, for some, the risks with non-food crops would not necessarily be mitigated since pollen dispersal could occur with insects or birds. In this case, 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.

Medical vs Industrial Products: Across the stakeholder groups that favoured PMF, there appeared to be little distinction made between medical products or industrial products in plants. A respondent from the agriculture sector and another from

government, perceived industrial products to be less harmful than medical products, if it involved production of benign precursor molecules, and not the compound itself which may be toxic. However, the idea of a pharmacologically active protein in plants was considered much more dangerous. Many respondents indicated that industrials, if shown to be safe, may be grown in the field in non-food crops. However, medical products should be physically contained for safety reasons and for reasons of public perceptions. Also, when discussing industrial products, the subject of appropriate land use was mentioned, suggesting the benefits of such applications would have to be justified. Among our public groups, health/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. The contrast was that if industrial applications were being judged and if the benefit was primarily to industry, the level of acceptability would be significantly lower.

Containment/Confinement Strategies: Throughout the entire survey, and across all stakeholder groups, the most significant concern of all was establishing appropriate containment and confinement strategies. Most agreed that these strategies should be determined on a case-by-case basis, since the risks vary with each application. Respondents were quick to cite prior breaches of containment in the United States such as the Starlink and Prodigene incidents, which have scarred the industry. These incidents are used as examples especially from individuals from the social/environmental sector, to show that regardless of what precautions have been taken, mistakes can still occur. Finally, there was general agreement from members of the public that growing these products in enclosed settings like a greenhouse would reduce the risks to a point where most applications would be acceptable, assuming appropriate regulatory provisions were in place. While about half of respondents overall remained uncomfortable about PMF in fields, the other half were more comfortable with this method if the plant were modified not to flower. However, some questioned the efficacy of plant sterility methods

Regulation: The development of a regulatory framework for PMF was stated as one of the biggest challenges facing PMF technology by the majority of respondents. One of the reasons is that PMF is an inter-disciplinary field that will require collaborations between different governmental agencies. In this context, plant molecular farming is

uncharted territory. The lack of a regulatory framework makes it a real challenge for the PMF industry to gain investor confidence. Similarly not having regulations in place, makes social/environmental groups uneasy since it appears to them, that the government does not have the capacity to appropriately regulate this field. Overall, individuals from each sector recommended that PMF should be regulated with input from all stakeholder groups to ensure the creation of balanced regulations. From the focus groups, perceptions and priorities in terms of policy and regulation were remarkably consistent across the groups. A regulatory overview was provided in the briefing document, indicating to participants that regulatory processes for this technology were still under development. Most did not possess a very high level of confidence in regulators to ensure that these applications and methods are safe before they are introduced. Most felt that government regulators would have to add resources and qualified staff in order to manage the technology.

Other critical issues

Although, potential contamination of the food supply, environmental issues, containment/confinement strategies, and regulations have been described as significant issues by the various stakeholder groups and the public, other issues have also been raised. From the stakeholder study, specific critical issues raised include public perception and education, the need to further the science of PMF, a determination of cost-effectiveness, the lack of financing and liability issues. These either individually or in combination could significantly impact the progression of this technology. From the focus group study, concerns were also raised with regard contamination of food crops either accidentally or malicious intent. A few mentioned the potential for bioterrorism. Generally, concerns were raised about the idea of some of these technologies “running wild” (i.e zebra mussels). The public members also raised the issue of long term risk, suggesting that these technologies might reveal impacts that won’t be detected for years, even decades after they are introduced. Finally, the potential of the profit motive to ultimately supersede the public interest in terms of safety was also raised.

Perception of risk

The perception of risk of each of the described PMF scenarios differed amongst the various stakeholder groups. Scientists from the PMF industry and academia often referred to the risk equation, where risk is defined as the product between the magnitude of the damage that can result from an event and the probability of occurrence of such an event (risk=hazard x exposure) (Arcand, 2004). However, representatives from social/environmental groups, when discussing risk, typically did not take into account the probability of occurrence of a particular hazard. To them, the fact that a hazard could happen even once was reason enough not to pursue the technology. Contamination of the food supply and contamination of the environment were described as high risk catastrophic events. However, scientists would argue that the likelihood of such events occurring are quite low, therefore indicating the risks are low. These differences in risk perception will be critical in determining the acceptability of these technologies and could characterize upcoming debates on this technology. In the focus groups, the purpose (or benefit) of the application was the most important factor in determining whether it was acceptable or not. 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 the 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 purpose variable would be lower. Generally, in cases where the benefits are seen to be substantial, they can overcome concerns about risk. These calculations by the public further took into account such factors as perceptions of long-term impacts on human health and the environment and confidence in regulatory systems. The focus groups did show that when provided with appropriate background information, they could assess the risks and benefits of the technology.

Limitations to Study

The main limitation of the stakeholder study was the small sample size. The results of the survey cannot be used to make generalizations about each sector due to the limited number of respondents interviewed from each sector. The intent of the survey

however, was to obtain qualitative assessments which may suggest concerns of each sector. It was also evident that respondents from the Food and Agriculture sectors had little awareness of PMF, and their responses were limited by this lack of knowledge. In the case of the GM food controversy, the food retail sector's involvement in Europe was sparked in response to consumer concerns and it is possible that PMF will remain low on the agenda of the food retail sector until it becomes an issue in the public arena. There were also more respondents from the PMF compared to the Food industry in this study.

With respect to the survey, some respondents indicated that there was insufficient information to appropriately identify the risks and benefits, therefore no speculation was made. More specific information was needed in terms of the plant biology (i.e. weediness) and confinement and containment methods. Focus group discussions are by their nature designed to provide depth and detail to views expressed; they are not meant to provide a statistical picture of public opinion.

CONCLUSION

Overall, across the stakeholder groups plant molecular farming was given a favourable risk/benefit assessment, provided that certain conditions were met. The conditions included having regulations in place and appropriate containment and confinement measures to ensure the safety of humans and the environment. In contrast, social/environmental and organic farming representatives from the Agriculture sector thought that plant molecular farming was unacceptable since the risks to human safety and the environment and to the organic industry far outweighed any benefits. The focus group participants were slightly less favorably predisposed than stakeholder participants. Judgments were made on the basis of risk-benefit trade-offs as well as confidence in regulatory capacities.

The findings of this study suggest important policy and regulation implications. First and foremost, it is imperative to have a regulatory framework in place that instills confidence; one that ensures that the regulating body has the knowledge and capacity to handle this new technology. The public indicated significant concerns about regulatory capacity for monitoring, particularly for surveillance for long term impacts. Secondly, procedures assuring that human safety and the environment are protected

need to be in place and communicated to the public. A strong preference for non-food over food crops was expressed by the public. In at least one instance however (vaccines in food plants), this general principle appeared to be relaxed so it is not clear whether there will be other conditions down the road where the use of food plants for PMF might also be acceptable.

The majority of stakeholder participants indicated that containment and confinement strategies should be determined on a case-by-case basis depending on the level of risk and the public preferred greenhouse-only conditions until thorough testing is complete and the use of non-flowering versions of plants. Furthermore, across all stakeholder groups the importance of communication was emphasized in two ways: 1) PMF should be regulated with input from all stakeholder groups and 2) greater communication is required for better understanding of the technology on the part of publics and other stakeholders. Such communication needs to be a two-way street where stakeholders and regulators also need to learn more about public concerns and values. Lastly, more research is required to further elucidate the basic science of PMF and the impacts on the environment and human health. Inclusion of these recommendations into policy development could warrant greater confidence in the technology and assurance of societal benefits.

REFERENCES

Animal and Plant Health Inspection Service (2002), Press release: USDA Investigates Biotech Company for Possible Permit Violations.

<http://www.aphis.usda.gov/lpa/news/2002/11/prodigene.html>

Arcand F, Arnison PG (2004). Development of Novel Protein-Production Systems and Economic Opportunities & Regulatory Challenges for Canada. April,

http://www.cmp2005.org/pdf/NPPS_040412.pdf

Barta, A. et.al. (1986), The expression of a nopaline synthase human growth hormone chimaeric gene in transformed tobacco and sunflower callus tissue. *Plant Molec Biol*, 6:347-357.

Canadian Food Inspection Agency (2002): Plant Molecular Farming Discussion Document- Glossary of Terms.

http://www.inspection.gc.ca/english/plaveg/bio/mf/mf_glose.shtml

Canadian Food Inspection Agency (2003): Interim Amendment to Dir2000-07 for Confined Research Field Trials of PNTs for Plant Molecular Farming (April 2003)

website: <http://www.inspection.gc.ca/english/plaveg/bio/dir/dir0007ie.shtml>

Ma, JK, PM Drake, and P. Christou (2003). The production of recombinant pharmaceutical proteins in plants. *Nature reviews-genetics*. October, 4:794-805.

Nevitt, J., G. Norton, B. Mills, ME Jones, M. Ellerbrock, D. Reaves, K. Tiller and G. Bullen (2003). “ Participatory assessment of social and economic effects of using transgenic tobacco to produce pharmaceuticals.” Report accessed at <http://www.agecon.vt.edu/biotechimpact/>

Office of Science and Technology Policy (2002), Proposed federal actions to update field test requirements for biotechnology-derived plants and to establish early food safety assessments for new proteins produced by such plants. Notice 67 , Federal Regist 149, 50577-50580. Cited in Stewart and Knight (2004).

Stewart, P. and A. Knight (2005). “Trends affecting the next generation of U.S. agricultural biotechnology: Politics, policy, and plant-made pharmaceuticals”. *Technological Forecasting and Social Change*. June, 72(5): 521-534.

USDA (2004), Permits for Pharmaceutical and Industrial-Expressing Crops. In www.aphis.usda.gov/brs/pharmaceutical.html. Retrieved 29-05-05

Appendix 1: Value chain of PMF Stakeholders

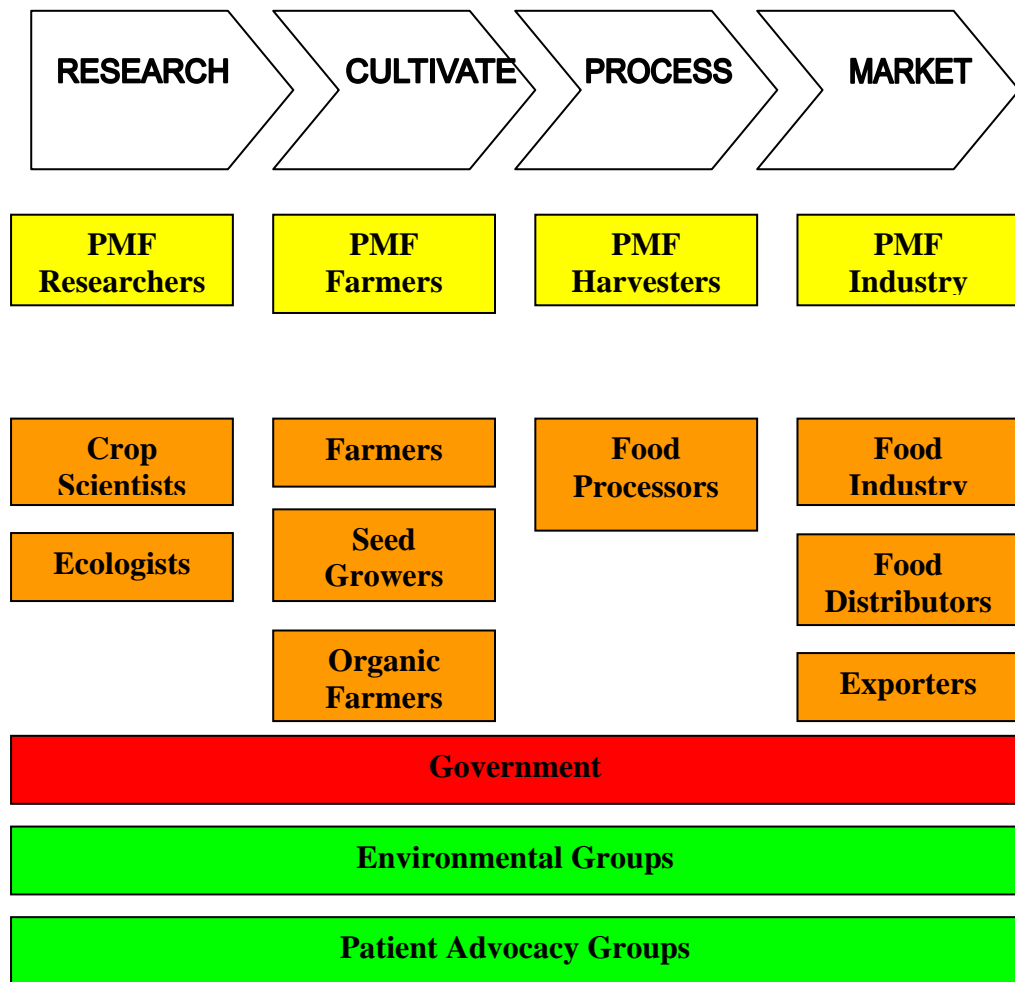


Figure 1: Value chain used to identify key PMF Stakeholders