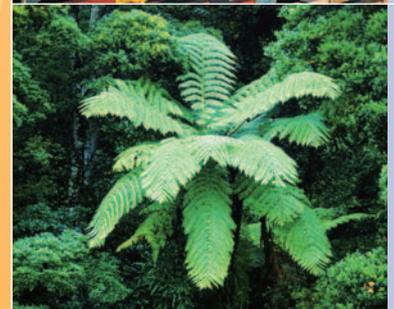
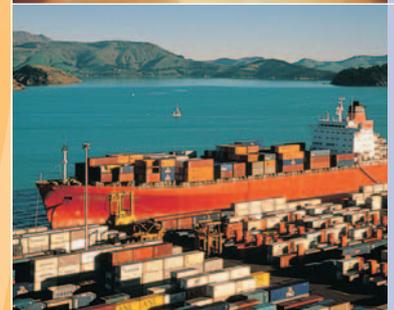




Preliminary Economic Evaluation of Biopharming in New Zealand

William Kaye-Blake
Caroline Saunders
Louise Ferguson

Research Report No. 296
March 2007



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Terms and Acronyms

ABARE	Australian Bureau of Agricultural and Resource Economics
BERL.....	Business and Economic Research Limited
cwe	carcass weight equivalent
FAO.....	Food and Agriculture Organisation
GDP.....	gross domestic product
GI.....	glycaemic index
GM	genetic modification
GMO.....	genetically modified organism
GST	Goods and Services Tax
GTAP	Global Trade Analysis Project
hLF	human lactoferrin
IBAC	Independent Biotechnology Advisory Council
LTEM.....	Lincoln Trade and Environment Model
MAF	Ministry of Agriculture and Forestry
MfE.....	Ministry for the Environment
NRB.....	National Research Bureau
OECD.....	Organisation for Economic Cooperation and Development
PRC	People's Republic of China
RCGM.....	Royal Commission on Genetic Modification
rhLF.....	recombinant human lactoferrin
ROW.....	Rest of World
TNZ.....	Trade New Zealand
trq	tarrif rate quota
USDA.....	United States Department of Agriculture
WHO	World Health Organisation

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The contributions of these people notwithstanding, the final responsibility for the report lies with the authors.

Preface

This report complements other research streams at the AERU. We have for several years been investigating the social and economic impacts of various biotechnologies, including genetic modification. We have also more recently been developing a research programme in emerging technologies, such as nanotechnologies and second-generation genetically modified foods. This report is thus the latest in a series of AERU Research Reports on biotechnology and emerging technologies. The research reported here will be useful and interesting for academics and others looking for a summary of the current state of the industry; government personnel interested in informing evidence-based policy-making; and industry people seeking an independent analysis of biopharming.

Professor Caroline Saunders
Director
AERU

Executive Summary

Biopharming – the production of pharmaceutical compounds in plant and animal tissue in agricultural systems – is touted as the next major development in both farming and pharmaceutical production. Biopharming represents new territory for both the agricultural and pharmaceutical industries, and presents novel challenges for government regulators. It presents both opportunities and challenges for the New Zealand economy. It is thus important to understand the current situation regarding biopharming and to assess the future directions and potentials of the industry.

The food, agricultural and tourism sectors in New Zealand are economically significant, contributing around 27 per cent of GDP. They are also export-focused industries therefore the reactions of overseas consumers are important. New Zealand and overseas research suggests that agricultural biotechnologies like biopharming can contribute to economic growth, but also may risk negative reactions if the technologies are not accepted by consumers. For example, biopharming currently uses genetic modification, so the experience with that technology may be instructive.

Production of a food or pharmaceutical compound can be viewed as a bundle of characteristics or a vector of dimensions, including technical issues of production, applicable regulations, political concerns, and consumer responses to the product. The literature indicates that biopharming differs from existing production methods in a large number of ways. The extent of the differences is generally unknown or known qualitatively. The analysis presented here suggests that not only are the sizes of the difference unknown, but their potential contributions to either costs or benefits are also unknown. Analyses that project future financial benefits from biopharming tend, on the other hand, to assume that technical, regulatory, political, and consumer issues are resolved.

From the academic literature, this report derives an economic model or framework for considering biopharming. This model is based on a cost-benefit approach to valuing changes in products and production methods. The model indicates the product dimensions that are likely to be affected by biopharming methods and how these dimensions may affect the costs and benefits of production. It also identifies the uncertainties in existing analyses. Finally, it demonstrates a method by which careful analysis of the economic costs and benefits of biopharming could proceed.

Two potential products are discussed using this model: recombinant human lactoferrin (rhLF) produced in cow's milk and low-GI potatoes. The analysis of rhLF suggests several things. First, all the necessary business information to assess the economic potential of producing recombinant human lactoferrin in milk in New Zealand is not available. Any assessment at this stage is necessarily preliminary. Secondly, it will be difficult to earn more than an economically normal profit by developing and marketing rhLF. There seem to be several close substitutes and competing technologies, so there appears to be little opportunity to create a dominant position in the market and earn oligopoly or monopoly profits. Finally, social science research suggests that introducing a GMO into the New Zealand dairy sector has a potential to cause a minimum of NZ\$539.6 million in losses to the dairy and tourism industries. Thus, such a biopharming endeavour would need to offset those losses before it could be viewed as a net positive for the New Zealand economy. Given that worldwide sales of lactoferrin are currently in the tens of millions of US dollars, offsetting hundreds of millions of NZ dollars of lost exports seems unlikely in the short to medium term.

By contrast, the low-GI potato could have clear consumer appeal in the functional foods market, a multibillion dollar and expanding market segment. As a functional food, it would have lower regulatory hurdles than a biopharmaceutical. Furthermore, potatoes are a commonly consumed food, and the total market is again a multi-billion dollar market. A final positive factor is that New Zealand has scientific expertise in the area and business experience in creating profits from Plant Variety Rights. However, the genetically modified status of the product could create problems in some markets, and there is the risk of losing at least NZ\$191.1 million in annual tourism earnings. It is unknown at this point what competing products would be developed, other types of low-GI potatoes, other low-GI foods, and even other dietary trends.

Thus, the economic potential of these products varies tremendously, depending on the overall size of the potential market, control of technology or proprietary information, and other factors. However, it is clearly early days for these products. The future impact of consumer concerns is unknown and contested. The regulatory regime and practices needed to segregate novel products from other food have not been set up and are untested. The potential contributions to cost savings or other benefits of the technology have not been quantified.

This is a preliminary piece of research. As more information becomes available on the potential products, the economics of their production, and consumer demand for them, future research will be able to improve the estimates of the economic impacts of biopharming in New Zealand.

Chapter 1

Introduction

Biopharming – the production of pharmaceutical compounds in plant and animal tissue in agricultural systems – is touted as the next major development in both farming and pharmaceutical production. For farmers, the appeal of biopharming is the production of high-value, niche products, which moves them away from commodity agriculture. For pharmaceutical firms, biopharming promises a method for reducing production costs. For the general public, the benefits of biopharming would be cheaper drugs produced more quickly.

Biopharming is new territory for the agricultural and pharmaceutical industries, and presents novel challenges for government regulators and others, particularly in New Zealand. This report examines the economics of the opportunities and challenges that biopharming presents. It investigates the research that has been done to this point in order to identify the key economic issues facing the development of biopharming. It also analyses the potential impacts, using a combination of economic theory and prior research. The result is an initial map that can help in charting New Zealand's way in this new territory.

The economic research on biopharming has two tasks. The first is to understand the current situation regarding biopharming. The second is to assess the future directions and potentials of the industry, to suggest what may happen and how the industry may develop. Both of these tasks are addressed in this report.

Chapter 2

Prior Research

2.1 Introduction

This chapter focuses on prior research that can help in understanding the potential impacts of biopharming in New Zealand. Because biopharming has arisen out of a confluence of agriculture, pharmaceutical production, and biotechnology, a number of topics need to be included in a review of prior research. This chapter first examines the literature that focuses specifically on biopharming. This examination considers the state of the industry and the economic issues that arise with biopharming. These issues then serve as departure points for several subsequent sections, which include the economy of New Zealand, potential economic impacts of genetically modified organisms (GMOs) in New Zealand, overseas research on GMOs, and consumer literature relevant to the economics of biopharming. Finally, the potential uses of the technology range from functional foods – food products enhanced to provide health benefits – to nutraceuticals – biologically produced compounds intended for sale as supplements – to biopharmaceuticals – compounds that have gone through the full drug testing regime.

2.2 Research on biopharming

2.2.1 Introduction

Whether the topic is the present or the future, it is very important to be precise when discussing biopharming. One necessary distinction is between actual and potential results. While much discussion focuses on the potential contribution that could result from successful production of pharmaceuticals in plants, the actuality is that this potential has not yet been realised. It is also necessary to distinguish amongst the different sectors being referred to in industry figures. Biopharming, in which compounds are produced in crops or livestock, is one part of a larger industry producing biological compounds. Biological compounds may also be produced through other technologies, such as cellular fermentation. A third distinction focuses on the risks and benefits of the technology: it is important to understand not only the size of the risks and benefits, but also who bears the risk and captures the benefits.

2.2.2 Current situation

The current situation in the biopharming industry is difficult to assess. It is a developing industry with a large number of companies entering and exiting. There is nearly no academic literature focused specifically on this industry, either on its structure or its technology. As a result, the economic information comes largely from two sources: the non-academic press and economic information contained in non-economic publications.

Biopharming is one area of a larger industry focused on producing biological compounds of pharmaceutical interest. In biopharming, these compounds are produced using crop plants or livestock. The plants and animals are genetically modified to produce or express the compounds. The expression may happen in any or all parts of an organism: for example, a maize plant may be modified to express the compound specifically in seeds, or a cow to express the compound in milk. The site of the expression is a key issue, because it affects the

costs of production as well as the risks. Thus, tobacco has been pursued as a biopharm crop when expression is in leaf tissue because tobacco produces a large amount of green matter, while maize is useful for compounds produced in seed.

These same compounds may be produced using other non-biopharming technology, however. In fact, according to Elbehri (2005) there are 84 biopharmaceuticals on the market, while Goldstein & Thomas (2004) stated that 'during the last two decades, approximately 95 biopharmaceutical products have been approved by one or more regulatory agencies for the treatment of various human diseases including diabetes mellitus, growth disorders, neurological and genetic maladies, inflammatory conditions, and blood dyscrasias'. All of these biologics, except perhaps one, are produced using non biopharming methods. Instead, they are produced using cell culture, in which vats of modified mammalian or plant cells are grown in containment and are then processed to extract the target compound. There is reference in the literature to one biopharmaceutical being produced using plant biopharming: the compound hirudin, produced in Canada (Giddings, Allison, Brooks, & Carter, 2000). The biopharmaceutical industry output is estimated to have a cumulative market value of \$41 billion, excluding pharma crop processes, with an annual growth rate of 20 per cent (Wisner, 2005b). Graff & Moschini (2004) suggested that global sales of therapeutic proteins are \$30 billion with sales estimated to approach \$60 billion by 2010. The market for industrial enzymes will be at about \$2 billion and growing at five per cent per year. Finally, biological compounds such as the above are just one part of the much larger pharmaceutical industry.

Biopharming differs from cell culture methods on several dimensions. The main differences are summarised in Table 1¹. This table appears to originate with Fischer & Emans (2000), but has been modified and repeated in a number of publications (Goldstein & Thomas, 2004; Kermode, 2006; Ma, Drake, & Christou, 2003; Stoger et al., 2002). The entries in the table indicate that biopharming is better than cell cultures in these ways: storage and distribution is easier and cheaper; gene size is not limited; it has multimeric protein assembly (SigA); production cost is lower; production scale is greater; propagation is easier; protein homogeneity may be higher; protein yield is slightly higher; biopharming is safer; scale-up costs are lower; and less time is required. However, there are issues that make biopharming less attractive than mammalian cell culture: there is a public perception that it entails greater risk; its glycosylation may not be correct; proteins may not fold accurately in transgenic plants; and therapeutic risks from the compounds is unknown.

Looking at this list, the dimensions that appear to be driving the interest in biopharming are largely related to the costs of producing these therapeutic proteins. The widely-cited estimate from Kusnadi, Nikolov, & Howard (1997) is that plant biopharming could produce compounds at one tenth to one fiftieth the cost of currently methods. The range of cost comparisons for producing pharmaceutical compounds with different technologies is presented in Table 2 (which extends over two pages). These cost savings are a result of lower costs for the factories that produce the feedstock and purify the compounds. Cellular fermentation facilities require an investment of around \$450 million and a time commitment of five to seven years for plant approval and construction, while the purification facilities required for plant biopharming would cost only \$80 million and require three to five years to finish (Elbehri, 2005). Related to the lower cost is the greater convenience of scaling production up or down. With biopharming, more feedstock for the purification can be

¹ The information in the table is repeated here without critical assessment. That is, the authors of the present economic report do not pretend to have the expertise to assess whether, for example, the protein folding in crop plants is different than protein folding in mammalian cell culture, or one method is 'safer' than another. Each of these dimensions could be further discussed, researched, and contested. The information is presented here in order to highlight that the literature on biopharming suggests that the differences between different methods of producing commercial biologic compounds are many and complex.

Table 1: Comparison of features of recombinant protein production in plants, animals, yeast and classical systems

	Transgenic Plants	Plant Viruses	Yeast	Bacteria	Mammalian Cell cultures	Transgenic Animals
Cost/storage	Cheap/RT	Cheap/-20°C	Cheap/-20°C	Cheap/-20°C	Expensive/N ₂	Expensive
Distribution	Easy	Easy	Feasible	Feasible	Difficult	Difficult
Gene size	Not limited	Limited	Unknown	Unknown	Limited	Limited
Glycosylation	‘Correct’?	‘Correct’?	Incorrect	Absent	‘Correct’	‘Correct’
Multimeric protein assembly (SIgA)	Yes	No	No	No	No	Yes
Production cost	Low	Low	Medium	Medium	High	High
Production scale	Worldwide	Worldwide	Limited	Limited	Limited	Limited
Production vehicle	Yes	Yes	Yes	Yes	Yes	Yes
Propagation	Easy	Feasible	Easy	Easy	Hard	Feasible
Protein folding accuracy	High?	High?	Medium	Low	High	High
Protein homogeneity	High?	Medium	Medium	Low	Medium	Low
Protein yield	High	Very high	High	Medium	Medium-high	High
Public perception of ‘risk’	High	High	Medium	Low	Medium	High
Safety	High	High	Unknown	Low	Medium	High
Scale up costs	Low	Low	High**	High**	High**	High
	(unlimited biomass)					
Therapeutic risk*	Unknown	Unknown	Unknown	Yes	Yes	Yes
Time required	Medium	Low	Medium	Low	High	High

* - residual viral sequences, oncogenes, endotoxins; ** - large, expensive fermenters etc; ? – unclear.

Source: (Fischer & Emans, 2000).

Table 2: Cost estimates for producing pharmaceutical compounds with different technologies

Production method	Cost Per Gram	Comment	Source
<i>Transgenic plant biopharming</i>			
IgG from alfalfa grown in a 250m ² greenhouse	US\$500 - 600	Expression levels will have a significant impact on the costs but, at the best expression level reported [500 µg g ⁻¹ leaf for a secretory IgA], the final cost should be well below US\$50 g ⁻¹ . The biggest component of cost with plantibodies will be purification. Assumed purification costs equivalent to industry costs for mammalian cell culture system.	(Daniell, Streatfield, & Wycoff, 2001)
Alfalfa leaves	US\$5.50 ^a	Cost based on commodity price of biomass and percentage of protein in the biomass, and assumed that 10% of total protein would be the target protein/compound.	(Kusnadi et al, 1997)
Canola	US\$8.95 ^a	Cost based on commodity price of biomass and percentage of protein in the biomass, and assumed that 10% of total protein would be the target protein/compound.	(Kusnadi et al., 1997)
Corn	US\$8.10 ^a	Cost based on commodity price of biomass and percentage of protein in the biomass, and assumed that 10% of total protein would be the target protein/compound.	(Kusnadi et al., 1997)
Peanuts	US\$26.40 ^a	Cost based on commodity price of biomass and percentage of protein in the biomass, and assumed that 10% of total protein would be the target protein/compound.	(Kusnadi et al., 1997)
Pharmaceutical corn	US\$80 - 250	Depending on scale; Fernandez et al., 2002.	(Elbehri, 2005)
Potato	US\$59.40 ^a	Cost based on commodity price of biomass and percentage of protein in the biomass, and assumed that 10% of total protein would be the target protein/compound.	(Kusnadi et al., 1997)
Soybeans	US\$4.95 ^a	Cost based on commodity price of biomass and percentage of protein in the biomass, and assumed that 10% of total protein would be the target protein/compound.	(Kusnadi et al., 1997)
Sunflower	US\$8.10 ^a	Cost based on commodity price of biomass and percentage of protein in the biomass, and assumed that 10% of total protein would be the target protein/compound.	(Kusnadi et al., 1997)
Transgenic plants	US\$13 - 14	Cost of growing protein.	(Drabenstott, 2002)
Transgenic plants (incl. potatoes)	US\$10 - 20	Applications: Cholera vaccine (tobacco; Chlorogen, Inc); gastric lipase (corn; Meristem); hepatitis B.	(Elbehri, 2005)

Production method	Cost Per Gram	Comment	Source
<i>Transgenic animal biopharming</i>			
Transgenic animal production systems	US\$100		(Daniell et al., 2001)
Transgenic animals	US\$23 - 25	Cost of growing protein.	(Drabenstott, 2002)
Transgenic animals.	US\$20 - 50	Applications: Lipase (sheep, rabbits; PPL Therapeutics); growth hormone (goats; Genzyme); factor VIII (cattle).	(Elbehri, 2005)
<i>Cell culture</i>			
Cell culture	US\$1000		(Daniell et al., 2001)
Hybridoma produced antibody	US\$5000		(Daniell et al., 2001)
Lab	US\$50 - 100	Cost of growing protein.	(Drabenstott, 2002)
Mammalian cell culture	US\$350 - 1,200	Depending on scale; Fernandez et al., 2002.	(Elbehri, 2005)
Mammalian cells	US\$500 - 5000	Applications: Tissue plasminogen activator; factor VII (glycoprotein); monoclonal antibodies (Herceptin).	(Elbehri, 2005)
Therapeutic production of antibody with animal cell bioreactors	US\$106 - 650	Based on estimates from industry.	(Morrow, 2002 in Elbehri, 2005)
<i>Other</i>			
Yeast	US\$50 - 100	Applications: beer fermentation; recombinant vaccines; hepatitis B viral vaccine; human insulin.	(Elbehri, 2005)

a. Actual figures in Kusnadi et al. (1997) indicated these prices as per kilogram. However, such prices are inconsistent with a fall in production costs to one-twentieth to one-fiftieth current levels. For example, Datar & Rosen (1990) gave a cost of production using fermenter technology at \$50 per gram, or \$50,000 per kilogram, while Petridis, Sapidou, & Calandranis (1995) conducted a profitability analysis based on \$110,000 per kilogram. Thus, prices from Kusnadi et al. are given here as per gram.

produced by growing more plants or animals, and creating more purification facilities is cheaper and less time consuming. Thus, creating more or less of a compound is easier than with current methods.

Whether this cost comparison describes the actual situation or rather biopharming's potential is unclear. The comparison has been repeated in one form or another in a variety of publications. However, commercial plant biopharming is not a current reality (again, with one exception), so there is likely to be an element of speculation in these figures. The one comparison of actual costs that was available for this research was that biotech company Agennix claimed that it could produce lactoferrin using cell culture methods at a cost comparable to Ventria Bioscience's biopharmed rice (Wisner, 2005b).

A further point raised in the above comparison of production methods is that the compounds produced through biopharming, in particular plant biopharming, are not exactly like those produced in cell culture/fermentation. These cost calculations, therefore, appear to presume that the technical issues facing biopharming, such as glycosylation or protein folding, have been overcome. The cost calculations indicating large cost savings through plant biopharming are in effect comparing the costs of producing two different compounds. This idea will be formulated more explicitly below.

The main idea that falls out of this discussion is that biopharming is still in a research stage; it is not a developed industry with commercial products and commercial revenue. Thus, the valuations of products and companies are not based on market transaction for final products. Instead, those valuations are based on projections of the future market value to be realised from present research. The research presently being conducted, however, has a wide scope, as shown in Tables A1 and A2, appended to this report. These tables contain information on the compounds being researched, the organisms modified to produce the compounds, and the companies involved.

2.2.3 Future possibilities

The future of biopharming is generally presented as bright and revolutionary. The technology can be used not only for pharmaceuticals, but also for nutraceuticals and industrial compounds. Biopharming is said to represent the future of biologic pharmaceutical production because of the cost savings and ease of matching the scale of production to market demand for the compounds. It is also said to have the added benefits of being safer than cell culture, since the therapeutic proteins are produced in media less likely to be infected with viruses that may affect humans.

Although the future looks bright, there are technical, regulatory, and political barriers to the development of the industry. The technical problems are outside the scope of an economic discussion; in fact, the economic and marketing literature around biopharming appears to assume that technical problems will be resolved with further research. Regulatory problems include issues of risk management and liability surrounding the genetic modified plants or animals; concerns for the purity of biopharmaceutical compounds and their exclusion from the food supply; and the standard regulatory process for the therapeutic compounds' themselves. Political pressures result from the lack of consensus amongst people and organisations regarding genetic modification in general and biopharming specifically.

2.3 The economy of New Zealand

2.3.1 Introduction

This report now turns to a discussion of the economy of New Zealand. In assessing the potential impacts of introducing biopharming to the country, it is important to understand what the economy currently looks like. Only then is it possible to describe how it might change.

New Zealand is widely recognised as having an economy with a strong foundation in biology and the environment. It is precisely in these areas that some of the largest impacts of biopharming may be felt. Economic impacts from biopharming are thus likely to affect predominantly the industries that rely on the country's natural resources: agriculture and tourism.

2.3.2 Agriculture

The primary sector is an important contributor to the New Zealand economy, both to Gross Domestic Product (GDP) and to export earnings. Together, agriculture, forestry, and their associated sectors contributed 18 per cent of the country's GDP in 2002/03 (Ministry of Agriculture and Forestry, 2005b). In addition, agricultural and silviculture exports accounted for over 60% of merchandise exports (Ministry of Agriculture and Forestry, 2005b).

What follows is a brief description of several parts of the primary sector in New Zealand. It provides an indication of the magnitude of production based on natural biological resources and the relative sizes of different primary commodities.

The dairy industry's 12,000 milk suppliers and their 5.15 million dairy cattle produced 1.21 million tonnes of milk solids in the 2005 season (Ministry of Agriculture and Forestry, 2005b). About four per cent of production was used to produce fresh milk for the domestic market; the other 96 per cent was processed into milk powder, cheese, butter, casein, and other products. The dairy industry is centrally organised, with Fonterra processing 96 per cent of New Zealand's milk. Over 90 per cent of milk products are exported, making the industry highly reliant on international markets. In addition, dairy products exports accounted for 18 per cent New Zealand's exports in the year to June 2006 (Statistics New Zealand, 2006b). In the year to March 2005, this amounted to \$5.678 billion (Ministry of Agriculture and Forestry, 2005b).

According to Statistics New Zealand (2006a), the national beef cattle herd was 4.4 million head at June 2005. Beef exports were 415,000 tonnes in 2005, at a total value of \$1.918 billion (Ministry of Agriculture and Forestry (MAF), 2005). About one-half of export beef goes to the US, with Asian markets as the next most important export destinations (Ministry of Agriculture and Forestry (MAF), 2005).

As at June 2005, New Zealand had 39.5 million head of sheep (Ministry of Agriculture and Forestry (MAF), 2005). In 2004, meat production was 107,000 tonnes of mutton and 411,000 tonnes of lamb, carcass weight equivalent (cwe). That same year, exports of mutton were 87,900 tonnes cwe earning \$255 million, while exports of lamb were 358,000 tonnes cwe or \$1.97 billion (Ministry of Agriculture and Forestry (MAF), 2004). In 2005, lamb exports had a lower volume at 292,000 tonnes, but higher prices meant they were valued at \$2.062 billion (Ministry of Agriculture and Forestry (MAF), 2005). The EU imports about one-half of the total volume of meat exports, paying above average prices for it. The US market is growing,

particularly after lifting the tariff rate quota (TRQ) in November 2001 (Ministry of Agriculture and Forestry (MAF), 2004).

Eighty per cent of New Zealand wool is produced along with meat from dual-purpose animals; only about five per cent of the country's wool is fine merino wool from specialty flocks (Ministry of Agriculture and Forestry (MAF), 2004). Production in 2005 was estimated to be 175,000 tonnes of wool, of which 148,000 tonnes were exported, earning \$698 million (Ministry of Agriculture and Forestry (MAF), 2005). The largest market for New Zealand wool is the People's Republic of China (PRC), with the UK and Italy also as significant importers (Ministry of Agriculture and Forestry (MAF), 2004).

Commercial forestry in New Zealand is focused largely on radiata pine. Forestry exports accounted for ten per cent of New Zealand's merchandise exports, or a value of NZ\$3,226 million for the year to March 2004 (Ministry of Foreign Affairs and Trade, 2004). Estimated roundwood removals for the year ended March 2005 were 19.3 million cubic metres (Ministry of Agriculture and Forestry, 2006). Removals have been decreasing by about eight per cent per year over the last two years because of reduced margins from lower prices and higher costs (Ministry of Agriculture and Forestry, 2006). Exports of all forestry products in the years ended June 2005 was \$3.184 billion (Ministry of Agriculture and Forestry, 2005a).

The horticulture subsector, including floriculture, accounted for over \$4.8 billion dollars in domestic spending and export revenues in 2004/2005 of which about \$2.3 billion was exported (HortResearch, 2005). The total area in horticulture in New Zealand is about 110,000 hectares, spread throughout the country. Major crops by area in 2002 were wine grapes (17,500 ha), apples (12,500 ha), kiwifruit (12,200 ha), potatoes (10,600) and onions (5,680) (Burt, 2004; Ministry of Agriculture and Forestry, 2003a). By 2005, wine grapes had increased to 21,002 ha, apples had fallen to 11,700 ha, kiwifruit was on 10,934 ha, and potatoes were on 11,289 ha (HortResearch, 2005). The major exports in 2005 were kiwifruit (\$720.2 million), wine (\$432.7 million), apples (\$387.0 million), and processed vegetables (\$263.7 million) (HortResearch, 2005). Floriculture exports were \$39 million in 2005 (HortResearch, 2005); the major export products were orchids, calla lilies, sandersonia, and proteacea (Ministry of Agriculture and Forestry, 2003a). In addition, domestic sales of cut flowers are estimated to be \$70 million (HortResearch, 2005), bringing the total value of floriculture to nearly \$110 million per year. The top markets for horticultural exports are the EU, Japan and the US, with Japan an important market for flowers, onions and squash and the UK an important market for wine (HortResearch, 2003).

The arable subsector contains a number of different crops, for which statistics on production, prices and trends are provided in MAF (2003b). The cereal crops of barley, wheat and maize accounted for about 136,000 hectares in 2003/04, with barley accounting for nearly half of that area. Cereal production amounted to about 856,000 tonnes in that year. Small seeds, such as ryegrass and clover seeds, are grown on about 33,000 hectares, and field peas account for another 10,000 hectares of production. A small but rising part of the arable subsector is vegetable seed growing, which earned \$25 million in 2003/04. Total exports of arable crops were \$111 million, comprising mainly grass seed, field peas, and vegetable seeds. Estimated total production in arable crops was \$389 million in 2003/04 (Kaye-Blake, Saunders, Emanuelsson, Dalziel, & Wreford, 2005).

It is possible to disaggregate the exports from different parts of the agricultural sector using data from *New Zealand External Trade Statistics* from the Ministry of Foreign Affairs and Trade. Table 3 is based on statistics from 2002:

Table 3: Disaggregated export statistics, 2002

Main export markets	Value (million NZ\$)
Australia	5,694
United States of America	4,793
Japan	3,698
United Kingdom	1,525
Republic of Korea	1,450
People's Republic of China	1,419

Main export products	Value (million NZ\$)
Dairy	5,925
Meat	4,423
Wood	2,371
Fish	1,401
Starch, Casein	1,386
Fruit (7 th ranked)	1,156
Vegetables (15 th ranked)	447

Main exports by market	Value (million NZ\$)
<i>Australia</i>	
Dairy	300
Meat	26
Wood	380
Fruit and Vegetables	215
<i>United States of America</i>	
Dairy	994
Meat	1,316
Wood	494
Fruit and Vegetables	154
<i>Japan</i>	
Dairy	551
Meat	253
Wool	600
Fruit and Vegetables	387
<i>United Kingdom</i>	
Dairy	229
Meat	540
Wood	2
Fruit and Vegetables	175
<i>Republic of Korea</i>	
Dairy	125
Meat	106
Wood	450
Fruit and Vegetables	28
<i>People's Republic of China</i>	
Dairy	207
Meat	111
Wood	200
Fruit and Vegetables	21

The agricultural sector, including forestry, is an important part of the New Zealand economy. Its contribution to the country's exports is even larger than its contribution to GDP, making New Zealand relatively dependent on primary products to generate income from international trade. In addition to indicating the overall size of the sector, the figures here provide a sense of the relative importance of different products. Dairy products are the most important agricultural products. Beef and sheep account for around \$2 billion each in exports, but forestry has even greater exports at over \$3 billion. Horticultural products taken together account for a greater portion of GDP than any other part of the agricultural sector bar dairy; this total value is spread over a number of economically important crops.

2.3.3 Tourism

The tourism industry is an important part of the New Zealand economy. The Tourism Satellite Account (Statistics New Zealand, 2006c), which calculates the contribution of tourism to the New Zealand economy, shows a total tourism expenditure of \$17.5 billion for the year ending March 2005, contributing nine per cent of gross domestic product. Of this amount, 54 per cent was contributed by domestic tourists and 46 per cent international tourists. International tourism expenditure accounts for 18.7 per cent of total national export earnings and is therefore New Zealand's largest export earner. It is important to note that international tourism is the only export sector that generates GST revenue for the government with a contribution of 10.5 per cent (\$526m) of GST receipts in 2005. Tourism is also an important part of the New Zealand workforce. It is estimated that tourism supports directly and indirectly 176,000 full-time-equivalent jobs involving 9.8 per cent of the labour force (Ministry of Tourism, 2006b).

Tourism is a growing sector. There was an average increase of 7.6 per cent in tourism expenditure between 1999 and 2003 (Tourism Research Council of New Zealand, 2004), and 1.25 per cent between 2003 and 2005. The recent slow-down in tourism expenditure is due to a decrease in domestic tourism. On the other hand, international tourism has been strong. International visitor arrivals passed one million in 1992 and two million in 2002 and reached an all-time high of 2.37 million in 2005 (Ministry of Tourism, 2006b). It is forecasted that international visitor arrivals will reach 2.8 million in 2008 if there is no presence of international shocks, such as the bird flu (Scanlon, April 11, 2006). The forecasted number of international visitors in 2012 is 3.11 million with an expected total expenditure of \$10.10 billion (Ministry of Tourism, 2006a).

Research confirms that tourists have a 'clean and green' image of New Zealand and that they are inclined to visit because of the unpolluted nature and beautiful landscapes (PA Consulting Group, 2001; Sanderson et al., 2003). A survey of international tourists in New Zealand and individuals in New Zealand's main overseas tourism markets indicated that they perceive the New Zealand environment to be above average and among the best in the world (Sanderson et al., 2003). Research conducted by TNZ and Colmar Brunton (New Zealand Tourism Board, 1995, 1997) also shows that it is the tourists' perception of the clean and green environment in New Zealand that motivates them to visit. Tourists are attracted to the beautiful scenery and landscapes, and the opportunity to engage in nature-focused experiences (PA Consulting Group, 2001). This suggests that New Zealand tourism is largely dependent on the 'clean and green image' and this image needs to be maintained to remain competitive in the global tourism market. For this reason, threats to the New Zealand environment may have a negative impact on tourism and the New Zealand economy.

A report published by the Ministry for the Environment (PA Consulting Group, 2001) estimated the export value of New Zealand's 'clean and green image', and surveyed the

change in tourists purchasing behaviours under worsened environmental conditions. Tourists from New Zealand's top five tourist markets (Australia, USA, UK, Japan and Korea) were provided with two sets of images. One set depicted the current state of the New Zealand environment with images typically used to promote New Zealand as a tourist destination overseas, and the second set depicted images of New Zealand with a degraded environment. The respondents had to indicate if the two different sets of images would have made them stay a different number of days in New Zealand, and if so, how many days they would have stayed under the different conditions. The results showed that the tourists were likely to spend less time in New Zealand under the degraded environmental condition and the estimated annual tourism expenditure loss was \$530 million (based on figures for the year ending 2001). This figure includes the loss of direct tourism expenditure and GST revenue. It is important to note that the loss figure only represents tourism expenditure from the top five tourist markets and the figure would be greater if all other tourist markets were included. The result from this study confirms that worsening environmental conditions negatively affect tourism expenditure.

The clean environment not only benefits international visitors, but also New Zealand residents (Hughey, Kerr, & Cullen, 2004). The high level of environmental quality in New Zealand can be attributed to the low population density resulting in modest environmental pressures (PA Consulting Group, 2001). However, there are some aspects of the New Zealand environment that are under pressure, such as rivers and lakes, marine fisheries and air quality (Hughey et al., 2004; PA Consulting Group, 2001). Hughey et al. (2004) found that New Zealanders believe that water pollution is the most important environmental issue and many of them are willing to pay a \$20 per year increase in rates to fund lowland stream enhancements. The value of park visits has been assessed in three main cities. The value per park visit for the Auckland Regional Council was estimated to be \$11.50 per person (Saunders, Cullen, & Ball, 1999). Another study found a similar figure for Wellington parks (Kerr, 1996). A Christchurch study for a single park found a much lower per-visit value, at only \$1.60 per person (Walker, 1992). This research suggests that the clean and green environment is also of value for domestic tourists.

2.3.4 New Zealand economy: conclusion

New Zealand's economy has a significant portion that is based on natural resources. The agricultural sector depends on the biological resources to produce not only food and fibre for the domestic population but also for a large percentage of the country's exports. International tourism also depends on the country's natural resources, its biology and landscape, and adds significantly to the country's export earnings. Tourism exploits New Zealand's image as a clean and green destination.

Biopharming also depends on natural resources, and is thus a potentially competing claim on these resources. Whether the net impact on the New Zealand economy is positive, negative, or neutral depends on the ability of these different industries to use the resources productively. It also depends on potential spill-over effects – externalities in the language of economists – and how large those effects are.

2.4 Economic analyses for New Zealand

While biopharming promises to revolutionise production of pharmaceuticals, there are elements of the industry that suggest comparisons with other areas of research. In particular,

the production of pharmaceutical compounds using biopharming relies on genetic modification to engineer the production of the novel compounds; the plants and animals used in biopharming are genetically modified organisms (GMOs). Thus, to understand the potential impact of introducing biopharming, one can examine the literature on the potential impact of GMOs in New Zealand.

2.4.1 Macroeconomic analyses

The Independent Biotechnology Advisory Council (IBAC) prepared an early economic analysis of the impact of GMOs, *Economic Implications of a First Release of Genetically Modified Organisms in New Zealand* (Campbell et al., 2003; IBAC, 2000). Jan Wright (a member of IBAC) relied on these findings for her submission to the Royal Commission on Genetic Modification (RCGM). The IBAC paper and Wright's submission indicated that there were serious economic issues with GM in agriculture, particularly with the 'first release'. Wright suggested that the RCGM look closely at economic issues (Campbell et al., 2003; Wright, 2000).

In the event, the RCGM did not fully explore the economics of GMOs, and in particular did not receive independent advice regarding the economics. A number of submissions came from entities with economic interests in GM, either for or against (Nana, 2000; Stroomborgen, 2000; Wright, 2000), but the economic research was remarkably thin (Campbell et al., 2003).

One example of economic research presented to the RCGM was Infometrics' analysis in support of the Life Sciences Network. Infometrics used a Computable General Equilibrium (CGE) model to simulate the effects of several scenarios regarding using or restricting the use of GM in New Zealand (Stroomborgen, 2000). While the findings were generally positive for GM crops, the results were unsurprising given the assumptions driving them. Nana (2000) reviewed this RCGM submission and noted that modelling the robustness of the effects or the impacts of closely related scenarios would have provided more useful results. Furthermore, Nana found that the actual model used probably overstated any impacts of GM crops on the NZ economy. Thus, Nana did not find that the result provided clear, unqualified empirical support for pursuing GM.

An important lesson from the Infometrics modelling was the importance of accurate and transparent assumptions for modelling. Campbell, et al. (2003) also suggested that comparing a future possible industry-wide practice with a minority sector like organic agriculture was problematic.

A second economic analysis presented to the Royal Commission was based on the Lincoln Trade and Environment Model (LTEM) (Saunders & Cagatay, 2001). The LTEM was initially used to simulate various scenarios relating to adoption of GM crops in NZ, including reduced costs of production, premiums for and against GM and bans for GM products in key markets Japan and the EU (Saunders & Cagatay, 2001, 2003). The results of the scenarios in which New Zealand adopted GM crops were generally negative for NZ, even when a preference for GM products and/or increased productivity was modelled. Saunders & Cagatay (2001) outlined their findings as being generally negative for the adoption of GM in primary production sectors. Further modelling work has in general supported these conclusions (Saunders, Kaye-Blake, & Cagatay, 2003). This later work found that for GM to have positive impact on producer returns NZ must be able to retain productivity benefits for itself and/or the GM product must have a premium.

Another source of economic analysis of GM crops in NZ is a report that the Ministry for the Environment (MfE) commissioned from Business and Economic Research Limited (BERL) and the AERU (Sanderson et al., 2003). As part of that research, surveys were conducted in several key overseas markets. These surveys found that New Zealand's image as an environmentally friendly country would be hurt by the release of GM organisms, and demand for NZ products would suffer. The report found that consumers' reactions were an important influence on New Zealand's international trade, but that productivity increases or cost savings on the farm were much less important. The overall effect on GDP from commercial use of GMOs in agriculture could be either negative or positive, depending on how consumer reactions affect actual trade and how GM technology affects actual production.

Research conducted to inform the economic modelling for the MfE report provided new information on how overseas consumer might react to the introduction of a GMO into the New Zealand environment. The survey research found that 27 per cent of Australians, 20 per cent of US citizens, and 30 per cent of Britons were opposed to the use of GMOs. These figures are on a par with the results of other research discussed below. In addition, the NRB research found that nine per cent of Australians, five per cent of US citizens, and six per cent of Britons would stop visiting New Zealand if a GMO were released in the country.

Further research has explored the dynamic interaction of consumer willingness to pay for premium products and the impacts of productivity on farmers' returns. Using results from a nationwide survey of New Zealanders' preferences regarding a variety of biotech products, Kaye-Blake, Saunders and Fairweather (2004) estimated the maximum gains that were possible from producing crops which commanded a premium. They found that growers of the most favoured GM product, anti-oxidant apples, would be able to charge a 17 per cent premium to 26 per cent of the apple market, leading to an average increase in industry revenues of 4.3 per cent. Anti-oxidant apples are an example of a functional food, so these findings are relevant for biopharming broadly defined.

There have also been some modelling activities in the Australian context that are relevant to the New Zealand economy. A Productivity Commission Report (Stone, Matysek, & Dolling, 2002) applied the global general equilibrium modelling framework GTAP (Global Trade Analysis Project) to examine potential impacts of GM technology on Australia's trade in non-wheat grains and oilseeds. The results of the three scenarios considered demonstrated that very small 'absolute changes' would occur in Australia's import and export flows. Rather, regions with currently significant GM sectors (such as North America) felt the most substantial impacts to trade and income. Two assumptions are critical to their findings: incompletely-adopting countries (Australia, New Zealand, and the EU) have an added regulatory burden that increases supply costs, whereas North America does not; and consumers who do not want GM crops do not have increased welfare from having access to sources of non-GM food. The authors conclude from their findings that a longer-term expansion of GM technology could have significant negative impacts on Australia's and New Zealand's trade position.

2.4.2 Consumer research

Finally, attitudes and perceptions of New Zealanders have been studied by social scientists at two Crown Research Institutes. One report compares the results of two telephone surveys (Gamble & Gunson, 2002). Generally, women are less sanguine about GM food than men, and are more likely to have changed their food purchasing behaviour due to concerns about GM. In addition, a product that is itself modified is less acceptable than a non-modified product produced using GM (such as beef fed with GM clover).

Another report (Small, Wilson, & Parminter, 2002) analyses the results of a postal survey. These results show somewhat less support in New Zealand than the above research. However, a majority of respondents were willing to support GM food in some circumstances. On the other hand, GM did not fit with respondents' personal beliefs.

Peer-reviewed research has also examined consumer reactions to genetically modified food. Kassardjian, Gamble, & Gunson (2005) used experimental auctions to determine the willingness of participants to exchange non-GM apples for GM apples with defined benefits. They found that 28 per cent of participants were not interested in the GM apples, while the majority was willing to pay between NZ\$0 and NZ\$0.50 extra for apples providing either environmental or health benefits. No difference in prices was found between the two types of products. They also found that participants felt a need to interact with the products, and that engagement in biotechnology positively affected willingness to pay. Kaye-Blake, Bicknell, & Saunders (2005) employed a choice modelling survey, which also collected information on willingness to pay for GM apples. They also found that a significant minority of consumers were not interested in GM apples. For some who were willing to buy GM apples, the price reductions were quite large, while for other respondents the price reductions were not statistically significant from zero. Thus, both of these articles suggest that a majority of consumers are willing to buy GM food, but that the prices demanded by these consumers have a considerable range.

2.5 Analyses of impacts on other countries

Further information about the potential impacts of introducing GMOs into New Zealand for the purposes of biopharming can be derived from overseas research. This research is particularly valuable as GMOs are currently commercially grown in some other countries, whereas they are not intentionally grown in New Zealand. From an economic perspective, it is helpful to divide impacts into those that affect production or supply and those that affect consumption or demand. These two sides of the market are then analysed together in the macroeconomic and trade literature. Production, consumption, and trade are thus handled in turn in the discussion below.

2.5.1 Production impacts

Much of the research on production impacts of biotechnology has focused on simple productivity gains. That is, they estimate the impacts of biotechnology from enabling farmers to produce commodity crops more efficiently (e.g., Frisvold, Sullivan, & Ranases, 2003). The impacts of biotechnology to date, especially in New Zealand, have been largely on productivity (Kaye-Blake, Saunders et al., 2005), so there is some merit to this focus.

However, biopharming produces a different kind of product. Rather than producing agricultural commodities in greater amounts, it produces a pharmaceutical product in a novel way. Analyses of productivity impacts are therefore of limited use. The literature on second-generation GM crops, which are products with enhanced attributes, such as nutraceuticals or functional foods, provides some guidance, however. The allure of these products is the increased profit from a price premium that consumers would pay. These would be value-added products that move producers out of the commodity market and into a market with higher profit margins. However, these products are also likely to lead to changes to the structure of agricultural sector, both through concentration of the control of inputs and desire

for quality control over these enhanced products (Caswell, Fuglie, & Klotz, 1998; Oehmke & Wolf, 2002).

Furthermore, the experience of an already-released functional food crop, the Flavr Savr tomato, shows that making a profit from enhanced products is not a foregone conclusion. As detailed in *First Fruit: The Creation of the Flavr Savr™ Tomato and the Birth of Genetically-Engineered Food*, (Martineau, 2001), genetically engineering a tomato to delay rotting was only part of the genetic work in producing a better-tasting, premium tomato. A significant problem was that commercial tomato varieties have been bred for toughness rather than taste, so they produce mediocre tomatoes whether rotting is delayed or not. A further problem had nothing to do with genetics and everything to do with business: Calgene, the company that developed the tomato, did not understand the fresh-market tomato business or its own product sufficiently to be successful. The GM tomato was pulled from the market after only a few years.

One peer-reviewed analysis of the economics of biopharming has been published (Kostandini, Mills, & Norton, 2006). It focused on the production of human serum albumin (HSA) in tobacco as a case study for biopharming. The market for HSA was modelled with linear supply and demand functions, and the results of a price reduction on the market were estimated both when the producer had monopoly power due to its innovation and when it did not. In the first case, the innovation resulted in excess (monopoly) profits for the firm. It did not benefit consumers, however. In addition, tobacco farmers were either unaffected or left worse off; they provided the tobacco at cost as a result of the relative market power of the farmers and the innovating firm. The latter case, without the monopoly, is assessed as unrealistic: the firm would not pursue the innovation unless it could secure monopoly pricing power. This modelling suggests that control of the innovation is important, and that widespread welfare gains from biopharming may be unlikely.

2.5.2 Consumption impacts

The impacts of biopharming on consumption can be considered at two levels. The first level is the consumption of the pharmaceutical compounds themselves: the market for the compounds, the maturity of the market, and the competitiveness of the market. These issues have received essentially no consideration in the academic economic literature, and it is thus difficult to reach any firm conclusions. However, given the information presented above regarding the types of compounds that are being produced with biopharming – well-understood compounds that may be manufactured in a number of ways – it would seem that the market for these compounds is relatively mature and stable. The size of the market for any individual compound could be assessed through industry sources, and competition is likely to be on the basis of cost.

The second level to consider for the consumption side of the market is the overall impact of releasing novel GMOs with biopharmaceutical properties. The consumer impacts of releasing GMOs has been studied extensively, so there is a body of literature from which to draw.

An important finding from this research is that all biotechnology applications do not provoke similar responses. Broadly speaking, medical uses of biotechnology are more acceptable than food uses, and biotechnology focused on plants is more acceptable than animal biotechnology or plant-animal genetic transfers. The same hierarchy of acceptance is evident in Australia, New Zealand, North America, and Europe (Campbell et al., 2003). The ramification of this hierarchy when medical compounds are produced in food plants is, however, unclear.

Another aspect of differential responses to biotechnology application is the variability amongst countries. Several researchers have found that North Americans are more accepting of biotechnology in general than are Europeans (Campbell et al., 2003; Hoban, 1997).

The impact of knowledge on attitudes towards biotechnology is a more difficult question. One early review of opinion polls found that people who learned more about GM became more accepting of it (Zechendorf, 1994). However, this finding does not always hold, and has been specifically countered in recent research in the UK, where people's attitudes hardened as they learned more about GM (Heller, 2003).

Risk perceptions regarding biotechnology are an important topic of research. Generally, lower acceptance of biotechnology is tied to greater risk perceptions. One specific concern that has been raised is concern for the unintended consequences of the technology (Norton, 1998 in Campbell et al., 2003; Heller, 2003). There is some question about how risks and benefits of the technology are perceived and assessed. Fischhoff & Fischhoff (2001) and Gaskell et al. (2004) have suggested that risks and benefits are not combined into a unidimensional scoring of the value of the technology, but that they act as thresholds in individuals' decision-making processes.

The PABE project (Marris, Wynne, Simmons, & Weldon, 2001) used in-depth research to examine these attitudes in more detail than is possible with opinion polls. Two important overall findings that challenged conventional wisdom in the area of consumer attitudes to GM were that attitudes did not vary much in the five countries studied, and that people were not simply 'for' or 'against' GM *per se*. The report focused on dispelling myths that have built up around consumer perceptions, suggesting that these myths have created a gulf of understanding between consumers on the one hand and government and industry on the other. The emphasis of this report is on the understandings and knowledge that consumers use to make decisions about biotechnology, and in particular about GM food. Although the general public may not have the specialist knowledge of a geneticist, they are not basing their decisions on that type of knowledge. Instead, they use their empirical knowledge of past institutional behaviour, especially of lapses in public safety. 'Signal' events (Flynn, Slovic, & Kunreuther, 2001) such as the BSE crisis are perceived to be examples of the normal behaviour of institutions charged with protecting the public safety.

Individuals have often expressed ambivalence about GM technology (Marris et al., 2001). They seem to recognise that there were both positives and negatives, and many factors came into play when they made decisions regarding specific biotechnology applications. Ambivalence is also how the UK public was described in a report synthesising results from the Eurobarometer surveys from 1996 to 2002 and additional surveys (Gaskell et al., 2003). The Eurobarometer polls are generally useful for assessing European attitudes towards biotechnology. Britons were found to be getting less negative towards GM in general between the 1999 and 2002 surveys, and significant percentages claimed to be keeping an open mind on the issue. In addition, it was clear that Britons also make clear distinctions between different types of biotechnology. The majority do not support GM food, while GM medical applications are generally acceptable.

The results of research into overseas consumers' attitudes towards biotechnology raise some important issues. First, given the apparent hierarchy of approval, with medical biotechnology more supported than food biotechnology, the reaction to producing medical compounds in food is potentially ambiguous. Secondly, consumer reactions are not unidimensional, but are complex and can be influenced in unpredictable ways. Factors like risk perceptions and knowledge of the technology do not have simple, unambiguous impacts on consumer reactions.

The literature on public and consumer perceptions of biotech food and the economic research described above suggest that the decision of what food to purchase is complex and affected by consumer awareness, environmental concerns, labelling, and product experience, in addition to the use of genetic technology. *Ceteris paribus*, non-GM food is preferred over GM food. However, if pharmaceutical or nutraceutical properties can be made available to consumers through genetic modification, some consumers may be willing to pay a premium for these products. Certainly, research in New Zealand suggests that there is a consumer segment that is comfortable with biotechnology and interested in improved food products (Kaye-Blake, O'Connell, & Lamb, 2007).

There are two broad conclusions that can be drawn from this review of consumer studies. The first is that there is a great degree of variability with regard to responses to and demand for biotech food crops. Levels of consumer concern vary by country and vary strongly by actual application of biotechnology. The second conclusion is that there is likely to be some resistance to biotech food as a potential export product from New Zealand. In every country studied, non-GM foods are preferred to GM foods. Furthermore, there is a market segment that finds GM foods unacceptable, regardless of other product attributes. Since around 1995-1996 this segment of the market in many Western countries has developed negative attitudes towards GM food. Levels of trust and perceptions of risk associated with biotechnologies are increasingly related to broader concerns about ethics, food morality, regulation and food safety, and the perceived politics of food trading. This resistance in key markets has become relatively stable and comprises a minority segment of some of New Zealand's key markets.

2.5.3 Environmental values

The previous sections reported on research conducted by social scientists that tended to focus on the distinction between food and medical uses of biotechnology. An important third area of interest in New Zealand is the potential for biopharming technologies to have environmental benefits.

Environmental values are an important part of perceptions of GM food (Bredahl, Grunert, & Frewer, 1998; Cook, 2000). However, the relationship is not straightforward. Researchers found that favourable attitudes towards nature correlated with negative attitudes towards GM (Bredahl, 2001). More specifically, survey respondents did not agree that GM is environmentally friendly (Small et al., 2002), and ecocentric respondents (those that value nature intrinsically) did not support GM (Siegrist, 1998). Likewise, those who felt that the costs of technological growth and energy consumption were too high tended to have negative attitudes towards GM (Sparks, Shepherd, & Frewer, 1994). In general, acceptance of GM was less likely when there is greater environmental risk (Macer, 1992; Small et al., 2002). In fact, the Organisation for Economic Cooperation and Development (OECD) has attributed the lack of acceptance of rBGH outside the US to concern for animal welfare (Organisation for Economic Co-operation and Development, 2000).

Some surveys that attribute environmental benefits to biotechnology in agriculture find positive reactions. In the IFSC/Wirthlin Group/Cogent Research surveys, respondents were asked whether they would buy biotechnologically derived food that required fewer pesticide applications and whether they would buy biotechnologically derived food engineered to taste better or stay fresher. Consistently, respondents express more support for the biotechnology application that has an environmental benefit (IFIC, 2002) than for applications that do not. Canadian, New Zealand, and Australian research has revealed a similar pattern (Macer, 1994; Sheehy, Legault, & Ireland, 1998).

What is apparent is that genetic modification of food and environmentally-friendly farming pull consumers in opposite directions. Choice modelling research in Western Australia found that respondents would purchase GM food at a 20 per cent to 47 per cent discount, but would also pay 36 per cent more to reduce agrochemical use by 30 per cent (James & Burton, 2001). The format of choice modelling surveys generally highlights tradeoffs that respondents could make, but this particular study was not designed in such a way to estimate the willingness to pay for GM food crops that used markedly fewer pesticides.

The combined effect of using genetic technology to achieve environmental goals was examined in research for the NZ Ministry for the Environment (Sanderson et al., 2003). Respondents from Australia, the U.K., and the U.S. were surveyed on how their image of New Zealand would change were the country to use genetic technology to control a pest population. Overall, 25 per cent said their image would improve, 29 per cent said it would remain the same, and 32 per cent said it would get worse. By contrast, if New Zealand were to be one of a few countries not to release GM organisms into the environment, 33 per cent said their image would improve, 59 per cent said it would remain the same, and six per cent said it would worsen. These results suggest that some people are comfortable with the use of genetic technology to achieve environmental goals, whilst others are not.

Environmental values seem to cut both ways. To the extent that biotechnology may represent a perceived threat to the environment, some consumers may see it as a negative development. To the extent that biotechnologies are perceived to reduce environmental damage, they may become more valuable.

2.5.4 Estimated trade impacts

The trade impact of introducing GM has been estimated by several studies. Moschini, et al. (2000) attempted to quantify the effects on production, price and welfare of adoption of roundup ready (RR) soybeans. This study used a three-region, US, South America and the Rest of the World (ROW), bilateral partial equilibrium trade model and they focused only on soybean and soybean products (meal and oil). To model the innovation at the production level, Moschini, et al. (2000) first quantified the per hectare cost, profit and yield effects of RR soybean seed adoption. They then calculated the price effects of quantified changes in the innovator country. The effect of trade policies in their model were assumed to be captured by price differentials between the regions. Finally, Moschini, et al. (2000) quantify the consumer and producer surplus measures of welfare effects of RR adoption in the innovator country and in the other regions. They also provided the welfare effects under the assumption of international technology spill-over from innovator country to other regions. They found that U.S. farmers are better off in the base scenario. However, they were worse off if the technology increased their yields, and they do not gain nearly as much if other countries also adopt the technology.

Nielsen, et al. (2000) analysed the impact of consumers' changing attitude toward genetically modified organisms (GMOs) on world trade patterns, with emphasis on the developing countries. They used a multi-regional computable general equilibrium (CGE) framework that modelled the bilateral trade among seven regions: High-Income Austral-Asia, Low-Income Asia, North America, South America, Western Europe, Sub-Saharan Africa and the ROW. Production was aggregated into ten sectors in each region, including five primary agricultural products (cereal grains, oilseeds, wheat, other crops, and livestock), three food processing industries and a manufacturing and services industry at aggregate level. The goods are assumed to be imperfect substitutes in the international market.

Nielsen, et al. (2000) included the GM and non-GM production of maize and soybeans sectors in their model. Initially, they assumed an identical production structure in terms of the composition of intermediate input and factor use in the GM and non-GM varieties and also the same structure of exports in terms of destinations for both varieties. The producers' and consumers' decision to use GM versus non-GM varieties in their production and final demand respectively was endogenised for maize and soybeans sector. For the other crops, intermediate demand was held fixed as proportions of output and final consumption of each composite good was also fixed as a share of total demand.

The policy scenarios were based on the assumption that the GM-adopting sectors did make a more productive use of the primary factors of production as compared with the non-GM sectors. Therefore, they introduced a ten per cent higher level of factor productivity in GM-adopting maize and soybean sectors in all regions as compared with their non-GM counterparts. The factor productivity shocks were introduced in alternative scenarios which differ in terms of the degree to which consumers and producers in high-income regions found GM and non-GM products substitutable. Starting from the perfect substitution case they lowered the degree of substitution among GM and non-GM maize and soybeans in production and consumption as the citizens of high-income, Western Europe and High-Income Austral-Asia, regions became more sceptical of the new GM varieties. In the other regions, the citizens were assumed to be indifferent, and hence the two crops remained highly substitutable in those production systems.

Nielsen, et al. (2000) included NZ in High Income Asia group. They found that trade diversion became significant when the GM-critical regions changed their preferences towards Non-GM products. The trade of GM-varieties was found to divert towards GM-indifferent markets and Non-GM varieties diverted towards GM-critical regions. This was explained as a result of the price differential between GM and Non-GM varieties, which was a consequence of factor productivity differences in the production of these varieties. However, the degree of the price differential and its impact on supply showed differences between the GM-critical and GM-favourable regions. In particular, in GM-favourable regions the prices of the Non-GM varieties declined as well as the price of GM-varieties, due to the high degree of substitution between the two varieties in consumption and to the increased production to supply to GM-critical regions. In the GM-critical regions on the other hand, the price differential impact on the supply of Non-GM goods was minor. Moreover, as there was not perfect substitutability between GM and Non-GM products in these regions, there was still the possibility for both varieties to access the GM-critical markets.

In a similar work that focuses on production of GM maize and soybean crops, Anderson & Nielsen (2000a) use a CGE model, GTAP (Global Trade Analysis Project), to quantify the effects on production, prices, trade patterns and welfare of certain countries adopting GM maize and soybean crops. They analyse the policy impacts in various scenarios with and without considering the trade policy and/or consumer reactions to GMOs. GTAP is a static CGE model that provides the bilateral trade relations among countries by using the Armington (1969) approach to differentiate the products. Anderson & Nielsen focus on 17 industries of which agricultural production is disaggregated into coarse grains, oilseeds, livestock, meat and dairy products, vegetable oils and fats, and other foods. The world is aggregated into 16 regions in which North America, Southern Cone, China, India, Western Europe, Sub-Saharan Africa, Other High-Incomes and Other Developing and Transition Economies are specified explicitly.

The policy scenarios are based on the assumption that the GM-adopting sectors experience a one-off increase in total factor productivity (including all primary factors and intermediate inputs) of 5 per cent thus lowering the supply price of the GM crop to that extent. Anderson

& Nielsen first analyse the impacts GM-driven productivity growth of 5 per cent in the related countries when others such as Western Europe, Japan, Other Sub-Saharan Africa are assumed to refrain from using or be unable to adopt GM crops in their production systems. In another scenario, the case of a policy and/or consumer response in Western Europe is introduced by banning the imports of maize and soybean products from GM-adopting regions. This scenario is based on the implicit assumption that labelling enables Western European importers to identify such shipments. The distinction between GM-inclusive and Non-GM products is based directly on the country of origin, and labelling costs are ignored. In a subsequent scenario, consumers in Western Europe are assumed to shift their preferences away from imported coarse grain and oilseeds and in favour of domestically produced crops. This scenario involves an exogenous 25 per cent reduction in final consumer and intermediate demand for all imported maize and soybeans. Incomplete information about the imported products in terms of whether they are non-GM or not is the implicit assumption behind this scenario.

Anderson & Nielsen (2000a) include NZ implicitly in Other High Income countries. They analyse the impact of policy scenarios on Other High Income economies by showing the change in economic welfare. In the case of GM adoption by other regions (except Western Europe), their findings show that the increase in economic welfare (equivalent variation) of Other High Income group is higher when Western Europe bans the GM imports, compared to 'no policy response' case. The same result also applies when consumer preferences in Western Europe shift towards non-GM varieties and away from GM products. The same results are reported in Anderson & Nielsen (2000b).

In addition, Anderson & Nielsen note that the analyses do not account for any increase in welfare Europe might derive from having access to non-GM products. A major weakness of measuring impacts of GM technology in terms of welfare changes is: if the demand for Non-GM food is not explicitly modelled, then the analysis of welfare gains or losses is incomplete. Furthermore, Anderson & Nielsen note that 'the cost of banning GMO imports in Western Europe amounts to barely US\$15 per capita per year – hardly a major impediment to imposing an import ban' (p. 14). Given such a low cost and the high willingness to pay for non-GM food, the likelihood that Europeans gain consumer welfare from a ban on GM food is quite high.

Jackson & Anderson (2003) use a similar GTAP model to estimate intra-national distributive impacts. They model several scenarios, including: increases in productivity enhancements alone and productivity increases with different regulatory and labelling policies. They find that aggregate welfare in North America increases in all model scenarios, but that Australasia gains when other countries ban GM products and lose welfare otherwise. Importantly, they show that European agricultural producers gain from a ban on GM imports, suggesting that pressure for a GM ban or GM labelling is not solely consumer-driven.

Another example of GTAP modelling is the report by the Productivity Commission in Australia (Stone et al., 2002) discussed above with the New Zealand research. The overall conclusion is that adoption of GM crops will not have a large impact on Australia's trade. The report does however suggest that Australia could lose market share in the long term and therefore export earnings if it does not expand its GM sector.

This message, that Australia and New Zealand could lose market share and income if they forego GM crops, is echoed in a report from the Australian Bureau of Agricultural and Resource Economics (ABARE) (Abdalla, Berry, Connell, Tran, & Buetre, 2003). Although the focus of the report is developing countries, it also reports that Australia and New Zealand

are unlikely to benefit from GM crops. The report advocates adopting GM crops, however, in order to limit losses in the event of worldwide adoption.

This above report demonstrates the difficulties inherent in relying on overseas research to assess impacts on New Zealand. Results are reported for Australia-New Zealand as a whole. Terms of trade for the region decline from large-scale adoption of cost-saving GM technology, but the region gains from reduced agricultural imports due to increased domestic production and cost savings in related industries, such as livestock production. However, New Zealand is likely to see less benefit than Australia from these impacts. Increased consumption of domestic production will be lower in New Zealand because of the products modelled. In addition, New Zealand's lower reliance on grain and oilseeds in its livestock production will see it gain relatively less than other countries. Thus, research that analyses New Zealand's specific situation is more helpful than more aggregated research.

Critically, Abdalla, et al. (2003) make no allowance for consumer attitudes. GM and non-GM products are assumed to trade at the same international price. The modelling therefore simulates the effect of a cost-saving technology that does not produce a differentiable product and whose adoption is geographically uneven. Consumers are not better off for being able to purchase products they prefer, and producers are unable to capture any premium from reaching those consumers. In essence, Abdalla, et al. (2003) present half a model. They consider the production impacts, but ignore the consumer impacts.

2.5.5 Actual impacts

Adoption of biotech commodities can affect the amount of goods traded and/or the price received. There has been only a little research on the trade price impact from adoption of biotech crops. The Tokyo Grain Exchange, for example, provides trading in futures contracts for non-GM soybeans. The premium over a standard contract is approximately the same as segregation costs (Parcell, 2001), suggesting that whilst there is a premium there are no excess profits for non-GM soybeans. Similar premiums are reported in Europe, with the USDA reporting premiums under US\$4.00 per ton to cover the costs of testing (USDA, 2001). In both Japan and the EU, it is suggested that there is sufficient supply of non-GM soybeans so that large premiums are not required (Parcell, 2001; USDA, 2001).

The impact on trade volumes is more difficult to assess, and evidence is largely anecdotal. A summary of the impacts is available in the ABARE report, 'Market access issues for GM products' (Foster, Berry, & Hogan, 2003): Canada lost the EU as a market for canola, the US lost most of its maize exports to the EU, and Brazil has gained ground in the world soybean market, possibly as a result of its non-GM soybeans. One common assertion is that the US has lost around US\$300 million per year in maize exports to the EU (INL Newspapers, 2003). Another impact is that the EU has shifted its in-quota supplier of maize, seemingly in reaction to the expansion of GM production in exporting countries (Agra Europe, 2000). Other similar anecdotes appear in the popular and trade press. However, no systematic study seems to have been made except the ABARE report, and that report is itself based on limited evidence.

The overall impression from the trade press is that international trade is fulfilling its basic function: it is getting the right products to the right markets at competitive prices. Non-GM commodities are going to GM-sensitive uses in GM-sensitive markets, whilst GM commodities (and co-mingled commodities) are going to GM-indifferent uses and markets. Inhibiting analysis in this area is the fact that data sources do not distinguish between GM and non-GM commodities. Comparisons of GM-indifferent and GM-sensitive markets are also difficult due to data reasons. A further question is the cross-commodity impact of the

commercial release of biotech products. Again, this topic has received scant attention. The ABARE report mentioned above does discuss the issue, if only to say that no cross-commodity impacts have been seen. Because of this lack of research, this report cannot provide any information on actual cross-commodity impacts of adoption of GM crops.

The actual impact that crops produced by biotechnology have had on international trade is an important topic, and it appears that there is scope for internationally important research in this area.

Chapter 3

Theory of Impacts

3.1 Introduction

The economic theory relevant to biopharming is extensive. It touches on supply and production, imperfect competition, demand and consumption, externalities, and risk. These topics form the basis of the following discussion.

3.2 Supply/production

There is currently nearly no commercial biopharming, in the sense of biopharmaceutical products being produced in agricultural systems for retail sale to final consumers. There is, however, much discussion of the potential. The question arises, then, of how to get from here to there, of what will happen when the industry moves from a situation of 84 biopharmaceuticals (Elbehri, 2005) on the market being produced in contained cell culture at a price of about \$1000 per gram to a situation in which therapeutic proteins are produced through biopharming at a cost of, for example, \$50 per gram.

It is possible to represent this change with a model. In this model, the cost of producing a compound is directly related to the characteristics of that compound; each compound may be viewed as a bundle of characteristics. If each characteristic is viewed as discrete, then it is possible to assign a cost to each one. The total cost of each compound is thus a function of the costs of the characteristics and the amount or level of the characteristics in each compound. For example, a biologic compound can be considered as a vector of characteristics (Fischer & Emans, 2000; Goldstein & Thomas, 2004; Kermode, 2006; Ma et al., 2003; Stoger et al., 2002):

[Cost/storage, Distribution, Gene size, Glycosylation, Multimeric protein assembly, Production cost, Production scale, Production vehicle, Propagation, Protein folding accuracy, Protein homogeneity, Protein yield, Public perception of risk, Safety, Scale-up costs, Therapeutic risk, Time required, Uncertainty].

A biologic compound could be produced using mammalian cell culture, which is current technology, or can be produced using biopharming. Using cell culture, the cost of the compound could be:

$$C_{cc} = \beta_n * k_{cc} = 1000 \text{ dollars per gram,}$$

where C is the cost, cc denote cell culture technology, β represents the costs of the characteristics, n is the number of characteristics, and k denotes the characteristics identified above. The sum of the characteristics multiplied by their costs is equal to the total cost of production. Using biopharming, the cost is estimated to be:

$$C_b = \beta_n * k_b = 50 \text{ dollars per gram,}$$

where b denotes biopharming and all other terms are as defined above. The values for the β s are constant across the technologies, weighted for each compound by the associated level of k . In principle, if the levels are known and given the prices of different compounds produced in different ways, it would be possible to estimate β s. However, they are largely notional, used to create a model for approaching the economics of the issue.

The economics can be shown as follows. The adoption of biopharming entails a movement from cell culture to biopharming. The cost shifts from \$1000 per gram to \$50 per gram. There are also associated changes in the levels of many characteristics. This may be summarised as follows (Fischer & Emans, 2000; Goldstein & Thomas, 2004; Kermode, 2006; Ma et al., 2003; Stoger et al., 2002):

$$C_{cc} - C_b = 1000 - 50 = \beta_n * (k_{cc} - k_b) = \beta_n [\begin{array}{l} \Delta \text{ Cost/storage} \\ \Delta \text{ Distribution} \\ \Delta \text{ Gene size} \\ \Delta \text{ Glycosylation} \\ \Delta \text{ Multimeric protein assembly} \\ \Delta \text{ Production cost} \\ \Delta \text{ Production scale} \\ \Delta \text{ Production vehicle} \\ \Delta \text{ Propagation} \\ \Delta \text{ Protein folding accuracy} \\ \Delta \text{ Protein homogeneity} \\ \Delta \text{ Protein yield} \\ \Delta \text{ Public perception of risk} \\ \Delta \text{ Safety} \\ \Delta \text{ Scale-up costs} \\ \Delta \text{ Therapeutic risk} \\ \Delta \text{ Time required} \\ \Delta \text{ Uncertainty} \end{array}]$$

The benefit of this approach is to help ultimately to understand the specific differences between production methods and consider how those differences contribute to the cost differences from biopharming.

3.3 Imperfect competition

The cost of developing a biopharmaceutical has been estimated at US\$1.2 billion (DiMasi, forthcoming). This amount pays for the technical development as well as moving the compound through successful clinical trials and securing regulatory approval for the compound. It is a fixed cost borne by the owner of the technology, a cost that must be recouped in order for a biopharmaceutical to be profitable. However, economic theory focuses

on the marginal cost of production as the main determinant of market price; fixed costs, particularly sunk costs, do not figure in calculations of marginal costs and thus price in a competitive market.

In order to allow the developer the opportunity to recoup these fixed costs, the government grants a temporary monopoly in the form of a patent. A monopoly reduces net social welfare by constraining supply of a product and raising its price. However, in the absence of an ability to raise the price of a biopharmaceutical above its marginal cost of production, the developer would not be able to recoup the development costs. If developers could not recoup these costs, they would cease to invest in developing new biopharmaceuticals. Thus, the granting of patents provides an incentive to invest in research and development that can be profitable over the medium term. Economists do discuss whether this institutional arrangement is better than alternative arrangements from the standpoint of social welfare.

To complicate the analysis of biopharmaceuticals, the situation in the industry is more like an oligopoly than a monopoly. In a monopoly, there is one supplier of the product. In an oligopoly, several firms sell products that are more or less similar. These firms may compete on price, quantity, or product qualities, depending on the specific model of oligopoly. Biopharming, as discussed above, is pursuing the production of existing pharmaceutical compounds but in a novel way. Thus, the product itself is potentially not unique. If it is not unique, then firms appear to be engaged in an oligopolistic competition based on price with potentially weakly differentiated products. The theoretical issue is complicated by the issue that the innovating firm has rights to a production technology that is potentially more efficient than its competitors. This issue suggests that competition could be price-based, but does raise the potential for excess profits as a result of the proprietary technology.

3.4 Demand for biopharming products

An important consideration is the impact of biopharming on the rest of New Zealand's agricultural and tourism industries. This depends on consumers in overseas markets. Some of the specific issues are: size of consumer segments; estimates of market size, given current purchases of agricultural products and consumer scepticism regarding biotech; and price impacts, again given current commodity prices, price trends, and consumer perceptions. Some specific questions relating to demand are listed below.

Markets for the commodity

- What are the intended markets for the commodity, by country and by market segment?
- What market share does NZ have, and how might this be affected?
- What are the trends in those markets, such as changes in tastes, income per capita, etc.?
- What is the elasticity of demand in those markets, that is, how sensitive are consumers to changes in price?
- What are NZ's competitors doing, and what impacts could they have?

The GMO/biotech issue

- How sensitive are the proposed markets to the issue of genetic modification?
- What proportion of the markets is particularly sensitive to the GM issue?
- Have any estimates been made of the likely discount facing GM products in the markets?

- Are ‘gatekeeper’ effects likely to exist? What is the level of concentration of food wholesalers, distributors and retailers in the market for the commodity?
- What are the requirements for labelling of GM products?
- What proportion of NZ’s exports are exposed to these labelling requirements?
- What costs will be incurred complying with labelling and other regulations?
- What are competitors doing regarding GM and biopharming?

3.5 Risk and uncertainty

Special consideration should be given to the idea of uncertainty. The uncertainty identified in the literature is technical, regulatory, and political. The *Constructive Conversations* project is specifically focused on regulatory aspects and potential impacts on the environment, health, and the economy. It is concerned with actual environments and practices that would be part of a biopharming system, especially with experiential knowledge regarding those environments and practices.

If the foregoing review has highlighted anything, it is that the economic impacts of commercial release of biotech products are uncertain and potentially very complex. The uncertainty and complexity make identifying risk evaluation criteria difficult. The following discussion should be seen in this light and should not be taken as exhaustive or predictive.

One way to think of risk is as the probability of an occurrence multiplied by its size or importance. This characterisation has been demonstrated to be incomplete, especially when discussing perceptions of risk (see, for example, Slovic, 2000). This incomplete formula is adopted here only as a starting point.

The second mental construct to consider is concentric circles (we are indebted to Tere Satterfield, Decision Research, for this observation). Each product, each crop, can be thought of as the centre of a set of concentric circles moving outward from related crops to the particular agricultural sector to wider categories up to the level of national effects.

In evaluating the risk posed by a particular application of genetic technology, it will be important to consider the probability of adverse reactions and the value of the sectors affected. Adverse reactions can come in different forms. For example, it may be that consumer reactions to a product are quite strong. On the other hand, the reaction might come from market gatekeepers, regardless of direct consumer reaction. Reactions in one market might be non-existent, but strong in another. The value of the sectors potentially affected is also hard to determine beforehand. A specific product is contained in many concentric circles, and although a biotech product may be intended for restricted use, it may be related or linked to products of much wider commercial importance.

There are some stylised facts to bear in mind:

- New Zealand’s largest export markets are: Australia, the US, the EU (ex. UK), Japan, and the UK.
- New Zealand’s largest exports are: Dairy, Meat, Wood, Fruit & Vegetables (combined), and Fish.
- Europeans are more sceptical than North Americans regarding GM.

- Cost-reducing GM products are much less valuable than consumer-oriented products.
- Consumers are sensitive to different types of genetic technologies, with food applications less acceptable than medical one, and transgenics less acceptable than other genetic technologies.
- The importance of New Zealand's image abroad is not well understood and needs more study.
- The sensitivity to consumers of cross-product GM 'contamination' is not well understood.

From these stylised facts a couple of observations can be made:

- Commercial release of a medically-oriented GMO that is unrelated to any of New Zealand's important exports, especially if it is not a transgenic organism, is potentially less risky.
- Commercial release of a food GMO, such as functional food, that will affect any of New Zealand's major products or markets (especially Europe) has a high probability of causing an adverse effect and can potentially affect large parts of the country's exports, so that it is overall probably more risky.

In addition, there is a body of research on risk perception that is outside the economic expertise at the AERU. Briefly, risks are perceptually evaluated not just on a 'probability times size' basis, but also on criteria such as control, dread, equity, certainty, voluntariness, etc. These perceptions of risk affect consumers and researchers alike.

One important concept from this literature is 'stigma'. It is possible for products to be stigmatised; producers and even countries can be similarly affected. One common example is the stigma that affected Johnson & Johnson as a result of the Tylenol poisonings. Another example is the possibility that Las Vegas tourism could be stigmatised by the siting of a nuclear waste storage facility in the same state, Nevada. Risk researchers have developed methods for assessing susceptibility to stigma and for considering its wider impact. Good resources for more information are Slovic (2000) and Flynn, Slovic, and Kunreuther (2001).

3.6 Conclusion

This chapter has quickly covered a wide range of economic theory. Biopharming products, whether functional foods, nutraceuticals, or biopharmaceuticals, will have both supply and demand effects. On the demand side, consumers will judge not only the biopharming product but also potentially a number of related products. On the supply side, it will be important to consider cost of production as well as industry structure. Finally, all of the available information represents a current approximation. All of the economic calculations are subject to the influences of risk and uncertainty.

Chapter 4

Analysis of Potential Impacts

4.1 Production through biopharming

The model set out earlier requires data to be estimated. The data that are available are not numbers, but descriptors. From the literature, the difference in cell culture and biopharming as method of production can be stated as follows:

= β_n [Cost/storage:	Expensive	→	Cheap
	Distribution:	Difficult	→	Easy
	Gene size:	Limited	→	Not limited
	Glycosylation:	Correct	→	Correct?
	Multimeric protein assembly:	No	→	Yes
	Production cost:	High	→	Low
	Production scale:	Limited	→	Worldwide
	Production vehicle:	0		
	Propagation:	Hard	→	Easy
	Protein folding accuracy:	High	→	High?
	Protein homogeneity:	Medium	→	High?
	Protein yield:	Medium-high	→	High
	Public perception of risk:	Medium	→	High
	Safety:	Medium	→	High
	Scale-up costs:	High	→	Low
	Therapeutic risk:	Yes	→	Unknown
	Time required:	High	→	Medium
	Uncertainty:	Current	→	Unknown].

The difference vector indicates that the biopharmed compounds are different to the cell culture compounds on nearly every dimension investigated. The differences fall into several categories. The first category is those dimensions that are cost-related and quantifiable, e.g., production cost and protein yield. Biopharming tends to outperform cell culture on most of these dimensions. Biopharming's success on these criteria appears to be driving the cost estimates that biopharmed compounds will be one-twentieth or less of the cost of current production techniques. The second category is those dimensions in which the results of biopharming are unknown. In the difference vector, these dimensions are those with a question mark (?) or labelled 'unknown', such as protein folding accuracy and protein homogeneity. A third category contains those dimensions whose values are known but qualitative. Because the differences are expressed qualitatively, there is insufficient information to generate an economic analysis. Thus, it is difficult to put on value on 'medium' safety versus 'high' safety. Finally, the risk profile of biopharming is, according to the difference vector, a potential concern. One risk dimension, public perception of risk, is worse for biopharming than for cell culture. The other risk dimension, therapeutic risk, is unknown.

The result of this model of biopharming, in which production is viewed as a bundle of dimensions with independent contributions to the cost of production, is that current information is insufficient. Some dimensions, particularly the quantitative cost dimension,

have received attention and are favourable for biopharming. Other dimensions are still largely qualitative and even unknown. Finally, there is insufficient information to determine the values of the betas, which indicate the contribution of each dimension to the final price of the compound. That is, the monetary impact of, for example, glycosylation versus worldwide distribution capacity is undetermined. As a result, the full cost of commercialised biopharmed therapeutic proteins, taking into account the technical differences, risks, and uncertainties, cannot be properly estimated from current data.

In addition, this model applies only to the biopharming product itself; it does not account for the concentric rings of influence into other industries. The theoretical model and other economic theory are applied below to two examples. One example is the production of lactoferrin in milk, and the other is low-GI (glycaemic index) potatoes.

4.2 Lactoferrin in milk

Lactoferrin is a protein produced by mammals and found in milk and even tears (www.pharming.com). It is a product that has considerable health benefits including positively affecting the immune system, proven ability to fight bacteria that cause eye and lung infections and limiting cancer growth in cells. There is still research being conducted on further benefits that could be provided by lactoferrin.

The world market for lactoferrin in 2004 was 90 metric tonnes per year and appears to be growing in global interest (AP-foodtechnology.com, 2004). The reported price for lactoferrin is at least US\$300 per kilogram, making the worldwide market valued at approximately US\$27 million per year. Fonterra reported that it is participating in the lactoferrin market with a new plant in Hautapu (Fonterra, 2005).

Presently, lactoferrin is extracted from cow's milk and added to food products, such as infant formula and yoghurt. Research has pursued producing a human version of lactoferrin in non-human organisms. The resulting product could be a functional food, nutraceutical, or biopharmaceutical, depending on how much the developing firm invests in following the regulatory process. Also, as a GMO product, it may require labelling.

Biopharming research has produced recombinant human lactoferrin (rhLF) in rice by Applied Phytologics and Ventria Bioscience. The company Agennix has announced that its microbial fermentation processes can produce lactoferrin too, and has production costs that were equal to the Ventria Bioscience biopharm rice (Wisner, 2005a). Meristem Therapeutics and Washington State University have also done research on lactoferrin production, but it is unclear as to the exact organisms used. Other research has produced rhLF in the milk of cows and mice (van Berkel et al., 2002).

Scientific research on rhLF provides information relating to some of the dimensions discussed above (Thomassen, van Venn, van Berket, Nuijens, & Abrahams, 2005; van Berkel et al., 2002). The protein structure appears similar to natural human lactoferrin (hLF) (Thomassen et al., 2005). The rhLF and hLF appear to be functionally similar, and to be safe in animal trials (van Berkel et al., 2002). The rhLF is also expressed at high concentration in cows' milk (van Berkel et al., 2002). This research thus seems to have determined that rhLF is physically similar to hLF, and that the protein yield may be commercially sufficient. Some dimensions for which information did not appear available and which are therefore continuing sources of uncertainty are: production cost, production scale, production vehicle, public perception of 'risk', scale up costs, time required.

A further issue with rhLF is that this scientific research has compared the human and recombinant human versions. From a business perspective, however, the comparison of bovine lactoferrin and rhLF is also germane. These two types of lactoferrin could be competing products in the marketplace. It is thus important to know whether the rhLF has any therapeutic benefits over the bovine version, and what the comparative costs of producing it are. One central question is the cost-benefit assessment of the two products. The information available is insufficient to make this assessment.

Furthermore, the rhLF has the further complication of the uncertainty surrounding consumer reactions to GM technology. If there are no adverse reactions, then the simple cost-benefit analysis suggested above would be sufficient to assess the business case. However, the research reviewed above indicates that there are adverse consumer reactions; the question thus becomes the extent and longevity of these reactions. Using the figures cited earlier regarding adverse reactions to GMOs (Sanderson et al., 2003) (27 per cent of Australians, 20 per cent of US citizens, and 30 per cent of Britons opposed to the use of GMOs) and figures on exports from 2002, the potential losses in these three markets from consumer rejection of New Zealand dairy products because of the introduction of a GMO into the dairy sector are NZ\$348.5 million per year. This figure does not include any price discounts that other consumers might demand, markets other than those three countries, or exports other than dairy products.

A similar calculation can be made of impacts on tourism. The same research found that nine per cent of Australians, five per cent of US citizens, and six per cent of Britons would stop visiting New Zealand if a GMO were introduced into the environment. Using tourism spending figures for these countries from the New Zealand Tourism Board, the potential losses in tourism amount to NZ\$191.1 million per year.

This analysis suggests several things. First, all the necessary business information to assess the economic potential of producing recombinant human lactoferrin in milk in New Zealand is not available. Any assessment at this stage is necessarily preliminary. Secondly, it will be difficult to earn more than an economically normal profit by developing and marketing rhLF. There seem to be several close substitutes and competing technologies, so there appears to be little opportunity to create a dominant position in the market and earn oligopoly or monopoly profits. Finally, social science research suggests that introducing a GMO into the New Zealand dairy sector has a potential to cause a minimum of NZ\$539.6 million in losses to the dairy and tourism industries. Thus, such a biopharming endeavour would need to offset those losses before it could be viewed as a net positive for the New Zealand economy. Given that sales of lactoferrin are currently in the tens of millions of US dollars, offsetting hundreds of millions of NZ dollars of lost exports seems unlikely in the short to medium term.

4.3 Low-GI potatoes

The glycaemic index (GI) measures the amount and speed at which different food types raise blood sugar levels. Foods with high GI ratings raise blood sugar levels quickly, making them potentially unsuitable for people with diabetes. Concern about GI ratings has also spilled out into the general public. The Human Nutrition Unit at the University of Sydney noted that 'the World Health Organisation (WHO) and Food and Agriculture Organisation (FAO) recommended that people in industrialised countries base their diets on low-GI foods in order to prevent the most common diseases of affluence, such as coronary heart disease, diabetes and obesity' (Glycemic Index Research, 2006). Links have also been drawn between low-GI diets and low-carbohydrate diets, such as the Atkins diet.

The value of the market for such foods with perceived health values is difficult to state. Euromonitor estimated the 2005 total world values of sales of naturally healthy, high-fibre foods at US\$25 billion (Euromonitor, 2006). Other research found estimated sales of functional and fortified foods in the United States in 2006 at US\$35.86 billion (Sloan, 2006). Low-GI foods are a growing sector of the functional foods market (Sloan, 2006).

The GI rates foods on a scale from 0 to 100, with higher ratings indicating that foods have greater impacts on blood sugar levels (Glycemic Index Research, 2006). Potatoes can have a range of GI ratings, depending on the source of the potato and preparation methods; some data from the University of Sydney on potato GI results are presented in Table 4. However, potatoes are not a processed food whose ingredients can be modified to lower the GI. Thus, a lower GI must result from modifying the potato itself.

A low-GI potato could replace some current potatoes and potato products. Low-GI potatoes, which might be produced through GM technology, would be a functional food rather than a biopharmaceutical or nutraceutical product. It could appeal to consumers who are currently wary of standard potatoes. It could also keep consumers eating potato products even as they become more concerned about GI. Impacts are thus defensive (preventing erosion of market share) and expansionary.

The current world market for potatoes is \$40 billion (FAO, 2006); New Zealand produces 500,000 tonnes of potatoes and has export sales of \$69.3 million in fresh and frozen potatoes for 2005 (HortResearch, 2005).

New Zealand also has scientific expertise in the area of potato research (Collins, 2003), so that the low-GI potato could be developed here. There are existing examples of proprietary control of a Plant Variety Rights that can provide suggestion for how such a new potato could be developed and marketed. One example is the Gold kiwifruit developed by HortResearch and controlled by ZESPRI. The growing of this cultivar has been tightly controlled in order to maintain good fruit quality and good prices for growers. The cultivar has also been planted in both Northern and Southern hemispheres to produce a year-round supply. As a result, Zespri has been able to deal with cultivation and quality issues and earn profits from proprietary control of the cultivar. A second example is the Jazz apple, a proprietary cross of Royal Gala and Braeburn. Commercial development of the cultivar is controlled by ENZA. The organisation has contracted growers in both hemispheres to produce Jazz, which enables year-round supply but also keeps profits from the cultivars flowing to New Zealand. The new variety is expected to yield an internal rate of return on the investment in research and development of 13 per cent by 2009, yielding a net present value of \$2.8 million (Growing Futures, 2005).

The model developed above for assessing biopharming provides useful information on low-GI potatoes. A number of the dimensions in the model concerned the specific proteins to be extracted from biopharmed crops. Because low-GI potatoes would be a functional food, many of these dimensions are moot. The issues surrounding this product are thus simpler. Some of the dimensions that would require assessment as the product is developed and marketed are cost/storage, distribution networks, production cost, production scale, propagation, public perception of risk, safety, time required, and uncertainty.

Table 4: GI Results for potatoes

Specific potato tested	GI	Serving size (grams)
Potato, Ontario, white, baked in skin (Canada)	60	150
Potato, Russet Burbank, baked without fat (Canada)	56	150
Potato, Russet Burbank, baked without fat, 45-60 min (USA)	78	150
Potato, Russet Burbank, baked without fat (USA)	94	200
Potato, Russet Burbank, baked without fat (USA)	111	150
Potato, Desiree, peeled, boiled 35 min (Australia)	101	150
Potato, Nadine, boiled (New Zealand)	70	150
Potato, Ontario, white, peeled, cut into cubes, boiled in salted water 15 min (Canada)	58	150
Potato, Pontiac, peeled, boiled whole for 30 min (Australia)	56	150
Potato, Pontiac, peeled, boiled 35 min (Australia)	88	150
Potato, Prince Edward Island, peeled, cubed, boiled in salted water 15 min (Canada)	63	150
Potato, Sebago, peeled, boiled 35 min (Australia)	87	150
Potato, unspecified type (Kenya, Africa)	24	150
Potato, white, cooked (Romania)	41	150
Potato, white, boiled (Canada)	54	150
Potato, boiled (Australia)	56	150
Potato, boiled in salted water (India)	76	150

Source: GI Database (2007)

Overall, the total economic potential of low-GI potatoes is uncertain at present. The product could have clear consumer appeal in the functional foods market, a multibillion dollar and expanding market segment (Sloan, 2006). As a functional food, it would have lower regulatory hurdles than a biopharmaceutical. Furthermore, potatoes are a commonly consumed food, and the total market is again a multi-billion dollar market. A final positive factor is that New Zealand has scientific expertise in the area and business experience in creating profits from Plant Variety Rights.

There are potentially difficulties, however. The GM status of the product could create problems in some markets, in terms of both meeting food safety and regulatory requirements and responding to consumer concerns. As with the earlier example of producing rhLF in milk, there is the risk of losing at least NZ\$191.1 million in annual tourism earnings. There would also be a risk of losing some export earnings from potato exports (total exports, NZ\$69.3 million). Whether earnings from other horticulture products or other agricultural exports would be affected is unknown. Other difficulties arise from the risks and uncertainties that exist for biopharming products. Finally, it is unknown at this point what competing products would be developed, either other types of low-GI potatoes, other low-GI foods, and even other dietary trends.

Chapter 5

Conclusion

This report has presented preliminary research into the economics of biopharming. The research has covered a wide range of economic theory and sources of data. The main reason to cover so much ground is that definitive information on the economics of biopharming is scant. Thus, this research has looked to economic theories of supply and demand, consumer behaviour, and industry structure; assessments of the impacts of prior biotechnologies; and the information that is available on biopharming. All of these elements together underpin the present assessment of biopharming.

This report has organised its assessment around a model or framework derived from the literature on biopharming. The potential impacts of biopharming are a function of the benefits and costs from changing from one type of production system to another, coupled with product advantages that the new system might afford. Clearly, there are a number of dimensions on which production systems differ. The impact of biopharming in its broad sense, including biopharmaceuticals, nutraceuticals, and functional foods, depends on how each of these dimensions changes and how those dimensions contribute to the value of the products.

This report has also considered two specific products: lactoferrin in milk and low-GI potatoes. The main result from this examination is that the necessary information to develop a robust economic analysis of these products is lacking. Much of the information on the relevant dimensions is simply unknown. A second result from this work is that the potential value of these products varies tremendously, depending on the overall size of the potential market, control of technology or proprietary information, and other factors. A third concern is adverse reactions in overseas markets. The future impact of consumer concerns is uncertain and contested. Nevertheless, since available information on adverse reactions suggests that the economic impact could be large compared to earnings from novel products, it is important to understand these potential reactions.

This has been a preliminary piece of research. As more information becomes available on the potential products, the economics of their production, and consumer demand for them, this area of research will be able to improve the estimates of the economic impacts of biopharming in New Zealand.

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Appendix

Table A1: Transgenic plant biopharming companies and products

Company	Plant	Drug	Comments
Agracetus	Corn		
Agragen	Pharma flax	Medicines for trauma patients who need a blood transfusion.	
AltaGen	Potato	Hemoglobin.	
Applied Phytologics	Rice	Factor VIII; human growth hormone. Human -1- antitrypsin Dirgent protein - origin: Forsythia intermedia. Laccase - origin: Forsythia intermedia. Lactoferrin - origin: human. Lysozyme - origin: human. Pinoresinol-lariciresinol reductase - origin: Forsythia intermedia. Secoisolariciresinol dehydrogenase NptII*. Hygromycin phosphotransferase* - origin: E. coli. Antithrombin - origin: human. Aminoglycoside 3'-adenylyltransferase - origin: human. Serum albumin - origin: human.	Human -1- antitrypsin is a protein of therapeutic potential in cystic fibrosis, liver disease and hemorrhages.
Biolex	Duckweed	α -interferon and other proteins.	Investigational new drug (IND) filing this year.
Biolex Inc	Lemna (duckweed)		Locteron (controlled-release α -interferon for hepatitis B and C), completed Phase 1; fibrinolytic clot buster, preclinical.
Biosource	Tobacco mosaic virus Tobacco etch virus	Phytoene synthase - origin: tomato. Trichosanthin - origin: Trichosanthes kirilowii. Alpha-amylase - origin: rice. Alpha-hemoglobin - origin: rice. Beta-hemoglobin - origin: human. Trichosanthin - origin: Trichosanthes kirilowii.	

Company	Plant	Drug	Comments
Biosource Technologies and Stanford University	Plant virus based transient expression system		Developed a technology to produce a tumor specific vaccine for the treatment of malignancies. Biosource Technologies is now named the Large Scale Biology Corporation.
Boyce Thompson Chlorogen, Inc	Potatoes Tobacco chloroplasts	Hepatitis B. Cholera vaccine. Human serum albumin. Interferon (hepatitis C). TGF- β for treatment of ovarian cancer. Animal vaccines.	
Cobento	Arabidopsis Thaliana	Human intrinsic factor (rhIF for diagnostics), in market rhIF plus vitamin B12 for B12 deficiency, in clinical trails.	
Cornell University Crop Tech	Potato Tobacco	Edible vaccine for Hepatitis B. Confidential business info; origin: human. NptII*.	Filed for bankruptcy in 2003.
CropTech Corp and Prodigene- Cramer Dow (Dow Plant Pharmaceuticals) (DowPharma)	Maize Corn A plant-based vaccine Beans of castor plants	Avidin. β -glucuronidase. Phosphinothricin acetyl transferase*. Confidential business information - origin: human. To protect poultry from Newcastle disease virus (NDV). RiVax.	Mechanical gene activation (MeGA) system that was developed. First commercial molecular-farming venture. Was approved by the USDA-APHIS' Center for Veterinary Biologics in 2006. Dow offers contract development and manufacturing of proteins in transgenic plants. RiVax was developed to protect against exposure to ricin toxin.
Dow AgroSciences	Maize Non-nicotine tobacco plant cell culture	Newcastle disease vaccine for poultry.	Described an adenosine deaminase selection system. Approved by USDA 2/2006.

Company	Plant	Drug	Comments
Emlay and Associates	Safflower	Growth hormone* - origin: carp. Oleosin* - origin: Arabidopsis thaliana.	
EpiCyte	Corn Maize/rice Transgenic soybean Chinese hamster ovary (CHO) cells	Phosphinothricin acetyl transferase. Monoclonal antibodies (plantibodies). EPI19 (bronchionliotis/pneumonia in infants)..	A full-length humanized IgG1 that recognizes herpes simplex virus (HSV)-2 glycoprotein B has been expressed in. This antibody, along with an IgG that recognizes the R9 protein of respiratory syncytial virus.
EPIcyte pharmaceuticals and ProdiGene	Plants	Antibodies.	
Farmacule BioIndustries	Tabacco Sugarcane	Virtonectin.	Available in late 2006-early 2007; proteases.
Garst	Corn	Acetolactate synthase*, confidential business information - origin: human and mouse.	
Greenovation Biotech	Moss	Humanization of glycosylation.	Homologous recombination in moss allows for easier engineering of strains.
Greenovation Inc., Freiburg	The moss Physcomitrella		
Guardian Biotechnologies	Canola Oriental Melon	Poultry vaccine for coccidiosis.	Phase 2.
Hawaii Agriculture Research Center	Sugarcane	Confidential business info; origin: human.	
Horan Bros. Agri. Enterprises	Corn	NptII*.	
Iowa State University	Corn	NptII*. Enterotoxin subunit B - origin: E. coli.	

Company	Plant	Drug	Comments
Large Scale Biology Corp	Tobacco mosaic virus		
	Tobacco	Non-Hodgkin lymphoma vaccine Alpha galactosidase.	Completed phase 1. For Fabry disease in clinical trails.
	Tobacco	B-Cell non-Hodgkin's lymphoma (Phase III). Alpha-galactosidase A (therapy for Fabry's disease). Patient-specific cancer vaccines. Hepatitis B surface antigen, scFvs and other recombinant proteins.	The antibodies were produced using virus-infected plants rather than transgenic plants, which is a strategy that is well suited to the rapid and small-scale production that is required to treat individual patients with unique antibodies. Has completed phase I trials.
Limagrain	Corn	Phosphinothricin acetyl transferase*. Procollagen - origin : human. G glycoprotein Serum albumin - origin: human. Alpha-hemoglobin - origin: human. Beta-hemoglobin - origin: human.	
Medicago Meristem Therapeutics	Alfalfa Corn Tobacco Maize Alfalfa	Hemoglobin Gastric lipase Hemoglobin;gastric lipase (cystic fibrosis, pancreatitis; Phase II). Albumin (surgery). Cancer therapeutic antibodies. Meripase (cystic fibrosis and lipid-storage disorders). Lactoferrin (gastrointestinal disorders).	To treat pancreatic insufficiency associated with cystic fibrosis in phase 2a. Meripase is in field trials and testing. Lactoferrin is in phase 1.
Monsanto	Soybean Corn	IgG anti-herpes simplex virus. C transcriptional activator.	
MPB Cologne GmbH	Potato Rapeseed	Antibody.	For detection of food/water borne pathogens.

Company	Plant	Drug	Comments
Nexgen Biotechnologies	Potato Cucumber Oriental Melo Tobacco	Thyroid-stimulating hormone receptor. Hemorrhagic fever virus antigens for diagnosis. Poultry vaccine for avian influenza (H5N1), epidermal growth factor, albumin fusion protein.	Thyroid-stimulating hormone receptor (diagnosis of Graves disease), projected marketed in 2006.
Noble Foundation	Alfalfa	NptII*. Cholera toxin B - origin: <i>Vibrio cholera</i> .	
Phytomedics	Tobacco		Manufacturing process secretes biologics from roots. Current product focus on plant extracts.
Pioneer	Rapeseed	Phosphinothricin acetyl transferase* - origin: <i>Strep. hygrosopicus</i> .	
Planet Biotechnology	Tobacco	CaroRx. RhinoRx. Antibodies- SIgA anti- <i>S. mutans</i> . Anti- <i>Streptococcus mutans</i> secretory IgA (SIgA) plantibody. <i>Streptococcus mutans</i> specific Guy's-13 antibody, which prevents dental caries.	CaroRx, proteins for tooth decay, in phase 2. RhinoRx, for common cold, in preclinical testing. Anti- <i>Streptococcus mutans</i> secretory IgA (SIgA) plantibody currently in phase II clinical trials for the prevention of dental caries. The first clinical trial of plant-based immunotherapy was by this company. This company has compared the cost per gram of purified IgA made by cell culture, transgenic goats, grain (7.5 tonne ha ⁻¹) and green biomass (120.0 tonne ha ⁻¹). Expression levels will have a significant impact on the costs but, at the best expression level reported [500 µg g ⁻¹ leaf for a secretory IgA, the final cost should be well below US\$50 g ⁻¹ . This significantly undercuts the costs of cell culture (US\$1000 g ⁻¹) or transgenic animal production systems (US\$100 g ⁻¹). The biggest component of cost with plantibodies will be purification.
Protalix	Plant cell culture	Glucocerebrosidase. Fully humanized IgG.	Glucocerebrosidase for Gaucher disease is in Phase 1. Fully humanized IgG is in preclinical development.

Company	Plant	Drug	Comments
ProdiGene	Corn Maize	Antibody for Traveler's diarrhea Trypsin. laccase. Subunit vaccines, recombinant antibodies and further technical enzymes, such as aprotinin and laccase. Recombinant bioactive avidin and β -glucuronidase.	Antibody for Traveler's diarrhoea completed phase 1. Trypsin which is produced using bovine DNA, is being marketed by Sigma Aldrich under the trademark name of TrypZean. Laccase which acts on lignine and could have applications in paper and textile production. This company demonstrated that feeding pigs an edible maize vaccine protects them from the transmissible gastroenteritis virus (TGEV). This company is an industry leader in cereal-based commercial protein. Recombinant bioactive avidin and β -glucuronidase are the first recombinant plant-derived proteins to be produced commercially made by Prodigene Inc and sold by Sigma Chemical company.
	Corn	Phosphinothricin acetyl transferase*. Aprotinin - origin: pig. Surface antigen - origin: Hepatitis virus B. Surface antigen - origin: transmissible gastroenteritis virus. gp120 (glycoprotein 120) - origin: simian immunodeficiency virus. Enterotoxin subunit B - origin: E. coli. NptII*. Phosphinothricin acetyl transferase*. Aprotinin - origin: Bos taurus. Enterotoxin subunit B - origin: E. coli. Surface antigen - origin: Hepatitis virus B.	
ProdiGene and EPIcyte Pharmaceuticals (strategic partnership)	Tomato Corn	NptII*. antibodies.	
RJ Reynolds	Tobacco mosaic virus		

Company	Plant	Drug	Comments
SemBioSys	Safflower	Antiobesity peptid; somatotropein Insulin. Apoplipoprotein A-1. Immunospheres.	Safflower is now being grown on a trial basis in Chile, US & Canada (Levinson, 2007).
Spanz	Transgenic oilseed Canola, (Brassica napus)	Human insulin and apolipoprotein in preclinical development. Hirudin.	The oleosin-fusion platform developed, in which the target recombinant protein is expressed in oilseed rape or safflower as a fusion with oleosin.
	Potatoes	Make proteins that will help the body repair itself after heart or circulatory system surgery or nervous diseases.	Spanz (Singapore and NZ) Biotech the 50-50 “biopharming” venture. Have since ceased operations.
U of Kentucky	Tobacco	Confidential business info; origin: human and mouse.	
UniCrop	Oilseed technology platform		The idea is to isolate recombinant proteins from the rapidly developing sprouts cultivated in bioreactors.
Ventria Bioscience	Rice	Product for iron deficiency and acute pediatric diarrhea in safety testing. Targeting Lactoferrin and lysozyme. Glucocerebrosidase production.	Have been conducting field trials, growing GM rice as a means for producing food additives with medical uses.
Virginia Tech and State University and CropTech; Cramer and colleagues.	Transgenic tobacco		Their studies ‘strongly support’ the future commercial viability of transgenic plants for the production of glucocerebrosidase, and of other lysosomal enzymes, for enzyme replacement therapy.
Washington State University	Barley	Green fluorescent protein*. Phosphinothricin acetyl transferase*. Amylase - origin: barley. Antithrombin - origin: human. Antitrypsin - origin: human. Lactoferrin - origin: human. Lysozyme - origin: human. Serum albumin - origin: human.	

Sources: (Cline, 2006; Collins, 2003; Colorado State University, n.d.; Daniell et al., 2001; DOR BioPharma Inc, 2006; Drabenstott, 2002; Elbehri, 2005; Fischer & Emans, 2000; Fischer, Stoger, Schillberg, Christou, & Twyman, 2004; Fox, 2006; GianCarlo, 2006; Giddings, Allison, Brooks, & Carter, 2000; Keefer, 2004; Larrick & Thomas, 2001; Leake, 2006; Leske, 2006; Levinson, 2007; Ma, Drake, & Christou, 2003; Schoebi, 2005; Tae-Gyu, 2006; Thiel, 2004; Wisner, 2005).

Table A2: Transgenic animal biopharming companies and products

Company	Animal	Drug	Comments
Avian Initiative	Transgenic chicken eggs	Recombinant proteins.	Avian Initiative is a collaboration between Viragen and the Roslin Institute.
AviGenics	Chicken eggs	Recombinant proteins.	
BioProtein Technologies	Transgenic rabbits	Recombinant proteins.	
Ecoarray	Transgenic fish	Recombinant human Factor VII	Ecoarray was formerly AquaGene.
Genzyme Transgenics	Goat herds	Tumor necrosis inhibitory monoclonal antibody, Remicade.	Remicade is marketed by Centocor for the treatment of inflammatory conditions, including Crohn's disease and rheumatoid arthritis. General growth hormone.
Genzyme Transgenics and Genzyme	Goats milk	Antithrombin III.	The protein is currently in phase III clinical trials to prevent blood clotting during cardiac surgery in heparin-resistant patients.
GTC Biotherapeutics, Inc	Transgenic goats	ATryn (antithrombin III) Monoclonal antibodies. Malaria vaccine.	European Medicines Agency (EMA) decided to recommend approval of ATryn for people with a rare inherited disease that leads to blood clotting.
	Cattle	Human serum albumin.	
	Milk of transgenic goats	MM-093. ATryn.	For people suffering from autoimmune disorders, such as rheumatoid arthritis, psoriasis or multiple sclerosis. The pioneering drug, an anti-clotting agent for people with a rare inherited disease that was developed to treat patients with hereditary antithrombin deficiency (HAD), which makes people vulnerable to deep-vein thrombosis.
Gyeongsang National University. Professor Kim Jin-hoi and a team of researchers.	Genetically engineered mice	Erythropoietin, the growth factor in blood.	

Company	Animal	Drug	Comments
Hematech	Cattle	Human polyclonal antibodies (vaccines).	Cattle that have, in addition to their own genome, an extra artificial minichromosome that contains genes for human immunoglobulins. Hermatech plans to use this technique to produce polyclonal human antibodies against a number of antigens, including anthrax.
Infigen Inc		Protein production.	
Nexia Biotechnologies	Transgenic goats	Protexia (human butyrylcholinesterase) Spider silk protein.	Protexia in preclinical development as a potential protectant against nerve gas.
Origen Therapeutics	Chicken eggs	Human poly- and monoclonal antibodies for therapeutic purposes.	
Pharming	Transgenic rabbits	Recombinant human C1 inhibitor.	For hereditary angiodema. In phase 3 trials.
	Cows	Rabbit-derived	RhC1INH.
			A potential treatment for angioedema, has received a fast track designation for review by the U.S. Food and Drug Administration. The Pharming drug candidate, rhC1INH, is a treatment for hereditary angioedema, which causes painful and potentially life-threatening swelling of the body's soft tissues. (Pharming produces therapeutic proteins in the milk of genetically modified animals and a fast track status provides an expedited review process for products used for life-threatening diseases with limited treatment options.)
	Transgenic animals	Rhucin.	Is intended to treat hereditary angioedema, a disease characterised by the painful, and sometimes fatal, swelling of soft tissues.
Pharming Group and Baxter Healthcare Corporation	Rabbit-milk	Derived recombinant human C1 inhibitor.	To treat patients with hereditary angioedema who exhibit C1 inhibitor deficiency.

Company	Animal	Drug	Comments
Pharming Group and Genzyme	Rabbits milk	Human α -glucosidase to treat infants with Pompe's disease, which results from a genetic deficiency in this enzyme.	Enzyme produced in rabbits milk was well-tolerated and showed clinical benefit in treated patients.
PPL Therapeutics	Sheep	Alpha-1 antitrypsin.	
	Rabbits	Lipase.	
TranXenoGen	Chicken eggs	Human proteins.	Company is essentially in liquidation, seeking to out-license patents and other assets.
UC Davis	Genetically engineered goats to produce an antibacterial milk	Lysozyme.	Could eventually protect children from diarrheal diseases. Lysozyme is an important antibacterial enzyme in human breast milk that is substantially lacking in the milk of diary animals.
US Transgenics	Plasma products		Now defunct.
Virage	Chickens	Recombinant proteins.	
Vivalis	Chickens	Recombinant proteins.	

Sources: (Cline, 2006; Collins, 2003; Colorado State University, n.d.; Daniell et al., 2001; DOR BioPharma Inc, 2006; Elbehri, 2005; Fischer & Emans, 2000; Fischer et al., 2004; Fox, 2006; GianCarlo, 2006; Giddings et al., 2000; Keefer, 2004; Larrick & Thomas, 2001; Leake, 2006; Leske, 2006; Ma et al., 2003; Schoebi, 2005; Tae-Gyu, 2006; Thiel, 2004; Wisner, 2005)

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