Food, Health and Biotechnology:

Consumer and Social Issues in Canada's New Food and Health Product Industries

A Report from the Advanced

Foods and Materials Network

Edited by Nola M. Ries and

Jacob J. Shelley

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Foreword

The Advanced Foods and Materials Network began in 2004 as one of Canada's Networks of Centres of Excellence. It is an innovative program of research and development that seeks to improve the quality and nutritional value of foods while applying new processes in biotechnology to the development of products, such as lower cost antibiotics and faster healing wound dressings, that contribute to better health. AFMNet has built a national network of hundreds of scientific researchers, professionals, industry partners and government agencies, who collaborate on a wide range of research projects.

A particularly innovative aspect of this project, one originating through the vision of AFMNet scientific director Rickey Yada, was the incorporation from the very outset of a stream of research to explore the ethical, environmental, economic, legal and social issues that are raised through these new developments in genomic science. Investigation of these so-called GE^{3}LS issues has formed a major component of the Network, bringing together many of the leading researchers in Canada from the social sciences, law and humanities to work in collaboration with the scientific researchers. The aim of the GE^{3}LS research is twofold: first, to incorporate social and ethical considerations at the early stages of scientific research, and second, to provide useful information to industry, consumers, public interest groups and government regulators, as well as the scientific developers themselves, on the deployment and use of these new technologies.

This report summarizes the results of the eight GE^{3}LS research projects that were conducted in the first three years of AFMNet's activities. These results were reported first at a national conference held in Victoria, British Columbia, in August 2006. They are published here so that they can be more widely disseminated to the various Canadian stakeholders in these scientific developments. They focus on issues related to consumer responses to new food and bio-materials; assessment of the new Canadian regulations governing natural health products; issues of intellectual property arising from these technologies; and the status of new regulatory risk assessment tools being developed to ensure the safety of novel foods and food processes.

It is our hope that this report will be a useful tool for communicating the results of GE^{3}LS research to the scientific community, to industry, to government, and to Canadian citizens.

Conrad G. Brunk
GE^{3}LS Theme Leader, AFMNet

1. Introduction

The Advanced Foods and Materials Network

The Advanced Foods and Materials Network (AFMNet) is a national network dedicated to research and innovation in foods and biomaterials. The Network brings together natural scientists, engineers, health researchers, social scientists, legal academics and researchers in humanities disciplines to work in multidisciplinary teams involving a total of 25 universities, 14 industries and 17 governmental bodies or other supporters.

AFMNet research is organized around three key themes:

1. the structure, dynamics and function of foods and bio-materials;
2. functional foods and nutraceuticals; and,
3. social, legal and ethical issues (such as regulations, risk assessment, policy, and consumer attitudes and perceptions).

The Network's mission is to enhance and cultivate Canada's leadership role in developing healthier foods, safer food processing, and commercial bio-materials. Its vision is a healthier Canada, new industry opportunities, and new, sustainable commercial materials and methods.

For additional information about AFMNet, visit www.afmnet.ca.

Research on GE^{3}LS Issues

One theme of AFMNet research focuses on "GE^{3}LS" issues, an acronym referring to ethical, economic, environmental, legal and social issues related to genomics. The GE^{3}LS theme involves researchers in fields of law, philosophy, economics, religious studies, political science, pharmacy, and molecular biology. In the first two years of AFMNet research (2003-2005), the following eight GE^{3}LS research initiatives were funded:

- *Factors Affecting Consumer Acceptance of Genetically Modified Foods Containing Transgenes from Sources Involving Moral, Religious and Cultural Dietary Prohibitions*
  Project leaders: Conrad G. Brunk and Harold Coward, University of Victoria
- *Accuracy and Nature of Media Representation of Food Biotechnology*
  Project leader: Timothy A. Caulfield, University of Alberta
- *Labelling of Genetically Modified Foods: Balancing Interests in Ethically Defensible Policy*
  Project leader: David Castle, University of Ottawa
- *Understanding Consumer Acceptability of Functional Foods*
  Project leader: Spencer Henson, University of Guelph
- *Understanding the Impact of Regulation on Advanced Food Innovation*
  Project leader: Spencer Henson, University of Guelph
- *Natural Health Products Regulations: Perceptions and Impact*
  Project leader: Heather S. Boon, University of Toronto
- *High Throughput Omics-Based Analytical Tools for Evaluating Food Safety*
  Project leaders: Cecil Forsberg, University of Guelph and Marc Fortin, McGill University
- *Comparative Intellectual Property Issues in Agricultural Biotechnology*
  Project leader: Richard Gold, McGill University

In August 2006, the first national AFMNet GE³LS conference was held in Victoria, British Columbia. This conference, *Food, Health and Biotechnology: Consumer and Social Issues in Canada's New Food and Health Product Industries*, profiled the findings of the research projects listed above. This conference brought together AFMNet-funded researchers, policy makers, industry representatives, and community stakeholders who are helping to shape the future policy and regulatory frameworks of Canada's emerging "novel" food industries.

This report summarizes research findings for specific GE³LS projects.

Several of the GE³LS projects listed above are still ongoing and new research in this theme began in spring 2006. The current GE³LS projects are:

- *Stakeholder Perspectives on the Ethical Issues in Animal Biotechnology and the Implications for Public Policy*
  Project leaders: Conrad G. Brunk, University of Victoria and Sarah Hartley, Genome British Columbia
- *Social Issues in Nutritional Genomics: The Design of Appropriate Regulatory Systems and Issues of Public Representations and Understanding*
  Project leaders: David Castle, University of Ottawa and Timothy Caulfield, University of Alberta
- *Natural Health Product Regulations: Perceptions and Impact*
  Project leader: Heather Boon, University of Toronto
- *Omics for Novel Plant and Animal Food Product Assessment and Risk Identification*
  Project leader: Cecil Forsberg, University of Guelph
- *Understanding Consumer Acceptance of Functional Foods and Nutraceuticals*
  Project leader: Spencer Henson, University of Guelph

For additional information on any of the research initiatives discussed in this report, or for additional copies of the report, please contact:

Nola M. Ries
AFMNet Research Associate
University of Victoria

Mailing address:
Advanced Foods and Materials Network
c/o Sedgewick B102, Vandekerkhove Wing
University of Victoria
PO Box 1700 STN CSC
Victoria BC V8W 2Y2

Email: nmries@uvic.ca
Telephone: (250) 721-6325

2. Acceptable Genes?: Factors Affecting Consumer Acceptance of Genetically Modified Foods Containing Transgenes from Sources Involving Moral, Religious and Cultural Dietary Prohibitions

Nola M. Ries and Conrad G. Brunk
University of Victoria[1]

Introduction

Consumer attitudes toward genetically modified (GM) foods are influenced by a variety of factors, including perceptions about safety and healthfulness of the food. For some consumers, religious, moral and cultural dietary practices also inform their willingness to consume GM foods. The goal of the "Acceptable Genes" project, led by Conrad Brunk and Harold Coward at the University of Victoria, was to investigate specific religious and ethical dietary traditions and examine the acceptability of GM foods that contain transgenes from sources that are prohibited within those traditions. For example, would a person committed to a Jewish kosher or Muslim halal diet consume food containing transgenes from unacceptable animal sources? How would ethical vegetarians view those same foods?

In studying the role of religious and cultural dietary prohibitions, the project included both expert and lay perspectives. As described in detail below, experts in theology and other disciplines engaged in novel scholarly analysis of the treatment of GM foods within specific faith traditions. Lay adherents of religious and cultural belief systems joined focus groups to share their views on transgenes in food. The resulting study combines interdisciplinary theoretical analysis with empirical data documenting lay attitudes and perspectives toward transgenic foods. This rich body of knowledge will be published in a forthcoming book by SUNY (State University of New York) Press as a 2007 volume in their Religion and Environment series.

No previous research work had examined these questions of consumer attitudes toward new food technologies in the context of values-based dietary practices as observed by religious and cultural communities. Our study in this area contributes to knowledge in fields of religious and cultural studies and also provides guidance to regulators who are interested in taking into account the views of diverse communities in developing law, regulations and policies to govern GM foods in the marketplace.

Methodology

The "Acceptable Genes" project used several research methods to acquire expert knowledge and lay perspectives to inform the study.

Expert scholars

The project leaders invited a multidisciplinary team of scholars with expertise in the theology and history of food and dietary practices in nine religious and cultural traditions.
The following experts participated in this project:

- Sam Abraham, British Columbia Cancer Agency – Scientific Background on

[1] Project team: Conrad G. Brunk and Harold Coward, Centre for Studies in Religion and Society, University of Victoria (Project Leaders); Lorenzo Magzul, Research Assistant, University of British Columbia; Shiri Pasternak, Research Assistant, University of Victoria.

Genetics and Genetically Modified Organisms
- Lyne Létourneau, Université Laval – Vegetarianism Perspectives
- Paul Thomson, Michigan State University – Ethical Perspectives on Food Biotechnology
- David R. Loy, Bunkyo University – Buddhist Perspectives
- Nancy Turner, University of Victoria, Lorenzo Magzul, University of British Columbia and Shiri Pasternak, University of Victoria – Indigenous Knowledge Systems
- Ping-chen Hsiung, Academia Sinica – Late Imperial Chinese Attitudes Toward Food
- Laurie Zoloth, Northwestern University – Jewish Traditions
- Ebrahim Moosa, Duke University – Muslim Ethics
- Donald Bruce, Church of Scotland – Christian Perspectives
- Vasudha Narayanan, University of Florida – Hindu Attitudes
- Nola M. Ries, University of Victoria – Regulatory Issues
- Leslie Rodgers, Praxis Pacific – Focus Group Facilitator

"The study was conducted by a multidisciplinary team of scholars with expertise in the theology of food and dietary practice within ten religious and cultural traditions."

The majority of these participants met at the outset of the project to define research parameters and goals and develop timelines for conducting their research. After writing and sharing their draft chapters with other members of the team, the research group convened again to do critiques of each draft. This process provided valuable peer review.

Lay focus groups

Eleven focus groups were conducted by Leslie Rodgers, a professional facilitator, between January and May 2005. These focus groups included volunteer participants in Vancouver and Victoria, British Columbia, from the following groups: vegan/vegetarian, Mennonite, Hindu, Orthodox Jewish, non-Orthodox Jewish, Seventh Day Adventist, Theravada Buddhist, Chinese, and Muslim. Indigenous Mayan peoples were interviewed in Guatemala in May 2005. The focus groups began with a short, informational presentation on GM food technology, and then the facilitator used a structured set of questions to elicit discussion. The focus group members explained their dietary practices and views on food, especially GM foods that contain transgenes from prohibited or problematic sources.

Data from the focus groups were compiled and summarized for review by the expert authors who sought to integrate the lay perspectives into their chapters. The focus groups were not intended as statistically representative samples that can provide generalizable statements about the views of the broader religious communities from which the interviewees were drawn. Rather, the purpose of conducting the focus groups was to incorporate a lay perspective into this research project. Views of the theological experts and lay practitioners on acceptable applications of GM technology often diverged and the chapter authors broadened the scope of their analysis by taking into account the focus group responses.

Results and Discussion

Among the religious traditions examined in this project, the teachings of Judaism are most open to GM foods. Jewish ethics have a fundamental concern with saving life and healing what is wrong in the world. Jewish law is relatively sympathetic to technological innovations that can be harnessed to address ill health and suffering. In regard to food, the kosher rules that prohibit mixing of specific plants and animals do not rule out gene transfers. While Jewish scholars express concern about greed and exploitation in biotechnology industries, GM foods nonetheless hold promise for enhancing food production and alleviating hunger.

Muslim teachings prohibit consumption of certain foods (e.g., pork). Aside from these specific prohibitions, the prophet Mohammed has instructed that choices about agriculture and other practical matters should be left to persons with experience and expertise. On the question of GM foods, Muslim authorities have divided into two camps: one that accepts GM foods provided risks are managed and another that urges considerable precaution to avoid social and environmental harm.

Hinduism, with its primarily vegetarian dietary prescription, divides food into pure and impure categories; impure foods are permissible for everyday consumption, but are unacceptable for meals on holy days and for ritual offerings. A fruit or vegetable that has been modified with a gene from an animal source would be considered impure but acceptable outside ritual meals. For most Hindus, one exception exists: a porcine gene transfer would preclude eating a GM food even for a routine, daily meal. GM foods are viewed as strictly unacceptable in worship.

Buddhism is concerned with reducing suffering and correcting the negative aspects of human motivation: greed, ill will and delusion. GM foods may mitigate suffering in some contexts, but avarice may drive industrial food production to the detriment of humans, animals and plants that share common ecosystems. Evaluation of GM technologies must consider the interrelatedness of species and the effect of food production and consumption on suffering.

Unlike other religions, Christianity does not have specific food prohibitions. Food does, however, have symbolic significance in Christian celebrations. There is little consensus on how Christian teachings are to be applied to guide the application of GM technologies. On one view, God has given people skill to develop modern science and technology; on the other, humans run the risk of disrupting God's natural creation.

The Chinese approach to diet is influenced by concern for balancing *yin* and *yang* foods to promote health. All food is believed to have medicinal effects in the body and concern exists that GM foods are unnatural and may have adverse effects on human health as well as the environment.

Indigenous peoples do not have uniform cultural beliefs and practices, but share a history of colonization and destruction of traditional ways of life. Genetic modification of foods, especially revered foods like maize for the Mayan community in Guatemala, is generally resented and rejected as another example of colonial powers foisting unwanted change on Indigenous peoples. In some Indigenous traditions, plants and animals are viewed as perfect creations and no lesser than human beings. Attempts to improve plants and animals through genetic modification are no more acceptable than similar efforts to improve people.

The analysis of vegetarianism distinguished between "health" vegetarians and "ethical" vegetarians; the former eschew food from animal sources because they believe such a diet offers personal health benefits, while the latter consider social justice, animal welfare and environmental considerations in making dietary choices. Health vegetarians are less likely to oppose GM foods containing transgenes from animal sources, provided the foods are evaluated to be safe and confer similar or greater health benefits. Ethical vegetarians have stronger opposition to GM foods due to worry that adopting such foods will have adverse social and environmental consequences.

Table 1: Religious and Cultural Groups Surveyed

1	Buddhist (Theraveda)
2	Chinese
3	Hindu
4	Jewish (Orthodox)
5	Jewish (Non-Orthodox)
6	Mennonite
7	Indigenous Mayans (Guatemalan)
8	Muslim
9	Seventh Day Adventist
10	Vegan/Vegetarian

"All of the groups investigated expressed some concern about genetic modification of food, especially where transgenes originate from a prohibited source."

Conclusions

This study suggests that religious and ethical concerns about appropriate and inappropriate foods are very likely to have a significant effect on consumer acceptance of GM foods in general and certain kinds of GM foods in particular. All religious faiths and other groups investigated in the project express some concern about genetic modification of food, especially where transgenes originate from a prohibited source.

Some faith communities are more receptive to GM foods, but all express worry about unforeseen harms, iniquitous motivations, and worsening gaps between privileged and non-privileged groups in the world.

Yet, almost no one among the expert scholars or the lay focus group participants argued that GM foods should not be approved for sale. However, common to all was a strong opinion that consumers should have access to information about transgenes in the food they eat. Information disclosure about the nature of transgenes in food would allow those with particular religious, cultural or ethical beliefs to avoid those foods. This finding has major implications for food labelling policy in Canada.

"The findings of this project support a change in regulatory policy to require mandatory labelling of GM foods."

The dominant regulatory stance in North America is that food label information should be confined to nutritional content and health and safety information (e.g., allergen warnings). The findings of this research project support a change in regulatory policy to require mandatory GM labelling or other means to make information available to interested consumers (e.g., bar codes that allow consumers to scan a product to learn more about method of production, ingredient content, and other details).

Our conclusion is that consumer sovereignty arguments made in free market societies support the right of these religious and ethical claimants to greater information disclosure about transgenes in foods. These claims are significantly strengthened by the appeal to rights of religious practice in liberal societies. People have a strong right in tolerant, liberal societies to live according to their most fundamental values and beliefs. Dietary practices mandated by religious and ethical beliefs certainly rise to this level and deserve to be respected.

3. Labelling Policies for Genetically Modified Foods

David Castle
University of Ottawa[1]

Introduction

Information is like money in the sense that people generally prefer to have more of it rather than less. An interesting fact about money, however, is that happiness does not always follow affluence. After a certain point, as reports from late-stage industrialized countries indicate, more money is actually associated with *less* happiness, and many people will trade money for other things they value like health or time. Does a similar pattern exist for information, such that the desire for more information implies little about the value of the information in the context of daily life, particularly when the information might be traded off for other considerations deemed more valuable?

"Our objective is to shed light on how GM labels rank in relation to other factors that influence food purchasing decisions."

When Canadians are asked if they would prefer to have information about whether their food is genetically modified (GM), or contains GM ingredients, nearly all will say they want the information. This result is consistent with research that studies the public's information needs regarding new technologies, for example in the energy, health care and biotechnology sectors. With respect to GM foods, the consistency with which survey respondents state they want information about GM foods suggests these foods should be labelled. In the United States, for example, consumers state they would prefer a text description accompanied by a symbol to indicate the presence of GM food or food ingredients (Harrison, 2003). Labels are thought to be the right way to convey information insofar as they have the potential to give point-of-sale control to consumers who want to make decisions about the products they consume. One approach is that if autonomous decision making by consumers is the issue, a label indicating whether the product is GM (or GM-free) should be able to provide enough information for a consumer to opt out of consuming GM foods.

Suppose two things can be taken for granted. First, people generally want more information about their food so they can decide if they should consume GM foods. Second, it is possible to develop a label that conveys enough information to allow consistent, autonomous decision making by consumers to opt out of buying GM foods. These conditions could be interpreted as counting in favour of a mandatory GM food labelling policy. But does the labelling of GM foods provide information to consumers they always desire? Or is this true only in the broad sense of a presumption that more information is better than less? Another option is that information about GM foods is desirable like money, but in the narrower sense that it can be traded for other valuable things, in which case there is less presumptive support for mandatory labels than it would first appear.

Our study attempts to go beyond studies and polls that suggest GM food labels are desired to investigate and understand *why* this information may be valuable to a point, and traded off thereafter. Our objective is to inform policies for GM food labels by shedding light on how labels rank in relation to other factors that influence food purchasing decisions.

Methodology

This study approaches the issue of GM food labelling with a methodology borrowed

[1] Project team: David Castle, Canada Research Chair in Science and Society, Department of Philosophy, University of Ottawa (Project Leader): Karen Finlay and Vinay Kanetka, School of Marketing and Consumer Studies, University of Guelph; Chris Norman and Anthony Vander Schaaf, Research Assistants, University of Guelph.

from pricing research, conjoint analysis. Labelling is one among several potential sources of increased costs for producers. Producers interested in the effect of labelling foods as GM will want to know whether meeting consumers' desire to have this information could be done while recouping the extra costs associated with the label change. Marketing products to consumers involves a complicated mix of label messages, consumer knowledge, and product category. All these factors can influence the extent to which consumers will be willing to pay for GM products. To discern the relative impact of different product attributes, including information on the label, consumer researchers use an experimental approach called conjoint analysis. One conjoint analysis method involves the "discrete choice" approach in which research participants make pair-wise trade-offs between a fixed set of product attributes. The results of these trade-offs can be analyzed into rankings of the relative importance of various product attributes without revealing which of the variables is of principal interest to the researchers.

"Consumers tend to be less accepting of organisms that are directly manipulated (such as fruits) than of processed foods with some GM ingredients (such as bread)."

To understand how the labelling of GM food might influence consumers' willingness to pay, and how label information would interact with other product attributes, three experimental hypotheses were developed:

> *Hypothesis 1*: Willingness to pay (WTP) for GM foods will vary according to the type of benefit conveyed on the label – highest for benefits to the consumer, lower for benefits to the environment, and lowest for benefits to the producers.
>
> *Hypothesis 2:* WTP will vary according to the product category – highest for processed foods (olive oil), lower for produce (tomatoes), and lowest for animals (ham).
>
> *Hypothesis 3:* WTP will vary according to how much the consumer knows about genetic modification in general – lower for more knowledgeable consumers, higher for less knowledgeable consumers.

To measure WTP, a discrete choice model was developed and administered to 367 participants in Guelph and Kitchener, Ontario, in the spring of 2006. Appropriate product attributes for olive oil, ham and tomatoes were derived from pre-test interviews, along with the three types of labels, and manipulated in a conjoint design. The study presented a series of paired options with varying levels of each attribute, and asked participants (15 for each of the three products) to indicate which option they would buy (the option to buy neither was also available). A four-item measure of consumer expertise was administered to gauge how much participants knew about genetic modification in general.

In addition to the conjoint analysis, participants responded to five open-ended questions that were intended to provide insight into the kind of labels consumers prefer, how much and what kind of information should be on the labels, how labels would affect their purchase decisions, and who they believe should be responsible for labelling in Canada. These questions were developed to elicit attitudes about normative issues associated with food labelling that would be help to explain, and to cross-validate, the quantitative results from the conjoint analysis.

Results

Results indicate qualified support for each of the three hypotheses. WTP for GM-labelled food varies significantly according to benefits associated with the product. Consumers are willing to pay a substantial premium – ranging from 10% to 19% over the average price – for GM products when the benefits, as explained on the label, are directly relevant to them personally (in this case, nutritional enhancement) The general trend, however is that foods labelled as GM otherwise experienced a substantial price discount, and the addition of benefits did not provide any overall relief for the price

discount in the foods studied. The highest price premium was found for tomatoes, but contrary to the hypothesized result, the lowest premium was for olive oil. Finally, consumer knowledge makes a significant difference in WTP, however the result in this case was opposite to the hypothesis since those who describe themselves as more informed about genetic modification were willing to pay a higher premium than those who describe themselves as less informed.

Analysis of the open-ended questions indicates that while most consumers want to see information about genetic modification on food labels, they tend to want this information in order to avoid buying those products. Those who indicated less negative attitudes responded that they wanted labels for genetic modification in order to make more informed decisions. Many respondents said they did not know enough about genetic modification to care about labelling one way or another, but they thought labels should be present to respect consumers' wishes to make informed purchasing decisions. Many respondents indicated they would like to see explanations on labels explaining how and why the products were modified, as well as more speculative information about the possible, but hitherto undocumented, risks associated with the product.

Few respondents mentioned ethical, economic or health concerns directly in their responses, but those who did expressed themselves forcefully. Some of these respondents indicated they were concerned about the naturalness of GM food. As one respondent stated, "I do have concerns about anything that is tampered with genetically, because I'm not sure it is something that we are morally supposed to be doing … what's more perfect than nature for our bodies?" This sentiment was echoed in other cases in which information about GM foods was associated with risk: "[It] matters because it is no longer 'nature'; it has 'man-made' attributes and humans make mistakes so current up-to-date info/research would be good." Another respondent stated, "I would like to be more generally informed on the nature of the modification so that I can decide on organic," a view another participant expressed in the language of choosing to opt out of the consumption of GM foods: "I do not want to participate in this experiment with nature."

Discussion

The findings of the study discussed here offer preliminary support for the idea that GM labels should include simple benefit messages that appeal to consumers' self-interest, that these messages should be tailored to specific product categories, and that producers may increase acceptance of GM products by improving the general level of knowledge about biotechnology through other channels.

Other studies on GM food labelling explore the contribution that label information could make to consumers' ability to make decisions based on "reliable" – which is to say verifiable as opposed to speculative or specious – information. The presumption of these studies is that consumers generally lack reliable information about genetic modification, and do not have sufficient background knowledge about food production, regulatory approval, nutrition sciences and so on. With reliable information and the background knowledge, they might be in a better position to make informed judgments about the risks and benefits of GM food (Bredahl, 2001; Castle, Finlay & Clark, 2005; Lambraki, 2002; Poortinga & Pidgeon, 2004). Labelling is regarded as one way to increase consumer knowledge and provide consumers with reliable information, thereby reducing their uncertainty about GM products (Runge & Jackson, 2000). Some authors suggest providing reliable information on food labels is an important way to avoid consumer assessments of risk and benefits that may be driven by heuristic-based reasoning that can lead to prejudicially negative attitudes toward GM foods (Bredahl 2001; Grunert, Bech-Larsen, Lahteenmaki, Ueland & Astrom, 2004).

Research on labelling aimed at determining consumers' needs for information suggests that labels should be relatively simple (Finlay, Morris, Londerville & Watts, 1999), should include admissions of risk or uncertainty about the consequences of GM technology (Bettman, Payne & Staelin, 1986) and should provide information about the reasons for the presence of genetic modification (Kutznesof & Ritson, 1996). Other research suggests that consumer understanding and evaluation of information on these labels may be driven by overall knowledge about the subject (Castle et al., 2005; Huffman, Shogren, Rosusu & Tegene, 2003). Bredahl, Grunet and Frewer (1998) suggest that consumers with greater expertise about genetic modification may be less motivated to process label information as thoroughly as would consumers who are less knowledgeable. Several researchers have also found that the type of organism being manipulated (animal, vegetable, micro-organism) affects attitudes towards GM products (Frewer, Howard, Hedderly & Shepherd, 1997; Hossain & Onyango, 2004). Consumers also tend to be less accepting of organisms that are directly manipulated (such as fruits) than of processed foods with some GM ingredients (such as bread).

If Canadian consumers want information on labels so they can choose between GM and conventional foods, and they are willing to price discriminate between the two, it would seem reasonable that Canada would have a policy requiring information about genetic modification to be included on food labels. Yet the present labelling standard for GM foods is voluntary, not mandatory. Parliament voted down a private members' bill for mandatory labelling of GM foods in 2001, and shortly thereafter the Canadian Biotechnology Advisory Committee recommended the adoption of a voluntary labelling scheme. After Parliament referred the matter to the Canadian General Standards Board, which had been considering the matter since 1999, two years elapsed before the voluntary labelling standard was released in 2004 (Canadian General Standards Board, 2004). The standard sets the terms, scope, verification and testing criteria, and standards for adventitious material, but is not widely adopted.

One might wonder if the voluntary labelling standard is out of step with consumers' desire for information about the products they buy. If a blanket demand for product information is given credence, the absence of a mandatory labelling policy seems out of step with what people desire. It would represent a policy failure to the extent that a "right to know" or "capacity to opt out" are interests that should have uptake in food labelling policy. Taken in the context of other information used to make purchasing decisions, however, genetic modification is not an overwhelmingly important consideration, and can be counter-balanced by a product's price, or other attributes (see Tables 1–3). One interpretation of this finding is that genetic modification is important enough to consumers that policy makers should adopt a mandatory labelling policy. Equally, however, it suggests that the lack of furor in Canada about genetic modification labelling is explained by the fact that label information is not in reality isolated from other factors. Product information on a label, such as product descriptions, country of origin, and genetic modification, will be traded off unequally against other considerations, such as price, nutrient content and overall product quality and appearance.

The conjoint analysis discussed here does not decisively lead to the conclusion that more information in general, or specific information about genetic modification in particular, is the highest priority for Canadian consumers making purchasing decisions. With respect to public policy implications, it may be the case that a mandatory labelling regime, were it to be adopted, would lead to regulatory and information overkill. In light of the evidence discussed here concerning the general demand for information about genetic modification, compared with information about other food attributes, genetic modification plays an important but not decisive role in consumer behaviour. People are willing to price-discount GM foods, but that is not

the same as wholesale avoidance or rejection. It might be conjectured that a voluntary labelling standard serves those who most wish to avoid GM food with the best of all standards. Food manufacturers wishing to expand markets in which people want label information to systematically avoid GM food have the appropriate labelling standards. They can communicate information that is valued highly by a self-selecting segment of the overall market. If the rest of the market considers information about genetic modification important, but not overwhelmingly so, arguments for mandating this information on labels are attenuated.

Table 1: Importance of various attributes in decision to purchase tomatoes. Ranking by percentage of respondents surveyed. N= 367

Product: Tomatoes		
Attribute	%	Rank
Price	26	1
Gm Info	22	2
Message: No GM	16	3
Appearance	16	4
Message: Contains GM	10	5
Colour	7	6
Purpose	3	7

Table 2: Importance of various attributes in decision to purchase ham. Ranking by percentage of respondents surveyed. N= 367

Product: Ham		
Attribute	%	Rank
GM Info	29	1
Price	27	2
Fat	17	3
Message: Contains GM	10	4
Grade	8	5
Message: No GM	7	6
Purpose	2	7

"Compared with information about other food attributes, genetic modification plays an important but not decisive role in consumer behaviour."

Table 3: Importance of various attributes in decision to purchase olive oil. Ranking by percentage of respondents surveyed. N= 367

Product: Olive Oil		
Attribute	%	Rank
Price	35	1
GM Info	25	2
Purpose	13	3
Processing	13	4
Message: No GM	6	5
Message: GM	5	6
Fat	3	7

*The attribute "GM Info" refers to whether a product has been genetically modified or not. The attribute "GM Message" refers to whether a message about potential health or environmental benefits of the genetic modification was included on the product.

"With respect to public policy, it may be that a mandatory labelling regime, were it to be adopted, would lead to regulatory and information overkill."

Conclusions

The National Institute of Nutrition's *Study on Voluntary Labelling of Foods from Biotechnology* (2006) thoughtfully explores the issue of *how* labels should communicate information to the public about the genetic modification of food. This is a good question to consider in the abstract, but it would be useful to know how much demand there is for label information on genetic modification among other factors that affect WTP for a GM product. Once one gives up the idea that label information is like money because one can never get enough of it, it becomes important to understand what people will trade in order to have information about genetic modification on product labels. The results of the discrete choice model discussed here give partial grounds for thinking that in the context of other factors that modulate WTP, genetic modification labels play an important, but not decisive role. Those seeking to substantiate a policy of either mandatory or voluntary labelling may find the clarity of their position muddied by evidence from studies that reveal how and why people use product label information. Information is not equally valuable to everyone. A policy about GM food labelling is, in this respect, as much a statement about anticipated value and utility of this information as it is a response to people's declaration about the value and utility of the information.

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4. Health Claims as Credence Attributes: Evidence From the Functional Foods and Nutraceutical Sector in Canada

Deepananda Herath, Spencer Henson and John Cranfield
University of Guelph

Introduction

This study explores the value that producers of functional foods and nutraceuticals perceive from the use of health claims in product marketing, and the extent to which this value is influenced by consumers' ability to verify the reliability of these claims. In so doing, the study addresses prevailing and contrary perspectives on the regulation of health claims, that is, whether such claims are a reliable way to deliver health-related measures to consumers, or are rather the basis of false product differentiation by food firms. Proponents of health claim regulations endorse greater regulatory intervention and, at the extreme, near prohibition of health claims. They argue that incentives are rampant for manufacturers to deceive and/or mislead consumers because the claimed health effects cannot be easily verified by consumers (Freimuth, Hammond & Stein, 1988; Galloway, 2003; International Association of Consumer Food Organizations, 1999; Jarvis, 1983; Silverglade, 1991; Silverglade & Heller, 1997). In contrast, opponents of restrictive regulations argue that providing direct information through product labelling is an effective approach to informing consumers about potential positive health effects that cannot be acquired through pre-consumption information-seeking and/or post-consumption experience (Calfee, 1997; Calfee & Pappalardo, 1991; Ippolitio & Mathios, 1990; Ippolito & Mathios, 1991; Keith, 1995; Steinborn & Todd, 1999).

The argument that firms are ignorant of, or disregard, consumer suspicions of possibly false health claims is not convincing. Why would a firm attempt to persuade consumers via false product differentiation, given the risk of losing market sales upon their discovery of the claim being false? Assuming competitive firms are not "fly-by-night" and/or myopic decision-makers, ignorance of consumer reactions to health claims and other forms of information is potentially detrimental to performance. Indeed, the threat of consumer rejection of products that do not deliver what is claimed would appear to be a strong incentive for firms to be truthful.

We specifically explore whether the motivation for functional food and nutraceutical firms to use different types of claims is consistent with the search, experience and credence characteristics of products[1]. We also explore the related difficulty in verifying the truthfulness of information about various product attributes, and the value of informing consumers about such attributes. If a firm's motivations can be explained by the notion of search and experience characteristics, regulatory policy can be based on a more meaningful premise than that of false product differentiation (see for example International Association of Consumer Food Organizations, 1999) or impulsive accusation. Perhaps the emphasis of regulatory policy should be shifted away from shielding consumers from potentially misleading information towards allowing greater access to meaningful and truthful information about functional foods and nutraceutical products that could improve consumers' overall health and well-being.

Data and Methods

Data from 146 firms was obtained from a 2003 survey of the functional food and

[1] Search attributes are characteristics consumers can examine before buying a product (e.g. price, colour, size). Experience attributes are characteristics that can be evaluated by the consumer after purchase (eg. taste). Credence attributes are factors consumers cannot evaluate even after purchase (eg. methods used to produce a good).

nutraceutical sector conducted by the Small Business and Special Survey Division of Statistics Canada on behalf of Agriculture and Agri-Food Canada. The survey asked respondents to assess the impact of various types of health claims, as well as recent changes to labelling requirements in Canada to more closely match those in the United States. Respondents were asked to assess these impacts in terms of 1) domestic sales, 2) export sales, 3) willingness to conduct research to support health claims, and 4) ability to compete with global competitors. Principal Component Analysis (PCA) was employed to identify a small number of business impact dimensions from the above four potential business impacts. For each of the above claims a sole factor was isolated from the PCA, capturing business impacts in a single dimension. These four factor scores were subjected to k-mean cluster analysis and the resultant two clusters were examined on the basis of the product specialization of the firm.

It was found that one of the two clusters (Group 1) was dominated by firms (n = 53) that specialize in products with "high credence" functional ingredients (related to vascular heart health, diabetes, cancer, gut health, bone health and immune system health) for which the associated health benefits are relatively difficult to verify by consumers. The other cluster (Group 2) was dominated by firms (n = 65) specializing in products with "low credence" functional ingredients (related to weight control, sexual performance, general well-being, level of energy, mental ability and other functions) for which the health benefits are arguably easier to verify by consumers. Perceptions of the business impacts of using different claims, which were captured by the four factor scores, were regressed against a variety of firm characteristics together with the dummy variable to arrive at a firm's "credence intensity" based on its specialized product category.

Results and Discussion

The average importance scores for the business impact of disease risk reduction product-specific claims were statistically significantly higher than the average scores for all other types of claim. This pattern was common across perceived impacts on domestic sales, export sales and the willingness to conduct research to support health claims. This suggests that functional food and nutraceutical firms attached much less importance to structure/function and generic health claims, which are not intended to be exclusive to specific products. In turn, this suggests that firms strive to communicate unique information about their products, while using product-specific claims to differentiate their product from those of competitors.

In view of the above, we should not find systematic differences in importance scores between firms in Groups 1 and 2. Irrespective of the credence intensity of the firm, there is a desire to communicate with consumers about the potential health benefits of products. Mann-Whitney U tests indicated, however, that the importance scores did differ significantly between firms in these two groups.[2] Firms with products having less visible health benefits ("high credence"), and which thus face greater difficulty in

Credence Ratings of Functional Foods and Nutraceuticals		
"High Credence"	Associated health benefits are difficult to verify by consumers	Products related to vascular heart health, diabetes, cancer, gut health, bone health, immune system health
"Low Credence"	Health benefits are easier to verify	Products related to weight loss, sexual performance, level of energy, mental ability, and general well-being

[2] P values for the average score difference for disease risk reduction product-specific claims between Group 1 and 2 were 0.002 for domestic sales, 0.000 for export sales, 0.000 for willingness to conduct research to support health claims and 0.000 for the ability to compete with global competitors.

communicating the associated health benefits to consumers, had higher importance scores for every type of claim. Further, the average importance scores for ability to use product-specific claims were generally highly significant and much larger than those observed for generic and structure/function claims. This suggests that firms with products providing health benefits that are not easy to verify place a much greater value on the use of claims to communicate with consumers compared to firms with products that offer more easily verifiable health benefits. This suggests that health claims are more likely to be used to communicate the real potential health benefits of functional foods and nutraceuticals rather than being the basis of false product differentiation.

"Firms with products providing health benefits that are not easy to verify place a much greater value on the use of health claims to communicate with consumers compared to firms with products that offer more easily verifiable health benefits."

Multiple regression analysis was used to explore whether other firm attributes were systematically associated with the importance of being able to use these four types of claims. The significant association between the importance of these claims and the degree of difficulty in verifying the health benefits of products, as described above, remained after controlling for other firm characteristics. Specifically, we used the factor scores from the PCA as dependent variables in four regression models. These indicated that the observed variation in the factor scores was reasonably well explained for a cross-section data set.[3] The *p*-value for the null hypothesis that the estimated parameters in each model were jointly equal to zero was rejected for all but the model explaining the factor scores related to the alignment of Canadian labelling regulations with those of the United States. Except for the dummy variable (*credence*) for firms in Group 1, none of the firm characteristics had a consistent relationship with the factor scores. However, some notable patterns did emerge.

The number of employees in a firm had a significant and inverse relationship with the factor scores related to alignment of Canadian labelling regulations in comparison with those of the United States. This result suggests that small Canadian functional food and nutraceutical firms did not feel harmonization with the United States' standards would prove beneficial to their business. This is perhaps unsurprising, since smaller firms are more likely to focus on the domestic market or to have already targeted specific export markets and have adjusted to differing labelling regulations accordingly.

Firms involved in retail activities had a negative perception of the impact of generic health claims on their business; the coefficient on this variable for the generic health claim regression model was negative and significant. This may reflect concerns that generic health claims will encourage the entry of new firms into the functional foods and nutraceutical sector, thus increasing market competition. Ownership structure did not appear to be an important factor, with only the coefficient on the private corporation dummy variable being significant in the disease risk, generic health and structure/ function claim models. However, this result does suggest that private corporations have positive perceptions of the impact of all three claim types on their business.

The use of particular distribution channels had a limited influence on the perceived business impact of health and nutrition claims. The coefficient on the dummy variable for firms who sold directly to customers was negative and significant in the structure/ function claim model, thus suggesting that these firms would be adversely impacted by the ability to make such claims. Again, the ability to make structure/function claims could attract firms into the functional foods and nutraceuticals sector, enhancing market competition and, potentially, a loss of market share for existing retail firms as other distribution channels are established. In partial support of this notion, the coefficient on the dummy variable for firms who sold through retailers/wholesalers was positive and significant in the disease risk and generic health claim models. Use of disease risk and generic health claims were perceived by these firms to have a positive impact on their business.

[3] The R^2 of the models ranges from 0.15 to 0.19.

The coefficient on the *partnership* dummy variable was positive and significant in the model for harmonization of Canadian labelling requirements with those of the United States, suggesting that firms in partnerships saw potential benefits. It may well be that participation in a partnership allows firms to develop experience and/or human capital which enables them to realize the potential benefits to trade in functional foods and nutraceuticals from harmonized labelling standards. The dummy variable representing firms with a product line addressing more than one disease state was negative and significant in the structure/function claim model. This suggests that these firms perceived that the ability to make structure/function claims would have a negative effect on their business, perhaps reflecting the fact that structure/function claims tend to focus on single disease states and are thus of less utility to firms that market products targeting multiple diseases.

Conclusions

The literature on regulation of health claims explores a range of associated business and market impacts, but lacks a coherent framework in which to understand the motivation of firms to use health or nutrition claims. In this paper we employ a search, experience and credence characteristics approach to help explain why firms might use claims in the absence of regulations: are such claims the basis of false product differentiation or a legitimate attempt to communicate the potential health benefits of products to consumers? The model underscores the trade-off between costly provision of a claim and the consumer's ability to verify any claims that are made. The conditions under which firms will rationally make claims are explored and related to the search, experience and credence characteristics of the health or nutrition benefits embodied in their products. The model suggests that the perceived business gains from the ability to use claims are systematically associated with the degree of difficulty consumers face in verifying such claims. This suggests that health and nutrition claims are driven more by attempts to communicate the potential longer term health benefits of products than by false product differentiation.

"The results of the study suggest that health and nutrition claims are driven more by attempts to communicate the potential longer term health benefits of products than by false product differentiation."

The ability of consumers to screen products and verify the associated health claims should play an important role in shaping the regulation of claims. Once the safety of a functional food or nutraceutical has been satisfactorily demonstrated, the market mechanism can play an important role in disciplining the use of health and nutrition claims where these can be easily and relatively cheaply verified through consumption experience. To date, the important function of information provision and assimilation by market participants (for example though the Internet and the media) has not been adequately appreciated in policies addressing the use of health and nutrition claims. The findings of the study reported here suggest that regulatory priorities could be set according to the level of credence intensity of the potential health benefits of a functional food or nutraceutical product. Perhaps such an approach could be based on the grouping of products according to the ease with which consumers can verify the purported health benefits, and regulatory priorities established accordingly. It is clear that functional food and nutraceutical firms are not ignorant of the ability of consumers to verify the claims that they make. Thus, we might expect that false product differentiation will occur in the limited cases where the potential health benefits can not be verified by consumers. In such cases there is a more pressing case for rigorous regulation in the pursuit of consumer protection.

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5. Understanding Consumer Acceptance of Functional Foods and Nutraceuticals

Andreas Boecker, Getu Hailu, Spencer Henson and John Cranfield
University of Guelph

Introduction

Diet-related diseases that impose high costs on society and reduce quality of life prevail in high-income societies. In addition to changes in lifestyle and eating habits, incorporating functional components into foods and other products is considered a promising route to reducing the burden of diet-related diseases. Functional foods and nutraceuticals can be directed at reducing the risk of disease and/or curtailing existing health problems. The steady increase in the size of the markets for such products worldwide, but particularly in the United States, European Union and Japan, reflects both increasing consumer interest and a major business opportunity for the food and life science industries. Although the Canadian market for functional foods and nutraceuticals is in its relative infancy, it is expanding rapidly and providing valuable opportunities for Canadian agri-food and bio-product companies (Agriculture and Agri-Food Canada, 2004).

At the same time, however, relatively little is known about the acceptance of, and reservations toward, functional foods and nutraceuticals among the Canadian population. Although there is a growing body of literature, in particular relating to the United States and European markets (see for example Cox, Koster & Russel, 2004; Moon, Balasubramanian & Russel, 2005; Verbeke, 2005; Verbeke, 2006), policy-makers and industry leaders in Canada have to make strategic decisions regarding the development of the functional foods and nutraceuticals sector with incomplete information on the demand side (an exception is Peng, Wang & West, 2006). For example, key questions remain over how consumers judge the efficacy and risks of these products, and how they make trade-offs between functional properties and other salient characteristics. More particularly, the role of information (e.g., the information available on labels) and trust in different sources of information have not been investigated in the slim body of research that is available on the Canadian market. Ideally, consumer acceptability should be incorporated at a very early stage into the development and commercialization of new product groups and technologies, which is problematic when we know so little about the Canadian consumer!

Hence, the overall aim of the project is to contribute to an enhanced understanding of the nature of consumer acceptance of functional foods and nutraceuticals in Canada. More specifically, based on the research results of the first stage of this project, the objectives are:

1. To quantify the interrelationships and trade-offs between the perceived benefits and risks associated with products containing functional components;
2. To assess the impact of factors determining consumers' decisions to purchase products containing functional components;
3. To quantify the trade-off that consumers make between functional properties and other characteristics of products, in particular price and information; and,
4. Determine the consequences of the above findings for the future development and marketing of functional foods and nutraceuticals in Canada.

As detailed in the next section, we used consumer surveys to gather the data needed to address these objectives. The specific functional components and health conditions being investigated are peptides for the treatment of hypertension, lycopene to reduce the risk of colon cancer, probiotics to improve digestive health and isoflavones to reduce the risk of heart disease.

Methods

The first stage of the project involved qualitative research methods, in particular focus groups, to identify possible concerns and the ways in which the risks and benefits associated with functional foods and nutraceuticals are perceived by consumers. Based on the results of the first stage, a survey tool was designed to enable us to assess both the factors determining individual choice and the evaluation of, and trade-offs between, functional properties and other characteristics of the products. Having both types of data for each respondent allows for an assessment of how individual characteristics influence attribute assessment and trade-offs.

Functional Food Ingredients

Investigated	Health Condition Addressed by the Product
Peptides	Hypertension
Lycopene	Colon Cancer
Probiotics	Digestive Health
Isoflavones	Heart Disease

The first part of the questionnaire addressed the factors influencing individual product assessment. Based on protection motivation theory, which belongs to a wider group of behavioural intentions models developed in cognitive psychology, two concepts are identified as of central importance, namely threat appraisal and coping appraisal. For the questionnaire design, these concepts were broken down further into groups of variables or questionnaire items. With respect to threat appraisal, these variables capture perceived vulnerability and the severity of the disease state a particular functional component is directed at – either in therapy or in prevention. Variables with respect to coping appraisal reflect the individual's perceived response efficacy (that is, the effectiveness of the product) and perceived self-efficacy (that is, the extent of control one has over one's own health in general and over applying the product as recommended).

Attributes Influencing Consumers' Choice of Functional Food Products

- Source of ingredient (plant, animal, mineral)
- Mode of delivery (drink, snack bar, yogurt, pill)
- Health claims/ information
- Price
- Regulatory approval

The second part of the survey used a conjoint design to elicit consumer evaluation of single product attributes and the interdependencies between these. The product attributes investigated were: 1) the material source of the functional ingredient; 2) the mode or product form in which the functional ingredient is delivered; 3) health claims about the functional ingredient; 4) sources of information about these claims; and 5) prices. Discrete-choice modeling based on random utility theory has become a standard in this type of stated-preference analysis. We employed traditional ranking or rating-based conjoint analysis combined with a statement on the respondent's purchase intentions for each of the product profiles. This reflects the expectation that most respondents would be unfamiliar with the choice situation. In light of this hypothetical bias, we judged that a more thorough consideration of all product attributes would be needed for respondents to rate and rank all product profiles.

Results

The data were collected through mall intercept surveys by face-to-face interviews in three waves over the period February 2006 to February 2007. At present, preliminary results are available for the peptides and probiotics surveys.

In the peptides survey, 196 questionnaires were completed in February 2006. The conjoint analysis investigated nine specific product profiles that were varied across four attributes with the following attribute levels. The product form or mode of delivery either was a non-prescription pill, a drink or a snack bar. The price was expressed as cost per week either at $10, $12 or $14. The product profiles described the sources of peptides as either from plants in general, from milk or from fish oil. Finally, the level of regulatory approval was described as either approved or as not required.

One key finding of the research points to the general difficulty of applying psychometric concepts in empirical research. Because measuring a concept with a single item yields low levels of reliability and no opportunity for cross-checking with other variables, multiple item scales are usually used in data collection which are then subjected to reliability analysis. We used the same four items to measure self and response efficacy for all three delivery modes. While collapsing all 12 items to a single average or summated scale yielded the highest score on the reliability measure Cronbach α, factor analysis suggested a different data structure that yielded lower but still satisfactory Cronbach α levels. In this "solution," the response efficacy items for the drink and snack bar options formed one group and were seen as separate from the response efficacy items for pills on the one hand, and from the self-efficacy scores across *all* three product formats on the other. The interpretation of this finding is that respondents clearly differentiated between the effectiveness of different product forms but judged their self-efficacy independently from a specific product form, at least for those considered in the conjoint analysis.

Classical conjoint analysis produced a pragmatic measure of relative importance for each attribute investigated. Although this measure is influenced directly by the (number of) attribute levels chosen for each attribute, it gives a first indication of how much weight an attribute has in the respondents' ranking decisions. In this analysis, product form was the most important attribute (with a weight of 34%) followed by cost per week (23%), source of peptides (22%) and regulatory approval (21%). Based on the average scores of the part-worth utilities for the three product forms across the whole sample, the drink was most preferred and fairly closely followed by the snack bar, while the pill was clearly the least preferred mode of delivery. Further, plants in general were preferred over milk, while milk was preferred over fish oil, as protein sources.

In a final step, a cluster analysis was performed on the individual estimates of the part-worth utilities for the 11 attribute levels included in the analysis. Four different segments were identified with clear preferences for a particular attribute level. The single largest segment (n = 73) placed a very high value on the presence of regulatory approval. Interestingly, this group was the only one that, simultaneously, placed a negative value on milk as a protein source. Food allergies, lactose intolerance or previous experiences might be the cause for this combination of preferences and thus should be considered in future empirical research. The second largest segment (n = 67) was most concerned about the preference for a particular product form. They had the strongest preference for the drink and, simultaneously, disliked the pill. Of the two smaller segments, the slightly larger one (n = 29) was the most price conscious, while the smallest one was identified via their evaluation of the protein source. These 27 participants disliked fish oil in this regard and had the highest preference for plants in general as the source of peptides. However, the link between these four segments with socio-economic, demographic and psycho-graphic variables was weak at best. In particular, the various protection motivation variables did not show any significant differences in means between the four segments.

In the probiotics survey 331 questionnaires were completed in October/November 2006. The conjoint analysis investigated nine specific product profiles that were varied on four attributes with the following attribute levels. The product form or mode of delivery either was a non-prescription pill, a yogurt or ice cream. The price was expressed as cost per month either at $8, $12 or $16. The product profiles also mentioned a health claim combined with a source of information for that claim. The claim was either "contributes to reduced risk of colon cancer," "promotes resistance to bacteria which can cause food poisoning" or "contributes to general well-being." The sources of information on the label were either from "an organization representing

product manufacturers," "label verified by government" or the "manufacturer of product."

The analysis of the probiotics data involved the same challenges concerning the right choice of efficacy items within the protection motivation theory variables as in the peptides analysis. Also, the empirical measures of relative attribute importance had the same direction as in the previous analysis. Product form was the most important attribute (with a weight of 40%), followed by type of health claim (23%), cost per month (19%) and source of information (21%). Based on the average scores of the part-worth utilities for the three product forms across the whole sample, yogurt was clearly most preferred, followed by ice cream and then the non-prescription pill. The average part-worth utility scores for the health claims referred to different combinations of probability and benefits as the inverse of the severity of disease states. Thus, "promotes resistance to bacteria causing food poisoning" scored low on probability and high on potential benefit, as did "contributes to reduced risk of colon cancer." The scores for benefits were considerably higher than we anticipated they would be. *A priori*, we would expect these claims to be rated more positively and to be closer to one another in respondent evaluations than the third claim "contributes to general well-being," which scored high on probability but fairly low on potential benefits. Overall, however, the reduction of colon cancer risk was valued highest, followed by the contribution to well-being, with increased resistance to pathogens being valued least. This supports the observation of previous studies on risk perception – that risk assessment by lay people involves more than the dimensions of likelihood and severity such that the wording of a claim may produce unanticipated responses. Finally, and as expected, government was the most trusted source of information, while the manufacturer was trusted least. However, the industry organization representing manufacturers was rated at an intermediate or neutral level, pointing to a more positive reception of industry-wide efforts and initiatives.

"We would stress that the appreciation of different attributes is not homogeneous among consumers. Consumers differ in both appreciation of attributes and in their assessment of labels and information sources."

Discussion

We do not know precisely how the hypothetical situation in which respondents were asked to make product rankings and to state purchase intentions may have impacted the role of the individual attributes in their stated preferences. It is almost certain that price is undervalued in such situations. However, the results of both studies clearly identify the mode of delivery as the single most important attribute for stated preferences, while costs or price followed as a distant second, at best being roughly of equal importance as the other two attributes.

From these results we can infer that consumers are willing to trade off price for other desired attributes. In particular, information that reduces uncertainty about the product's safety and efficacy must be taken into consideration. In the case of the peptides study, it was the label indicating that a product had regulatory approval that was valued highest by the single largest segment. The demand for government intervention or involvement in the authorization, distribution and monitoring of functional foods and nutraceuticals was also expressed in the probiotics study, where the government was by far the most trusted source of information. However, with regard to the precise wording of health claim labels, the results of the probiotics study call for a case-by-case approach. While it is obvious that unproven or unrealistic claims have no place on such labels, any regulating body, as well as industries or companies making claims, must be aware of the additional perceptions and valuations consumers associate with specific words or phrases. Although our study was not intended to analyze the wording of health claims in detail, the results of the probiotics study illustrate how consumer perceptions and evaluation of a claim may deviate from that of a more technical assessment of likelihood and severity of the described effect. To

avoid unjustified positive associations that may result from emotional advertising, we recommend that regulators subject proposed claims to an intensive pre-test with consumers.

Finally, we would stress that the appreciation of certain attribute levels is not homogeneous among consumers. Rather, as shown by the greatly differing values placed by sub-groups on attribute levels in the peptides study, consumers differ both in their appreciation of attributes and in their perception and assessment of labels and information sources. The lack of clearly corresponding differences in socio-economic, demographic or psychographic characteristics, however, makes it difficult to design and manage information campaigns in the fragmented markets for nutraceuticals and functional foods. Regulating bodies have to be aware of this and should respond, perhaps, by keeping publicly-financed and initiated communication at the most general levels and by considering closely the possibilities and potentials of industry self-governance for more specific aspects of communication.

"As expected, government was the most trusted source of information, while the manufacturer was trusted least. However, industry organizations were rated at an intermediate or neutral level, pointing to a more positive reception of industry-wide initiatives."

Conclusions

The project has provided a rich data set on individual perceptions and evaluations of a variety of functional foods and nutraceuticals. These data provide detailed insight into how consumers make trade-offs between functional and other product characteristics and their response to different information regimes. However, the data analysis also reveals two areas where additional research is needed. First, the lack of correspondence between individual characteristics and preferences for product attributes suggests future consumer studies need to be based on a more complete understanding of health-related behaviour. In particular, valid instruments for measuring health involvement and relevant personal experiences need to be developed. The same applies to the linkages between consumption of food in general, consumption of functional foods and nutraceuticals, and other health-related behaviors. Second, the unanticipated order of the valuation of health claims calls for closer investigation of wording issues in labelling regulation. More particularly, the interaction with news and media reports, advertising, other information sources have to be taken into consideration to assess the potential impacts of labels on consumer choice.

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6. Popular Representations of Science, Research and Technology

Timothy Caulfield and Tania M. Bubela
University of Alberta[1]

"First we explored how research on homeopathy is presented in peer-reviewed journals. Our sample included 251 articles published in English over the past 10 years."

Introduction

There is growing recognition that popular representations of science, research and technology can have a profound impact on public perceptions, policy development, and implementation and utilization of new products and technologies. The popular media plays a particularly important role in shaping public views and has emerged as one of the most significant sources of scientific information for both the general public and health care professionals (Geller, Tambor, Bernhardt, Rodgers & Holtzman, 2003). Media portrayals can have an enduring impact on how the public frames social issues and even influence research agendas. Indeed, in a recent report, the United Kingdom Royal Society (2006) called for the scientific community to consider the public interest when communicating scientific results, suggesting that "Many of the biggest controversies in science over the past few years have arisen at least partly from problems in the process of communicating research results to the public" (p. 4).

Given the role of popular representations as a key part of the knowledge translation process, our research team thought it essential to explore their accuracy and tone. In addition, we wanted to investigate social forces that may impact the nature of the science communication processes, particularly the role of commercialization pressures. There is a growing body of literature on how the media covers biotechnology, particularly in the areas of genetics and stem cell research (e.g., Bubela & Caulfield, 2004; Geller et al., 2003; Nisbet & Lewenstein, 2001). This work has found that though media coverage is often less than ideal, frequently relying on oversimplification of important scientific concepts, it is usually relatively accurate and error free. However, key information is often left out, including information about risks, conflicts of interest and funding sources – all information that can impact the perceived credibility of the research.

Much of our AFMNet work focused on complementary and alternative medicines (CAM), such as homeopathy and herbal remedies. The socio-economic forces relevant to these areas differ from those in conventional biomedical research. As such, we felt that research on communication issues in this context would produce some interesting comparisons. In addition, the use of CAM is a significant economic and health care phenomenon. The CAM industry is a $30 billion a year business in the United States alone, and use of CAM in Europe and North America has increased significantly in recent years (Park, 2005). For example, a 1998 phone survey of 1539 adults in the United States found that 42.1% of respondents had used at least one CAM within a 12-month period and that usage had increased since 1990. The most common treatments were herbal remedies, massage, megavitamins, self-help groups, folk remedies, energy healing and homeopathy. In 2003, 20% of all Canadians visited a CAM practitioner, up from 15% in 1994–95 (Park, 2005).

Methodology

We used a variety of different approaches in our projects First, we explored how research on homeopathy is presented in peer-reviewed journals. We started with

[1] Project team: Timothy Caulfield, Canada Research Chair in Health Law and Policy, Health Law Institute, University of Alberta (Project Leader); Tania Bubela, School of Business, University of Alberta; Ubaka Ogbogu, Research Associate, University of Alberta; Suzanne Debow, Kanchana Fernando, Megan Koper and Thomas Moran, Research Assistants, University of Alberta.

this project for several reasons. Homeopathy is a popular CAM and there have been numerous clinical trials published in a variety of biomedical and CAM journals. The efficacy of homeopathy is highly contested and, as such, it seemed an ideal CAM to study for a publication bias. Literature searches were performed using a variety of standard biomedical online databases. All articles published in English over the past ten years were included. Our search yielded 251 articles overall, of which 46 systematically examined the efficacy of homeopathic treatment. We categorized the overall results of each paper as having either "positive" or "negative" outcomes depending on the reported effects of homeopathy. We also examined and compared 15 meta-analyses and review articles on homeopathy to ensure our collection of clinical trials was reasonably comprehensive.

Our second and larger study sought to explore more directly how knowledge is translated in the socio-economic-political context of CAM. Specifically, we were interested in the nature of the information provided by clinical trials and the media and how this might impact decision making regarding the use of CAM versus conventional pharmaceuticals. We also examined the reporting of conflicts of interest and industry funding of research.

"Our second and larger study examined reports of herbal remedy clinical trials in 73 newspapers from across Canada, the United States and the U.K."

We first searched for reports of herbal remedy clinical trials in newspapers between 1995 and 2005 from Canada, the United States, and the United Kingdom. We then narrowed our results to include only those newspaper articles that discussed the results of at least one identifiable clinical trial and attempted to locate the results of those trials as published in the academic literature. Our final sample included 58 clinical trials and 388 newspaper articles published in 73 different newspapers from across Canada, the United States, and the United Kingdom.

Using a coding frame similar to that used in Bubela and Caulfield (2004), we first examined the clinical trial reports in the medical literature to assess the quality of the clinical trial, reporting of efficacy and risks, disclosure of funding information and conflicts of interest, as well as overall tone. We then compared the newspaper articles to their corresponding reports in the medical literature to assess how the same information was portrayed to the general public. Newspaper articles were also rated on the basis of technical accuracy and level of exaggeration.

It is important to note that we took a very broad view of what constitutes a conflict of interest in assessing if a conflict was present. Specifically, we considered a conflict of interest to exist 1) if a researcher declared a personal conflict of interest (a minority of cases), 2) if the research was funded by a pharmaceutical or other company that manufactured the herbal remedy in question and 3) if industry researchers were members of the research team. Future research will parse these categories so that the influence of industry funding can be distinguished from conflicts of interest declared by researchers.

Results and Discussion

The homeopathy study found that a considerable difference exists between the number of clinical trials showing positive results published in CAM journals compared with traditional biomedical journals (Caulfield & Debow, 2005). Forty-six peer-reviewed articles published in a total of 23 different journals were compared (26 in CAM journals and 20 in conventional journals). Of those in conventional journals, 69% reported negative findings compared to only 30% in CAM journals. Very few articles presented a negative tone, and most used neutral or unbiased language.

These results suggest that a publication bias against homeopathy exists in mainstream journals. Conversely, the same type of publication bias does not appear to exist between review and meta-analysis articles published in the two types of journals.

These results suggest that a possible publication bias exists in the homeopathic literature. It is interesting to note that other studies have found, in the context of industry supported biomedical research, a bias toward the publication of positive results (Council on Scientific Affairs, 2004). While preliminary, our research highlights another piece of the knowledge translation picture – that socio-economic forces can impact what is published in peer-reviewed publications.

Though the analysis of the data from the herbal remedies project is continuing, some interesting conclusions can be reported (for preliminary papers, see Bubela, Caulfield & Boon, 2006; Koper, Bubela, Caulfield & Boon, 2006). First, the media reporting on CAM does not seem to be closely tied to the number of clinical trials. The fact that many commentators have noted the high level of media coverage of CAM may indicate that most CAM stories are not based on experimental evidence and instead tend to be what one former CAM journalist for a women's magazine termed "feel good" and "lifestyle" articles (Bowerman, 2004). This again highlights that CAM reporting is driven by social forces that differ from those associated with conventional biomedical research.

Factors Determining Conflict of Interest in Biomedical Product Research

- Researcher declares a personal conflict of interest
- The research was funded by a company involved in the manufacture of the product
- Industry researchers were members of the research team

A second major finding is that the media significantly under-reports the risks associated with CAM and is more likely to report on clinical trials with negative results. It is difficult to ascertain whether this apparent bias toward the reporting of negative trials is a reflection of a greater number of negative trials being published in conventional medical journals, the main source of the information in newspaper articles. However, it should be noted that an under-reporting of risk is consistent with other areas of science reporting but the emphasis on the negative seems somewhat unique (Bubela & Caulfield, 2004). Consumers, who often self-administer CAM, are not being provided with information sufficient to make informed choices about treatment alternatives.

Finally, a preliminary analysis of the data indicates that the overall tone of the article varied depending on whether a conflict of interest was made apparent. Newspaper articles that discussed conflict of interest were less likely to portray the herbal remedy as beneficial and more likely to report a higher level of potential risk associated with the treatment. This latter finding is particularly significant, given the general tendency of newspaper articles to under-report risks in the context of CAM as well as other biological research. In addition, the study provides another piece of information about the impact of commercial involvement on reporting. A perceived involvement with commercial interests has an adverse impact on the credibility of the research and the opinions of the researcher (Caulfield, Einsiedel, Merz & Nicol, 2006).

In sum, there is a welcome trend toward evidence-based medicine in the application of herbal remedies. This trend, however, is not necessarily reflected by mainstream news media in Canada, the United States and the United Kingdom. In the media coverage of herbal remedy clinical trials a subtle trend toward the reporting of negative results is evident. In addition, newspaper articles do not provide readers with adequate information to assess the quality of the trial and its outcomes. The next steps in this study on knowledge translation in a biomedical context will be to compare media coverage of CAM with coverage of conventional pharmaceuticals used to treat the same medical conditions as those covered in the present study on CAM.

Conclusions

This project provides additional information about the nature and source of both popular representations and media reports of research. This work also informed our conceptual work on the nature of biomedical reporting (e.g., Caulfield, 2005). Below are some key conclusions and policy recommendations:

- Both peer-reviewed publications and media reports are influenced by forces

other than the quality and value of the research.

- Efforts should be made to ensure that conflicts of interest and funding sources are appropriately disclosed in peer-reviewed publications. When possible, these should also be disclosed in media reports.
- Researchers, funding agencies and the media should work together to develop a science communication strategy that provides the public with the information necessary to make informed choices about health care alternatives.

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"Efforts should be made to ensure that conflicts of interest are appropriately disclosed in peer-reviewed publications and, when possible, in media reports."

7. Natural Health Product Regulations: Perceptions and Impact

Heather Boon and Natasha Kachan
University of Toronto[1]

Introduction

New regulations governing the manufacture, packaging, labelling, importation and sale of natural health products (NHP) in Canada became law on January 1, 2004. NHPs are defined as products derived from plant, animal or mineral sources (and not significantly modified) that are promoted for a medicinal purpose including the treatment or prevention of a disease or disorder. Examples include herbal medicines, vitamins, minerals, probiotics, homeopathics and traditional medicine. Tobacco, marijuana, products currently categorized as biologics (e.g., blood-based products and insulin) and any product sold in an injectible formulation are specifically excluded from the NHP category. All NHPs must be shown to be safe for direct consumer use, i.e., without any intervention from a health care practitioner.

The NHP regulations specifically define good manufacturing practices and the information required on labels. Manufacturers, packagers, labellers and importers were required to apply for site licenses by December 31, 2005. In addition, each specific product requires a product license. For those products already for sale in Canada on January 1, 2004, product licensing applications are due sometime prior to December 31, 2010, based on a schedule provided by the Natural Health Products Directorate (NHPD) of Health Canada. Pre-approval of licenses is needed for any new product introduced to the Canadian market. The license applications must provide details of the safety and efficacy of the product so that these can be assessed by Health Canada.

The Canadian NHP regulations are unique and it is not yet known how they will affect the public's use of these products. As such, the overall objective of this research program was to begin to assess the regulations and their impact on a range of stakeholders. The research, which represents one phase of a larger initiative, consisted of three specific projects, each with its own set of objectives.

Project 1 – Industry Compliance

The objectives of this study were to 1) identify which firms are complying with Canada's new NHP regulations (for example, by submitting their product licensing applications on time), 2) explore the factors that affect regulatory compliance and 3) investigate compliance motivations.

Project 2 – Practitioners' Perceptions

The objective of the second project was to explore the perceptions of complementary and alternative medicine (CAM) practitioners concerning how the new regulations may affect their practices and their relationships with patients and consumers.

Project 3 – Legislative Processes

The objectives of the third project were to 1) compare and contrast the legislative schemes for the current regulations and a proposed amendment to them, Bill C-420, and 2) examine the political processes that led to the creation of the regulations and

[1] Project Team: Heather Boon, Leslie Dan Faculty of Pharmacy, University of Toronto (Project Leader); Jillian Clare Cohen, Leslie Dan Faculty of Pharmacy, University of Toronto; Natasha Kachan, Project Manager, University of Toronto; Hina Laeeque and Karen Moss, Research Assistants, University of Toronto; Timothy Caulfield, Tracey M. Bailey and Jane Steblecki, Health Law Institute, University of Alberta.

proposed amendment, identifying in particular party stances.

Methodology

The research program used a multi-method approach combining qualitative and quantitative methods. Key methodological components were focus groups, key informant interviews, and documentary analysis of legislation, regulations and market surveillance.

Project 1

To assess compliance, twenty interviews were conducted with representatives from Canadian firms involved in the manufacture of glucosamine or chondroitin products. These were among the firms required by the NHP regulations to meet the first compliance deadline. The structured interviews focused on the firms' level of satisfaction with the regulations and their perceptions of compliance and non-compliance. Data from the interviews was coded, using qualitative content analysis. Team meetings were held after every three to four interviews to discuss emerging themes.

Project 2

Qualitative interviews with 37 Canadian leaders from four CAM groups that use natural products as a core part of their practice were conducted in the fall of 2004. The four CAM groups represented were naturopathic medicine, traditional Chinese medicine, homeopathic medicine and Western herbalism. The interviews were transcribed verbatim and coded independently by a minimum of two investigators using qualitative content analysis.

Project 3

To investigate the legislative processes involved, researchers conducted a legal documentary analysis of the NHP regulations and the proposed amendment, Bill C-420. In addition, political debate around these pieces of legislation was identified from House of Commons records, including Question Period transcripts, statements by Members, Petitions by Members; records from the House of Commons Standing Committees on Health; and Senate records from the Oral Question Period. These records were compared and contrasted along party lines.

Highlights of the New Canadian Natural Health Product Regulations (2004)

- Product must be shown to be safe for direct consumer use
- Producers must meet established manufacturing standards
- Producers must demonstrate the safety and efficacy of the product
- Product license required for each existing product by December 31, 2010
- Pre-approval of license applications by Health Canada required for all new products
- Site licenses required by all NHP manufacturers, packages, labellers and importers

Results

Project 1

The key finding from Project 1 was that a majority of the companies interviewed (17 out of 20) were at least partially compliant with the NHP regulations. Only small and medium sized enterprises (SMEs) were either non-compliant or under-compliant, in comparison with large companies which were either semi- or fully compliant[2] Qualitative content analysis enabled the identification of factors that contribute to regulatory compliance, including perceptions and knowledge of the regulations and business size. Perceptions of compliance among competitors did not affect firm compliance. For example, although large firm representatives felt that industry competitors were not complying, and that enforcement of the regulations would not be likely, these firms were nonetheless compliant. Findings also show that the rationale for compliance differs for large enterprises compared with SMEs. Large firms are motivated to comply with the regulations because of social motivations, ability to comply, the desire to maintain a competitive market advantage and the deterrent fear

[2] Firms were defined as non-compliant that failed to submit a product licensing application (PLA) by the deadline date, as under-compliant that submitted a PLA after the deadline date, as semi-compliant that submitted some of the company PLAs by the deadline, and as fully compliant that submitted all PLA by the deadline.

of negative media coverage. By contrast, SMEs are motivated to comply due to the deterrent fear of prosecution and a sense of duty. An unintended consequence of the NHP regulations suggested by our findings, which may result in a significant change in the structure of the NHP industry, is that the majority of people interviewed expressed concerns about the ability of SMEs to comply with the regulations due to the costs associated with doing so.

Project 2

Three key findings emerged from the data on practitioners' perceptions. First, all CAM leaders were concerned with the issue of their own access to natural health products. Second, all of the CAM groups, with the exception of the homeopathic leaders, specifically indicated a desire to have a restricted schedule of NHPs. Third, only naturopathic leaders were concerned that the NHP regulations could potentially endanger patients if they self-medicate incorrectly. Additional analysis focused specifically on the Western herbalists. As the NHP regulations establish "good manufacturing practices," Western herbalist leaders are concerned that many small companies will find the regulations too costly to implement, causing them to reduce the number and diversity of the products they manufacture, or go out of business altogether. Furthermore, lack of availability of whole plant products could severely restrict the practice of Canadian Western herbalists. In response to this challenge, herbalists are attempting to organize as a more cohesive group to define their unique body of knowledge and increase the perceived legitimacy of their practices in the eyes of the public, conventional health care practitioners, and regulators.

"A majority of the companies interviewed were at least partially compliant with the NHP regulations. Factors contributing to regulatory compliance include business size (large enterprises were more compliant than small ones) and knowledge of the regulations."

Project 3

The success of the NHP regulations and the likelihood of their being adopted as a model were directly threatened by Bill C-420. If Bill C-420 had been brought into force it would have changed the *Food and Drugs Act's* definition of food and drugs as well as repealing the Act's current health claims prohibition, raising serious problems for interpretation and application of the regulations. Notwithstanding these significant implications, our documentary analysis found that the parliamentary debate did not consider the broad merits and risks of this amendment. Rather, the debate focused on the appropriateness of classifying NHPs as foods for the purpose of enabling consumer access. On this point, the political parties were largely in agreement that amendments to the current regulatory scheme were required to improve consumer access. The divergence noted across party lines was relatively minimal and was restricted to how such amendments should be framed so as to best balance consumer access with consumer protection. While some suggestion was made that the Act be amended so that NHPs fall within an entirely new and distinct category, the scheme of classification as proposed by Bill C-420 was largely supported. In fact, a substantial fraction of the party in opposition to the party responsible for introducing Bill C-420 voted in favour of the bill passing second reading. Since the completion of this analysis, Bill C-420 was defeated in the Commons Standing Committee on Health.

Discussion

This project highlights the importance of assessing the impact of new policy decisions on the end users. Often research is conducted prior to making a policy decision, but then once the decision is made, there is little interest in additional research. Our work provides feedback to those who are implementing the regulatory changes so that the process of implementation can be adjusted to enhance the likelihood of compliance, which as our results indicate, is highly dependent on knowledge and understanding of what is expected.

Our work also highlights the gap between regulations as written in law (almost no one

we talked to had actually read the formal legislation) and the policy documents created to aid interpretation and compliance. The drafting of regulations is only the very first step in a long and complicated process of changing a system as large and diverse as that involved in the manufacturing, labelling, packaging and importing of NHPs in Canada. This project allows us to identify strategies that are working and areas where new ideas are needed.

The NHP Directorate consulted widely during the drafting of the regulations and this has proven to be an extremely effective strategy. It helped to ensure that the new regulations are perceived to be necessary, the product of consultation and therefore relevant to the industry being regulated and at the same time meeting the needs of those they are supposed to protect – Canadian consumers. Many people we talked to, especially from medium and large NHP companies, were involved in some kind of consultation exercise, and in many cases their knowledge of the regulations came at least partially from their participation in creating them. However, it was obviously not possible or practical to engage everyone in consultation. Small companies, and to some extent CAM practitioners, felt left out of the process of designing the regulations. And it was among these groups that we found either a lack of knowledge or some degree of misunderstanding about the substance of the regulations. Although wide consultation is to be encouraged, it is not a way to ensure that all constituents are aware of new policy changes.

"Western herbalist leaders are concerned that many small companies will find the regulations too costly to implement, causing them to reduce the number of products they manufacture or to go out of business altogether."

Guidance documents that interpret the new regulations in practical terms were found to be helpful by most of the large company representatives we spoke with, but assumed a baseline level of knowledge that was not often present in the smallest companies in the sector. The guidance documents were focused on things like how one would apply for a site or product license. CAM practitioner groups also found them to be of little help for example in interpreting how the federal product regulations interface with their professional scopes of practice as set out in provincial legislation. This concern is just now beginning to be addressed through focused discussions with specific groups who perceive potential unexpected impacts from the regulations on their ability to practice.

Finally, the key to acceptance of and compliance with new policies such as the NHP regulations is knowledge of what is expected. Those industry members with the greatest level of understanding were the most likely to be in compliance, while the CAM practitioners with the best understanding were the least likely to be worried about negative impacts to their practices. Thus it appears that a key to implementing any policy change is widespread knowledge translation.

Summary of Recommendations

1. Wide consultation to inform policy development will help to increase the knowledge and ability to comply with newly formed policies.
2. Guidance documents that provide practical interpretation of new policies are necessary.
3. Focused discussions with groups who perceive that they are impacted by the new policies are required.
4. The key to implementing policy change is effective knowledge translation.

Conclusion

Although most people agree that some form of regulation for NHPs is necessary, there are a variety of concerns about how the new standards will affect Canadians. The initial stage of implementation has been marked by a degree of confusion and apprehension about what is going to happen. As the implementation continues,

however, we will continue to explore the actual impact of the regulations on a variety of stakeholders to determine how the rules are affecting the public's use of, and access to, NHPs. Future research will include assessing consumers' perceptions of the risks associated with NHPs as well as the professional roles of conventional health care providers, such as pharmacists and dietitians, regarding these products.

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8. Linking Transcript Profiles to Metabolites and Metabolic Pathways: A Systems Biology Approach to Transgene Risk Management

Dionysos Kiambi, Julie Beaulieu, Genevieve Morin, Kei Chin Cheng,
Martina V. Stromvik and Marc G. Fortin
McGill University

Introduction

Plant biotechnology and genetic modifications offer potential for increasing crop production and for nutritional enhancement. However, one of the major concerns is the possibility of unintended effects caused by transgene integration. Upon random insertion of specific DNA sequences into the plant genome (intended effect), the disruption, modification or silencing of active genes or the activation of silent genes may occur. This could result in the formation of new metabolites, altered levels of existing metabolites, modified metabolism, novel fusion proteins, or other pleiotropic effects that could compromise safety, such as production of new allergens or toxins (Cellini et al., 2004; Kuiper, Kleter, Noteborn & Kok, 2001). Unintended effects may be partly predictable on the basis of knowledge of the place of the transgenic DNA insertion, the function of the inserted trait, or its involvement in metabolic pathways, while other effects are unpredictable due to the limited knowledge of gene regulation and gene-gene interactions.

Pleiotropic effects such as multiple metabolic changes in tocopherol, chlorophyll, fatty acids and phytoene have been reported by Shewmaker, Sheely, Daley, Colburn and Ke (1999) while engineering canola for over-expression of phytoene-synthase. Similarly, in the process of manipulating potato to express yeast invertase, Engel, Gerstner and Ross (1998) reported up to 48% reduction in glycoalkaloid levels while Momma et al. (1999) reported a 50% increase in vitamin B6-content in their work on expression of soybean glycin in rice. Pleitropic effects have also been demonstrated through gain of function analysis. As reported by Fernie, Trethewey, Krotzky and Willmitzer (2004), the analysis of a gene of known function introduced into *A. thaliana* confirmed the expected function but also revealed new effects on the metabolic network. This included the up-regulation of the methionine pathway with up to two- to four-fold increases and the down-regulation of the isoleucine pathway, with isoleucine decreasing to 15% compared to levels in the wild-type. However, it should be emphasized that the occurrence of unintended effects is not specific to genetically modified (GM) organisms as it also occurs frequently in conventional breeding as reported in Thomas et al. (1998), Coulston and Kolbye (1990) and Beier (1990). We briefly review molecular approaches to transgene safety assessment and also provide an update of the ongoing work in linking transcript profiling, metabolite profiling and metabolic pathways as a systems biology approach to studying risks associated with transgenes.

Assessing changes in genetically modified plants (or plants with novel traits)

The comparison of the chemical composition of the GM plant to that of a traditionally bred counterpart has been a key element in the safety assessment of GM crops. Such a comparative approach reveals similarities as well as differences between the transgenic crop and the selected comparator and will thus provide information on the status of "substantial equivalence" (König et al., 2004; Ye et al., 2000).

Different approaches and strategies have been applied in the identification of potential secondary effects of genetic modifications. Traditionally, unintended effects have been identified through a targeted approach where an analysis of the agronomical and morphological characteristics of the new plant is followed by proximate or chemical analysis of key nutrients, anti-nutrients and toxicants typical for the plant. Limitations of this analytical, comparative approach are the possible occurrence of unknown natural toxins and anti-nutrients, particularly in food plant species with no history of safe use, and the availability of adequate detection methods. In addition, there are no generally accepted and harmonized guidelines that define the full extent of the analyses required. Furthermore, the targeted approach is considered to be biased and focuses on known compounds and expected or predictable changes (Millstone, Brunner & Mayer, 1999).

"In this new generation of transgenic crops, there is a possibility of...unpredictable effects not revealed by [the traditional profiling] approach, and new methods are therefore necessary. These methods include transcript profiling, proteomics and metabolomics."

To avoid biases, non-targeted methods are now being used as an alternative approach for the detection of unintended effects using profiling techniques. This type of screening for potential changes in GM organisms becomes important since the next generation of GM crops is likely to include varieties with improved nutritional properties. In the development of this new generation of transgenic crops, there is a possibility of far- reaching effects on metabolic processes due to complexities associated with metabolic perturbations and/or generation of new biosynthetic pathways. This could lead to the occurrence of unpredictable unintended effects not revealed by a targeted approach and new methods are therefore necessary. These methods include transcript profiling, proteomics and metabolomics. They allow for the screening of potential physiological, cyclical, developmental or environmental changes of the modified host organism at different cellular integration levels, at the genome level during gene expression and protein translation, and at the level of metabolic pathways (Cellini et al., 2004; Kuiper et al., 2001). When these methods are integrated with bioinformatics technologies it becomes possible to investigate global unintended effects through the analysis of transcripts, proteins and metabolite profiles using a systems biology approach (Jonsson et al., 2005).

Methodology

Metabolomics as a profiling approach for transgene risk assessment

Metabolomics is a comprehensive analysis in which all the metabolites of an organism are identified and quantified (Bino et al., 2004). The accurate identification and the relative quantification of a high number of metabolites in a multitude of samples makes it possible to study dynamic metabolomic networks (Fiehn & Weckwerth, 2003) and also undertake comparative studies between GM crops and their traditional comparators that are "generally recognized as safe (GRAS)" based on the extent of their natural variation (Lehesranta et al., 2005).

Transcript profiling in detecting differential gene expression for transgene risk assessment

Functional genomics refers to the study of direct expression products of genes, the mRNA transcripts and the related regulatory elements. It can therefore provide insight into the complex metabolic relationships within an organism including pathways that are relevant for the safety of food crops. It may also lead to an in-depth understanding of the natural variation in the expression of genes under different environmental conditions (Sommerville & Sommerville, 1999). The scale and resolution of DNA microarrays that are used to generate transcripts facilitates the detection of alterations in gene expression and the possible consequences for food safety, if the relevant pathways are known.

Integrating transcript profiling and metabolite profiling through a systems biology approach

Both theoretical and experimental disciplines have seen the emergence of systems-based approaches to biology in the past few years as typified shifts from the more traditional reductionist approach towards more holistic approaches, with experimental strategies aimed at understanding interactions, such as links between transcripts and metabolites, across multiple molecular entities (Oksman-Caldentey, Inzé & Oreši , 2004). This holistic understanding of the biological behavior of a complex system enables the careful tracking of the response of an organism to conditional perturbations at different molecular and genetic levels. Through holistic profiling within a systems biology approach it is possible to identify markers and mechanisms that are important to the function of the perturbed system, with the ultimate goal of developing computational models that enable the prediction of the response of the system to any given perturbation (Sweetlove, Last & Fernie, 2003). This "systems" approach to biology involves the comprehensive characterization of the components of a biological system at the transcriptome, proteome and metabolome levels (Fiehn & Weckwerth, 2003).

Potential Unintended Consequences of Transgene Insertion: Plant Genome

- Disruption, modification or silencing of active genes
- Activation of silent genes
- Formation of new metabolites
- Altered levels of existing metabolites
- Modified metabolism
- Novel fusion proteins
- Production of new allergens or toxins
- Other pleiotropic effects

Results

Here we report progress made in the development of an open source database for integrating soybean expression data with metabolic pathways and other annotation data. The main objective is to enhance and enable the exploration of changes in gene expression and metabolite production in normal, GM, environmental and pathogen-challenged soybean plants. The database exploits and integrates publicly available data using bioinformatics methods. It contains 309,486 soybean EST sequences and data from 85 EST libraries; BLAST hits to Swiss-Prot protein sequences; Gene Ontology annotations and Enzyme Commission (EC) numbers for Swiss-Prot; KEGG pathways and EC numbers from each map; TIGR tentative consensus identifiers; Affymetrix soybean probe IDs and soybean viral sequences. This web application enables users to query the database with biologically interesting questions such as "Which metabolic pathways differ between young leaves and expanded leaves?" Through the different query features, users can find information for up-regulated genes by microarray probe set identifiers. In future, metabolite and microarray data will be integrated into the database to enable comparisons between GM and non-GM soybeans. Through this integrated approach, it may eventually be possible to visualize the effects of transgenes on gene expression, metabolic pathways and metabolite profiles as a result of up or down regulation of genes.

Using Affymetrix chips, gene expression was measured for five soybean varieties, including two GM varieties. Our analysis was limited to one plant tissue (first trifoliate leaf) collected from five varieties of soybean grown in a controlled environment, and to genes that were represented on the Affymetrix Soybean GeneChip®. However, it appears that some genes were differentially expressed in GM soybean varieties 2601R and PS46R under these conditions. Also, to distinguish the "genotype" effect from the "GM" effect, we would have to conduct a separate, model-based statistical analysis. Results from this analysis indicate that high density oligoarrays constitute a highly sensitive exploratory tool for the substantial equivalence assessment of GM crops.

Metabolomic analysis supports the results observed using gene expression analysis. Generally:

- little variation is observed between samples of one variety;
- some cultivars are more different from each other than in comparison with the GM varieties;
- reproducibility of the analysis is high; and,
- metabolomics and transcriptomics analyses provide similar results.

Discussion

Implications for plants with novel traits risk assessment and regulation

For these technologies to be even more effective tools for plants with novel traits (PNT) risk assessment and regulation, further progress will need to be made in the validation of the vast information generation. More comprehensive bioinformatic tools need to be developed to extract relevant biological information from raw data sets using a systems biology approach that integrates data sets from both metabolomics and genomics platforms. As this comprehensiveness increases and bioinformatic tools mature, it will become easier to visualize and assess the effects of transgenes and perturbations resulting from their integration in biological entities. The combination of the new techniques of metabolic and gene expression profiling will also make tangible contributions towards comparisons of PNTs with the traditional comparators that are generally recognized as safe. However, for this to be accomplished, the development of publicly available databases of crop composition and profiles is an absolute requirement in order to determine natural variation of compounds within and between given plant species. As information is gathered, evolving baselines and benchmarks with which to compare PNTs could be envisaged. These databases would also greatly aid the robustness of targeted analyses.

"There is little doubt that existing profiling techniques, when used in an integrated manner using a systems biology approach, provide sufficient basis for science-based regulation of plants with novel traits."

Conclusions

There is little doubt that the existing profiling techniques, when used in an integrated manner using a systems biology approach, provide sufficient basis for science-based regulation of PNTs. They have proven successful in revealing unintended effects but it may be argued, however, that unintended effects do not automatically or necessarily imply health hazards. Ideally, only those parameters that fall outside the range of natural variation should be considered further in safety assessment. The main impediment is the lack of information on the natural variation within and between plant cultivars for all the parameters that can be measured. Safety assessments could be simplified if the identification and safety significance of any observed differences are known. The regulators need to develop guidelines on how different a particular parameter should be from its GRAS comparator for it to be considered a risk. However, one major drawback is the lack of adequate toxicity databases to aid the interpretation of the safety significance of compounds with unknown identity and/or function. Major differences based on quantities and/or novelty of unintended effects may lead to the consideration of more extensive safety testing but this becomes a regulatory issue.

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9. High Throughput Omics-Based Analytical Tools for Evaluating Food Safety: Genetically Modified Meat Products and other Novel Foods

Serguei P. Golovan[1], Chris Verschoor[1], Tom C. Wright[3], Chris Elsik[5], Sandra Walters[2], John P. Phillips[2], John M. Kelly[4] and Cecil W. Forsberg[2]

"The primary question is whether the novel meat products are substantially equivalent to the conventional meat products. In answering this question, the challenging aspect is determining whether there are any unintended effects or changes in the animal that may have a deleterious effect on the healthful nature of the food for human consumption."

Introduction

Novel foods produced through genetic modification are assessed for regulatory approval based on composition, toxicity, allergenicity, nature of the transgene product, location of the transgene in the chromosome and environmental impact. Guidelines are not in place for genetically modified (GM) food animals, but the approach may include an initial screen of growth, reproduction and health. If there are no detectable differences in the performance at this level, the assessment presumably will move to the next level, which corresponds closely to that for assessment of GM plants. The primary question is whether the novel meat products are substantially equivalent to the conventional meat products. In answering this question, the challenging aspect is determining whether there are any unintended effects or changes in the animal that may have a deleterious effect on the healthful nature of the food for human consumption.

Detection of unintended effects relies primarily on basic chemical analysis, which may include determinations for total protein, amino acids, fatty acids, carbohydrate and minerals. Despite the fact that these comparatively superficial instruments for assessing changes arising from the genetic modification have served us well in the past, they may not meet the test for transgenic food animals. For example, they may not detect unintended effects that involve a change in a physiological pathway arising from the novel protein, or interference with endogenous gene expression (gene disruption, production of chimeric proteins, competition with the transgene for cellular machinery, microRNA-like interference by transgene mRNA, etc.). These effects may influence transcription, translation or post-translational modifications of endogenous proteins, resulting in the production of novel cellular metabolites with potentially toxic, carcinogenic or mutagenic potential, or may decrease metabolites with health-promoting properties in any number of tissues.

Due to the sheer complexity of the animal genome and proteome, it is exceedingly difficult to assess the occurrence of these unintended effects via traditional means of analysis. Thus, the focus of this research program has been to assess high-throughput molecular profiling techniques, including analysis of the transcriptome and proteome, and the integration of these different hierarchical levels of organization with traditional composition analysis to create more "holistic" multidimensional tissue models that eventually can be assembled into a whole-animal model of the GM animal. In other words, this approach enables the assessment of the function of either individual genes or groups of genes that contribute to biological pathways for individual proteins within selected tissues. This comprehensive approach should enable improved detection of any changes in metabolic function within a tissue, including the influence of transgene expression at the cellular and whole organism levels that may lead to undesirable effects on food safety, animal production characteristics or animal welfare (health, growth characteristics, reproduction, etc.). Our model for this research is the transgenic Enviropig™ breed with an enhanced capacity to digest plant phytate phosphorus

[1]Department of Animal and Poultry Science, University of Guelph; [2]Department of Molecular and Cellular Biology, University of Guelph; [3]Ontario Ministry of Agriculture, Food and Rural Affairs, Fergus, ON; [4]MaRS Landing, Guelph, ON; [5]Texas A&M University, College Station, TX, USA

enabled by expression of phytase in the salivary glands (Golovan, Hayes, Phillips & Forsberg, *2001*).

This program of research is unique in that we have a transgenic pig model with well-documented data on transgene stability and expression, growth, health status, and gross physical and chemical compositional information on tissues over which we can layer transcriptome and proteome information. This array of data is in the process of being integrated to develop tissue models linked to an animal model. The focus of this research program is transcriptome and proteome analysis of major food tissues. The initial objective has been development of a model for parotid gland function in relation to secretion of phytase. With the data pipeline developed we are now examining the major food tissues.

"Due to the sheer complexity of the animal genome and proteome, it is difficult to assess the occurrence of unintended effects [of genetic modification] via traditional means of analysis."

Methodology

Forty-eight pigs consisting of 24 transgenic pigs (12 males and 12 females) and a comparable numbers of conventional male and female Yorkshire pigs were raised to finisher weight, slaughtered, and tissues samples collected and prepared for analysis. Chemical analyses of 12 tissues from each animal were used to provide baseline data for protein (and amino acids on major food tissues), fat (and fatty acids), minerals and carbohydrates by difference. Transcriptome and proteome profiling were performed using Affymetrix Gene Chip® chips (porcine genome arrays involving 23,256 unique porcine transcripts – see http://www.affymetrix.com/index.affx) and iTRAQ analysis. ITRAQ analysis is a tool for protein identification and relative quantification using "isotope tags for relative and absolute quantification" (Ross et al., 2004). Analyses have been completed on parotid tissue, which serves as a positive control since it is the tissue with high phytase transgene synthesis and a key candidate for any significant changes. ITRAQ analysis was conducted on the major consumable tissues including muscle, liver, kidney and skin. Microarray analysis of the parotid gland and muscle tissue has been completed and liver analysis is in progress. Bioinformatic processing of the massive quantity of data collected is in progress.

Results

We have raised transgenic and non-transgenic pigs under standard conditions, assessed animal health during all phases of growth, isolated all major tissues and prepared them for chemical and "omics" analysis. These analyses have demonstrated that any statistically significant differences between GM tissue samples and conventional tissue samples were usually within the normal range. The greatest number of statistically significant differences observed between the major food tissues from transgenic and conventional pigs was in kidney tissue. The majority of the differences might be explained by increased availability of phosphorus and some minerals as a result of digestion of phytate-mineral complexes in the transgenic Enviropig™. These data have provided an important baseline data set for comparison with the omics analysis.

Omics technologies were tested with parotid glands to develop a data collection, analysis and integration pipeline for other tissues. While the parotid is not a major food tissue, it is the tissue most likely to be affected due to the high parotid gland specific phytase transgene expression in the Enviropig™.

We selected the Affymetrix Porcine Gene Chip for assessing messenger RNA (mRNA) production because it provides the highest coverage of the porcine transcriptome and has higher accuracy and reproducibility of data including the absolute quantification of mRNA. Therefore, the resulting data can be used both in-house and in other laboratories because of its reproducibility. Quality assurance and data analysis were performed using freely available Bioconductor and D-Chip software packages. Analysis

of the swine parotid gland transcriptome using six transgenic pigs (three males and three females) and six conventional Yorkshire pigs identified 12,388 transcripts (53%) present in parotid glands, which is comparable with the number of gene transcripts detected in other studies, including mouse (7,303), human skeletal muscle (9,194) and human brain (11,587). We believe that the actual number of expressed genes is larger, as the porcine array has only half as many genes as the corresponding human and mouse arrays. Also, our proteome profiling by iTRAQ indicates a more complex proteome in parotid glands as compared with muscle. Different analysis methods identified almost 800 differentially expressed genes (at ≥ 1.5 fold-change; ($p \leq 0.05$) or ~8% of total transcriptome. There was a decrease in expression of parotid specific genes (parotid secretory protein, alpha-amylase, lysozyme and salivary lipocalin) in the Enviropig™, which probably is due to competition for transcriptional/folding/modification/secretion machinery with the highly expressed transgenic phytase protein. Similar results were reported for endogenous milk proteins when transgenes were highly expressed in the mammary glands of mice and cows (McClenaghan, Springbett, Wallace, Wilde & Clark, 1995; Wilde, Clark, Kerr, Knight, McClenaghan & Simons, 1992).

Proteomics deals with qualitative and quantitative changes in the proteins expressed by the genome. A main advantage over microarray analysis is that it detects functional changes in protein production in contrast to microarray analyses that detect mRNA molecules that are precursors of the proteins. ITRAQ was chosen as it allows a quantitative comparison of protein composition of four separate protein samples in one analysis (i.e., whether a protein such as albumin is increased or decreased in the GM tissue as compared to the same tissue from the conventional animal. In the experimental design, a single iTRAQ run compares the relative concentration of individual proteins in samples of the same tissue from each of 1) a male transgenic Enviropig™, 2) a female transgenic Enviropig™, 3) a male conventional Yorkshire pig and 4) a female conventional Yorkshire pig.

The original mass spectroscopy data were also analyzed by the program MASCOT (http://www.matrixscience.com/), an independent program used to confirm protein identities. Analysis of the parotid glands resulted in the identification of 395 unique proteins or ~4% of proteins predicted by transcriptome analysis. This is approximately two times the number of proteins we identified in a single analysis of the porcine skeletal muscle proteome. Relative quantification of proteins in the parotid using iTRAQ revealed 26 proteins that were differentially expressed at ≥1.5 fold-changes ($p \leq 0.05$) between transgenic and control animals. Validation of proteome profiling results by an independent method is a difficult and extremely time consuming task because it requires the production of specific antibodies for each protein to be tested. Therefore, we tested the applicability of Real Time reverse transcriptase polymerase chain reaction (RT-PCR) to confirm the results from proteomic profiling. While the usual concordance of ~60% is observed between mRNA and protein due to differential protein modification and proteolysis, out of seven genes tested, five demonstrated the same directional change, one gene showed no change and one gene showed an opposite change in mRNA concentration. This demonstrated that Real Time RT-PCR can be used for quickly validating changes in the majority of proteins detected by proteome profiling.

This is the first time the parotid transcriptome and proteome have been analyzed on a large scale in any species. This type of "gene/protein catalogue" will advance our understanding of parotid gland physiology, the role saliva plays in reducing disease susceptibility and its function in promoting overall oral health and feed digestion. In addition, a molecular index will aid areas of research where swine are increasingly being used as animal models for salivary diseases such as Sjögren's syndrome and

radiation-induced salivary gland injury arising from medical treatments, and gene transfer to salivary glands. Our results demonstrate that despite a relatively moderate level of transgene expression in the analyzed Enviropig™ line, up to ~6% of endogenous parotid proteins might be affected in the Enviropig™ breed. This estimate is close to those of gene expression changes assessed by microarray, where ~8% of parotid genes were affected by transgene expression.

The Enviropig™, a transgenic pig developed at the University of Guelph, has enhanced digestive abilities resulting in a 60% reduction in the environmentally toxic phosphorus content of manure produced by pigs. Tissue samples from the genetically engineered pigs were compared with those from conventional pigs using high-throughput molecular profiling techniques to detect the presence of undesireable effects in the transgenic tissue.

Using the strategies developed for parotid analysis, similar iTRAQ analyses were done in triplicate on the major food tissues including muscle, liver, kidney and skin. Acknowledging some redundancy in the recording of protein identifications that may give a slight overestimation for this preliminary report, a total of 398 different proteins were identified and catalogued for muscle tissue at the 99% level of confidence: 929 for liver, 1093 for kidney, and 824 for skin. This is the largest proteome profiling done for any livestock animal. From an assessment of the log ratios of proteins in transgenic pigs over conventional pigs, we have calculated that in three replicate runs in which proteins were identified in all three runs, none out of the 15 proteins tested differed by more than one standard deviation from the mean. In liver, four out of 65 were greater than one standard deviation, but less than two standard deviations; for kidney, three of 57 proteins were greater than one standard deviation, but none were greater than two standard deviations. In skin, all 29 proteins detected in three of three replicate runs were within one standard deviation of the mean. With few exceptions, there were no significant differences in the observed ratios between sexes of either the GM pigs or Yorkshire pigs. As one might expect, more deviations were detected in proteins which appeared in only two out of three runs and one out of three runs because the number of replicates making up the mean was fewer. This data demonstrates that the secretory tissues including parotid, liver and kidney appear to have larger proteomes than muscle. Phytase was detected as a major protein in parotid tissue by iTRAQ, but was not detected in other tissues analyzed by iTRAQ, which is consistent with immunohistochemistry and enzyme analysis for phytase in these tissues. This is the first time such a detailed proteomic analysis has been completed for porcine tissues.

All data will be deposited in publicly available Omics databases using MIAME and MIAPE formats. The biggest obstacle to mining porcine Omics data is lack of sufficient annotation of porcine genes where only 10% of genes have been annotated. To

overcome this challenge, we are both annotating the genes of interest and integrating our iTRAQ and Affymetrix data into a single data set.

The parotid genes and proteins have been classified in Gene Ontology categories of i) cellular components, ii) biological processes and iii) molecular functions. Differentially expressed genes are currently mapped to known metabolic and signalling pathways using a variety of software programs (KEGG, Bind, BioCarta, GeneMapp, etc.) to enable identification of specific functional pathways affected by transgene expression. We are also testing MetaCore (GeneGo) and PathwayStudio Central (Ariadne Genomics) pathways analysis software to study their suitability for the analysis of porcine data. These programs provide a database of manually curated pathways, and, in addition, allow expansion beyond traditional models for identification of novel pathways using text mining with Natural Language Processing algorithms, which detect co-occurrence of gene/protein names in the same text in PubMed articles (Dr. A. Yuryev, personal communication). By overlaying changes in gene expression over existing pathways, one will also be able to analyze the flow of metabolites and information through affected pathways. Biological pathway analysis will allow an increased depth of data mining by identifying pathways affected in a statistically significantly manner by revisiting the Omics data to reanalyze other genes in the same, or in interconnected pathways, which may not have been detected by initial analysis. We will also integrate Omics information with previously collected compositional analysis of the tissues to see if predicted pathway changes manifested themselves in compositional changes. This is the first time such comprehensive analysis was done on GM livestock animals. It will enable testing of the application of molecular profiling technologies to analysis of substantial equivalence of GM organisms, and contribute to better understanding of the effect of expression of novel genes on existing cellular metabolic networks. This integration of traditional compositional data with Omics-based data at the molecular level will provide the highest degree of analysis of GM organisms from a molecular systems biology and whole-animal perspective to ensure a rigorous determination of food safety.

"This comprehensive approach should enable improved detection of any changes in metabolic function within a tissue...that may lead to undesirable effects on food safety, animal production, or animal welfare."

Discussion and Conclusions

Current requirements for regulatory approval of GM organisms include little molecular-level analysis other than genomic characterization of the transgene insert. This leaves a greater opportunity for error in the final assessment of food safety, environmental and animal welfare issues. There is also the question of social acceptability. A paradigm shift in biology, with widespread use of Omics technologies for high through-put profiling of gene expression, proteins and metabolites, has not yet been applied to the evaluation of food safety of GM organisms. We recommend the establishment of an international database for food animals that includes information on a range of natural variation in compositional characteristics and in molecular profiles (transcriptome, proteome and metabolome). With a greater in-depth knowledge of whole organism characteristics at the molecular level achieved by Omics technology, it would seem that more decisive regulatory decisions on food safety will be possible. This should lead to greater consumer acceptance in terms of food safety of GM food animals. With increased use of Omics technologies for novel foods testing, the costs for testing ultimately will be reduced, and the software for analysis of data will be both improved and more user-friendly. These changes may ultimately lead to a reduced time-to-market for some types of GM food animals. However, as with most scientific advances, their application and acceptance are entirely dependent upon the social acceptability of the product.

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10. Comparative Intellectual Property Issues in Biotechnology

Karen Durell and Richard Gold
McGill University[1]

Introduction

Agricultural biotechnology (ag-biotech) research is a growing sector within Canada and globally. As projects in this area flourish, the quantity of intellectual assets in the biotechnology market simultaneously grows. This creates an interesting situation, as researchers who were previously unaccustomed to dealing with intellectual property (IP) are now creating valuable assets they are often unequipped to deal with. Furthermore, due to the freshness of this sector, new categories of IP are being created. Thus, the ag-biotech sector is ripe for an IP review.

This project, led by Richard Gold at the Centre for Intellectual Property Policy at McGill University, examined the IP issues facing agricultural-biotechnology research, with a special emphasis on matters encountered by Advanced Foods and Materials Network (AFMNet) participants as they worked to bring their research to fruition. AFMNet presents a particularly interesting forum for this research as it offers a wide range of scientific projects – from functional food development to information technology software to the delivery of nutraceuticals. Furthermore, AFMNet scientists possess varying levels of understanding about intellectual property, which is instructive to the research project.

The "Comparative IP Issues in Biotechnology" project addressed several issues, including means of protecting intangible aspects of research, licensing strategies, contracting arrangements, and IP management initiatives. As these are wide topics, the research team identified some key concerns facing the ag-biotech research sector. These include the role of public-private technology transfer in public research dissemination; IP protections that may be sought at various stages of research and development of an ag-biotech product; means of ensuring more effective IP protection in the future; strategies for managing the various forms of IP protection that may be sought for single research projects or projects within the ag-biotech sector and AFMNet in general; and knowledge and attitudes towards IP of AFMNet researchers.

An important goal of the project was to disseminate information to enhance the understanding of researchers in the ag-biotech sphere. The project thus concentrated on developing a number of instructional tools (publications, databases, conference presentations and workshops, etc.) to educate researchers about the integration of IP in their research programs.

Methodology and Results

This research set several interesting goals focused on the role of IP in biotechnology research. This is a broad topic as aspects of the means for obtaining intellectual property rights (IPR), including scope of IPR and sharing of protected products and information, all come into play. Consequently this project involved two steps: 1) an identification of the present environment and issues facing IPR in the biotechnology sphere; and 2) consideration of management strategies for IPR. A variety of research methods were employed: literature review, public forums, conference presentations and

[1] Project Team: Richard Gold, Centre for Intellectual Property Policy, McGill University (Project Leader); Tim Caulfield, Health Law Institute, University of Alberta; David Castle, University of Ottawa; Peter Phillips, University of Saskatchewan; Karen Durell, Researcher, McGill University; Lorraine Sheremeta, Research Associate, University of Alberta; Roxanne Kaminski, Research Assistant, University of Saskatchewan.

survey results. The following describes the sub-projects the research team addressed.

Public-private technology transfer

A crucial dilemma facing researchers is the appropriate means of transferring technologies and knowledge, both within the research community and across the public/private divide. To better understand the issues that are of particular concern to researchers and industry in this area we organized a Technology Transfer workshop that was held on April 20, 2004 at Blakes LLP in Montreal, Quebec. The participants included academics, government representatives, and industry members, all of whom actively engaged in the debate facilitated during the meeting, offering their input and commentary about technology transfer issues in Canada.

The Technology Transfer Workshop revealed that several hurdles presently inhibit the transfer of ideas from public laboratories to private industry for commercialization. Participants identified four types of action needed to address these barriers. These include 1) better harmonization of IP policies; 2) development of a guiding framework and model agreements; 3) development of means to bridge the present funding gap for technology development; and 4) training and education for researchers on IP and technology transfer strategies.

To capture the discussion at the workshop and to make the materials available to a wider audience, the project team prepared a post-meeting report describing the prevalent technology transfer issues raised by the participants as well as potential solutions that were suggested. A copy of this report, entitled the *Technology Transfer Workshop Issue Paper*, is published on the McGill Centre for Intellectual Property Policy website at http://www.cipp.mcgill.ca/db/published/00000005.pdf.

"Traditional intellectual property rights regimes, such as patents, copyright and trademarks, continue to play an important role in ag-biotech research, but new forms of rights are also being introduced."

Identification of intellectual property in research projects

As a further means of understanding the scope of IP issues in biotechnology research, the project undertook a review of the AFMNet research projects, identifying the types of intellectual property that would be produced at various stages of the research, as well as the issues that may arise as a result of that IP creation. The purpose of this activity was to situate IP creation at particular stages in the research and development of publicly funded ag-biotech products.

As an initial step, the researchers conducted a review of projects funded within AFMNet. This allowed for a greater understanding of the variety and forms of ag-biotech research and allowed the investigators to identify the research steps likely to be part of these projects. From this base we undertook a wide literature review to identify IP issues relating to various stages of research and the types of IP protection that may be sought at each research stage.

This sub-project brought forth interesting results; in particular it pointed out the changing face of IPR in ag-biotech. Traditional IPR regimes, such as patents, copyright and trademarks, continue to play an important role in the protection of aspects of ag-biotech research projects, but new forms of rights are also being introduced. For example, geographical indicators (rights derived from the geographical source of certain food varieties) are growing in importance and global application. The research also highlighted the tug-of-war that exists between plant patent rights (exclusionary rights over an entire plant) and plant breeders' rights (rights over propagating materials). These examples demonstrate the importance of recognizing the different forms of IPR available (patent rights are different from copyright, which is different from trademarks, etc.) as well as jurisdictional variations within the territories where

a research product may ultimately be marketed (e.g., the United States offers plant patents and Canada offers plant breeders' rights).

A table was developed to capture the results of the review. As the project progressed and brought further relevant information to light, the table was developed into a simple database so that further research could easily be updated into the report. A copy of this report was provided to the AFMNet directorate.

Survey of attitudes of researchers to intellectual property in agricultural biotechnology

Intellectual Property in Agricultural Biotechnology: Priorities for Researchers

- Identifying the types of intellectual property produced at various stages of the research and how to protect them
- Knowledge of IP protections available, e.g., patents, copyright, trademarks, plant breeders' rights
- Knowledge of IP law, management, ethics and liabilities
- Methods for protecting intangible aspects of research
- Methods for sharing protected information among peers
- Technology transfer methods for publicly funded research
- IP training and education for researchers

A questionnaire was developed for circulation to the AFMNet project leaders, graduate students and other trainees to capture information about the innovations that may result from their research, as well as steps they are taking to seek IP protection for elements of their research, including the end product. After establishing goals for the survey, the investigators reviewed existing surveys to consider the wording and format each utilized. From this base, the AFMNet survey was designed.

This questionnaire project has grown from its initial concept to a much larger endeavour. In particular, the research team joined its initiative with a survey project being conducted under a Genome Prairie grant. This will allow comparison of IP issues and knowledge within AFMNet to those faced by a broader group of biotechnology researchers in Canada. This addition will provide important information about the comparative level of IP understanding within AFMNet. This survey was distributed at the Genome Canada national conference in October 2006 and will be administered to other research networks in the coming months.

Intellectual property and agricultural biotechnology workshop

Results from other aspects of this project were integrated into the development of an IP seminar for AFMNet graduate students and trainees. This full-day seminar, entitled "Intellectual Property: Foods and Materials Research," was presented on November 10, 2005 in Montreal, Quebec, and covered IP law, IP management, ethics and liabilities. The agenda reflected the wide variety of topics and concerns raised by IP in the research sphere, moving from basic information about existing IP regimes to ethical issues in patenting and practical IP management considerations. A variety of speakers were invited to participate, including Canadian academics, a patent practitioner, a representative from McGill's Office of Technology Transfer and a European scholar. Each speaker presented a unique view and important information about intellectual property and its relation to research. The major portion of the seminar was presented by graduate scholars from the AFMNet IP Project.

The research team received useful input and feedback during the initial presentation of this seminar. In particular, attendees noted that they are interested in increasing their understanding of how IPR and the information gleaned from research can be easily shared among their peers. This generation of researchers is not solely interested in utilizing IPR to commercialize research products. This interest in the free flow of information and IPR may be supported through emerging initiatives, such as the open source movement.

Discussion

The research team has had several opportunities to share results from this project. Most notably, the team gave a panel presentation in London to the Queen Mary Patenting Lives Conference in December 2005. The opportunity to have a multidisciplinary group offer commentary further enhances the primary finding of the project — the

importance of appropriate IP management strategies.

IP management is the development of strategies that allow for the application of intellectual property rights within an entity (firm, research group, etc.) for the purpose of achieving the entity's goals (e.g., commercialization, commercial advantage through exclusion, free-sharing of information between entities, etc.). There is no one-size-fits-all approach to IPR. Not all entities will share the same goals or methods, and thus tailored IP management strategies are required.

An important aspect of IP management is knowledge of IPR – the differences between types of protection, for example, as well as how and when each form of IPR may be applicable to aspects of a research project. The power of IPR is not necessarily the rights themselves, but that they can be applied in multiple ways. Moreover, the combination of different forms of IP can produce unique levels of protection. A strategic approach to IPR within a research project can ensure that a specific form of IP protection (whether that be high or low protection) can be achieved for protectable aspects of the research (research tools, data, etc.) as well as the ultimate research product. Knowledge of all available IP forms is integral to creating the most appropriate management strategy – and this knowledge can be gleaned from education about IP, its nature and possible applications.

"Researchers must take their role as initial protectors of intellectual property rights seriously. Private industry will likely pass over products that have not achieved the critical forms of IP protection available during the research stage."

Many researchers blindly strive for patent rights, but ignore other forms of IPR available to them. This can have two effects: (1) inferior IP protection; and (2) the protection may not be secure because measures that should be applied in earlier research stages may have been missed. In the former case, a researcher could find that solely seeking patent rights while ignoring geographical indicators, plant breeders' rights, trademarks (particularly certification marks that assure quality), trade secrets, or copyright (over documents that disclose integral or design information) may result in a lesser form of IPR protection than may have been achieved if all these forms of rights were held in a portfolio. An example of the latter case is often experienced by IPR holders if the right is challenged in court. There are steps that researchers can take during their project to help secure their rights in the face of a challenge in the future.

This research teaches that viewing IPR as a group of rights to be managed in accordance with a guiding goal is important to the achievement of effective IPR. It also points out that ag-biotech research that is intended for wide dissemination should consider the value and role of an integrated IPR strategy. In sum, clear goals for research results and a corresponding management strategy are integral for all research projects, to ensure that appropriate IP protection is achieved.

Conclusions

Intellectual property rights play an important role in ag-biotech research projects. As new forms of IPR emerge, such as geographical indicators, it seems that the significance of IPR in research will only grow. Moreover, as technology transfer is recognized as a vital step in the progression of research products from the laboratory to the public, researchers must take their role as initial protectors of IPR seriously. Private industry will likely pass over research products that have not achieved the critical forms of IPR protection available during the research stage. Even if a private company does not intend to exert them, the basis for the rights must exist. Thus, researchers must consider more than just their laboratory procedure. As this study has shown, however, it is possible, through education and the development of IP management strategies, to ensure the necessary steps for establishing an effective IPR foundation become part of laboratory procedure. What is clear is that IPR and ag-biotech research are now linked and will likely become more completely entwined in the future.

11. Summary of Findings and Recommendations

Acceptable Genes?: Religious and Ethical Perspectives on Genetically Modified Foods

- Religious and ethical concerns about appropriate and inappropriate foods will likely have a significant effect on consumer acceptance of genetically modified foods in general and certain kinds of GM foods in particular.
- While almost none of the project participants, including scholars and lay focus group members, argued against the approval of GM foods for sale, they all believe strongly that consumers should have access to information about transgenes in the food they eat. This finding has major implications for food labelling policy in Canada.
- The research findings support a change in regulatory policy to require mandatory GM labelling or other means (e.g., websites) to make information available to interested consumers.
- Consumer sovereignty arguments made in free market societies support the right of those with religious and ethical food prohibitions to greater information disclosure about transgenes in foods. People have a strong right in tolerant, liberal societies to live according to their most fundamental values and beliefs. Dietary practices mandated by religious and ethical beliefs certainly rise to this level and deserve to be respected.

Labelling Policies for Genetically Modified Foods

- In developing labelling policies for GM foods, it is important to understand what factors people weigh in determining the value of additional label information.
- Our results suggest that most consumers want information about genetic modification on food labels, largely to be able to avoid buying those products. Those with less negative attitudes wanted labels to be able to make more informed decisions. Many respondents said they did not know enough about genetic modification to care about labelling one way or another, but they thought labels should be present to respect consumers' wishes to make informed purchasing decisions.
- Many respondents indicated they would like information on labels explaining how and why the products were modified, as well as information about possible risks associated with the product.
- Willingness to pay for GM-labelled food varies significantly according to benefits associated with the product. Consumers are willing to pay a substantial premium for GM products when the benefits, as explained on the label, are directly relevant to them personally (e.g., nutritional enhancement).
- The general trend, however, is that foods labelled as GM experienced a substantial price discount, and the addition of benefits did not provide any overall relief for the price discount in the foods studied.
- GM labels should include simple benefit messages that are tailored to specific product categories and that appeal to consumers' self-interest. Producers may

also increase acceptance of GM products by improving the general level of knowledge about biotechnology through other channels.

Use of Health Claims in Marketing of Functional and Nutraceutical Food Products

- Functional food and nutraceutical firms strive to communicate unique information about their products, while using product-specific claims to differentiate their product from those of competitors.
- Firms with products providing health benefits that are not easy to verify place greater value on the use of health claims compared with firms with products offering more easily verifiable health benefits. This suggests that health claims are more likely to be used to communicate the real potential health benefits of functional foods and nutraceuticals than as the basis of false product differentiation. The perceived business gains from the ability to use claims are systematically associated with the degree of difficulty consumers face in verifying such claims.
- Small Canadian functional food and nutraceutical firms did not feel harmonization with the United States' standards would prove beneficial to their business.
- Once the safety of a functional food or nutraceutical has been satisfactorily demonstrated, the market mechanism can play an important role in disciplining the use of health and nutrition claims where these can be easily and relatively cheaply verified through consumer experience.
- Regulatory priorities could be set according to the "credence intensity" of a product's potential health benefits, meaning the degree to which the truth of the claim can be verified by consumers.

Understanding Consumer Acceptance of Functional Foods and Nutraceuticals

- Although the Canadian market for functional foods and nutraceuticals is expanding rapidly, relatively little is known about the acceptance of, and reservation toward, these products among the Canadian population.
- There is demand for government intervention or involvement in the authorization, distribution and monitoring of functional foods and nutraceuticals. The government was the most trusted source of information by consumers, while the manufacturer was trusted least. However, industry organizations representing manufacturers are rated at an intermediate or neutral level, pointing to a more positive reception of industry-wide efforts and initiatives.
- The mode of delivery is the single most important attribute for stated preferences, while costs or price followed as a distant second, at best, being roughly of equal importance as the other two attributes. Consumers are willing to trade off price for other desired attributes. In particular, information that reduces uncertainty about the product's safety and efficacy must be taken into consideration.
- Consumers differ both in their appreciation of attributes and in their perception and assessment of labels and information sources. The lack of clearly corresponding differences in socio-economic, demographic or psychographic characteristics makes it difficult to design and manage information campaigns in the fragmented markets for nutraceuticals and functional foods.

- Two areas of additional research are needed: (1) the development of valid instruments for measuring health involvement and relevant personal experiences; and, (2) an investigation of wording issues in labelling regulation.

Media and Popular Representations of Science, Research and Technology

- Popular representations of science, research and technology can have a profound impact on public perceptions, policy development, and implementation and utilization of new products and technologies.
- Media coverage of biotechnology often oversimplifies important scientific concepts. It is usually relatively accurate and error free; however, key information is often left out, including information about risks, conflicts of interest and funding sources – all information that can impact the perceived credibility of the research.
- Both peer-reviewed publications and media reports are influenced by forces other than the quality and value of the research.
- Efforts should be made to ensure that conflicts of interest and funding sources are appropriately disclosed in peer-reviewed publications. When possible, this should also be disclosed in media reports.
- Researchers, funding agencies and the media should work together to develop a science communication strategy that provides the public with the information necessary to make informed choices about health care alternatives.

Natural Health Product Regulations: Perceptions and Impact

- New regulations governing the manufacturing, packaging, labelling, importation and sale of natural health products in Canada became law on January 1, 2004. The Canadian NHP regulations are unique and it is not yet known how they will affect the public's use of these products.
- A key finding of this study is that the majority of companies interviewed were at least partially compliant with the new regulations. The main factors contributing to regulatory compliance are business size (large enterprises are more compliant than small ones) and knowledge and perceptions of the regulations.
- Small companies and some complementary and alternative medicine practitioners felt left out of the process of designing the regulations. These groups were more likely to lack of knowledge of the regulations.
- Wide consultation to inform policy development will help to increase the ability of firms and practitioners to comply with newly formed policies.
- The key to implementing policy change is effective knowledge translation.

New Developments in Transgene Risk Management of Genetically Modified Plants

- Plant biotechnology and genetic modifications offer potential for increasing crop production and for nutritional enhancement. However, one of the major concerns is the possibility of unintended effects caused by transgene integration.
- The comparison of the chemical composition of the GM plant to that of a traditionally bred counterpart has been a key element in the safety assessment

of GM crops. The next generation of plant genetic modification requires new assessment methods.

- New methods – transcript profiling, proteomics and metabolomics – allow for the screening of potential physiological, cyclical, developmental or environmental changes of the modified organism. When these methods are integrated with bioinformatics technologies, it becomes possible to investigate global unintended effects through the analysis of transcripts, proteins and metabolite profiles using a systems biology approach.
- Safety assessments of GM plants could be simplified if the identification and safety significance of any observed differences between GM and conventional plants are known. Regulators need to develop guidelines on how different a particular parameter should be from its "generally recognized as safe" comparator for it to be considered a risk.

Evaluating the Safety of Genetically Modified Meat Products and other Novel Foods

- Novel foods produced through genetic modification are assessed for regulatory approval based on composition, toxicity, allergenicity, nature of the transgene product, location of the transgene in the chromosome and environmental impact.
- Current requirements for regulatory approval of GM organisms include little molecular-level analysis other than genomic characterization of the transgene insert. This leaves greater opportunity for error in the final assessment of food safety and environmental and animal welfare issues.
- The complexity of the animal genome and proteome seriously impedes assessment of unintended effects via traditional means of analysis. High-throughput molecular profiling techniques – including analysis of the transcriptome and proteome – can improve detection of any changes in metabolic function within a tissue and help identify changes that may lead to undesirable effects on food safety, animal production characteristics, and animal welfare.
- We recommend the establishment of an international database for food animals that includes information on a range of natural variation in compositional characteristics and in molecular profiles (transcriptome, proteome, metabolome).
- Greater in-depth knowledge of whole organism characteristics at the molecular level achieved by Omics technology would facilitate more decisive regulatory decisions on food safety. This should lead to greater consumer acceptance in terms of food safety of GM food animals.
- As with most scientific advances, application and acceptance of Omics technologies for novel food testing are entirely dependent upon the social acceptability of the product.

Comparative Intellectual Property Issues in Agricultural Biotechnology

- Agricultural biotechnology research is a growing sector within Canada and globally. As projects in this area flourish, the quantity of intellectual assets simultaneously grows and many researchers now find they are creating valuable assets in need of intellectual property protection.
- Emerging intellectual property (IP) issues in agricultural biotechnology

include the need for awareness of the various types of IP protections available at different stages in the development of agricultural biotechnology products, and better understanding of the role of public-private technology transfer in publicly funded research.

- A strategic approach to the management of intellectual property rights within a research project can ensure appropriate protection of the research process (research tools, data, etc.) as well as the final research product.
- Strategies to facilitate a more effective transfer of ideas from public laboratories to private industry would include 1) better harmonization of IP policies; 2) development of a guiding framework and model agreements for the management of IP; 3) development of means to bridge the present funding gap for technology development; and 4) training and education for researchers on IP and technology transfer strategies.
- As technology transfer is looked to as a vital step in the progression of research products from the laboratory to the public, researchers must take their role as an initial protector of IPR seriously. Private industry will likely pass over research products that have not achieved critical forms of IPR available during the research stage.

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Réseau des aliments et des matériaux d'avant-garde
ADVANCED FOODS & MATERIALS NETWORK

Inspiration from the ground up | Aux racines de l'inspiration

Advanced Foods and Materials Network
c/o University of Victoria
Sedgewick Bldg,
Vandekerkhove Wing, Room B102
P.O. Box 1700 Stn CSC
Victoria, B.C. V8W 2Y2
Ph: 250-721-6325
Fax: 250-721-6234
Email: csrs@uvic.ca

University of Victoria

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