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Social Acceptance of Plant-Made Vaccines: Indications from a Public Survey

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The use of transgenic plants for production and oral delivery of vaccines has been shown effective in animal trials and Phase I human clinical testing. The use of edible plants for production of vaccines represents an interesting intersection between medical treatments and the use of genetically modified (GM) food crops. Public acceptance of GM foods is highly variable on a global scale, and similar issues of social acceptance will influence the commercial feasibility of a plant-made vaccine. The recipient of a plant-made vaccine may have to weigh the perceived benefits of vaccination against the perceived risks associated with consumption of GM plant materials. A public opinion survey of 706 respondents was conducted to gain an indication of the prospects for public acceptance of this technology and demonstrated strong potential support for a plant-made vaccine.

Key words: pharmaceuticals, public acceptance, risk, transgenic plants, vaccines.

Introduction

The expression of vaccines in plants is an exciting application of biotechnology. There are several benefits to this method of vaccine production: the elimination of the risk of contamination by animal pathogens; the provision of a heat-stable environment in processed plant tissues; oral delivery eliminates injection-related hazards. A situational analysis including the strengths, weaknesses, opportunities, and threats associated with this technology has been performed by Kirk & Webb (2005). Plant-made vaccines (PMVs) have shown a fundamental ability to induce systemic and mucosal immune responses, and Phase I initial clinical studies have demonstrated PMVs to be safe and functional. (For review see Twyman, Schillberg, & Fischer, 2005 and Walmsley & Arntzen, 2003.) Despite advances in agricultural biotechnology that have resulted in the approved release of several GM food crops, the extension of plant engineering technologies for human vaccines has been comparatively slow.

A product development model for PMVs has been suggested by Kirk & Webb (2005), who also described the most likely scenario for commercial development as one where agricultural biotechnology companies might leverage their existing GM plant technologies to venture into pharmaceutical development, rather than the pharmaceutical sector attempting to conduct R&D in the agricultural sector. Underlying this suggestion is the assumption that social acceptance will not prevent introduction of an effective PMV to the market, or perhaps more importantly, that the potential for nonacceptance would not prevent commercial parties from exploring and developing this technology. As demonstrated by attempts to widely introduce GM crops in Europe, biotechnology innovations which are successful on technical merits must also be accompanied by social acceptance—assuming market demand—for commercial success.

If social acceptance is of sufficient importance, then gauging public attitudes toward any new technology becomes an important step in market assessment and justification of financial investment to conduct research and development. There are several ways that public opinion can be evaluated. One method is to examine what people are buying. People express their preferences directly in the marketplace. As with any new product, probable acceptance in the marketplace should be assessed before major investment ever begins. Another method of gauging consumer preference is by forming focus groups. Focus groups provide the opinions of a small number of people but the personal feedback from these individuals can be very useful.

In general, public opinion is best evaluated through direct survey. Surveys can be cumbersome to administer but the information obtained through thoughtful questioning can be invaluable. Surveys about technology can be designed to determine the true public perception of a specific technology, to understand the public perception of specific needs and risks, and/or to gauge general public acceptance of novel technologies.

Public perceptions of biotechnology are extremely complex and cannot be generalized easily. Separate studies and surveys cannot be compared empirically if different questions were asked (Peterson, 2000). There

are numerous opinion studies about genetically modified foods, but few address the use of biotechnology to produce pharmaceuticals. Consumer preference for PMVs could be crudely estimated by evaluating the acceptance of genetically modified foods; however, the risks and benefits of vaccines are significantly different than those of food commodities, and inferring either acceptance or rejection of PMVs based on these trends would be inaccurate.

There have been two previous attempts to gauge public attitudes specifically toward plant-made pharmaceuticals that might include vaccines. Although these have been positive studies regarding public *perception* of risks and benefits, we believe that neither study specifically addresses public *acceptance* of a PMV. In the earliest study, by Nevitt et al. (2003), 672 respondents answered questions related to perception of risks and benefits for a pharmaceutical produced in transgenic tobacco.[1] Although this study did show support for medicines produced in tobacco, the two survey questions (out of 19 total) that related to acceptance of a plant-made pharmaceutical were focused on medicines available from a store and subject to price comparisons with alternative, non-GMO products. It is difficult to draw any specific comparisons between the results of this study and potential acceptance of PMVs, because vaccines are not available from retailers or pharmacists, are generally not price-sensitive in nature, and rarely have multiple brands available for consumer choice.

In the most recent study, reported by Einsiedel and Medlock (2005), a focus group was assembled and questioned on their views and perceptions related to six different plant-made pharmaceuticals, including a Norwalk virus vaccine expressed in transgenic potato. In that survey, respondents were given extensive information in the form of a discussion document for each potential product and polled for their acceptance of each application. In the case of the PMV example, 27% (13 out of 48) of the respondents described this application as "unacceptable" or "less acceptable," while 52% (25) described it as "more acceptable" and 21% (10) described it as "fully acceptable." The potato vaccine was the most accepted application of the six that were used. Previous studies based on applications of biotechnology have also shown that there is more support for medical biotechnology than for agricultural biotechnology (Fischhoff & Fischhoff, 2001).

In more detailed responses, focus group participants felt that PMVs might be an effective way to administer vaccines (although this might be confounded if the discussion document described the PMV as an edible food rather than as a tightly regulated pharmaceutical—the title of this application in the survey was "edible vaccines," a term now avoided by researchers in this field to prevent the idea of distribution as a specialty food item). Respondents also felt that PMVs were advantageous for use in developing countries, offer significant cost benefits, and are more appropriate than other transgenic plant technologies due to the preventative medical application. Although this survey also showed very positive results in general and raised questions as to how acceptable each technology might be, it did not ask whether respondents would personally be willing to accept and use the product. Depending on how the edible vaccine discussion document was framed, the responses could be interpreted as an indication of support for a technology intended for predominant use in developing countries, where the risk and benefits equation may be seen to be significantly different and where any risks may be remote and of less personal importance to the survey respondents. The interpretation of delivering edible vaccines to developing countries is not dissimilar to much of the literature on this topic (see Castle & Dalgleish, 2005; Robert & Kirk, in press) but is not strongly aligned with the issues of market acceptance as a feasibility criteria for investment by industry in development of PMVs as a profitable technology.

In addition to commercial investments, research funding by government and nonprofit agencies and oversight by regulatory agencies can also be influenced by public attitudes—and the argued balance between perceived risks and benefits of a new technology. As indicated in Figure 1, PMV technology represents a unique intersection between the fields of agriculture, biotechnology, and pharmaceuticals.

There are numerous risks and ethical issues arising from each of the fields indicated in Figure 1, which might influence public acceptance of PMV technology. The environmental and human health risks of PMVs have been discussed by Kirk, McIntosh, Walmsley, and Peterson (2005), and the ethical questions related to the development and use of this technology—particularly in developing countries—has been described in detail by Robert and Kirk (in press). Even if technical development of PMVs is successful, and even if effective risk management practices are adopted by manufacturers, the ability of the public to withhold approval for this technology based on misperception of risk, or due ethi-

1. *For survey design and results see http://www.agecon.vt.edu/biotechimpact/surveys/surveymain.htm.*

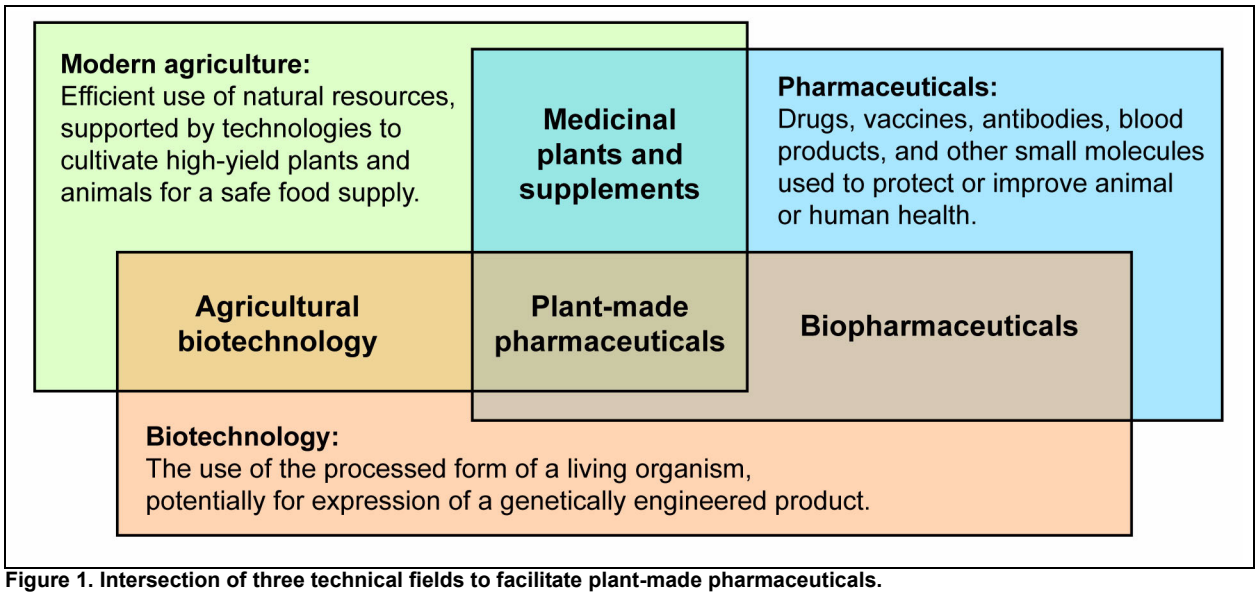

Figure 1. Intersection of three technical fields to facilitate plant-made pharmaceuticals.

cal, social, or moral issues is a significant issue for any third party with commercial interests. Unformed public opinion can be unpredictable, and although certain societies (such as the United States) tend to be optimistic toward science-related issues, it can be misleading to assume that public opinion will not ultimately be negative at the time a choice is required (Priest, 2001). The purpose of this study was to investigate the existing level of general acceptance (as opposed to risk perceptions) for a potential PMV by means of a public survey.

Survey Design and Administration

A survey comprising three multiple choice questions was posed to 706 respondents in the greater Phoenix (Arizona) area over a period of two weeks. The survey was conducted using classroom questionnaires, public venue interviews, and random telephone interviews. The questionnaires did not contain any identifying information, and all responses were voluntary and without compensation or other rewards. Classroom surveys were conducted by handing out questionnaires at the beginning of randomly selected senior- or graduate-level courses at Arizona State University (Tempe, Arizona, USA) with prior permission from instructors. Public-venue interviews were conducted by randomly selecting willing interviewees at concentrated business locations such as shopping malls. Telephone interviews were conducted by professional telemarketers using commercially available randomized lists of telephone numbers. Additional demographics were collected as part of the questionnaire to allow analysis by sex, frequency of travel (frequent travelers defined as undertaking air travel more than twice per year), and survey location (university or general public environments).

The objective of the first question was to evaluate the market preference among the general population for noninjectable vaccines. One of the major expected advantages of PMVs is the ability to produce an oral product; this might also allow a competitive business advantage if introduced to replace an existing injectable vaccine. This issue is a common consideration for new product development within the pharmaceutical field (one of the three fields indicated in Figure 1). Question 1 of the survey was "If your doctor advised you to obtain a vaccine before traveling on a cruise ship or to a foreign country, how would you rate your preference between an injection and an orally administered vaccine in the form of a capsule, a liquid, or a chewable tablet?" The travel scenario was included for the purpose of setting a realistic scenario for an adult who would be receiving a vaccine, because the majority of vaccinations currently occur in infants.

The objective of the second question was to investigate the general perception regarding use of biotechnology in existing vaccines. Aspects of genetic manipulation are foremost within the risks and ethical concerns for any biotechnology product (another of the three fields in Figure 1). This question was not designed to elicit any indication of approval or rejection for biotechnology per se but rather to give an indication of public perception about how prevalent biotechnology is within the existing vaccine portfolio. Question 2 of the

Table 1. Public opinion survey data sorted by response.

Response options		No. of respondents	% of respondents
Question 1	Very likely to choose oral	339	**48.0%**
	Somewhat likely to choose oral	83	11.8%
	No preference	152	21.5%
	Somewhat likely to choose injection	40	5.7%
	Very likely to choose injection	92	13.0%
	Total	706	100.0%
Question 2	All of them (90–100%)	85	12.0%
	Most of them (60–80%)	289	**40.9%**
	Some of them (30–50%	213	30.2%
	A few of them (10–20%)	83	11.8%
	None of them (0%)	36	5.1%
	Total	706	100.0%
Question 3	Very likely to accept	212	30.0%
	Somewhat likely to accept	268	**38.0%**
	Somewhat unlikely to accept	91	12.9%
	Very unlikely to accept	41	5.8%
	No opinion	94	13.3%
	Total	706	100.0%

survey was "What percentage of current vaccines would you say are made from a genetically modified source?"

The objective of the third question was to elicit specific approval or rejection for a PMV. This question is grounded mostly in the agricultural field (from Figure 1), in that the question focused on description of a GM plant. Question 3 of the survey was "How likely would you be to accept the use of a vaccine that is produced in a genetically modified plant (such as a powdered tomato)?"

Results and Discussion

The response data is summarized in Table 1. Table 2 provides the response data sorted according to demographics. The demographics suggest that each category was generally evenly sampled and that there were no significant interrelations between these groups. Approximately 53% of frequent travelers were from the university environment, while 49.3% of infrequent travelers were from the university environment. The female respondents were more evenly distributed between frequent (49.2%) and infrequent travelers (50.8%), while male respondents showed a slight bias toward frequent travel (53.9%). Approximately 59% of female respondents were from the general public sector, whereas 61.9% of the male respondents were from the university environment.

Preference between orally administered vaccines and injectible vaccines was evaluated in Question 1. It was found that 59.8% of respondents expressed some preference for an oral vaccine. Only 18.7% of respondents expressed a preference for injection, and 21.5% of respondents expressed no preference between oral administration and injection. The demographics for this question suggest that education level does not influence preference, and frequency of travel does not influence preference, but there is a marginally stronger preference—63% for oral vaccines among female respondents compared to 56% preference for oral vaccines among male respondents. This small difference in male and female responses could indicate a culturally based male bravado toward needles—or at least indifference, as supported by the higher proportion of responses in the "no preference" category. It may also reflect that females are the predominant caretakers of children and take them to a physician for vaccinations, possibly resulting in elevated general discomfort with injections. It may also reflect that females are more familiar with preventative oral medication such as contraceptives.

The responses to Question 2 show that 40.9% of respondents believed that most vaccines are genetically modified. However, of the 35 vaccines licensed for immunization and distribution in the United States by the FDA, only two (6%) are produced by genetically engineered subunit technologies.[2] The high response

Table 2. Public opinion survey data sorted by response and demographics.

Question 1	Very likely oral		Somewhat likely oral		No preference		Somewhat likely injection		Very likely injection	
Frequent travelers	176	**48%**	30	8%	78	21%	20	6%	59	16%
Infrequent travelers	163	**48%**	53	15%	74	22%	20	6%	33	10%
University sample	160	**44%**	50	14%	88	24%	24	7%	39	11%
General public	179	**52%**	33	10%	64	19%	16	5%	53	15%
Female	194	**52%**	40	11%	69	19%	24	6%	45	12%
Male	145	**43%**	43	13%	83	25%	16	5%	47	14%
Question 2	**All (90–100%)**		**Most (60–80%)**		**Some (30–50%)**		**Few (10–20%)**		**None (0%)**	
Frequent travelers	42	12%	159	**44%**	107	29%	40	11%	15	4%
Infrequent travelers	43	13%	130	**38%**	106	31%	43	13%	21	6%
University sample	52	14%	175	**48%**	100	28%	29	8%	5	1%
General public	33	10%	114	**33%**	113	33%	54	16%	31	9%
Female	42	11%	145	**39%**	116	31%	47	13%	22	6%
Male	43	13%	144	**43%**	97	29%	36	11%	14	4%
Question 3	**Very likely**		**Somewhat likely**		**Somewhat unlikely**		**Very unlikely**		**No opinion**	
Frequent travelers	117	**32%**	133	**37%**	41	11%	20	6%	52	14%
Infrequent travelers	95	**28%**	135	**39%**	50	15%	21	6%	42	12%
University sample	132	**37%**	136	**38%**	38	11%	15	4%	40	11%
General public	80	**23%**	132	**38%**	53	15%	26	8%	54	16%
Female	88	**24%**	150	**40%**	60	16%	27	7%	47	13%
Male	124	**37%**	118	**35%**	31	9%	14	4%	47	14%

Note. Survey results yield a margin of error for the sample of 3.7%. The use of stratigraphic sampling (surveying higher-educated public and the general public by telephone and personal interviews) yields a margin of error for the educated sector of 5.2% and a margin of error for the general public sector of 5.3% (Weiss, 2002).

rate in the "most of them" category suggests that people believe that biotechnology is already being extensively commercialized. This positive response rate could be caused by increased focus on the biotechnology industry in the Phoenix area[3] including several new biotechnology facilities[4] and extensive media coverage by local newspapers.[5] The demographics indicate that frequent travelers believe "most" vaccines are genetically modified, more so than infrequent travelers by a difference of 6%. Forty-eight percent of the university sample responded that "most" vaccines are genetically modified, whereas only 33% of the general public responded this way. The general public responses show a less positive impression of the proliferation of genetically modified vaccines with 33% responding in the "some" category compared to 28% of the university sample, 16% responding in the "few" category compared to 8% of the university sample, and 9% responding in the "none" category compared with 1% of the university sample. This could be a result of the university public receiving greater exposure to information about genetic modification technologies. There was little difference between the responses of males and females to this question.

2. *For US licensed vaccines see http://www.fda.gov/cber/vaccine/licvacc.html.*
3. *For more information see http://www.flinn.org/docs/Arizona_Biosci_Roadmap_revised_540.pdf.*
4. *For more information see http://phoenix.bizjournals.com/phoenix/stories/2004/03/15/focus2.html or http://www.azcentral.com/arizonarepublic/business/articles/0911biotech11.html.*
5. *The Business Journal (Phoenix) featured more than 130 stories on biotechnology in Arizona during 2003-2004 (see http://phoenix.bizjournals.com/phoenix/stories/), and the Arizona Republic (newspaper) published more than 120 stories on biotechnology in Arizona during 2003–2004 (see http://www.azcentral.com/arizonarepublic/); keyword = biotechnology.*

As shown in Table 1, 68% of respondents expressed some level of acceptance for use of a PMV. This is a good indication to support commercial development of a vaccine candidate with an appropriate market opportunity in developed countries. The positive response rate is in agreement with a survey conducted by Hallman (1996) that revealed several aspects of risk perception of biotechnology products. Nearly 20% of respondents in that survey had negative initial thoughts about genetic engineering, but approximately 50% of the respondents who believed genetic engineering is morally wrong also indicated they approved of its use to create new drugs and more nutritious grain to feed people in poor countries. An opinion survey by the Pew Institute to gauge public perception of genetic engineering showed that 48% of the sample agreed with the idea of genetically modifying plants to contain vaccines to prevent disease, while only 39% of the sample expressed agreement with genetically modifying insects to prevent them from carrying diseases (Pew Initiative on Food and Biotechnology, 2001). In the present survey we found that males were slightly more accepting of genetically modified vaccines (72%) than females (64%), which may be grounded in the same trends shown by Fischhoff and Fischhoff (2001), who found by looking across previous biotechnology surveys that more positive views of science are expressed by people who are young, male, politically conservative, and wealthy. The survey conducted by the Pew Institute showed that men were more likely than women to agree with genetically modifying insects, fish, and plants. Other studies have also shown this gender gap regarding perception of genetic technology. Women perceive lower benefits and are less accepting of genetic technology than men, but more empirical studies need to be done to specifically address why this is so (Siegrist, 2000). The demographics of this survey show that there is little difference in PMV acceptance between frequent (69%) and infrequent travelers (67%). Some difference in acceptance of the tomato vaccine was evident with 75% of the university sample expressing acceptance compared to 61% of the general public sample. The greater acceptance in the university sample might be indicative of their exposure to more information about genetic technologies and could show the need for more communication and education opportunities about the technology to the general public.

Conclusion

As shown by the survey, there appears to be a positive public outlook for PMVs and genetically engineered vaccines in general. The development of PMVs may promise significant advantages for production of vaccines and other pharmaceuticals; however, we suggest that the benefits and risks associated with new technologies must still be communicated to the public early to maximize social acceptance. The data and conclusions provided here should not be construed as demonstration that risks associated with this technology are not important to the general public. Studies have shown that even if people associate technology with relatively high risks and unknown consequences (especially genetic technologies), they still might not reject the technology (Siegrist, 2000; Zechendorf, 1994). Oversight by regulatory agencies (such as the US Department of Agriculture and the US Food and Drug Administration) may give confidence to the general public and facilitate acceptance of new technologies, despite negative perceptions with regard to specific risks. More empirical research on public perceptions of agricultural biotechnology specific to producing novel vaccines is needed before substantive generalizations can be made. We believe this survey shows an acceptance of PMVs as a rare combination of medical and agricultural biotechnologies. Given that oral vaccines are preferred, that people believe that most vaccines are genetically modified, and that the public has expressed a high acceptance for PMVs, further development of this technology by commercial parties is favorable, if paralleled with appropriate market demand for specific products. Investment in clear communication by scientists and regulators will further enhance the public trust, optimism, and ultimate acceptance for PMVs.

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