MBA 823.3

BIOTECHNOLOGY COMMERCIALIZATION

PROFESSOR GRANT ISAAC

REGULATORY PROFILE: SOMATIC EMBRYOGENESIS

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Introduction

Somatic Embryogenesis is a biotechnology process that allows for immature embryos to be selected from seed stock of superior trees and applied to a growth culture to create embryogenic tissues, or a germplasm, from which several thousands of somatic embryos can be obtained. The regulations in place pertaining to the use of somatic embryogenesis varies from country to country and is most often closely tied to the regulations in place with utilizing other plant biotechnologies.

This analysis explores the regulations in place pertaining to somatic embryogenesis in both the Canadian and United States markets as well as identifying the regulating authorities that monitor and enforce these regulations. In addition to exploring these North American markets, a cursory review of the regulations pertaining to forest biotechnology in the UK is also reviewed.

The analysis will then explore the external opportunities and threats as well as internal strengths and weaknesses of somatic embryogenesis for ArborGen™. These factors will then be used to frame a strategic recommendation on how to best manage and anticipate regulations on forest biotechnology for the future.

Canada

As the process is defined for Canadian regulation, somatic embryogenesis products are considered animate products of biotechnology. Regulations in Canada pertaining specifically to forest biotechnology are not firmly in place however are currently regulated under the Canadian Environmental Protection Act, 1999 (CEPA, 1999), Part 6 under the authority of Environment Canada. The Act states:

> *Part 6: Animate Products of Biotechnology (Sections 104-115)*
> *This act outlines the requirements for the assessment and introduction of living organisms that are the products of biotechnology where:*
> - *"living organism" means a substance that is an animate product of biotechnology.*
> - *"significant new activity" includes, in respect of a living organism, any activity that results or may result in the entry or release of the living organism into the environment in a quantity or concentration that, in the Ministers' opinion, is significantly greater than the quantity or concentration of the living organism or the exposure or potential exposure of the environment to the living organism that previously entered or was released into the environment.*[1]

The Act further details requirements for information and reporting pertaining to new organisms and the inclusion of its characteristics and parameters in the Domestic Substances List (DSL). The New Substances Notification Regulations (NSNR), also regulated by Environment Canada, requires this information on any substance intended for import or manufacture and is not listed on the DSL. CEPA, 1999 provides Environment Canada with authority to address pollution problems on land, in water, and through all layers of the atmosphere. Currently, forest biotechnology is considered a toxic innovation as defined by CEPA, 1999 and is prohibited for use in Canada. Other forest biotechnology products are regulated under several acts, which assess products for safety. These include the Seeds Act for genetically modified trees, the Plant Protection Act for imports, the Fertilizers Act for bio-fertilizers and mycorrhizae all of which are regulated by the Canadian Food Inspection Agency.

In addition to federal regulation, forest biotechnology products are also subject to regulation from provincial authorities. The provincial Acts and Regulations that regulate the use of biotechnology in the Forestry sector are administered by several different departments including labour, transportation and environment.[2]

Currently in Canada, there are no forestry biotechnology products that have been approved for introduction into the environment.

United States

Biotechnology is regulated by three agencies in the United States (US). The United States Department of Agriculture (USDA) regulates plant pests, plants and veterinary biologics products. The Environmental Protection Agency (EPA) regulates microbial and plant pesticides, new uses of existing pesticides, and novel micro-organisms. And lastly, the Food and Drug Administration (FDA) which has oversight on products including food, feed, food additives, veterinary drugs, human drugs and medical devices. For the purposes of somatic embryogenesis and the creation of new plants, specifically species of Pine and Eucalyptus developed by ArborGen™, the USDA is the regulating authority for the US. The USDA regulates somatic embryogenesis with the following process:

> *Within USDA, the Animal and Plant Health Inspection Service (APHIS) is responsible for protecting US agriculture from pests and diseases. Under the authority of the Federal Plant Pest Act, APHIS regulations provide procedures for obtaining a permit or for providing notification, prior to "introducing" a regulated article in the United States. Regulated articles are considered to be organisms and products altered or produced through genetic engineering that are plant pests of that there is reason to believe are plant pests. The act of introducing includes any movement into (import) or through (interstate) the United States, or release into the environment outside an area of physical confinement. The regulations also provide for a petition process for the determination of nonregulated status. Once a determination of nonregulated status has been made, the product (and its offspring) no longer requires APHIS review for movement or release in the US.*[3]

The field trials and monitoring programs stipulated in the regulations continue through four phases of approval: pending, acknowledged, issued approval, and finally nonregulated status. Appendix 1 shows the status of all applications to the USDA for somatic embryogenic seedlings. This data shows that approvals have been issued only for Walnut to the University of California at Berkeley. ArborGen™ applications are all acknowledged status with the exception of one denied application in 2003 and six pending applications filed in February of 2004.

The US regulatory system is quite transparent and the status of all applications is easy to acquire.

United Kingdom

In the United Kingdom (UK), there are strict regulatory policies regarding the use of genetically modified organisms (GMO's) In order to qualify for release into the environment, an incremental monitoring and testing program is implemented with explicit regulatory consent required at every step. There are two broad categories of release of GMO's, namely, Part B releases for research and development and small incremental research field trials, and Part C releases for the commercial application of an approved product. A thorough environmental risk assessment is initially implemented to assess impacts, after which the Joint Regulatory Authority from the Department for Environment, Food and Rural Affairs review in consultation with expert committees. In order to qualify, the release must be considered a very low risk, which means that the modified variety does not pose any greater risk than the natural equivalent of the variety. These Part B trials continue in the field at incrementally increased volumes and as approvals exist. Should these incremental tests be satisfied, consent from the Secretary of State for the Environment, Food and Rural Affairs. Each release carries comprehensive risk management conditions and inspections and monitoring are implemented by the Central Science Laboratory (CSL) and by the Scottish Agriculture and Science Agency (SASA) to ensure that these conditions are adhered to. With respect to seed regulations, the new variety, whether or not the production involves genetic modification, must satisfy the same requirements as conventional varieties. In order to be included in the National List of Seeds or the European Common Catalogue, a series of tests to demonstrate distinctiveness, uniformity and stability must be met. This list is maintained and regulated also by the Department for Environment, Food and Rural Affairs.[4]

As the European Union (EU) becomes more solidified in the world economy, regulatory policies may also become more uniform. If this is the case, The UK will have to adopt policies more in line with their member countries such as Finland, Sweden and Norway which have much more flourishing forestry industries.

ArborGen™

With respect to regulatory acknowledgement of the somatic embryogenesis of selected pine species and commercial use of the product, ArborGen™ states the following on their corporate website:

> *Science- based regulatory systems are essential for commercializing trees with modified traits. Essential elements of a working system include:*
>
> - *Responsible Use Of The Technology*
> - *Benefits and risks associated with the technology and its deployment are addressed.*
> - *Appropriate post-launch management mechanisms are in place, including performance and safety assessments.*
> - *Dialog with the public, including universities, landowners, industry, government and nongovernmental organizations and other research institutions, is incorporated in such a way as to allow advancement of the technology when the science indicates it is safe.*

These statements acknowledge that there is much work to be done in the development of release consent for their products and that commercial approval has not yet been granted, which is evident from the data presented in Appendix I. They acknowledge the depth of knowledge required for consent and identify the critical decision groups and stakeholders that should be included in the development of this approval.

Social, Economic and Political Factors of Forest Biotechnology

The societal and systemic influences on forest biotechnology are different for each country where forest biotechnology is regulated. Specifically to Canada, First Nation groups and special interest groups, such as the Sierra Club and Greenpeace, have massive influence on public perceptions and Canadian governmental reactions which occasionally lead to subsequent imposition of regulations or changes to forest management policy. The pressure from Sierra Club combined with the subsequent public outcry of logging in places such as the Stein Valley and Clayoquot Sound in the late 1990's prompted the British Columbia government to completely revise their forest management policies, resulting in the Forest Practices Code of 1997. These groups pose the greatest influence on policy makers and as such should be integrated into decision making to anticipate the impacts their concerns may have on novel, sustainable and environmentally safe forest product innovations.

Strategic Recommendations

The regulatory systems vary for each of the major forestry markets in the world. The strategic planning required to penetrate each market will depend heavily on which market is chosen. Currently, only the United States maintains transparent and systematic regulatory systems that are conducive to commercialization. Canada has a much larger resource base and, as such, has much more sensitive environmental concerns and involved stakeholders and regulatory systems reflect the social perception regarding environmental contamination of forest biotechnology.

ArborGen™ must first focus on the most accessible market, the United States. Their regulatory approvals are in currently process for most of their derived products as shown in Appendix I. Once nonregulated status has been achieved for the selected species of pine and eucalyptus, the collected environmental monitoring data will enable them to strengthen their petitions for regulatory approval in the other prime markets, namely Canada and the EU.

Appendix I – Regulatory Status of Somatic Embryogenesis in the United States

Permit	Institution	Organism	Received	Status	Issued	Effective	Release Location(s)
04-049-03n	ArborGen	Pine	02/18/04	Pending		03/19/04	SC
04-049-04n	ArborGen	Pine	02/18/04	Pending		03/19/04	SC
04-049-05n	ArborGen	Pine	02/18/04	Pending		03/19/04	SC
04-049-06n	ArborGen	Pine	02/18/04	Pending		03/19/04	SC
04-040-09n	ArborGen	Pine	02/09/04	Pending		03/10/04	SC
04-040-10n	ArborGen	Pine	02/09/04	Pending		03/10/04	SC
03-358-02n	ArborGen	Pine	12/24/03	Acknowledged		01/23/04	SC
03-329-01n	ArborGen	Pine	11/25/03	Acknowledged		12/25/03	SC
03-275-01n	ArborGen	Pine	10/02/03	Acknowledged		11/01/03	SC
03-274-02n	ArborGen	Pine	10/01/03	Acknowledged		10/31/03	SC
03-265-01n	ArborGen	Eucalyptus grandis	09/22/03	Acknowledged		10/22/03	FL
03-247-05n	ArborGen	Pine	09/04/03	Acknowledged		10/04/03	SC
03-239-03n	ArborGen	Eucalyptus grandis	08/27/03	Acknowledged		09/26/03	FL
03-232-06n	ArborGen	Pine	08/20/03	Acknowledged		09/19/03	SC
03-232-07n	ArborGen	Pine	08/20/03	Acknowledged		09/19/03	SC
03-232-08n	ArborGen	Pine	08/20/03	Acknowledged		09/19/03	SC
03-209-01n	ArborGen	Pine	07/28/03	Denied		08/27/03	SC
03-203-09n	ArborGen	Eucalyptus grandis	07/22/03	Acknowledged		08/21/03	FL, SC
03-184-07n	ArborGen	Eucalyptus grandis	07/03/03	Acknowledged		08/02/03	FL, SC
03-147-04n	ArborGen	Pine	05/27/03	Acknowledged		06/26/03	SC
03-121-04n	ArborGen	Eucalyptus grandis	05/01/03	Acknowledged		05/31/03	SC
03-112-01n	New York State U	American Chestnut	04/22/03	Acknowledged		05/22/03	NY
03-091-15n	ArborGen	Pine	04/01/03	Acknowledged		05/01/03	SC
03-076-06n	ArborGen	Pine	03/17/03	Acknowledged		04/16/03	SC
02-214-02n	ArborGen	Eucalyptus grandis	08/02/02	Acknowledged		09/01/02	SC
02-112-02n	ArborGen	Pine	04/22/02	Acknowledged		05/22/02	SC
02-112-01n	ArborGen	Pine	04/22/02	Acknowledged		05/22/02	SC
01-124-09n	Westvaco	Pine	05/04/01	Acknowledged		06/03/01	SC
01-124-08n	Westvaco	Pine	05/04/01	Acknowledged		06/03/01	SC
01-124-07n	Westvaco	Pine	05/04/01	Acknowledged		06/03/01	SC
01-092-06n	Westvaco	Pine	04/02/01	Acknowledged		05/02/01	SC
01-079-03n	Westvaco	Pine	03/20/01	Acknowledged		04/19/01	SC
01-079-05n	Westvaco	Pine	03/20/01	Acknowledged		04/19/01	SC
01-079-04n	Westvaco	Pine	03/20/01	Acknowledged		04/19/01	SC
00-353-10n	U of California/Davis	Walnut	12/18/00	Acknowledged		01/17/01	CA
00-305-01n	Westvaco	Pine	10/31/00	Acknowledged		11/30/00	SC
00-220-03n	Westvaco	Pine	08/07/00	Acknowledged		09/06/00	SC
00-167-03n	Westvaco	Pine	06/15/00	Acknowledged		07/15/00	SC
00-126-01n	Westvaco	Pine	05/05/00	Acknowledged		06/04/00	SC
00-034-18n	U of California	Walnut	02/03/00	Acknowledged		03/04/00	CA
99-174-02n	Westvaco	Pine	06/23/99	Acknowledged		07/23/99	SC
99-158-02n	Westvaco	Pine	06/07/99	Acknowledged		07/07/99	SC
99-158-01n	Westvaco	Pine	06/07/99	Acknowledged		07/07/99	SC
98-141-10n	Westvaco	Pine	05/21/98	Acknowledged		06/20/98	SC
98-042-07n	U of California/Davis	Walnut	02/11/98	Acknowledged		03/13/98	CA
98-042-08n	U of California/Davis	Walnut	02/11/98	Acknowledged		03/13/98	CA
97-210-02n	U of California/Davis	Walnut	07/29/97	Void		08/28/97	CA
97-209-04n	U of California/Davis	Walnut	07/28/97	Void		08/27/97	CA
97-189-01n	U of California/Davis	Walnut	07/08/97	Acknowledged		08/07/97	CA
97-189-02n	U of California/Davis	Walnut	07/08/97	Acknowledged		08/07/97	CA
97-182-09n	U of California/Davis	Walnut	07/01/97	Denied		07/31/97	CA
97-163-01n	ARS	Walnut	06/12/97	Acknowledged		07/12/97	CA
97-163-02n	U of California/Davis	Walnut	06/12/97	Acknowledged		07/12/97	CA
95-272-02r	U of California/Davis	Walnut	09/29/95	Issued	1/16/95		CA
93-004-02r	U of California/Davis	Walnut	01/04/93	Issued	3/26/93		CA
90-351-01r	ARS	Walnut	12/17/90	Issued	3/15/91		CA
89-220-01r	U of California/Davis	Walnut	08/08/89	Issued	2/15/90		CA

References

[1] Canadian Environmental Protection Act -
http://www.ec.gc.ca/EnviroRegs/Eng/SearchDetail.cfm?intCategory=10&intAct=1001

[2] Canadian Provincial Regulating Authorities –
http://strategis.ic.gc.ca/epic/internet/inbravo-canada.nsf/vwGeneratedInterE/h_ak00197e.html

[3] About the USDA –
http://www.aphis.usda.gov/brs/usregs.htm

[4] Genetically Modified Organisms – The Regulatory Process (UK-Europe)
http://www.defra.gov.uk/environment/gm/background/regulate/index.htm