The Genomics "Regulatory-Science" Regime: Issues and Options

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Editor's Preface

Launched in 2009, *GPS: Where Genomics, Public Policy and Society Meet* is a series hosted by Genome Canada to facilitate a dialogue between federal policymakers and researchers exploring issues at the interface of genomics and its ethical, environmental, economic, legal and social aspects (or GE^{3}LS).

Overarching themes for the series and specific topics are selected on the basis of their importance and timeliness, as well as the "ripeness" of the underlying scholarship. Accordingly, the first series focused on "Genetic Information," whereas in year two, attention shifted to "Translational Genomics."

At the core of these exchanges is the development of policy briefs that explore options to balance the promotion of science and technology while respecting the many other considerations that affect the cultural, social or economic well-being of our society.

Co-authors of the briefs are leaders in their field and are commissioned by Genome Canada to synthesize and translate current academic scholarship and policy documentation into a range of policy options. The briefs also benefit from valuable input provided by invited commentators and other experts who participate in GPS events.

Briefs are not intended to reflect the authors' personal views, nor those of Genome Canada. Rather than advocating a unique recommendation, briefs attempt to establish a broader evidence base that can inform various policy-making needs at a time when emerging genomic technologies across the life sciences stand to have a profound impact on Canada.

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Executive Summary

The current and future development of Genomics as a science and as a set of products and processes in Canada and globally is being shaped by "regulatory-science regimes". The economic and social development of genomics is dependent of course on many factors ranging from research funding, to patenting, commercialization, entrepreneurial skill and financing. Regulatory-science regimes are one such factor that require an accurate mapping and understanding. Those already in place include: a) an amalgam of regulatory and governance structures, values and varied types of democracy; and b) systems of science, evidence and knowledge in support of regulation generally, and the regulation of genomics research. These regimes involve processes related to regulation-making, pre-market assessment of products, and post-market monitoring of products, as well as other compliance phases.

Genomics has been promoted by the state while its applications have been regulated by it. If genomics-based product development is regulated in a sectoral sense, it is also part of cross-sector regulation, precisely because genomics is an enabling and transformative science and technology affecting many industries based on the life sciences, as well as other aspects of society.

In this context, the brief explores what broad strategic policy and governance options are available and need to be debated. These include: 1) the extent and nature of federal regulatory jurisdiction regarding genomic-based applications; 2) the scope and impacts of regulatory-science based on cooperation and greater use of guidance and soft-law forms of regulation rather than hard rules; 3) the need for greater joint Canada-U.S. cooperation/harmonization for regulatory assessment of genomics-based applications, given demands by Canadians for access to products already being advertised and sold in the U.S. but not yet approved in Canada; and d) the nature and extent of self-regulation and self-knowledge regarding genomics-based products and processes, especially by lay individuals who interact with professional knowledge and monitoring networks.

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I. The Context

The current and future development of genomics as a science and as a set of products and processes in Canada and globally is being shaped by the "genomics regulatory-science" regime. A regime is a set of interacting ideas, agencies, laws, rules, processes, and interests in a given defined policy field. While Canadian regulators focus on the 'coordinated framework' of empowered actors and institutions that delivers services to the public and industry, there is significant value in framing any analysis at the broader and all-encompassing regime level. The genomics regulatory-science regime includes an amalgam of multi-level regulatory and governance structures and national and globalized systems of science, evidence and knowledge in support of decision making around genomics and its applications (Doern and Prince 2012). The regulatory role of the state is further complicated because genomics is an activity both promoted and regulated by the state (Phillips 2007; Bunton and Peterson 2005; Carolan 2010). This Policy Brief draws on a wide range of published empirical and conceptual studies, including the authors' own research, both to develop and substantiate where positive developments have emerged and where obstacles still undoubtedly exist.

Regulations, at the core of the regime, are "rules of behaviour backed up by the sanctions of the state" (Doern, Hill, Prince and Schultz 1999, 1) and anchored in compliance approaches and practices, including crucial product assessments and approvals and, more recently, initial steps regarding post-market monitoring. Regulation is usually delegated law (the "regs") but some operational provisions occur in parent statutes. To make things more complex, regulation extends to, and is expressed through, guidelines, formal and informal codes and standards, sometimes cast as soft law or 'rule-making in the shadow of the law' (Organization for Economic Cooperation and Development 2012; Prince 2010; 1999; May 2007).

In the Canadian federation rules must conform to the division of powers between the federal and provincial jurisdictions and to the overarching Charter of Rights and Freedoms. Regulation inevitably encompasses a world of administrative law and principles (Jones and de Villars 1999). The early stages of regime development in different regulatory fields often set precedents for later add-on rules, products and processes.

The common characterization of the genomics regulatory system is that it is "science-based" and fundamentally built upon "sound science." This typically empowers two types of scientific expertise in the system: the theoretical and basic science that underpins regulators' efforts in regulation-making and the scientific knowledge and related expertise possessed by front-line regulatory staff engaged in assessing products, what is sometimes labelled 'related science activities' (RSA) (Kinder 2010; Doern and Kinder 2007; Jarvis 2000). More recently, regulatory regimes have been described as 'evidence-based or evidence-informed', which variably includes and empowers socio-economic expertise and networks of citizens, patients, families and workers with local, front-line knowledge of diverse spatial and product uses and their potential impacts (Maheu and Macdonald 2010; Knoppers and Isasi 2004). In the context of genomics, a diverse set of scholars and practitioners interested in the ethical, legal and social aspects of technology (called GE3LS in Canada, ELSI in the US and ELSA in the EU) are increasingly involved in defining and monitoring the ethical dimension of the science and its uses.

The underlying structure and principles of the regulatory system predates the technology. Genomics-based applications in the agricultural, forestry, fishery and health and environment fields are generally handled in comparable but separate streams (Doern and Prince 2012). While the system adapted efficiently to the introduction of first-generation, single-trait GM crops (yielding a handful of herbicide-tolerant and insect-resistant canola, corn and soybean varieties that now dominate their market segments), it has to a large extent stalled since then. Some stacked trait crops have been adopted but second and third generation GM varieties are largely caught in the regulatory regime. GM trees and GM animals, including fish, await adjudication and, apart from a few drugs designed with the aid of genomics, human applications such as gene therapy and personalized medicine are only slowly emerging.

While some of the delayed assessments are undoubtedly due to proponents not aggressively prosecuting their cases, many of the delays are attributed by proponents and observers to hesitant responses from regulators when new applications are beings assessed. Canada is often viewed as in the middle of the field internationally—the domestic regulatory regime tends to be a bit slower than in the US, but much faster and more predictable than in the EU. A recent study for CropLife International reports that regulatory costs globally account for about 26% of the cost and 37% of the time to develop and commercialize a new GM crop product and that the regulatory process has increased from an average of 45 months for events introduced before 2002 to more than 65 months for current events (Phillips McDougall 2011). CropLife Canada undertook an internal study on Canada's regulatory performance and found "that the total time from submission to approval is generally increasing, timelines for new submissions are less predictable (some are fairly quick while others are longer, but the length of review does not appear to be correlated to complexity of the submission) and the time from the last information request to the letter of approval has increased (which the regulators assert is strictly administration time that could easily be improved)" (Tranberg 2012).

In the health field, DNA testing, in both the justice system and human therapy, and the range of techniques related to human reproductive technologies all have had long gestation periods and have been challenged by controversial and partial development of law and regulation (Supreme Court of Canada 2011; Deckha 2009; Miller-Chenier 2002; 1994; Royal Commission on New Reproductive Technologies 1993). Indeed, Assisted Human Reproduction Canada (AHRC), which was only established in 2007 after a decade of delay, was abruptly cancelled in Budget 2012 due in part to a Supreme Court of Canada ruling that had significantly reduced the federal regulatory role in assisted human reproduction.

The genomics regulatory-science regime involves intricate governance boundary problems regarding bio-food, bio-health and bio-life—engineered foods and the prospects of more invasive genetic human health interventions have triggered concerns about what is "natural" and what should be viewed as private property and commoditized as opposed to treated as a public good (Castle 2009; Brunk and Coward 2009; Wiles 2007; Phillips et al 2010; Andree 2009).

II. The Issues

Three genomics regulatory-science issues stand out as major concerns, each related to different aspects of the overall regime. There are of course other particular issues that arise in more specific contexts and in the diverse nature of changing genomic-centred product and process developments in food, health and life. Some of these issues are mentioned below but they are not among the three main overriding issues we focus on in this very brief paper.

The first issue relates to how regulations can and should be made. The federal government made a strategic decision in the 1990s to review biotechnology and genomics research through existing institutions and in the context of their application and intended uses, rather than through purpose-built or technology specific structures. In that context, the 2007 federal Cabinet Directive on Streamlining Regulation (CDSR), the main regulatory policy of the current Conservative Government, asserts that, when regulating, the federal government will: protect and advance the public interest in health, safety and security, the quality of the environment, and social and economic well-being of Canadians as expressed by Parliament in legislation; and promote a fair and competitive market economy that encourages entrepreneurship, investment, and innovation (Canada 2007, 1).

The CDSR seeks to move the federal regulation-making process away from its historic 'one regulation at a time' approach to one where regulatory priorities are more explicit (Doern 2007 and 2011). In this way the CDSR seeks to garner better evaluation of regulatory regimes and not simply line-by-line reviews. While well intentioned, this may not come to pass. This may be complicated by the 2012 federal commitment to a 'one-for-one' rule and burden test (where any new regulations require offsetting deletions of regulations and must not add to the net cost of regulatory compliance for business) which may narrow the focus of regulatory development. A complicating factor for comprehensive review is that regulatory oversight is triggered by the novelty of the product and not the methodology used in the production, which means that specific opportunities or challenges triggered by genomics may only be fully engaged at one of the pre-planned reviews of the system related to food, drugs, forestry, energy and the environment. The federal government is not alone in trying to work through and implement a new approach to regulation. A recent OECD review of regulatory policy highlighted the growing complexity and numerous inherent partial contradictions in delivering on the core principles of efficiency, effectiveness, transparency and engagement (Organization for Economic Cooperation and Development 2012; Pal 2012).

The second issue relates to whether and how a life-cycle approach might be adapted and embodied in product assessments for food, drugs and environmental effects of new products (National Round-

table on Environment and the Economy 2012; Health Canada 2006 and 2007). The Health Canada life-cycle concept has been proposed to move the focus away from a single "point-in-time" pre-market assessment system for new products to one that follows products and processes in post-market phases, including their ultimate use in households and the environment. The 2006 federal Blueprint for renewal in health and drug regulation has gone the furthest in recommending moving to a product life-cycle approach, which would involve post-release monitoring and reporting (Health Canada 2006, 6-25). But the Blueprint plans are not a statutory policy provision and in times of restraint may not be implemented as proposed. The extension to post-market monitoring of products and product use would necessarily include networks of varied and dispersed expertise and knowledge in both the federal-provincial knowledge system and beyond the national borders to other scientific communities and markets, which would be a major challenge even in the best of circumstances. The 2012 report by the National Roundtable on Environment and the Economy (NRTEE) also stresses the value of life-cycle approaches to foster sustainable economic development in Canada but it also points to many practical obstacles along the way, including limited conceptual understanding, complexity, and serious gaps both in the science and in the front-line capacity to deliver science-based regulations and policy.

The third issue is whether any national regulatory system can be fully capable of assessing the diversity of genomics applications. Of all the sciences, genomics is probably the most global. No country is self-sufficient in the science used to develop new products and processes or that is needed to undertake assessments. This is a particular challenge as much of the knowledge embedded in these new products is protected and exploited under proprietary regimes (protected by patents, trademarks, trade secrets and various commercial and contractual mechanisms). This system privileges some actors and forms of evidence at the expense of others—at least partly because most regulators prefer to work with owners of new products so that they can more easily assign fiduciary and residual obligations related to unintended and unanticipated consequences. This becomes more of a challenge once a product enters the market—consumers in Canada and globally have high expectations that they will be able to make their own choices about accessing and using foods, drugs and other products (Phillips and McNeil 2001).

While food labelling has been a hot topic, the health area is even more challenging as Internet-savvy Canadians and their families often have knowledge about, and access to, products well before they are approved in Canada, especially from the US. This has triggered what one author has called the "wow" to "whoa" phenomenon, as new discoveries and products with human health impacts are announced with excitement—almost immediately followed in the same rhetorical breath with human and social fears about such products and processes (Harris 2010; Wade 2010).

One particularly troubling trend is that some Canadians are beginning to buy direct-to-consumer genetic testing for health, disease and ancestry from such providers as 23andMe—these relatively inexpensive services can cause significant angst and demands on the public health system in Canada as people seek help interpreting and responding to their results (Caulfield et al. 2010). This issue is in some ways the flip side of the continuing concern that such tests could lead to genetic discrimination. With the support of the Canadian Coalition for Genetic Fairness (2010), a Member of Parliament from the New Democratic Party has proposed a bill to amend the Canadian Human Rights Act to prevent discrimination of people based on genetic characteristics (New Democratic Party 2010). While numerous US state governments have introduced such laws, Canada has no such restrictions in place.

III. Policy Background

Who then are the regulators and what are their science, evidence and knowledge capacities? A minimal mapping of the system would be centred on government regulators, but there are many others who contribute to making choices about new technologies.

The story and the foundation for the genomics "regulatory-science" regime begins with the genomics research itself (Doern and Prince 2012, Chapter 3). There are two main streams of government investment: Genome Canada and tri-Council investments in basic genomics research discovery and development; and government intra-mural investment in the science needed to underpin public policy and regulation. Provinces, foundations and especially private capital come on-line only as the research advances and commercial opportunities become clear. At the federal level, the Genomics R&D Initiative (GRDI) (Canada 2012; National Research Council Canada 2010) funds and coordinates seven federal departments in the fields of genomics research. Over one billion dollars has been invested since 1999 in five three-year funding cycles. This has generated quite a number of projects and discoveries which have importance to researchers and client genomic networks but the links to regulatory issues are complex and often hard to track in any detail. The general GRDI website says that "independent evaluations have found that GRDI is successfully supporting the core public policy, regulatory, and operational mandates of government" (Canada 2012, 1). While regulatory science is part of the GRDI mandate, the most recent evaluation of the program does not offer any specific insight into how this work has supported Canadian regulatory capacity (National Research Council Canada 2010).

Each of the federal and related research organizations undertakes de facto pre-market regulatory assessments, in that each has its own norms, rules and processes for making choices which effectively pre-screens genomics applications before they reach the main product and process regulators. Almost all organizations now adhere to some articulated set of ethical norms (such as the Canadian Tri-Council Policy Statement: Ethical Conduct for Research In-

volving Humans) embodied in corporate pledges, corporate social responsibility (CSR) processes or in mission and mandate statements.

Most institutions also set practices for codifying, disseminating and asserting ownership for any inventions or discoveries or for biosafety (e.g. embedded in Good Laboratory Practices or other professional or industrial standards). The early phase regulatory process thus includes federal research granting bodies such as the CIHR, NSERC, SSHRC, the Networks of Centres of Excellence, Genome Canada and the Canadian Foundation for Innovation, as they impose and enforce processes and norms through their grants, including the requirement for "leveraged money" and the structure and role of peer review (Lopreite and Murphy 2009; Doern and Stoney 2009; Atkinson-Grosjean 2006).

As long as the efforts and the outcomes of research remain contained in laboratories or greenhouses, formal regulatory oversight does not really begin. If and when a genomics application is proposed for use beyond containment, then governments in Canada and around the world begin to respond. Canada uniquely uses the novelty of the product to trigger assessments—in conformity with World Trade Organization (WTO) norms. Thus the regulator examines product attributes rather than the production and processing methods (PPM) used to produce the product. Novelty can arise either by simply transferring organisms to the eco-system from other areas or by mutagenic or transgenic techniques. Other national systems tend to trigger assessments based on the use of transgenic methods, but still focus their efforts on assessing the risk of using or consuming the resulting products. The practical effect is that the Canadian system catches and assesses more products (e.g. mutagenic crop varieties) than other competing systems. The actual assessment in Canada (and most other countries) is then based on the internationally accepted risk analysis framework (RAF), which encompasses three distinct phases—risk assessment, risk management and risk communications—with different actors assigned different tasks (National Research Council 1983, 1994 and 1996).

At the federal level, the regulators with partial direct or indirect genomic-related mandates, laws, regulations and guidance roles include: Health Canada (and several of its directorates such as the Health Products and Food Branch Inspectorate and Therapeutic Products Directorate); the Canadian Food Inspection Agency; Environment Canada (for those products that do not have Acts listed under the Canadian Environmental Protection Act); Fisheries and Oceans Canada; the Public Health Agency of Canada; the Canadian Intellectual Property Office; the Patented Medicine Prices Review Board; the Canadian Agency for Drugs and Technologies in Health; and the Privacy Commissioner of Canada. All of these agencies operate in analogous and complementary ways, with delegated groups undertaking risk analysis that is then adjudicated by a risk management group and communicated more broadly to the public and interested parties. Each system attempts to reflect the 'common regulatory principles' articulated in the 2007 Regulatory Cooperation Framework between Canada, the US and Mexico.

Genomics-based products are generally evaluated only once in Canada, at the federal level. Nevertheless, provinces at times can be key actors. Given shared constitutional jurisdiction in agriculture, provinces are often important actors in priority setting, funding and management of agri-food research, while many provinces have carved out niches in the genomics research area targeted on their specific economic priorities (often related to health, forestry or the fisheries). BC and Quebec, through Genome BC and Genome Quebec, in particular, have invested in provincially-targeted research competitions. At least as important are the universities which undertake much of the foundational research on genomics. As provincial entities governed on an arms-length basis, universities have their own internal regulatory and policy provisions and processes regarding research ethics, patenting, commercialization, and public-good science (Doern and Stoney 2009).

At the other end of the research chain, provincial agencies are often the most important market for technologies and services. Health departments and drug formularies make decisions about whether to purchase or fund within provincial Medicare programs new genomics-based products or services, including drugs, devices and tests. While products may have been granted patent rights and Health Canada approval, this does not mean that they all will be funded or used in the provincial systems (Canadian Agency for Drugs and Technologies in Health 2008). Numerous provincially-based groups of medical professionals, patients, carers and disease advocates aggressively engage with provincial authorities, seeking to bring forth new and improved prospects. The combination of variable uptake of technology and uneven lobbying by interest groups opens up potential for conflict and differential access to drugs under healthcare.

The story does not stop at the national boundary. International regulatory and policy bodies exert considerable direct and indirect influence on Canada, both through harmonizing the evidence and processes for regulating genomics research and applications and through various kinds of exhortative demonstration effects. In addition to the important scientific, commercial and regulatory links we have built with our major trading partners—especially the US, the European Union and other OECD member states—Canada belongs to a range of international organizations that work to normalize the models, methods and metrics of regulatory practice. Regulators communicate almost daily with colleagues in competent regulatory agencies in other states to identify the appropriate ways to undertake the vital tasks of hazard identification, hazard characterization, exposure assessment and risk characterization. Recent reforms to the US Food and Drug Administration (FDA) have also been important to Canada's potential regulatory reform agenda (Carpenter 2010). The Obama Administration's more aggressive stance in monitoring genomics-related research ethics is also noteworthy (Meslin

2010). And in the larger political-regulatory context, the role of religion in embryonic stem-cell research in the US has served as a cautionary tale in Canada's somewhat more secular political culture (Knowles 2010).

IV. Policy and Governance Options

The overriding challenge is that Canadian regulators have got themselves boxed in, on the one hand, with rising expectations from industry and consumers that recent large public investments in genomics will deliver real benefits soon and, on the other hand, with slowing regulatory processes. As the Phillips McDougal and CropLife Canada studies noted, while a number of genomics-aided technologies and products have run the regulatory gauntlet, many more remain locked in the system. A number of broad policy approaches appear possible, including (1) renewing federal leadership to complete the system, (2) optimizing international regulatory cooperation and harmonization in a global effort to efficiently and effectively regulate genomics-based innovations, (3) opening up space for industry and others to self-regulate and (4) setting a tabula rasa to better engage socio-economic considerations. As with any broadly-defined approach, there are inevitably more specific sub-options within or across each of these (we make some reference to a few of them in our set of further research questions).

4.1 Renewing Federal Leadership to Complete the System

If one interprets the apparent lags in commercialization as simply a lack of federal effort, the most straightforward and direct approach would be for the federal government to complete the regulatory system in this domain and then to appropriately resource it. There are actionable proposals in the federal system regarding some genomic products that would enable regulators to quickly and cleanly create or amend existing rules that could then be used to guide and adjudicate any products now languishing in the system. This would entail completing the regulatory system for second and third generation crop traits, implementing rules for assessing GM animals and fish, clarifying the rules for genetic tests and revamping the processes and procedures for drugs, medical devices and gene therapies. Complementing this, one would expect there might need to be some review of the intellectual property rules for genomics-based inventions (de Beer, Gold and Guaranga 2011; Doern and Prince 2012).

While this seems simple and straightforward, it is not clear that it would necessarily on its own lead to more economically and socially appropriate outcomes. While federal regulators offer an opportunity for a Pre-Notification Consultation, which can provide product proponents with an opportunity to identify the steps required to achieve regulatory approval, many proponents have been hesitant to interact in advance. So part of the challenge is to get more effective engagement between regulators and the regulated. Moreover, in some cases, delays may not be due to a lack of resolve but reflect underlying concerns about the technologies and the scientific and regulatory knowledge available to assess and use these innovations.

There is also evidence that there are real limits to the power of the state, so that even definitive government action may not translate into effective outcomes. Consumers and citizens are able and willing to defy government decisions, acquiring and using technologies and products in unapproved and untested ways. A more subtle yet perhaps more fundamental challenge is that the contingent nature of defining risks, hazards and errors makes it impossible for any jurisdiction to have a clean, straightforward system. This is compounded by the diffusion of responsibility and authority—regulatory authority vested in national agencies is shared with other agencies (e.g. via mutual recognition agreements) and various international intergovernmental organizations while the proponents themselves are heavily involved in any assessment.

One particularly complex issue is personalized medicine, which is fundamentally built upon the genomics revolution (Boyer 2010; Crawley 2008; Economist 2010; Personalized Medicine Coalition 2009). If this application of genomics proves to add value to the medical system, it promises to cause significant changes in the regulatory system, as the current 3-stage clinical trials process and related drug approval system may be fundamentally incompatible with the personalization of drugs and dosage in the context of a person's genome and lifestyle.

The end result is that most product assessments now involve significant reference to other authorities, with many nested decision-making sub-systems contributing to the overall decision.

4.2 Optimizing International Regulatory Cooperation and Harmonization

The processes of coordination and harmonization have varied widely in pace and scope in the recent past. The internationalization of both science and trade has led both to more coordination (i.e., gradual narrowing of differences between systems based on voluntary international codes of practice) and harmonization (i.e., standardization of regulation in identical form) (Davies 2002).The earliest and still the most extensive international collaboration has focused on human health related to food, drugs and chemical pollutants in the environment. An array of international organizations has been created to coordinate and harmonize risk. Over the years membership in these organizations has grown to involve most countries in the world and hundreds of technical committees of regulators, scientists and industrial managers who meet regularly to consider new risks and to develop procedures for managing the processes of evaluating and managing those risks.

These groups are for the most part closed, with admission controlled by the expert group in charge (be it national regulators, policy advisors or research scientists). At times, organizations such as the Food and Agriculture Organization (FAO) and the World Health Organization (WHO) have sought to extend beyond this closed system by commissioning expert panels of independent scientists to consider areas of uncertainty in the international food or health sys-

tems, seeking to contribute to greater understanding of how a risk or an event might assert itself.

Other regional and functional configurations of countries and experts are also engaged in the debate about regulating risks. The Organization for Economic Cooperation and Development (OECD), involving 34 high-income democracies, engages in an array of efforts to harmonize international regulatory requirements, standards and policies in the chemical and biotechnology areas. Apart from codifying practices and providing a forum for coordinating policy development, the OECD has created a new quasi-regulatory instrument in the biotechnology area called a Consensus Document. These mutually accepted scientific reports (52 as of January 2012) codify the biology of a host crop plant or characterization of an introduced trait or transgenic method, thereby providing a common base to be used in a regulatory assessment of an agricultural or food product derived through modern biotechnology.

The above institutions and others centred on the WTO produce practical interdependence that narrows the range of options but also offers an array of fora and processes for examining difficult aspects of emerging risks and, as required, for testing options and resolving disputes about different interpretations of any attendant risk.

4.3 Opening up Space for Industry and Others to Self-Regulate

One response to the slow development of national and international rules has been for individual companies or parts of the industry to implement self-regulation to develop and sustain market access. Generally these systems are effective where it is possible to safely and economically produce a product or service but there are gaps in the regulatory architecture. Provided tort laws exist and are judiciable, governments and the courts, sometimes prodded by disgruntled consumers through class-action law suits, can effectively focus the market in ways that governments alone sometimes find difficult. It is perhaps worth noting in passing that most individuals involved in genomics research and regulation are part of peer, epistemic groups that impose rules and norms that govern individual actions, which undoubtedly have a moderating influence on the actions of the institutions employing them.

There are a number of cases where parts of the agri-food industry, in particular, have developed systems to deliver products with higher standards than domestic or even international minimum standards. The red meats industry in Australia (Spriggs and Isaac 2001), the canola industry in Canada (Gray, Malla and Phillips 2006; Phillips and Smyth 2004), retailers and processors in the EU, North America and Asia (Phillips and McNeill 2001) and the corn industry in the US, have all adopted private standards to differentiate and control quality in the supply chain. For example, the Canola Council of Canada has an industry constructed Export Ready Program that binds seed developers to acquire foreign regulatory approval before they commercialize new varieties while the Canadian soybean industry has an industry-operated identity preservation system to differentiate conventional soy from GM soy, facilitating high-value export markets in Japan.

This approach is increasingly subsumed in the broader debate and effort to sustain co-existence of GM and non-GM production in core agri-food markets (GMCC 2011). Over time, private standards, supplemented by Hazard Analysis and Critical Control Processes (HACCP) protocols or International Standards Organization ratings (particularly ISO 9000 and 14000 series) could realistically supplement public regulation—especially regulation that goes beyond considering the narrow public health and safety agenda. In order to address market demands for traceability and separability, new physical and organizational infrastructure are emerging. Already the ISO has developed new eco-labeling standards (ISO 14020 and ISO 14024) which offer industry the opportunity to use the standards to support environmental goals but also as a way to avoid some environmental challenges to their products in domestic or foreign markets.

While currently underdeveloped, this approach represents an interesting possibility for industry to manage its own regulatory space through creating and promoting higher industry standards that ensure both regulatory and market acceptance of their products. A major advantage is that such an approach would not require industry to carve off large chunks of the regulatory pie. Instead, problems can be resolved in bite-sized pieces as problems and opportunities are identified—as in the past, private standards setting can then be institutionalized through reference and recognition in the formal regulatory system.

4.4 Setting a Tabula Rasa to Better Engage Socio-Economic Considerations

Genomics applications at times challenge the current architecture for science, regulation and intellectual property rights, opening the door to new actors with new questions and new values, interests and beliefs.

To many, 'science' is simply not adequate. In the absence of agreement on what makes a 'scientific consensus' (Kuhn 1970 called consensus a 'paradigm' which incorporates known theories and known evidence, or his known-knowns), it is not clear when there is enough science. Simply filling in Kuhn's unknowns (i.e., where we either have a lack of theory or evidence) will not satisfy many, as they assert paradigms are simply reflections of the prevailing power systems and not ultimate truths.

Those unwilling to simply continue the slow, patient work of filling in the unknowns generally fall into two camps. Some want a whole new set of rules that reflect new norms while others simply want a way to pause the process for a while. Both camps have looked to use the emerging norm of 'precaution' as a way to achieve a different outcome (Vogel 2012). All countries have some form of precaution in their systems, either formally articulated or informally used, that enables them to delay or suspend judgment on a product that is suspected to pose unacceptable and irreversible risks.

The first articulation of precaution was in the World Charter for Nature in 1982. Since that time the policy has been expressed in numerous national and international regulatory systems. Principle 15

of the 1992 Rio Declaration on the Environment and Development states: "(i) in order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation." The Commission of European Communities offered guidelines for using its version in a politically transparent manner: "measures … must not be disproportionate to the desired level of protection and must not aim at zero risk … comparable situations should not be treated differently and … different situations should not be treated in the same way, unless there are objective grounds for doing so … measures … should be comparable in nature and scope with measures already taken in equivalent areas in which all the scientific data are available … measures must be of a provisional nature pending the availability of more reliable scientific data … scientific research shall be continued with a view to obtaining more complete data" (Commission of the European Communities 2000, 19-21). International law is conflicted about how to deal with precaution—the World Trade Organization (WTO) offers a narrow and science-based process for managing precaution while the Cartegena Protocol on Biosafety (CPB) embodies a definition of precaution that is more expansive and could lead to extended delays. While Canada and the US reject the EU and CPB conception of the precautionary principle (which they argue has been used to delay decisions excessively), they both have precaution as a guiding principle in their assessment systems. The difference would appear to be more in intent and effect rather than in general principles.

Those who want a more permanent change in the power system are seeking to place socio-economic considerations (SEC) at the centre of decision making. Some assert that the scope for SEC in the WTO is not fully tested—the preamble of the Marrakesh Agreement (1994) affirms "…the objective of sustainable development, seeking both to protect and preserve the environment…" It is not clear what flexibility and policy space is available in the sub-agreements, in particular. Risk assessment under the WTO Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement), for example, already involves a mix of scientific and economic considerations: "Members shall take into account as relevant economic factors: the potential damage in terms of loss of production or sales in the event of the entry, establishment or spread of a pest or disease; the costs of control or eradication in the territory of the importing Member; and the relative cost-effectiveness of alternative approaches to limiting risks" (Article 5.3). In the meantime, other venues have emerged where socio-economic considerations are accepted and at times are more influential than science in determining decisions.

Those opposed to opening the regulatory system to more non-scientific considerations express concern that it would generate more red-tape, undermine regulatory predictability and delay innovation. Such measures could also undermine Canada's trade advocacy work, which often relies on scientific arguments to open and maintain foreign markets for Canadian goods. Changing Canada's policy for genomics applications might create a precedent that would have unintended consequences for other aspects of Canada's economy.

V. Practical Application and Considerations

A number of practical issues that emerge from the above analysis were discussed by three commentators at the Canadian Science Policy Conference in November 2011, by other reviewers and by participants in the workshop session that followed. Three specific considerations flow from the ongoing evolution of the genomics regulatory-science regime.

First, while all four of the policy and governance options provide different separate focal points for change, they also overlap and interact with each other. Thus the federal, international, self-regulatory, and socio-economic arenas are likely to change both in response to internal pressures and due to their deepening links and complexities. Each represents simultaneously multi-level and spatial arenas of politics, power, government versus governance, values, science and knowledge related to and involved with genomics. Indeed, one of the specific suggestions to emerge from the discussion was that the federal government, in concert with other players, needed to take explicit steps to foster better basic public understanding of the current system.

A second practical matter is whether the current system is up to the challenges to be faced and whether overall these challenges require new laws and regulations or whether, on balance, it is best to work towards gradual and incremental change. There are already laws and regulations in place—many regulatory practitioners, in the face of considerable technical and political uncertainty, assert that laws and regulations are complex and time consuming to change and implement through the full Parliamentary or Cabinet processes, especially if they require federal-provincial or international coordination and agreement. This logic then leads one to consider softer guidance and guideline approaches and for governance rather than just government approaches. The dilemmas were illustrated by discussion in the workshop. While the federal Cabinet Directive on Streamlining Regulation (CDSR) and Health Canada Blueprint announcements related to life-cycle approaches suggests major changes are in the offing, both so far are more aspirational than operational. Similarly, while there is extensive effort to develop greater coordination and harmonization at the international level, the extent of change that is possible depends on differences in the core political economy of North American and Europe. Currently there appears to be more opportunity for convergence in processes guiding the regulation of health products, but less in the areas of agriculture, food, fisheries and the environment.

A third concern is whether greater practical clarity can be provided to differentiate the regulatory functions from promotional considerations. The Canadian government is quite legitimately concerned about and engaged in regulation making and assessment of genomics applications and in the development and promotion of genomics-based innovation. The challenge is that both roles create new linkages domestically and internationally that would be difficult

if not impossible to codify in statute or regulation. It is far from clear whether further guidance is possible or whether this is inevitably an area of regulatory judgement and discretion left to front-line regulators.

VI. Future Research Questions

Five areas for further research emerged in the context of the development of this policy brief.

6.1 Precisely how, and to what extent, can different forms of self-regulation complement or reinforce the current science-based formal regulatory system?

6.2 What forms should the federal CDSR and Health Canada post-market monitoring life-cycle approach take? Should it remain a policy and governance aspiration or can it actually be implemented? How can or should we balance effectiveness, efficiency and democratic ideals in the full life cycle ?

6.3 Are periodic large-scale technology assessment processes desirable as a complement to the current novel-product-centred assessment system? The current genomics regulatory-science regime does not purport to regulate genomics as a transformative technology per se but rather focusses on particular novel products and applications. If a more comprehensive review is needed, how could it be structured (e.g., as periodic reviews every five to seven years)? How should it engage experts and the public?

6.4 Rather than try to tinker with the current nationally-based set of regulatory assessments to accommodate new perspectives, is there any potential for an entirely new approach that might instead offer an authoritative, globally-based, open-source regulatory science and assessment process? Given that no single country is fully competent to undertake the current tasks, is there some way to pool our resources and competencies to strengthen the system that will enhance both safety and innovation?

6.5 In the context of federal austerity measures and budget and staff cuts, are the core science and evidence-based regulatory capacities of the current system being maintained? Moreover, will there be adequate resourcing to develop the new capacities that may be needed as genomic research and products increase in volume and complexity?

References

Andree, Peter (2009) Genetically Modified Diplomacy: The Global Politics of Agricultural Biotechnology and the Environment. Vancouver: University of British Columbia Press.

Atkinson-Grosjean, Janet (2006) Public Science, Private Interests: Culture and Commerce in Canada's Networks of Centres of Excellence. Toronto: University of Toronto Press.

Boyer, Peter J. (2010) "The Covenant", The New Yorker, September 6, 60-67.

Brunk, Conrad B., and Harold Coward, eds. (2009) Acceptable Genes: Religious Traditions and Genetically Modified Foods. Albany: State University of New York Press.

Bunton, Robin and Alan R. Petersen (2005) Genetic Governance: Health, Risk and Ethics in the Biotech Era, (London: Routledge).

Canada (2007) Cabinet Directive on Streamlining Regulation (CDSR) (Government of Canada).

Canada, (2012) About the Genomics R&D Initiative (Genomics R&D Initiative) http://grdi-irdg.collaboration.gc.ca.

Canadian Agency for Drugs and Technologies in Health (2008) Annual Report. Ottawa: Canadian Agency for Drugs and Technologies in Health.

Canadian Coalition for Genetic Fairness (2010) "About CCGF," http://ww.ccgf-cceg.ca/en/about-ccgf.

Carolan, Michael S. (2010) "The Mutability of Biotechnology Patents: From Unwieldy Productsof Nature to Independent 'Objects'", Theory, Culture and Society, 27, 110-129.

Carpenter, Daniel (2010) Reputation and Power: Organizational Image and Pharmaceutical Regulation at the FDA (Princeton University Press).

Castle, David (2009) (Ed.) The Role of Intellectual Property Rights in Biotechnology Innovation. (Cheltenham: Edward Elgar).

Caulfield, T., Ries, N., Ray, P., Shuman, C. and Wilson, B. (2010), Direct-to-consumer genetic testing: good, bad or benign?. Clinical Genetics, 77: 101–105. doi: 10.1111/j.1399-0004.2009.01291.x

Commission of the European Communities (2000) Communication From the Commission on the Precautionary Principle. COM(2000). Brussels: European Commission, February 2.

Crawley, Richard H. (2008) Edging Towards BioUtopia: A New Politics of Reordering Life and the Democratic Challenge (University of Western Australia Press).

Davies, L. 2002. "Technical cooperation and the international coordination of biotechnology inventions". Journal of Law and Society, 29(1), 137-62.

de Beer, Jeremy, Richard Gold and Mauricio Guaranga (2011) Intellectual Property Management: Policy Issues and Options, Genome Canada, Policy Brief No. 4, August.

Deckha, M. (2009) "Holding on to Humanity: Animals, Dignity, and Anxiety in Canada's Assisted Human Reproduction Act," Unbound, 5: 21-54.

Doern, Bruce (2007) Red-Tape, Red-Flags: Regulation in the Innovation Age. (Ottawa: Conference Board of Canada).

Doern, Bruce (2011) Strengthening the Governance Oversight of Regulation and Red Tape Reduction: Improving Transparency, Predictability and Accountability. Paper Prepared for the Red Tape Reduction Commission.

Doern, Bruce, M.Hill, M.Prince, and R.Schultz, eds. (1999) Changing the Rules: Canada's Changing Regulatory Regimes and Institutions (University of Toronto Press).

Doern, Bruce and Jeffrey Kinder (2007) Strategic Science in the Public Interest: Canada's Government Laboratories and Science-based Agencies. (Toronto: University of Toronto Press).

Doern, Bruce, and Michael J. Prince (2012) Three Bio-Realms: Biotechnology and the Governance of Food, Health and Life in Canada (University of Toronto Press).

Doern, Bruce, and Christopher Stoney (2009) Research and Innovation Policy: Changing Federal Government-University Relations. (Toronto: University of Toronto Press).

Economist (2010) "Biology 2.0: A Special Report on the Human Genome", The Economist, June 10, 3-16.

GM Co-existence Conference (2011) Coexistence 2.0: Achieving Coexistence of Biotech, Conventional & Organic Foods in the Marketplace, Vancouver, October 26-28. www.gmcc-11.com.

Gray, R., S. Malla and P. Phillips (2006). "Product innovation in the Canadian canola sector" Supply Chain Management: An International Journal 11(1), 65 – 74.

Harris, John (2010) "Promise and The Risks From Life Not As We Know It", Financial Times, 27 May, 8.

Health Canada (2006) Blueprint for Renewal: Transforming Canada's Approach to Regulating Health Products and Food. (Ottawa: Health Canada).

Health Canada (2007) Blueprint for Renewal II: Modernizing Canada's Regulatory System for Health Products and Food. (Ottawa: Health Canada).

Jarvis, Bill (2000) "A Question of Balance: New Approaches for Science-Based Regulation" In G. Bruce Doern and Ted Reeds, (Eds.) Risky Business: Canada's Changing Science-Based Policy and Regulatory Regime. (Toronto: University of Toronto Press) 307-333.

Jones, David P. and Anne S. de Villars (1999) Principles of Administrative Law Third Edition. (Toronto: Carswell).

Kinder, Jeffrey S. (2010) Government Laboratories: Institutional Variety, Change and Design Space. Ottawa: Unpublished Doctoral Dissertation, School of Public Pol-

icy and Administration, Carleton University.

Knoppers, Bartha M., and Rosario M. Isasi (2004) "Regulatory Approaches to Reproductive Genetic Testing," Human Reproduction, Vol. 19, no. 12, 2695-2701.

Knowles, Lori P. (2010) "Religion and Stem Cell Research", Stem Cell Network.http://www.stemcellnetwork.ca/index.php.

Kuhn, T. (1970), The Structure of Scientific Revolutions, 2nd Edition (Chicago: University of Chicago Press).

Lopreite, Debora, and Joan Murphy (2009), "The Canada Foundation for Innovation as Patron and Regulator", in Bruce Doern and Chris Stoney, (Eds.) Research and Innovation Policy: Changing Federal Government-University Relations. Toronto: (University of Toronto Press), 123-147.

Maheu, Louis, and Roderick A. Macdonald (Eds) (2010) Challenging Genetic Determinism: New Perspectives on the Gene in Its Multiple Environments. (Montreal and Kingston: McGill-Queen's University Press).

May, Peter J. (2007) "Regulatory Regimes and Accountability," Regulation and Governance, Vol. 1, No. 1, March, 8-26.

Meslin, Eric M. (2010). What to Expect From the New Bioethics Commission, Science Progress. http//www.scienceprogress.org/2010/05/problemsolvers.

Miller Chenier, Nancy (1994) Reproductive Technologies: Royal Commission Final Report. Ottawa: Library of Parliament, Political and Social Affairs Division, April 22.

Miller Chenier, Nancy (2002) Intergovernmental Consultations on Health: Toward a National Framework on Reproductive Technologies, 2002. http://dsp-psd.pwgsc.gc.ca/Collection-R/LoPBdP/PRB-e/PRB0234-e.pdf

National Research Council (1983). Risk Assessment in the Federal Government: Managing the Process. (Washington D.C. National Academy Press).

National Research Council (1994). Science and Judgment in Risk Assessment. (Washington D.C. National Academy Press).

National Research Council 1996. Understanding Risk: Informing decisions in a Democratic Society. (Washington D.C.:National Academy Press).

National Research Council Canada (2010) Evaluation of The Genomics R&D Initiative (GRDI) (National Research Council of Canada).

National Roundtable on the Environment and the Economy (2011) Canada's Opportunity: Adopting Life Cycle Approaches For Sustainable Development (Ottawa: National Roundtable on the Environment and the Economy).

New Democratic Party (2010) NDP Moves to Outlaw Genetic Discrimination. Press Release by New Democratic Party. http://www.NDPCOM@parl.gc.ca. April 14.

Organization for Economic Cooperation and Development (2012) Recommendation of the Council on Regulatory Policy and Governance (Paris: OECD).

Pal, Leslie A. (2012) Frontiers of Governance: The OECD and Global Public Management Reform (Palgrave Macmillan).

Personalized Medicine Coalition (2009) The Case For Personalized Medicine. (Washington, D.C.: Personalized Medicine Coalition).

Phillips, Peter, and S. Smyth (2004). "Managing the Value of New-Trait Varieties in the Canola Supply Chain in Canada". Supply Chain Management, 9(4), pp. 313-322.

Phillips, Peter, and H. McNeill (2001). "National Labelling Policy for GM Foods". AgBioForum 3(4), pp. 219-224.

Phillips, Peter W.B. (2007) Governing Transformative Technological Innovation: Who's in Charge? (London: Edward Elgar).

Phillips, Peter, et al. (2010) A Response to the Nuffield Council on Bioethics Consultation Paper: New Approaches to Biofuels. University of Saskatchewan, April 27.

Phillips McDougall. (2011) The cost and time involved in the discovery, development and authorization of a new plant biotechnology derived trait: A consultancy study for Crop Life International. http://www.biotech.ucdavis.edu/PDFs/Getting_a_Biotech_Crop_to_Market_Phillips_McDougall_Study.pdf. September.

Prince, Michael J. (1999) "Civic Regulation: Regulating Citizenship, Morality, Social Order and the Welfare State," in G.B. Doern, M. Hill, M. J. Prince and R. Schultz, (Eds.) Changing the Rules: Canadian Regulatory Regimes and Institutions. (Toronto: University of Toronto Press) 201-227.

Prince, Michael J. (2010) "Self-Regulation, Exhortation, and Symbolic Politics: Gently Coercive Governing?" in G. Toner, L.A. Pal, and M.J. Prince, Eds. Policy: From Ideas to Implementation – A Book in Honour of Professor G. Bruce Doern. (Montreal and Kingston: McGill-Queen's University Press), 77-108.

Royal Commission on New Reproductive Technologies (1993) Proceed with Care – Final Report (Ottawa: Minister of Government Services Canada).

Supreme Court of Canada (2011) Reference Re: Assisted Human Reproduction Act (2010) Supreme Court of Canada.

Spriggs, J. and G. Isaac (2001) Food Safety and International Competitiveness: The Case of Beef. Oxon UK: CABI Publishing.

Tranberg, J. (2012) Raising Regulatory Efficiency. Presentation to VALGEN's Bioproducts and Crops Regulation: Challenges and Opportunities International Workshop, Vancouver, March 6-7.

Vogel, David (2012) The Politics of Precaution: Regulating Health, Safety, and Environmental Risks in Europe and the United States (Princeton University Press).

Wade, Nicholas (2010) "A Decade Later, Genetic Map Yields Few New Cures", New York Times, Jun 12, 21.

Wiles, Anne (2007) Strategically Natural: Nature, Social Trust and Risk Regulation of Genetically Modified Foods and Natural Health Products in Canada. Ottawa: Unpublished Doctoral Thesis, Department of Geography, Carleton University.

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