Genome Canada – Strategic Research Theme:

Securing Canada's Future Bio-Based Economy through Genomics

Prepared by:

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July 3rd, 2007

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Executive Summary

The bioproducts sector offers a unique avenue for Canada to pursue concrete environmental targets, while building a future foundation of the Canadian economy. A multitude of drivers are pointing to continued and rapid growth of the bioproducts sector in Canada and around the world, including the growing gap between demand and supply of petroleum and the increasingly unsupportable burden of greenhouse gas emissions from the production and consumption of petroleum fuels products. Governments throughout the world are investing heavily in the development of their bioproducts sectors. If Canada is to capitalize on its huge landmass and store of renewable resources, its world leading bioproducts companies, and its strengths in genomics and related science and technology areas, it must build upon the many significant federal funding programs recently put in place, and tackle areas of central concern to the Canadian bioproducts sector with a comprehensive multidisciplinary approach that includes a strong genomic component. A key step towards this goal will be the adoption by Genome Canada of the Biofuels and Bioproducts Strategic Research Theme as a priority.

There is an undeniably profound relationship between genomics and bioproducts. Genomics will allow us to understand and manipulate the underlying biological processes that are the engine of the bioeconomy. While the production of a vast range of bioproducts is currently possible, only a small fraction is economically viable given existing technology. Genomics holds the promise to revolutionize the bioproducts sector by its ability to directly impact three of the biggest challenges in advancing bioproducts value chains:

Area of Impact #1 - Feedstock Optimization: Significant work is required to help ensure the right feedstock is available at the right place and at the right price to support a rapidly expanding Canadian bioproducts and biofuels sector. The challenges to Canada involve both the optimization of feedstocks for the diversity of Canadian climatic regions, and the optimization of feedstock traits for industrial applications. Canada has specific research strengths, genomics and otherwise, in all three primary classes of industrial feedstocks: lignocellulosic crops, oilseeds, and cereals and grasses.

Area of Impact #2 – Microorganisms for Sustainable Processing Technologies: To achieve sustainability, the conversion of biomass into fuels and products calls for the massive deployment of novel enzymes and new fermentation processes. Genomics will greatly accelerate the identification, development and optimization of enzymes and microorganisms for a myriad of uses in the bioproducts sector, including the production of biofuels, biochemicals, and biomaterials, as well as the extraction and production of high-value bioactive compounds.

Area of Impact #3 – Value Added-Bioproducts: A key to the realization of viable biorefineries is the development of processes whereby low or negative value biomass residue from one industrial process is transformed into higher value bioproducts. Closely related is the need to identify high-value compounds from biological sources, which can anchor and make viable the production of a much larger range of bioproducts.

In addition, the intersection of bioproducts and genomics raises a number of exciting research opportunities and challenges concerning various ethical, economic, environmental, social and legal issues related to sustainability.

Existing Canadian bioproducts initiatives have not adequately acknowledged the role and potential of genomics, and none have exploited the broader community of genomic researchers and existing infrastructure. The lack of a unified approach to the application of genomics to the opportunities of the bioproducts sector in Canada flies in the face of efforts elsewhere, and is limiting the effectiveness and depth of the potentially huge contributions that could be made. Aggressively pursuing this research theme would fill a distinct gap in existing efforts, while simultaneously strengthening the research and commercialization efforts already underway and capturing important future international market niches for Canadian industry.

Capitalizing on substantial previous investments in infrastructure and expertise, the Canadian genomic research community is poised to make significant contributions to the bioproducts sector, with multiple beneficial environmental, social, and economic outcomes. To aggressively pursue this Strategic Research Theme, it is estimated that an investment from Genome Canada of approximately $75M will be required.

Table of Contents

1 - Introduction 1
2 - Relevance of the Bioproducts Sector to Canada's Future 1
3 - The Role of Genomics in Growing the Canadian Bioproducts Sector 3
4 - Areas of Impact 4
Area of Impact #1 – Feedstock Optimization 4
Area of Impact #2 – Microorganisms for Sustainable Processing Technologies 5
Area of Impact #3 – Value-Added Bioproducts 6
5 - Capacity 7
6 - Stakeholder interest and support 8
7 - Socio-Economic Outcomes 9
8 - Budget Request 10
9 - The consultative process used to develop this Position Paper 10
References 11
Charts and Tables 12

Acknowledgements:

Financial support for the preparation of this Position Paper was provided by Genome Canada, Génome Québec and Genome British Columbia. In addition, Genome Prairie organized a workshop in Saskatoon on March 1, 2007 that included this Strategic Research Theme. We thank Faye Pagdonsolan of Genome Prairie for her help in compiling the coordinates of supporters and Genny Cardin of Genome Canada for her organization of the National Workshop. We are also grateful for the strong support provided by the Chief Scientific Officers of all the genome centres and other staff members at Génome Québec and Genome British Columbia.

1 - Introduction

The magnitude of the opportunity represented by the bioproducts sector cannot be overstated. It can be said with certainty that the Canadian (and global) economy has begun an inevitable shift towards a bio-base. As the increase in demand for energy continues to accelerate, we are seeing mounting pressure to switch production from the petroleum-based materials, chemicals and fuels that underpin our economy to a more sustainable basis, with renewable resources as the foundation. Add to this the promise of a reduced carbon footprint that the bioproducts sector offers, and the need for significant action to stimulate Canada's emerging bioproducts sector is clear.

A broad definition of the term "bioproducts" has been adopted in developing this Position Paper. Bioproducts are commercial or industrial products that are composed in whole or in significant part of biological, renewable materials derived from plants, animals, or microorganisms. Bioproducts include chemicals, materials, fuels, and energy, but exclude food, feed, timber, and conventional wood products. Examples of bioproducts include biofuels such as ethanol and biodiesel, electricity from biomass, bioplastics, natural fibre composites, as well as biologically-derived paints, lubricating oils and fine chemicals. Similarly, the term "genomics" as used in this paper includes a broad group of related sciences, including proteomics, metabolomics, bioinformatics, and systems biology.

The field of bioproducts is fundamentally about harnessing the output of living systems to create the energy, chemicals and materials that sustain modern society. The field of genomics concerns the understanding of these living systems at the most fundamental level. Clearly, the field of genomics will shape and drive the development of the bioproducts sector in profound ways. This Position Paper makes the case for adopting the strategic research theme "Securing Canada's Future Bio-based Economy through Genomics" as a major focus for Genome Canada in the immediate future.

2 - Relevance of the Bioproducts Sector to Canada's Future

The 20th century witnessed unprecedented global economic growth, boosted by the exploitation of cheap fossil fuels. However, continued reliance on fossil fuels to feed society's voracious appetite for petroleum-based energy, chemicals and materials promises unsupportable negative impacts, both environmental and economic.

Environmentally, the massive injection of carbon into the atmosphere caused by the combustion of fossil fuels has been identified as a critical contributor to anthropogenic climate change – perhaps the greatest crisis the global community has yet faced. The mountain of evidence being developed by international bodies such as the International Panel on Climate Change [1] points to the impending onset of massive climatic disruptions. The Stern Review [2] has estimated the economic costs of the damage caused by a business-as-usual approach to climate change will be equivalent to a 5 to 20% reduction in global GDP. If the reality proves to reflect even the very bottom end of the range of predictions, the consequences will be devastating. Although Canada generates 2% of the world's greenhouse gas emissions, on a per capita basis Canada is one of the worst emitters. Our obligation to take dramatic action is correspondingly great.

In addition to addressing the challenge of greenhouse gas emissions, a robust bioproducts sector promises to seriously reduce a broad range of environmental pollutants currently released in the production and use of fossil fuel, with corresponding positive impacts on human and ecosystem health.

Economically, the growing fragility of our economy's overwhelming dependence on petroleum must be recognized. Issues of global energy security and cost are permeating economic and policy agendas. Factors such as the dramatic increases in the price of oil and the volatility in energy markets cannot be seen as isolated phenomena, but represent the growing gap between supply and demand. Climatic disruptions such as hurricane activity in the Gulf of Mexico are now having direct and substantial impacts on petroleum prices, and the threat of geopolitical conflict, such as open hostilities with Iran, is seen by many as an even greater risk. Despite Canada's rare status among developed countries as a net exporter of energy, the Canadian economy is in no way shielded from these risks.

The transition to a bioeconomy, if done in a sustainable manner, promises to mitigate the substantial economic and environmental risks outlined above. The development of biomaterials and biochemicals, and their successful introduction in the market, will displace petroleum-based counterparts, placing the Canadian economy on the sustainable basis needed to maintain and enhance the quality of life of Canadians beyond the petroleum era. Vital areas of the Canadian economy such as the energy, chemical, and automotive sectors, not to mention the forestry

and agricultural sectors, will be among the first to benefit from this transition, but bioproducts will increasingly permeate all sectors of the market.

In addition to the overwhelming economic and environmental drivers pointing to the importance of the bioeconomy for Canada's future, there are a host of other drivers relevant to the Canadian situation that reinforce this sector's growing importance, some of which are:

- A growing focus on resource upgrading – enhancing the benefits to Canada by adding value to our natural resources;
- New enabling technologies that are being developed;
- Serious "pain points" in the agricultural and forestry sectors, and in some of the industries that have been large consumers of renewable resources, which are motivating stakeholders to consider new opportunities. This is closely related to the pressing need for economic renewal in rural areas;
- Growing awareness of bioproducts opportunities among business leaders;
- Accelerated development of bioproducts, particularly in biofuels, amongst Canada's major trading partners;
- Regulatory changes which have eliminated the traditional management of various potential feedstocks, including deadstock, septage, biosolids, and some industrial organics;
- Increasing market pull (public and commercial) for "green" products; and
- Increasing validation of bio-based business models.

Underlying the above discussion is the fact that bioproducts are now beginning to successfully compete in the open market on strictly economic terms. With process and technology improvements driving down the costs of production, combined with volatile petroleum prices, the bioproducts sector increasingly offers equivalent or superior functionality at an attractive price point.

International Relevance

That Canada has begun a transition to an economy that is increasingly bio-based is not in doubt. What is in question is whether we as a country will be at the front of this wave, capitalizing on our vast biomass availability and innovative capacity, or whether we will cede leadership to other players. Reacting to many of the same economic and environmental drivers in play within Canada, other developed countries are pursuing integrated national bioproducts strategies, and investing heavily in strategic areas such as biofuels, bioenergy, and biochemicals. With the global bioproducts sector anticipated to grow to $300 Billion by 2010 (up from $60 Billion in 2003) [3], the stakes are high.

International competition in this space is heating up rapidly. A bill committing $4.5B US for biomass research and loans through to 2012 has recently passed the House [4], on top of the more than $750M US being invested by the Department of Energy in a variety of renewable energy programs [5,6]. The European Union's 7th Framework Program, with a budget of 5B Euros, has targeted bioproducts projects for support for the period 2007-2013 [7]. China has announced an astounding $180B US investment in renewable energy through to 2022 [8].

Given Canada's huge landmass and store of renewable resources, our world leading bioproducts companies [9], and our strengths in many relevant S&T areas, we have the capacity to carve unique areas of leadership for Canada. However, concerted action on a national scale is necessary now to ensure that this happens.

The bioproducts sector's combination of substantial economic and environmental outcomes represents a unique opportunity for Canada. It is an avenue that allows us to directly pursue concrete environmental targets while simultaneously building a foundational sector of the Canadian economy. The international commercialization of Canadian innovation in the bioproducts sector not only strengthens Canadian industry and Canada's global competitive position, but contributes to reducing the carbon intensity of industry wherever uptake is achieved.

Alignment with Federal and Provincial Priorities

The bioproducts theme resonates with multiple federal and provincial priorities, including but not limited to sustainable development, climate change initiatives, pollution prevention initiatives, rural and regional development initiatives, and the greening of government operations. The broader field of biotechnology has been front and centre in recent commercialization, innovation, and S&T initiatives, with the bioproducts sector increasingly prominent. The bioproducts sector is also beginning to be seen as a growing vehicle for regional and rural economic development.

While Canada does not yet have an integrated national bioproducts strategy, the new science and innovation policy emerging from the Office of the Prime Minister / Industry Canada [10] is creating a policy environment that is strongly supportive of the bioproducts sector. Encouraged by this favourable policy climate, the bioproducts efforts that have been developing within many federal departments and institutions are gaining increasing priority and visibility. Table 1 lists recent high profile federal bioproducts programs. Provincial government bioproducts initiatives are equally compelling. Several provinces have set targets for renewable energy content (Table 2), and significant provincial funding programs are available in virtually all provinces [11].

This Strategic Research Theme dovetails naturally with the various federal and provincial initiatives. None of the existing Canadian bioproducts programs adequately acknowledges the role and potential of genomics, and none exploits the broader community of genomic researchers and existing infrastructure. The lack of a unified approach to the application of genomics to the opportunities of the bioproducts sector in Canada flies in the face of efforts elsewhere (e.g., the Genome-to-Life Program of the US Department of Energy), and is limiting the effectiveness and depth of the potentially huge contributions that could be made. Aggressively pursuing this research theme would fill a distinct gap in existing programs, while simultaneously reinforcing and completing the research and commercialization efforts already underway, and assist in capturing important future international market niches for the Canadian economy.

3 - The Role of Genomics in Growing the Canadian Bioproducts Sector

While it is clear that Canada and the world have begun an inevitable transformation towards a bioeconomy, it is also true that this transformation is in its infancy. A number of challenges must be met if this transition is to be accelerated. Investment in Genomics at this time will allow Canada to gain maximum benefit from substantial existing genomic resources and build on these to make a major impact in the bioproducts sector. There is an undeniably profound relationship between genomics and bioproducts and the marriage of these fields will have revolutionary consequences, both long term and in the more immediate future. Genomics will allow us to understand and manipulate the underlying biological processes that are the engine of the bioeconomy. Sections 4 & 5 map out the areas where Canada's strengths in genomics can directly benefit the Canadian and international bioproducts sectors.

The fundamental issue facing the bioproducts sector is the necessity for it to compete on strictly economic terms. Of the vast range of bioproducts that is currently possible to produce, only a small fraction is at present economically viable. For the bioproducts sector to grow, strong bioproduct companies must be competing successfully on the open market. Optimization of the entire value chain is required, from feedstock production through to the delivery of end products. As noted by McKinsey & Company, in addition to the price of petroleum, two of the biggest determinants of the cost of production are the cost and availability of feedstocks, and the conversion technologies that are available [12]. The Canadian genomic community has the capacity to directly impact both these challenges.

The biorefinery concept can be defined as the co-location of a suite of synergistic industrial processes for the purposes of maximizing the value derived from a particular feedstock stream while minimizing the environmental footprint. The model is an important component of achieving economic competitiveness in the bioproducts sector. The identification and development of value-added bioproducts is the third area of impact, addressing the utilizing the residual biomass from one industrial process as the starting feedstock for a complementary processing line. The development of value-added bioproducts is a key to realizing maximum value for the Canadian bioproducts sector. Closely related to this is the identification and development of high-value bioproducts, which can make viable the production of a much broader range of products in a biorefinery model. Section 4 examines each of these three areas of impact in more detail.

GE^{3}LS – Genomics and Ethical, Economic, Environmental, Legal and Social Implications

The transition to a bioeconomy is a cornerstone of a sustainable and prosperous future for Canada. Sustainability is measured along three axes: the economy, the environment and society. Bioproducts and genomics simultaneously raise a number of exciting research opportunities and challenges pertinent to sustainability, including (but certainly not limited to):

- Appropriate economic and policy structures for developing and governing the bioproducts sector;
- The economic and social impacts of redirecting traditional food and feed crops for industrial purposes, and from converting food producing agricultural land over to producing industrial crops;

- The myriad of issues surrounding the engineering of new crop platforms, including risk mitigation, avoidance of unintended cross-breeding, and public acceptance;
- The ecological and other environmental ramifications of greatly increased biomass output, including the use of marginal agricultural lands, the use of crop residue, water utilization, soil quality, as well as implications for biodiversity and conservation;
- Issues of rural economic renewal, and of aligning rural and urban agendas; and,
- Challenges around performance evaluations, life cycle analysis, and other systems for validating environmental performance.

GE^{3}LS research into these and a host of other issues will be embedded within the projects arising from this Strategic Research Theme.

4 - Areas of Impact

The following discussion will focus on the short to medium term impacts that could be realized within three areas of focus – feedstock optimization, utilization of microorganisms in bioprocesses, and the development of value-added bioproducts. Each of these areas represents a constellation of specific strengths in Canadian genomic research capacity that can be aligned with the identified needs of industry stakeholders to accelerate the Canadian bioproducts sector. It should be noted that coordinated research in the three areas of impact will generate new interdisciplinary synergies, and they should therefore be viewed not in isolation, but as an integrated package. For example, it will be essential to coordinate research on plant feedstock optimization with research on biomass conversion, so that potential new feedstocks can provide the substrate for novel conversion processes. Similarly, research in value-added bioproducts will greatly benefit from the identification of genes affecting fundamental cellular processes underlying plant and microbial metabolic regulation, which will enable the engineering of a broader repertoire of new feedstocks as well as novel processing opportunities. Thus, a coordinated and sustained genomic research investment in all three of the impact areas outlined below will be required to achieve the goals of ensuring Canadian competitiveness in the emerging global bioeconomy.

Area of Impact #1 – Feedstock Optimization

Problems to be tackled: While Canada has a huge landmass compared to other countries, this does not necessarily translate to a corresponding advantage in biomass availability. The major portion of the biomass is too remote, and / or too expensive to produce / harvest. Significant work is required to help ensure the right feedstock is available at the right place and at the right price to support a rapidly expanding Canadian bioproducts sector. The challenges to Canada are two-fold with respect to optimizing feedstocks for the production of bioproducts:

1) Agricultural and forestry feedstocks must be optimized for the diversity of Canadian climatic regions. Significant value will also be delivered in optimizing feedstocks for production on more marginal lands, and for reduced input growing regimes (e.g., fertilizer and irrigation). At the same time, maximization of biomass production must be realized without compromising the properties of the plant (oil content, fibres, starches) that make it valuable for industrial purposes.

2) Feedstock quality must be optimized to align with bioproducts applications. While crops have long been optimized for food and feed, a similar process of optimization has now begun in earnest for industrial end-purposes.

Canada has specific research strengths (genomics and otherwise) in all three primary classes of industrial feedstocks, each of which has its specific challenges and research goals:

a) Lignocellulosic crops: A thorough understanding of secondary cell wall / lignocellulose deposition and structure will reveal avenues for efficient cell wall deconstruction and sugar release for fermentation. The goal is to produce biomass that has abundant and high quality cellulose / fibre, reduced and/or easily extracted lignin, and low content of factors inhibitory to fermentation.

b) Oilseeds: Increased understanding of oil synthesis in oilseeds and the factors that control fatty acid composition and diversity. The goal is to develop oilseeds with increased oil content with emphasis on the production of oil tailored to the needs of specific industrial sectors; e.g. the production of biodiesel, plastics and industrial chemicals.

c) Cereals and grasses: Optimizing suites of the value of low cost starch/sucrose crops in a biorefinery model, in

which higher-value bioproducts are extracted, and ethanol and other fuels are produced from the process residue.

In addition to the three feedstock categories above, lipid-rich algae are re-emerging within Canada as an area of significant interest as a potential feedstock for the production of biodiesel, ethanol, and chemicals.

Optimizing traits that are industrially desirable is a challenge that is highly amenable to the application of genomic tools. Genomic approaches to genetic improvement of our bioproduct feedstocks will involve three general steps: 1) Identification of genes and gene networks in feedstock and model plant systems that control feedstock quality and biomass production in the Canadian context; 2) Identification or manipulation of genetic variants to enhance feedstock quality and production; and 3) Incorporation of genes or gene variants into feedstocks by marker assisted breeding or direct gene transfer to accelerate the development of new commercial varieties.

Impacts and Outcomes: Investment in this area will result in large-scale identification and functional characterization of genes and gene networks responsible for important cellular processes related to biomass and bioproducts, and translation of this information into biomass crop improvement. Genomic researchers in Canada have access to extensive breeding populations and/or germplasm collections representing natural genetic variation in key crops, which will facilitate transfer of knowledge to the user community after gene discovery. Partnerships among genomic scientists, feedstock growers, and those involved in downstream processing will allow continual testing of new improved varieties and incorporation of these into the feedstock production stream, leading to the continual improvement of these agricultural and forest crops. Although short- to medium-term benefits will be achievable, investment in this cluster will also impact crop improvement for many decades to come. Genes discovered and characterized will also impact traditional forestry and agriculture improvement programs, since many of the mechanisms that control biomass are important for plant improvement in these sectors.

Area of Impact #2 – Microorganisms for Sustainable Processing Technologies

Problems to be tackled: To achieve sustainability, the conversion of biomass into fuels and products calls for the massive deployment of novel enzymes and new processes [13]. Microorganisms are the major decomposers of biomass and the pivotal role that microorganisms play in bioproducts development is universally recognized. By way of example, the three bioenergy research centres recently announced by the US Department of Energy [5] are all headed by researchers working with microorganisms, and one of them is a genomicist. Using genomic approaches, the phenomenal diversity of the microbial world will be tapped to reveal novel metabolic pathways and enzymes with expanded functionalities and beneficial properties. As well, "workhorse" microorganisms for discovering and producing novel enzymes for biomass conversion and bioproducts development will be established. Uses of enzymes and processes to achieve the sustainable development of bioproducts include: (i) hydrolysis of lignocellulose to simple sugars; (ii) conversion of sugars or solar energy to bioproducts; (iii) conversion of oil and fatty biomass into diesel and industrial feedstock; (iv) conversion of non-fuel biomass into chemicals and materials; and (v) extraction and production of high-value bioactive compounds.

Beyond accelerating the development of bioproducts, advancing the genomics of microorganisms will be of significant benefit to important sectors of the Canadian economy; including:

1) Canada is a world leader in the forestry sector, contributing some $45 billion a year to the trade balance of the country [14]. The Canadian forestry sector has been the largest generator of bioenergy in the country, and has assumed a clear leadership position in the integration of bioprocesses into their operations. For example, enzymes are used extensively in Canadian pulp mills to reduce the use of bleaching chemicals. The microbial enzymes and processes uncovered through genomics will increasingly replace the use of polluting chemicals, reducing the consumption of energy, and facilitating the development of co-products to enhance the international competitiveness of the industry.

2) The large tracts of forests in British Columbia damaged by pine beetles represent an enormous source of underutilized biomass. The efficient conversion of this biomass into fuels and useful products will require specialized enzymes and processes that can be revealed by genomics.

3) Microbial pathogens inflict significant damage to the Canadian forestry and agricultural industries; e.g., Fusarium head blight is causing over $ 1 billion in damage to cereal crops [15], and white pine blister rust is estimated to cost the Canadian softwood industry $1.5-4.0 billion [16]. The powerful enzymes evolved by these pathogens to invade

plants can be harnessed for biomass deconstruction. Thus the genomic analysis of microbial pathogens of economic importance to Canada, such as *Cronartium ribicola* (white pine blister rust) and *Leptosphaeria maculans* (blackleg in canola), will result in at least two unrelated outcomes: fertile source for discovering biomass-deconstruction enzymes and the development of biocontrol agents against the pathogens.

4) Genomic characterization of microbial communities inhabiting unique environments such as the oil sands of Alberta will enable the development of bioprocesses to improve product recovery, reduce water use, and minimize pollution and greenhouse gas emissions.

Another critical area is the genomic analysis of individual microbes and microbial communities in terrestrial and marine ecosystems in order to elucidate the processes involved in chemical cycling, a central factor in understanding climate change and essential to the modeling of these cycling processes and the development of enabling technologies to sequester greenhouse gases.

Impacts and outcomes to be realized: Community resources that would be realized from efforts in this area include enriched databases, new gene and enzyme libraries, methods and microbial strains that produce novel molecules and catalysts, improved bioinformatics tools, high through-put screening protocols, and models to evaluate the socioeconomic and environmental impact of both new sustainable technologies and current practices. Within two years, the biofuels and forest products industries will begin to receive from the genomic and proteomic initiatives large numbers of enzymes and processes for applications testing. A wide range of other industries including food, animal feed, textile, detergent, coal liquefaction and composites will also benefit from these research deliverables within the same time span. Novel technologies for oil extraction and greenhouse gas sequestration are thought to be realistic within five years.

Area of Impact #3 – Value-Added Bioproducts

Problems to be tackled: The growth of the bioproducts sector is dependent on its ability to produce products that can compete on the open market. The biorefinery model is a key component of achieving this market competitiveness, in which the maximum possible value is realized from a given feedstock stream. The identification and development of value-added bioproducts – i.e. the development of processes whereby low or negative value biomass residue from one industrial process is transformed into higher value bioproducts.

Closely related is the need to identify high-value compounds from biological sources. High-value bioproducts can anchor and make viable the production of a much larger range of bioproducts, within a biorefinery model. Plants and microorganisms are capable of producing a broad range of compounds that are important to human health, or are of high value to industry (industrial chemicals and compounds). These products can be derived as by-products of other industrial bioprocesses, or developed in specialized or engineered plants or microorganisms. One example is the use of the abundant phenolic polymer lignin as source of specialty organic chemicals after its extraction from wood during processing for pulp and paper or biofuels applications.

Due to their low production cost, flexibility and storage capability, plants and microorganisms provide attractive platforms for metabolic engineering of high-value, bioactive molecules. A comprehensive systems biology approach has the potential to reveal the fundamental mechanisms of natural product metabolism in key organisms and, ultimately, to facilitate the engineering of bioactive ingredients for human health, or for the production of chemicals via manipulation of biosynthetic pathways in fermentation systems.

Metagenomic approaches, involving direct analysis of DNA from highly complex microbial communities, have the potential to identify new or improved biosynthetic pathways and processes for production of valuable biomolecules. In energy crops, plant polymers not used for energy production may be converted by enzymatic action and microbial fermentation into materials, fine and bulk chemicals, and high-value bioproducts.

Impacts and Outcomes: In addition to the timely release of genomic, proteomic and metabolomic information in organized databases, advanced informatic tools to decipher complex pathways and pioneer mechanisms will be made available to the community. New approaches to producing such known bioproducts as flavouring agents and nutraceuticals are expected to emerge within three years. With the cost of DNA sequencing plummeting and with rapid advances being made in proteomics, metabolomics, synthetic biology and genome shuffling, truly novel bioproducts and bioactive molecules will be developed within five years.

5 - Capacity

State of the Science

The development of genomic information and tools for plants and microorganisms oriented towards industrial bioprocesses is emerging as a priority in many regions, including Canada, the USA, and Europe as well as countries with rapidly developing economies such as China, Brazil, and India. Ongoing genomic research is helping to identify genes and pathways integral to the production, degradation and conversion of biomass.

This research is facilitated by the continued development of genomic resources and information for plants and microbes. Partial genome sequences exist for about 2,000 microorganisms, scores of microbial communities and many plants [17]. Complete plant genome sequences are available for *Arabidopsis* [18], *Populus* [19], and rice [20]. The genomes of many microorganisms with relevance to biomass conversion and energy production have been determined; and these include: degraders of lignocellulose [21,22]; fermenters of 5-carbon and 6-carbon sugars into ethanol [23,24]; producers of hydrogen and butanol [25,56]; a methane utilizer [27]; cell factories for enzyme production [28,29], a symbiont of poplar [30], and such phytopathogens as the causative agent of scab in wheat and barley [31] and the noble rot fungus [32]. The Joint Genome Institute of the US Department of Energy has established multiple programs to support sequencing projects related to bioenergy conversion, and Canadian scientists are active participants in these programs (see Attachment A).

The microbial world is marked by extraordinary diversity and specialization. For example, highly similar fungal species can establish vastly different relationships with humans. *Aspergillus fumigatus* [33] is the second most devastating fungal pathogen of humans while its evolutionary cousins *Aspergillus oryzae* [28] and *Aspergillus niger* [29] have been used safely in the food industry for centuries. In some cases different strains of the same species benefit humans in distinct ways: one strain [29] of *Aspergillus niger* is a robust producer of biomass-degrading enzymes while another strain with minor sequence variations [34] produces most of the citric acid that we consume. Comparative genomics has thus become a standard tool [33,35] in the identification of genes and pathways involved in bioprocesses. Due to the common evolutionary origin of land plants, and the associated conservation of metabolic processes and genes, comparative genomics between models such as *Arabidopsis*, new models, and potential feedstock plants, has also been extremely valuable in helping to identify genes relevant to biomass and bioproduct production. The importance of comparative approaches is recognized by the US Department of Energy's current plant genome sequencing projects [36], which focus on genome sequencing both in existing crop species such as cotton and cassava, and in informative model systems such as, *Brachypodium* (model for cereal grains), *Physcomitrella* (model for a basal plant genome), *Eucalyptus* (second model tree), and *Mimulus* (model for adaptation).

Significant genetic mapping has been done on many important plants with bioproducts potential, including *Populus*, *Salix*, spruce, *Brassica*, and wheat. However, there are crops that are especially relevant to Canada that have yet to be comprehensively addressed; including: rye, triticale, flax, hemp and camelina. These maps, coupled with genome sequence and the repertoire of ancillary tools open the door to genetic selection for accelerating feedstock optimization. Canadian leadership in the genomics of these plants and corresponding bioprocesses and value-added bioproducts will provide Canadian industry with enhanced access to leading genomics-based intellectual property.

Genome sequence information provides an essential foundation for the application of advanced genetic tools and techniques for tackling challenges in bioproducts development. In the global context, microarrays, large scale metabolite analyses, genome-wide mutagenesis, and proteomic analyses provide increasingly incisive tools and databases for monitoring gene activity, and elaboration of the protein and chemical constituents of cells and organs with bioproduct applications. Other approaches include comparative genomics, metagenomic analysis, directed evolution, genome shuffling, synthetic biology, and targeted gene transfer. Among many applications, the knowledge gained from genomics has already led to the design of synthetic life forms dedicated to energy production [37].

Canadian infrastructure, resources and strengths in genomics

Attachment A outlines the genomic resources and infrastructure available to fast-track biofuels and bioproducts development. It also illustrates some of the contributions that Canadian scientists have made to the community.

Canada has established an international reputation for excellence in plant-based genomics. Canadian genomic scientists were major contributors to sequencing and interpreting the *Populus* genome, and are leaders in forestry genomics and the applications of genomics to tree improvement. Knowledge of wheat genetics has been the result of 100 years of development of varieties adapted to all parts of Canada. Canadian researchers have contributed about one-sixth of the 800,000 EST sequences available, high density microarrays, end-sequenced BAC libraries and transformation expertise. Markers to accelerate breeding for many traits have been mapped and are currently in use by breeders. A further example is Canadian leadership in the development of genomic resources for *Brassica* species (particularly canola) and flax. A collection of nearly 450,000 EST sequences has been established, representing the major international resource for these crops.

Canadian genomics researchers have also been key contributors to the significant progress that is being made in analyzing microbial diversity. Functional genomic programs have been launched on about 100 microorganisms with over 800,000 ESTs generated. Large sets of mutant strains and microarrays have been constructed. Canadians are leading the international effort to construct synthetic lethal mutants for the budding yeast. Novel pathways in the degradation of persistent pollutants and nitrogen fixation have been uncovered. Programs to elucidate the metagenome of bioremediating microbial communities, and marine viruses that are critical to global carbon cycles, are harnessing the enormous progress in genomic technologies that has ensued over the last decade. The integrative approach of metagenomic research is improving our ability to control complex bioprocess technologies, and discover novel, industrially favorable biocatalysts. It is noteworthy that Canadian researchers were the first to use an integrated genomics approach to link gene discovery with industrial applications. With over 500 functionally expressed fungal recombinant proteins, Canadian researchers hold one of the largest collections of novel biomass-degrading enzymes in the world. These enzymes are being used by industry players in Canada and Europe in the development of new bioproducts and biofuels.

Canadian scientists have been very active in developing and using sequence enabled genomic tools in bioproduct feedstock related research. This includes development and application of microarrays for gene expression profiling in trees, crops, fungi, and bacteria; development of proteomic and metabolite profiling approaches; protocols for large scale genetic diversity studies, genotype-phenotype association studies, and development of novel functional genomics tools in plants and trees such as “TILLING” and activation tagging, which are powerful approaches for genome-wide discovery of novel genes involved in plant processes of interest.

State-of-the art infrastructure for bioproducts genomic research is in place in the genome centres and research institutions across the country. This includes bioinformatics, DNA sequencing, mass spectrometers for protein and metabolite analyses, peptide synthesis, microarray construction, nuclear magnetic resonance and synchrotron for structural studies, fermentation facilities, robotic platforms, and medium-throughput protein production platforms and screening facilities. Large collections of microorganisms are being maintained by institutions such as the National Mycological Herbarium in Ottawa.

Canada’s strengths in genomics are complemented by strengths in the chemistry of lignocellulose, outstanding research expertise in the breeding of trees and northern-climate agricultural crops and assembling range-wide tree collections that capture genetic diversity, an international reputation as a centre for plant biochemistry research, as well as leading expertise in some target platforms such as canola, wheat, flax, hemp, and triticale. Canada also has international leaders in the fields of microbial metabolism and enzymology. Canada is home to global leaders in biofuels and biorefinery development (e.g., Tembec, Iogen, and FPInnovation). Overall, Canada is ranked an impressive 4th internationally in the number of patents held in bioproducts and bioprocesses [3].

Support for this Strategic Research Theme will capitalize significantly on previous genomic investments. These investments have allowed Canadian scientists to collaborate on large-scale international projects related to the genomics of bioproducts (see Attachment A). Continued investment by Genome Canada in this sector is essential to ensure that Canadian scientists have the resources to maintain and expand such collaborations, facilitating Canada’s acquisition of and access to the latest information and technology related to bioproduct development.

6 - Stakeholder interest and support

Stakeholders who have provided support letters for the bioproducts and biofuels theme are listed in Attachment B. Strong support for this research theme was found from the following sources:

- Representatives from federal departments and agencies with biotechnology portfolios (Agriculture and Agri-Food, Environment, Fisheries and Oceans, Industry, Natural Resources, and the National Research Council) and provincial agencies (Alberta Research Council, BC Ministry of Forests, and INRS-Institute Armand-Frappier) are supporters of the theme.
- Over thirty NGOs and private enterprises wrote in support of the theme.
- Thirty-eight of the 47 participants of the National Workshop on this theme were non-academic stakeholders.
- Partners of current bioeconomy genomic projects in Canada include: Agriculture and Agri-Food Canada, Natural Resources Canada, FPInnovations (the world's largest forest products research organization), Tembec (a global leader in forest-based biorefineries), Iogen Corporation (a world leading cellulosic ethanol company), DSM B/V (a multinational industrial biotechnology company), and Ocean Nutrition Canada (manufacturer of nutraceuticals).
- Additional companies which have expressed interest in partnering with future Genome Canada projects in biofuels and bioproducts include: Novozymes (the largest enzyme producer in the world), Greenfield Ethanol (the largest Canadian producer of fuel ethanol), and Lallemand (a multinational yeast producer based in Montreal).
- Representatives from various provincial governments, including British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, and Québec, participated in the development of this position paper and have expressed strong support for this research theme.

The extensive partnership opportunities with global and national enterprises are indicative of the short to mid-term return on investment potential of Canadian genomic projects within this Strategic Research Theme.

7 - Socio-Economic Outcomes

The bioproducts sector is unique in delivering powerful economic, environmental and social outcomes from what is fundamentally an industrial pursuit. The contributions of genomics to this sector will accelerate competitiveness and corresponding market penetration, enabling and enhancing a suite of beneficial impacts.

Economic

On a fundamental level, rapid and continued growth of the bioproducts sector is necessary to ensure Canada successfully navigates the inevitable transition to a post-petroleum economy. In the short to medium term, aggressively pursuing this Strategic Research Theme will directly contribute to the growth and success of Canada's bioproducts companies. There are over 230 bioproducts companies in Canada, including many with proven international leadership, that collectively have $12 billion in annual sales, $3 billion of which is directly related to bioproducts, and almost half of which is from export [38].

Genomics-driven process and feedstock breakthroughs will link Canada's agriculture, forest, energy, chemical, and manufacturing sectors in new value chains, carving out distinct Canadian competitive advantages during the defining early years of the bio-based economy. The economic stakes are enormous, given the growth predicted in key bioproducts markets (see Table 3).

Environmental

In addition to reductions in greenhouse gas emissions, the use of bioproducts and bioprocesses typically involves significantly less environmental pollutants, impacting both human and ecosystem health. Biosolvents are already beginning to offer more benign substitutes for environmentally damaging products, such as phenol formaldehyde. Biofuels, such as biodiesel and ethanol, yield fewer airborne particulates, which are becoming particularly acute in Greater Toronto and other urban centres in Canada. Enzymatic transformation, referred to as green chemistry, is highly specific and efficient, greatly reducing unwanted byproducts and the use of hazardous chemical catalysts. The transition to bioproducts will reduce hidden health costs that are not easily quantifiable, but will constitute very significant economic benefit.

Social

The social impacts of genomics-based advancements in the bioproducts sector are harder to quantify, but no less important. Short to medium term impacts include the potential to increase the farm gate value delivered to farmers for their crops, and to offer an expanding choice of crops and target markets to pursue. With the extreme stresses that

have been felt in Canada's agricultural and forestry communities for an extended period of time, the importance of this outcome must not be minimized.

The bioproducts sector also holds out the promise of helping to connect rural and urban agendas. The bioproducts sector calls for a careful alignment of industry with feedstock, typically in close proximity. This brings traditionally urban industries into more rural areas, and compels industrial centres to form more intimate relationships with sources of feedstock, which in many cases will be from the local community.

Aggressively pursuing this Strategic Research Theme will also serve to significantly build Canadian genomic capacity in this critical area. The highly qualified people trained and retained through these efforts will be necessary to meet future growth in the bioproducts sector, allowing Canadian industry to have continued access to cutting-edge research capacity – a hallmark of an effective innovation system.

This brief discussion of social impacts would not be complete without a mention of the job-creation potential within the bioproducts sector itself, and closely related sectors such as forest and agriculture. The most recent figures on bioproduct sector employment in Canada (2003) indicate that over 24,000 Canadians were employed [3], although this figure has certainly risen substantially. It must also be remembered that growth in this sector provides employment for an extended value chain, from feedstock providers through to retail outlets.

As a final thought, it is important to point out that significant Canadian contributions to the bioproduct sector have the potential to be rapidly commercialized throughout the world, magnifying the economic, environmental and social benefits achieved.

8 - Budget Request

It was not straightforward how best to estimate the budget request that should accompany this Strategic Research Theme. On the one hand, the need for research funding to facilitate the transition to a bioeconomy is immense. On the other, the human capital to conduct large-scale genomic research in Canada is finite.

For the purposes of this Position Paper, the budget request is based on the available capacity to conduct large-scale genomic research in bioproducts within Canada, as judged in part by participation of Canadian scientists in past Genome Canada competitions[1]. The proposed overall budget request for the competition is $150 million. Taking the current Genome Canada co-funding policy into consideration, the estimated request from Genome Canada is $75M.

9 - The consultative process used to develop this Position Paper

In preparing this Position Paper, the "Biofuels and Bioproducts Genomics" Working Group engaged in an extensive consultative process, with a special emphasis placed on involving representatives from all stages of current and potential bioproducts value chains. Over 200 stakeholders were consulted. At a workshop held on May 23rd, over 75% of the attendees were from industry and government. A constant dialogue was maintained throughout the development process, facilitated by such tools as a dedicated website (www.biogenomicscanada.com). A more comprehensive breakdown of the consultative process is provided as Attachment C.

The consultative process adopted a philosophy that a strong focus must be on research that will enhance the competitiveness of Canadian companies. It is only companies that produce products. It is only by products (fuels, chemicals, materials) successfully competing in the marketplace that the positive outcomes and impacts of the bioproducts sector will be realized. A systems approach was adopted, acknowledging that research is but one of many contributing factors in the creation of strong Canadian bio-based industries. The wide range of perspectives and inputs realized through the inclusion of a broad spectrum of stakeholders contributed significantly to the quality of this document.

[1] In the most recent competition of Genome Canada held in 2005, twenty-eight proposals related bioproducts with a total request of $350 million were submitted. An informal survey shows an increase of 25% in the number new independent investigators, appointed in the past five years, interested in large-scale bioproducts genomics. From this assessment, it can be estimated that a request for proposals in biofuels and bioproducts genomics will generate a budget request of about $450 million. Approximately one-third of these are expected to be judged of top caliber, and thus would qualify for funding.

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Charts and Tables

Table 1: Recent Federal Bioproducts Initiatives of Note
Agriculture and Agri-Food Canada's (AAFC) Agricultural Bioproducts Innovation Program (ABIP) has $145M in funding in support of research networks.
AAFC's ecoAgriculture Biofuels Capital Initiative (ecoABC) program provides capital assistance to farmers to become biofuel producers, with $200M in funding.
AAFC has allocated $134M for the scale-up of commercially ready technologies for the manufacture of bioproducts and novel food processing.
Natural Resource Canada's (NRCan) EcoEnergy program provides $1.5B to stimulate renewable energy consumption, and $230M for clean energy technology development.
Sustainable Development Technology Canada is investing very heavily in the bioenergy sector, with over $1B in funding and $500 million forthcoming in 2008 dedicated towards support for next generation cellulose to ethanol production facilities;.
The National Research Council has announced that bioproducts will be the theme of its first ever national initiative, judging that this is the area where it can make the most profound contribution to Canadians.
The joint Environment Canada / NRCan / AAFC Renewable Fuels Strategy announced in Dec. 2006 mandating a 5% threshold level for ethanol in all ground transportation fuels sold in Canada by 2010 and 2% biodiesel in ground transportation and heating oil by 2012
The Natural Sciences and Engineering Research Council of Canada (NSERC) has allocated $37M for networks and promising young researchers in the areas of renewable energy, environmental and information technologies.
The 2007 budget allocates $1.5 billion over seven years for an operating incentive to producers of renewable alternatives to conventional fuels.

Table 2: Provincial Biofuel Mandates
Ontario established a requirement for 5 percent ethanol for 2007
Saskatchewan requires 7.5 percent ethanol since 2006
Manitoba has passed legislation requiring 10 percent ethanol content in 85 percent of the province's fuel, but has not yet set a date for entry into force
Quebec has set a goal of 5 percent ethanol in gasoline by 2012
British Columbia has announced it intends to require 5 percent renewable content in diesel fuel by 2010.

Table 3: Growth in Key International Markets

Global Markets	Predicted Growth
Biofuels and bioenergy	Global market in 2003: $3-5B US Global market by 2050: $150B US [A]
Biomaterials and Biochemicals.	The markets for biomaterials and biochemicals are hard to quantify, due to the breadth of potential products. Some indicative market sector predictions: • Global market for biochemicals and bioplastics in 2003 - $60B US. Global market in 2010 - $140-210B US. [A] • The market potential for biochemicals (primarily platform chemicals) made from corn in Canada, including acetic acid derivates, has been conservatively estimated at over $200M Cdn per annum. [B]. The international markets for these products is immense. [C] • The European market for biodegradable lubricants, currently estimated at between $35-100M Euros, is predicted to grow to between $1025-4340M Euros by 2010, including all of the chain bar, 75% of the mould release, 40% of hydraulic fluids and greases, and 30% of the anti-corrosion markets. [D,E] • Biosurfactants have the potential to capture 40% of the European market by 2010, up from 20% in 2000. The biopolymers market is estimated at a half million tonnes in 2010, up from 25 000 tonnes in 2000. [F]
Biocatalysts and Industrial Enzymes	Global market in 2005: $3.7B 6.5% growth is expected per year over the next five years [A].

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