


# Biopharming in New Zealand: Risk and Governance Implications

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## Abbreviations

| | |
|---|---|
| AMA | Aquaculture Management Areas |
| BSE | Bovine spongioform encephalopathy |
| CRI | Crown Research Institute |
| DNA | Deoxyribonucleic acid |
| ERMA | Environmental Risk Management Authority |
| FDA | U.S. Food and Drug Administration |
| FRST | Foundation for Research, Science and Technology |
| FSANZ | Food Standards Australia and New Zealand |
| GM | Genetic modification / genetically modified |
| HGT | Horizontal gene transfer |
| IAO | Iwi Aquaculture Organisation |
| IPM | Integrated pest management |
| IVF | In vitro fertilisation |
| MAF | Ministry of Agriculture and Forestry |
| MoRST | Ministry of Research, Science and Technology |
| OTS | Office of Treaty Settlements |
| QA | Quality assurance |
| rhLF | Recombinant human lactoferrin |
| RMA | Resource Management Act |
| SCID | Seed Crop Isolation Distances |
| TOKM | Te Ohu Kai Moana Trustee Ltd |
| TRONT | Te Runanga o Ngai Tahu |
| TSE | Transmissible Spongioform Encephalopathies |
| vCJD | Variant Creutzfeldt-Jakob disease |

# Executive Summary

This report is not intended as a comprehensive review of biopharming *per se*. Rather it emphasises those aspects addressed by the Constructive Conversations / Kōrero Whakaaetanga approach, and it specifically addresses the implications of biopharming in and for New Zealand contexts.

The Constructive Conversations / Kōrero Whakaaetanga research on biopharming addressed what we see as three common deficiencies in the process of assessing technologies. First, the projected benefits of developing or applying a technology are rarely given the same scrutiny as its potential harms. Second, there is insufficient recognition of the importance of context to evaluating the implications of developing and deploying a technology. Third, insufficient attention is paid to the kind of detailed knowledge of context necessary to evaluate this interaction. This knowledge is often more experiential than formalised.

The Constructive Conversations / Kōrero Whakaaetanga approach thus involved identifying those with experiential expertise in relevant contexts and eliciting relevant knowledge from them. People who are unfamiliar with the technology in question may nonetheless have knowledge of context that is highly relevant to assessing that technology. Such people are rarely part of formal risk assessment processes. The Constructive Conversations / Kōrero Whakaaetanga approach also involves conversations among those with diverse formal expertise. Pathways to harm or benefits are often "hybrid" in nature; that is, they entail interactions of biophysical and social events.

Those who see biopharming as beneficial for New Zealand have emphasised returns to farmers, the composition of exports, and a related transformation of the New Zealand economy. These benefits depend on the commercial success of biopharming as a drug-production process, which in turn hinges on whether it will significantly lower the costs of drug production. Unresolved issues in relation to cost include: difficulty of comparison, purification costs, costs of negotiating the "patent thicket", developments in competing platforms, and regulatory issues, particularly regarding biosimilars.

Whether or not farmers will benefit from biopharming depends on a number of factors, including ownership and management arrangements and relative market power. With regard to animal biopharming, our research suggests that the most likely arrangement would be a self-contained commercial research enterprise producing the transgenic animals, farming them, and extracting the product. It is likely that such an enterprise would require some degree of foreign ownership and unlikely that it would offer significant benefits to New Zealand farmers. With regard to plant biopharming, the most likely arrangement may be local seed producers contracting with a multinational biotechnology company. Because the market power of the contracting biotechnology or pharmaceutical companies is much greater than that of the potential biopharm-crop growers, benefits to growers are likely to be limited. We have not identified a likely scenario for biopharming in aquaculture because practitioners were almost unanimously

of the opinion that containment was impossible and contamination would seriously threaten their industry.

Other issues impacting on potential returns to New Zealand include: involvement of low-cost competitors in biopharming, use of New Zealand-sourced animals in overseas biopharming enterprises, the current expectations regarding CRI commercialisation of products, and the challenges of establishing the necessary commercial partnerships.

Biopharmed drugs avoid some risks of human-derived drugs but entail other risks. These are related to infection, allergenic responses, immunogenic responses, and autoimmune reactions. Risk issues include viral pathogens and prions, unanticipated changes resulting from transgenesis, and impacts of differences in glycosylation processes.

Unlike other forms of drug production, biopharming poses the risk of contamination of the food supply chain. The potential pathways to food contamination are many and complex, including both biophysical and social components. We review pathways for plant and animal biopharming, in connection with impacts on human, animal and ecosystem health. We also review the potential for economic harm, including damage to trade and tourism, additional costs to non-biopharm producers, and opportunity costs.

The risk of social and cultural harms is difficult to assess. Social and cultural impacts extend beyond economic returns or employment opportunities to include such things as ability to engage in a valued way of life, community relations, the distribution of harms and benefits, and the socio-cultural implications of the intensified instrumentalisation of life forms. Exploring such harms was not the primary focus of much of our research; however, socio-cultural issues emerged strongly within the research on Māori assessments of biopharming in aquaculture. Key issues included: the wider social and cultural implications of damage to ecosystems, the impacts on cultural practices around mana moana and kaimoana, and implications of this for self-determination.

Our research findings have implications for various groups in the governance arena. With regard to ERMA, our research raises questions about whether it is practical to assume that mandated controls will be consistently implemented. Relevant elements of context include: economic (dis)incentives, attitudes of practitioners toward risk, labour conditions, and the unavoidability of human error.

Our research on Māori assessments of biopharming in aquaculture, which led to wider discussion of Māori involvement in aquaculture more generally, has raised a number of issues regarding iwi governance as well as national legislation and policy. Despite policies and legislation that promote Māori involvement in the aquaculture industry, it is questionable whether hāpū and iwi are able to participate in ways that fulfill their cultural, environmental, and development aspirations. The legislative parameters that iwi operate within, the relationships between iwi and hāpū, and the lived realities of whānau make Māori involvement in aquaculture development and biopharming fraught. Of particular concern is the potential use of biotechnologies to advance aquaculture development and the impact (both positive and negative) that such technology may have

on hāpū and iwi rights as mana whenua/mana moana to practice and fulfill kaitiakitanga obligations.

Biopharming is also of significance for private governance systems, including quality assurance regimes such as GLOBAL-GAP, which are important regulators of New Zealand producers' access to premium markets. Biopharmed products have the potential to raise three issues around the emerging necessity to preserve market access for exporters: biopharmed products themselves will be required to meet strict standards of safety and risk management in order to achieve market access; non-biopharmed products produced by the same company will face increased scrutiny and risk, and will have to maintain strict protocols of containment; and most significantly, other companies exporting products will have to implement measures to ensure that there is no cross-contamination of products in the same ecosystem. If introduced into the arable sector, biopharming would require reform of the current SCID system. In its current voluntary, self-regulatory form, the SCID system cannot be relied upon to provide the kind of high-quality information that would be needed in order to assess the contamination potential of a biopharm crop in any particular location.

Biopharming raises issues in connection with the Resource Management Act. It is essential that reforms of the RMA not undermine the ability to harness local knowledge when assessing risks of biopharming operations. Further, it is important that the question of whether or not the RMA would protect residents from any potential negative impacts of a neighbouring biopharm facility be publicly clarified.

# 1. Introduction

The Constructive Conversations / Kōrero Whakaaetanga research on biopharming addressed what we see as three common deficiencies in the process of assessing technologies.

First, the projected benefits of developing or applying a technology are rarely given the same scrutiny as its potential harms. Projected benefits are a key element in funding agencies' decisions to fund the technology's development, and they are weighed against risks in regulatory agencies' decisions to permit the deployment of a technology. Insufficient scrutiny of benefit claims can thus lead to poor investment and regulatory decisions.

Second, there is insufficient recognition of the importance of context to evaluating the implications of developing and deploying a technology. This includes not only the biophysical context, but also the social context. Technologies never operate outside a biophysical and social context, and their effects cannot be understood independently of that context. In order to evaluate the potential harms and benefits of a technology, we must know how it is likely to interact with its context.

This leads us to the third deficiency, which is that insufficient attention is paid to the kind of detailed knowledge of context necessary to evaluate this interaction. This knowledge is often more experiential than formalised. The Constructive Conversations/Kōrero Whakaaetanga approach thus involved identifying those with experiential expertise in relevant contexts and eliciting relevant knowledge from them. People who are unfamiliar with the technology in question may nonetheless have knowledge of context that is highly relevant to assessing that technology. Such people are typically not involved in formal risk assessment processes.

The Constructive Conversations / Kōrero Whakaaetanga approach also involves conversations among those with diverse formal expertise. Pathways to harm or benefits are often "hybrid" in nature; that is, they entail interactions of biophysical and social events. Our intention in bringing the biophysical and social researchers into conversation with each other was to enable us to construct a more realistic understanding of the possible effects of biopharming in New Zealand contexts.

This report is not intended as a comprehensive review of biopharming *per se*. Rather it emphasises those aspects addressed by the Constructive Conversations/Kōrero Whakaaetanga approach, and it specifically addresses the implications of biopharming in and for New Zealand contexts. In Chapter 2, we present and scrutinise the benefits claimed for biopharming in New Zealand. In Chapter 3, we present the potential harms of biopharming in New Zealand contexts, utilising both experiential knowledge of contexts and the contribution of formal expertise in biophysical and social sciences. In Chapter 4, we address the implications of our research for public and private regulation.

Previous reports in this series have looked in greater depth at biopharming in relation to particular *sectors*, including dairy (Goven et al. 2008), aquaculture (Campbell et al. 2008; Cram et al. 2008; Phillips 2008), and arable farming (Morris et al. 2009); *domains*, including economy and trade (Kaye-Blake et al. 2007; Kaye-Blake et al. 2008) and biosafety (Heinemann 2008); and *governance* issues (Cram et al. 2008, Phillips 2008). For access to these reports, please refer to www.conversations.canterbury.ac.nz.

# 2. Potential benefits and their uncertainties

In this chapter, we focus on the benefits that have been claimed for the relevant technologies by their New Zealand proponents. For a more comprehensive discussion of benefits claimed for biopharming, please see Goven et al. (2008), Kaye-Blake et al. (2007; 2008), and Morris et al. (2009). Benefits claimed in a New Zealand context fall into two main categories: economic benefits and benefits to human health.

## 2.1. Economic benefits

### 2.1.1. Projected benefits

The discussion of the benefits of biopharming for New Zealand has emphasised returns to farmers, the composition of exports, and a related transformation of the New Zealand economy. A 2000 article promoting biopharming in the official publication of the Government's trade promotion agency (Trade NZ) argued that biopharming would benefit farmers directly and would increase export returns by producing goods that are both more valuable and less likely to encounter trade barriers.

> The key benefit of bio-pharming is that the financial returns to growers and farmers are many times higher than those in conventional farming… Bio-pharming is also of interest because the high value pharmaceutical products produced will escape the current food-based quotas that many of our exports are penalised or prohibited under, further expanding marketing possibilities (Powell 2001: 15).

A Foundation for Research, Science and Technology (FRST) 2001 case study of AgResearch's FRST-funded biopharming programme described it as:

> [A] comprehensive research programme that aims to build underpinning expertise in reproductive and transgenic technologies in order to assist in *transforming NZ farming operations and to develop new NZ industries* over the next 10-20 years. (FRST 2001; emphasis added)

The development of biopharming is seen as a strategy to increase New Zealand's economic competitiveness. New Zealand has traditionally relied on efficient production methods to produce large quantities of commodities that are price-competitive in overseas markets. It is argued that New Zealand will soon be out-competed in these markets by "low-cost competitors", particularly in Asia, South America and Eastern Europe (see, e.g., MAF 2008a). Biopharming is said to meet the oft-cited need for New Zealand's agricultural sector to shift from the production of commodity goods to higher-value-added goods for export.

A science manager associated with biopharming told us:

> Already certain countries, for example, in Eastern Europe and probably South America, have got lower cost of production than what we've got, so therefore we can't maintain an edge. …We are not a low-cost commodity player anymore, therefore we have to get into some aspects of higher value.

The 2004 booklet *New Zealand Biotechnology Strengths* from the Ministry of Research, Science and Technology (MoRST), which prominently features biopharming, portrays this and other applications of biotechnology as leading to the creation of "new industries": "Today, our biology-based enterprises are being combined with new scientific knowledge, particularly that based on genetics, to create new industries and opportunities" (MoRST 2004).

MoRST's *Biotechnology to 2025* (2005) presents biopharming as a key trend and a significant emerging application in the primary sector. It characterises biopharming as a means to increase returns to the primary sector by producing higher-value-added products:

> FROM "HIGH-VOLUME, LOW-VALUE" TO "LOW-VOLUME, HIGH-VALUE" PRIMARY PRODUCTION
> Primary industry products have traditionally been characterised by the production of high volumes for relatively low returns. Biotechnology is enabling a move towards more value added products being produced in the primary industries (for example, pharmaceutical proteins produced in livestock and plants). (MoRST 2005: 10)

The goal of AgResearch's FRST-funded biopharming programme entitled "Transgenic cattle producing valuable proteins" is described as: "to build, through cloned-transgenic cattle, a new biotechnology based bioreactor industry in NZ that will *transform New Zealand's traditional farming operations* into biological enterprises producing an array of products including not only pharmaceuticals, neutraceuticals [*sic*] and high quality health foods but also value-added farm commodities" (Laible 2004; emphasis added).

Regarding its current FRST-funded project, "TG [transgenic] livestock", AgResearch declares: "We aim to build, through TG livestock producing valuable proteins in milk, a new biotechnology based biopharmaceutical industry which will contribute approximately $5 million p.a to the NZ economy by 2016" (FRST 2008).

### 2.1.2. Profitability of biopharming

The benefits claimed above depend on the commercial success of biopharming as a drug-production process. The commercial appeal of biophaming is based primarily on the claim that it will significantly lower the costs of drug production.

*2.1.2.1. Low cost?*

Dyck et al. (2003), who argue that transgenic technology offers the lowest-cost method for producing biopharmaceuticals, acknowledge that it is difficult to carry out a direct comparison with other platforms because of the wide range of unknowns, which include "lack of data on protein yield, purification rates and production scale…[and] specific recombinant protein being produced" (394-395). They posit that the cost of purification once the protein has been produced will be similar whatever the production system.

Spök (2007) argues that the major costs of drug production derive from processing, particularly the purification process, and these costs are unlikely to be lower for pharmaceuticals produced by plants. Some argue that costs of purification may even be greater for biopharm plant and animal production platforms:

> [T]ransgenic crops or animal milk, just like cell culture media, must be purified before a final product is achieved. Transgenics don't necessarily have an advantage here and in fact may require additional processing and purification steps in some cases. (Thiel 2004: 1371)

The costs of managing the risks of commercially biopharming plants and animals (e.g., containment measures, veterinary needs and auditing systems), still unknown, must also be figured into the cost profile of biopharmed drugs. Thiel quotes one industry participant's view that "[t]here are a lot of hidden costs in producing transgenics that I'm not sure anyone really understands, and I'm not sure they will until they do it at scale," and relates the opinion of a second that "estimating the true costs of transgenic production is an 'angels-dancing-on-the-head-of-a-pin question' because of the unknowns" (Thiel 2004: 1371).

Another issue impacting on costs, and indeed overall viability, is intellectual property. According to Kind and Schnieke (2008: 1027):

> [B]ecause all pharming companies were founded on a means of production rather than product discovery, access to potential products has been a considerable problem. Most proteins with biomedical indications are protected by patent or proprietary information, and this has forced reliance on industrial partnerships, sometimes making pharming companies vulnerable to third-party decisions….

They also see the current patent system as presenting obstacles to biopharming development:

> The current patent system is widely viewed as poorly suited to the realities of biotechnology, and practices such as the granting of overbroad claims have been criticised as protectionist and stifling innovation. For example, a patent granted within the US to GTC Biotherapeutics claims ''any therapeutic protein in the milk of any transgenic mammal'' making it difficult for other companies to compete

> (www.transgenics.com). While patent rights can of course be disputed, financial costs are high. (ibid: 1028)

*2.1.2.2. Competing platforms*

Biopharming has been promoted as having cost and flexibility advantages over traditional biopharmaceutical production methods. This view, however, may not have given sufficient consideration to developments in traditional methods.

Improvements have been made in cell-line yields, and disposable bioreactors have been developed, introducing more flexibility into cell-based production. As Thiel (2004: 1365-1370) notes:

> Traditional cell-line manufacturing, whether in microbial or mammalian hosts, is advancing in ways that could dramatically change how facilities are built and operated…. [R]apid advancements in cell-based manufacturing technologies and strategies…pose considerable threats to companies hoping to do contract manufacturing in transgenic plants or animals…. [B]iotech companies looking at options for commercial production of biologics see available capacity and a future of increasing efficiency in traditional cell-line production…. [T]here is little immediate pressure for companies to move to alternative platforms that are as yet commercially unproven.

Thiel relates an industry participant's view that "the cost advantage boasted by transgenics will dwindle as traditional cell culture manufacturing becomes more productive with new, more efficient cell lines" (ibid: 1370). Similarly, Kind and Schnieke (2008: 1032) note: "Cell culture is increasingly well established and the possibility of increased yields (Butler 2005), such as those reported by Wyeth (Ledford 2006) may yet overturn the cost advantages of animals."

It is perhaps worth noting that the Texas-based firm Agennix claims that it can produce recombinant human lactoferrin through microbial fermentation processes at costs similar to those expected to be incurred by Ventria Bioscience's plant biopharming platform (rice engineered with the genes for the production of human lactoferrin) (Wisner 2005: 27). This suggests that biopharming's putative cost advantages may be whittled away by competing platforms.

It has been suggested that animal biopharming may make it possible to produce new biopharmaceuticals that cannot be produced through other existing platforms (see, for example, Keefer et al. 2007). Indeed, Kind and Schnieke (2008: 1025) argue that the long-term success of animal biopharming may depend upon its ability to produce biopharmaceuticals that are unique to transgenic animals. If this were to be achieved, the economic problem of competing platforms would be (at least temporarily) mitigated for producers of these compounds. For more on biopharming as a producer of new drugs, see section 2.2.1.

*2.1.2.3. Regulatory issues*

The economic case for biopharming emphasises its use as a new, lower-cost method to produce versions of existing biopharmaceutical drugs, particularly once they have come off-patent. Such drugs are called biosimilars (or follow-on protein products). Biosimilars, however, are not the same as generic versions of conventional pharmaceuticals.

> Conventional generics are considered to be therapeutically equivalent to a reference once pharmaceutical equivalence (i.e. identical active substances) and bioequivalence (i.e. comparable pharmacokinetics) have been established and do not require formal clinical efficacy and safety studies. The term 'biogeneric' would imply that the active substance of a biosimilar could be readily characterized and shown to be identical to the active substance of the reference product. This is simply not the case with biosimilars. The active substance of a biopharmaceutical is a collection of large protein isoforms and not a single molecular entity, which is generally the case with conventional small-molecule drugs. Thus, it is highly unlikely that the active substances are identical between two products, and there are currently no analytical techniques to establish biopharmaceutical equivalence. (Schellekens 2009: i27)

Regulatory agencies face particular challenges when it comes to evaluating biosimilars.

> [Biopharmaceutical proteins] are in general 100-1,000 times larger than small molecules [produced through chemical synthesis], they can't be fully characterized physiochemically by current analytical methods, which are often insufficiently sensitive, and their mode of action can confound biological characterization *in vitro*. Unlike the chemical processes used to synthesize the small molecules, therapeutic proteins are manufactured in living cells, which are very sensitive to culture conditions. … For regulatory agencies, a key question is how similar the physiochemical characteristics of the biosimilar and its patented counterpart need to be to qualify for the biosimilar route of marketing authorization. Even if the biosimilar product has the same gene sequence, vector, host cell line, culture conditions and purification methods as the innovative protein, it can still differ substantially in its biological and clinical properties. (Schellekens 2004: 1358)

If this is true of biosimilars using the same production platform as the original biopharmaceutical, it will presumably apply *a fortiori* to those using a different production platform.

In the United States, whether and under what conditions biosimilars should be approved is still under debate; as of this writing, legal and regulatory pathways do not exist. In Europe, the EMEA has issued a set of guidelines, which "advocate pre-clinical and clinical testing of biosimilars to demonstrate safety and efficacy prior to market authorization, followed by tailored pharmacovigilance plans to monitor potential

immunogenicity" (Schellekens 2009: i31). The regulatory requirements (such as clinical trials and post-marketing pharmacovigilance programmes) developed to ensure that biosimilars have safety and efficacy profiles equivalent to the original may significantly erode the profitability of biosimilar production and thus of biopharming.

While these issues apply to biosimilars in general, there are additional issues relevant to biopharmed drugs. Dyck et al. (2003: 396; see also Gavin 2001) identified the regulatory implications of the technical challenges of purification as a potential obstacle to animal biopharming's commercialisation:

> [T]he raw potential for producing valuable proteins with transgenic animals seems apparent. However, the purification of these proteins from their source, whether milk, eggs or semen, is still a hurdle to be overcome and creates, often undefined, regulatory issues.

Purification of a recombinant protein in commercially viable amounts from the milk of transgenic animals is a complicated process with a number of unknowns (Goldman 2003: 5).

A relevant consideration for plant biopharming is that the number of modifications induced in the biopharm plant and the concentration of the introduced protein in it are much higher than for first-generation genetically modified plants. This is expected to increase the number of unintended effects on the plant and therefore the potential for harm to human health and the environment, raising regulatory issues. The resulting additional assessment and risk-management costs could significantly reduce the cost advantages of plant biopharming (Spök 2007).

### 2.1.3. Returns to New Zealand

#### *2.1.3.1. Returns to farmers*

Whether or not farmers will benefit from biopharming depends on a number of factors, including ownership and management arrangements and relative market power.

*Plant biopharming*

There has been more discussion internationally around farmers' returns from plant biopharming than from animal biopharming. Ann Marie Thro, from the USDA, makes a common claim when she argues that "there could be benefits from pursuing a more diverse group of crops [than the usual corn] … allowing more rural farm communities to gain income via production of transgenic pharmaceutical plants" (in Fernandez et al. 2002: 12). Robert Wisner, a specialist in agricultural economics at Iowa State University, examined the likely distribution of benefits and liabilities from plant biopharming and summarised the situation for growers:

> The economic benefits for pharma crop producers will depend on:
>
> - returns per acre paid by the pharma crop firm for use of the farmer's land and for any expenses needed to maintain crop separation and multiyear land isolation;
> - returns paid for labor and management;
> - the total number of acres needed;
> - any costs required to meet contractual obligations; and
> - any risk of liabilities that must be assumed by the farmer in producing a crop that could seriously jeopardize food and feed supplies if commingling with commodity production occurs. (Wisner 2005)

Wisner concluded that farmers are unlikely to be the beneficiaries of biopharming, primarily because the market power of the contracting biotechnology or pharmaceutical companies is much greater than that of the potential biopharm-crop growers.

Kaye-Blake et al. (2007: 17) report on a peer-reviewed analysis of the economics of biopharming focusing on the production of human serum albumin (HSA) in tobacco (Kostandini et al. 2006), which also cast doubt on the prospects of increasing returns to farmers.

> 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.

Our study of the arable industry (Morris et al. 2009) confirmed this distribution of power and likely returns; our informants pointed out the increasing concentration of ownership of the vegetable seed industry and related intellectual property, with seed industry players also being major biotechnology and pharmaceutical companies:

> A lot of those companies are now owned by the likes of Monsanto and Bayer and those sort of people who are driving the industry from behind the scenes with some of this new technology. … So there is almost a cartel behind the scenes. A lot of people don't realise that Monsanto own this company, this company and this company. … So a little bit hidden from public view probably, but we in the industry know who they are and where they are.

This market power also provides a driver for the introduction of biopharming into New Zealand's arable industry, as described by an interviewee from an intermediary seed-production company:

> If it's one of the big fellows and we're doing a significant amount of business with them, you'd have to weigh that up. And saying, well, no, we're not going to do that one, but we'll do all the others, they might just turn round and say: either you're doing that one and those ones, or you're not doing any of them. [*So you think that could happen?]* It could. Some of those companies would be that way inclined. If push came to shove. A lot of these customers aren't exclusive necessarily with us. A significant number deal with each of us. … As we do with our growers, yes. We growl at them saying: the best approach would be to be exclusive with us, we'd get all the good growers and everything else. I mean, put yourself in their shoes, they're not going to do it. And I can understand that, too, I suppose. I suppose if this type of push was coming from the Monsanto-type companies, it's going to be hitting us, it's going to be hitting others as well at the same time. I'm sure we're all going to get pinged at the same time.

It was assumed that, like current specialty vegetable and seed growing, the company that owns the IP in the crop would supply the seed, receive the crop (in the form of seeds or plant) and process it. Farmers could be contracted either directly or through local seed-production intermediary companies (such as PGG Wrightsons and Cropmark), though some in the industry thought it unlikely that the IP-owning companies would use New Zealand intermediaries:

> At the level of intellectual content, the breeding, the transgenics, whatever goes into the seed, it becomes so valuable that it may come to the point where production companies that are contracted become less and less acceptable to someone who's got $10 million in the variety. Instead they'll put their own production people on the ground.
>
> Are they going to have a use for [us] when they have a $12 million research budget? And are they going to entrust it to a couple of yokels who are used to putting ear tags on gates? Probably not. They're going to open an office in Christchurch and they're going to hire us for our local knowledge, but basically control it.

*Animal biopharming*

Animal biopharming presents a different set of possibilities for farmers. First, the transgenic animals have to be (repeatedly) produced. Second, these animals are farmed to produce the raw unprocessed form of the product. If this is milk, then the process of farming involves not only the feeding and care of the animals, but also milking them and keeping them lactating. Third, the raw product is taken somewhere to be purified and processed or formulated into a marketable product. Each of these stages could be carried out by the same organisation or by different ones.

Our research into animal biopharming (Goven et al. 2008) derived the following possibilities for the organisation of production:

- A corporate owner employs a farm manager – farm and animals are owned by a corporate entity which employs a manager to manage the everyday running of the farm.
- The farmer owns and manages the farm and the animals, producing on contract to a biotechnology or pharmaceutical company.
- A coalition of farmers within a geographical area owns and manages the operation, producing on contract to a biotechnology or pharmaceutical company.
- A self-contained commercial research enterprise produces the transgenic animals, farms them, and produces the product.

We concluded that the final option was the most likely.

To farmers, the costs of entering biopharm production would be considerable. Farmers did not generally think it would be possible to include both biopharm and conventional dairying in the same operation if commingling and contamination issues were to be addressed. In their view, it would be necessary for a farm property to be devoted exclusively to biopharming in order to protect the integrity of both the biopharm and the conventional products. An operation involving a small specialist herd producing a product requiring high levels of segregation and containment would require a dedicated infrastructure: not only dedicated paddocks and special fencing, but also milking and transport infrastructures suitable for relatively small quantities of milk and high levels of containment. Constraints on other practices, such as off-farm wintering, imply being able to afford a higher land-to-stock ratio and buying in winter feed. Other constraints include not being able to sell bobby calves and other culled stock. There is also the risk of long-term costs associated with contamination of the land, e.g., through biopharming's impact on soil microorganisms (see section 3.1.3).

When assessing the costs of establishing a specialist biopharm, a farmer would also need to consider the longer-term consequences of opting out of their current supply relationship with Fonterra (or other cooperative); that is, the farmer must consider whether it would be possible to resume that relationship should the biopharm venture prove unsatisfactory or unviable. Our interviews suggested that this is a significant risk for a dairy farmer to take. Similarly, it is likely that a farmer producing biopharm milk would supply a single company, which is very unlikely to be a farmers' cooperative. The considerable power differentials likely to be present in such a relationship (i.e., relative market power, as discussed above) may impact negatively on returns to the farmer. Such an arrangement would also be associated with the risk to the farmer that the company would withdraw from the business or go into liquidation, as has occurred previously with a number of companies involved in biopharming.

In interviews with promoters of animal biopharming in New Zealand, we sought more detail about how, if the research were successful, it would be translated into implementation in the pastoral sector.

> I think what we look at is if you have large-scale animal biopharming in New Zealand., sure the ultimate consumer is overseas, it's a pharmaceutical company, it's a biotech company that has developed this. But no doubt there will be significant value capture for New Zealand, in terms of the basic product that would come out of the animal and would be trucked off the farm, would be worth far more than the current commodity. So instead of x dollars per litre, or kg, milk solid, you may be talking 100 dollars for the same amount, or whatever….[*Would the farmers own their cows?*] I would suspect though, that no, what you would get effectively is farm managers farming the animals that are owned by a biotech company or a pharmaceutical company…. [*So the farmer would be paid a salary?*] Oh yeah, farm management basically, share milker, or, I don't know. Purely speculative at this point.
>
> If I were a farmer and was asked by a company to develop a herd or purchase a herd to produce a pharmaceutical product I would be interested in what returns, additional returns, I was going to get for that product. But also what the issues were in terms of flexibility of production, because if I had a 600 cow herd, and I was going to have to run 20 transgenic animals, essentially you would have to duplicate your facilities for that 20 animals, and so there's a costing issue associated with that. And then the milk is going to have to be kept separate. Cows might need to be kept in a separate mob. 20 animals is a relatively small mob, so there's going to be some big farming decisions a farmer is going to make, before the decision comes simply to go and do this. … There will be more, smaller mobs which will put the cost of handling these animals up.
>
> [*Who would own them, do you think, if this comes to fruition?*] Ideally, owned by the commercial enterprise that is actually processing that particular milk….I don't see this as being a huge enterprise for many thousands of cows running around the countryside. It'll be sort of a small, discrete lots, maybe 50, 100 cows and maybe two or three enterprises

Neither in these discussions nor in the literature have we found evidence or argument to substantiate the claim that animal biopharming would translate into higher returns to New Zealand farmers. In particular, the issue of the market power of the farmer relative to the contracting company does not appear to have received sufficient consideration.

*Biopharming in aquaculture*

In our view it is unlikely that (GM) biopharming will be pursued at all in New Zealand aquaculture during at least the next 10-15 years. Most practitioners dismissed the feasibility of containment and noted that contamination would pose a very considerable threat to the industry. Given our informants' reaction to aquacultural biopharming in

general, and the feedback we received on the current state of both the aquaculture sector and the research likely to be of use to the aquaculture sector, there was little point in putting to our informants a variety of specific biopharming scenarios. We therefore adjusted our research focus to look at aquacultural innovation strategies more broadly, with an emphasis on biotechnology and medical applications where possible. We adapted our approach to investigate the practical, experiential knowledge relevant to these areas. For our findings, please see Campbell et al. (2008).

*2.1.3.2. Competitiveness of New Zealand agriculture*

It is unclear how biopharming would enhance the competitiveness of New Zealand agriculture. The products are aimed at the pharmaceutical market (or will be sold to pharmaceutical companies), rather than the market for agricultural products. It is more likely that biopharming will, firstly, compete with the agricultural sector for resources; and, secondly result in added costs in the form of additional systems and measures to prevent commingling and contamination.

*2.1.3.3. New industries and higher-value exports*

It may be that what is intended by claims about competitiveness of agriculture is instead about the ability to use resources currently used to produce agricultural commodities to produce higher-value products, and in this way move out of the markets in which we may be outcompeted by countries with lower production costs. It is, however, unclear why it is assumed that biopharming activity will not be carried out in countries with lower costs of production. It is worth noting that Canadian firm SemBioSys is growing biopharm safflower in Mexico and Chile (Murphy 2007).

The case may be different for animal biopharming; here it is argued that New Zealand has the significant advantage of being free from scrapie and the related prion diseases, Transmissible Spongiform Encephalopathies (TSEs). However, GTC Biotherapeutics has addressed the issue of animal disease by importing goats, certified as scrapie-free by the USDA, from New Zealand into the U.S. It has developed its biopharm herd there in a self-contained commercial research enterprise that produces the transgenic animals, farms them, and purifies the product.

Moreover, gaining access to pharmaceutical profits involves far more than the ability to grow biopharm plants or animals. As a New Zealand scientist involved in biopharm research told us:

> It's more than just producing a vaccine or a useful medical compound or any health-benefiting compound in the plant. When it comes to medicines, there's a huge cost downstream…. The next step is you've got to bring on these big multi-national partners and unless you've got good connections it's not going to work. And there's no point starting out, unless you've got those connections. And those connections need to be well and truly entrenched in place before you need to start. Because

> although you might have a bright idea, if there's a real market for it, some other bugger's already thought of it and is already doing it.

In our interviews with scientists it was also suggested that benefits would not accrue to New Zealand for biopharm plants (or animals) developed by Crown Research Institutes (CRIs), because of the way in which CRIs are constituted:

> [W]e're not allowed to market our own plant breeding. It's got to be licensed to another company …. We sell it, we get a royalty on it, but we're not allowed to do any of our own marketing.
>
> I think that is one of the problems with the CRI setup, is that basically CRIs, as soon as they get a product, they're forced to sell it off. I would imagine if a company like [CRI] came up with one of these magic foods, [or] plants, that … as soon as we'd showed that it was of value, we would be forced to sell it to a multinational who would just make big money on it.

Publicly available information on AgResearch's commercial partnerships in the biopharming area indicates that production of recombinant human lactoferrin (rhLF) would be done under license to Pharming NL, who retain ownership of the intellectual property in the production technology.

> The two companies [Pharming NL and AgResearch] have now pooled their resources for the manufacturing of rhLF, with the NZ company taking responsibility for the production of rhLF and purification, as well as providing research capabilities for product development. AgResearch will also fund the initial production of rhLF and support the commercialisation of the ingredient in the South Pacific and Asia.
>
> Pharming has granted AgResearch a research license to its proprietary technology for the production of recombinant proteins, and in return the Dutch firm will have the first right to review new products arising out of AgResearch's protein discovery and R&D projects. The commercial rights of Pharming will cover recombinant bovine and human proteins produced using its proprietary technology. (Taylor 2005)

We are not in a position to evaluate the benefit to the New Zealand economy of this arrangement, but we suggest that any claims of significant benefits to New Zealand from such an arrangement should be scrutinised from the perspective of the issues raised in this report.

## 2.2. Benefits to human health

In some arenas, biopharming is promoted as a way to generate benefits for human health. (For examples from New Zealand, see New Zealand Life Sciences Network [1999], AgResearch [2002], and AgResearch [2008]). Such claims centre on possible new therapies, safer drugs and/or more accessible drugs.

### 2.2.1. New therapies

Biopharming is one potential method for producing biopharmaceuticals. As noted above, there are other methods. Some have suggested that biopharming may be able to avoid certain problems associated with other biopharmaceutical production platforms (that is, bacteria, yeast, and insect, metazoan and mammalian cells) and thereby enable production of novel drugs that could not otherwise be produced (Ma et al. 2005; Dyck et al. 2003; Thiel, 2004). There may be such novel drugs in development; however, all biopharm drugs in commercial development of which we are aware can be produced through other platforms.

While AgResearch (2008) has described its biopharm programme as possibly leading to "exciting new therapies for previously untreatable diseases in humans", all of the pharmaceutical substances that have been identified by AgResearch in its applications and publicity materials – i.e., recombinant human lactoferrin, myelin basic protein, Herceptin and Interferon[1] – are currently being produced through other production platforms.

### 2.2.2. Safer drugs

According to Kind and Schnieke (2008: 1028):

> An important motivation for the production of proteins in animals and animal cells has been to provide safe replacements for human-derived products. These carry a risk of associated pathogens if not properly screened. …Recombinant proteins dramatically reduce these dangers…

However, as they also acknowledge, animal production platforms also incur new risks, including "possible zoonotic disease, contamination with animal proteins and DNA, and alterations in the structure of recombinant protein" (ibid.).

It has been argued that biopharmaceuticals can be produced more safely in plant production platforms than in either biopharm animals or mammalian cell lines. The large evolutionary divergence between plants and animals is assumed to imply a similarly large divergence between the viruses or other infectious elements that normally infect either plants or animals (Spök 2007). Somewhat contradictorily, it has also been argued that plant platforms are less safe than animal platforms because their glycosylation patterns differ more significantly from those of humans. For a discussion of these points, please see section 3.1.1.

[1] For references to Herceptin and Interferon, see Wallace (2008).

### 2.2.3. Cheaper drugs; better access for developing countries

Even if biopharming does prove to be a cheaper method for producing drugs, it does not necessarily follow that either patients or health services will benefit from lower drug costs. As Ma et al. (2005: 594) note: "'Cost of goods' has relatively little impact on the market price of new pharmaceuticals." Moreover, complex biopharmaceutical production processes may mean that cheaper generic drugs will be harder to produce, in which case it is possible to question whether the cheaper production methods of biopharming will necessarily lead to a greater availability or affordability of drugs for patients (Herrera 2005).

These considerations apply to both developed and developing countries. According to Mich Heim of Epicyte Pharmaceuticals, Inc., risk management and processing requirements further limit the potential benefits of biopharming for developing countries:

> He noted that producing the vaccine would still involve both state-of-the-art manufacturing facilities and careful regulatory review, neither of which are generally available in the developing world. Therefore, Hein said, the benefits pharma plants may hold for developing countries may be less dramatic than what was contemplated several years ago[2]. (Fernandez et al. 2002: 12)

[2] He is referring here to ideas such as the vaccine banana, which are now considered to be unlikely developments largely because of the difficulty of controlling doses.

# 3. Potential harms and their contexts

## 3.1. Harm to human health

### 3.1.1. Biopharm drugs

Biopharmaceutical production processes can generate health risks and related challenges for drug regulatory agencies. Beyond the potential for toxicity that characterises drugs in general and biopharmaceuticals in particular, health risks related to drugs produced through biopharming have been categorised by Amy Rosenberg of the U.S. Food and Drug Administration (FDA) as: infection; allergenic responses; immunogenic responses; and "autoimmune reactions arising should transgenic proteins break tolerance to their endogenous, self-protein counterparts" (quoted in Schmidt 2006).

According to Schellekens (2009), immunogenicity is the primary safety concern for biosimilars (and for biopharmaceuticals in general).

> The use of biopharmaceuticals to replace endogenous proteins, which may be present at insufficient concentrations (e.g. the use of ESAs in CKD patients with anaemia), carries the serious risk of stimulating the immune system to develop anti-product antibodies (Abs) that may cross-react with endogenous protein. Although these proteins are designed to closely mimic human proteins, they have the potential to induce an immune response, especially when administered as multiple doses over prolonged periods. The level of immunogenicity can be markedly different for products considered to be very similar. (Schellekens 2009: i29)

This applies to all production platforms. However, there is also a range of issues specific to plant and animal biopharming.

*3.1.1.1. Drugs from biopharm animals*

Drug safety issues include, for example, the possibility of passing on infectious agents such as viruses or prions and the possibility of triggering immune reactions. Amy Rosenberg of the U.S. FDA notes:

> We would really need assurance that the animals aren't infected with any kind of prion disease. And each product poses its own unique risk – for instance, recombinant versions of endogenous proteins might pose immunogenicity risks that you might not encounter if the protein doesn't have a human counterpart. (quoted in Schmidt 2006)

Prions are associated with Transmissible Spongioform Encephalopathies (TSEs) in both humans and animals, including bovine spongiform encephalopathy (BSE), sheep scrapie, chronic wasting disease (cervids), Creutzfeldt-Jakob disease (CJD) and variant Creutzfeldt-Jakob disease (vCJD). Prion proteins are parts of protein aggregates that transmit a trait as if they were based on DNA (Campbell 1998; Keyes 1999; Weld and Heinemann 2002). Prion diseases can be infectiously spread through food, as the origins of the BSE and vCJD epidemics in the UK attest (Caughey and Baron 2006). Some suggest that prion diseases could develop in the community through the use of genetically modified animals (Weaver 2003: 25). This may happen if a prion is consumed through drinking the modified cow's milk (U.S National Research Council, 2002: 52). In the case of prions, the infection requires a highly similar, but not necessarily identical, protein to be part of the normal proteins in the exposed recipient. However, all proteins have the capacity to aggregate, even if all do not become infectious, and there remains the formal possibility that other deleterious effects arise from aggregation itself (for example see Bucciantini et al. 2002). Transgenic animals may be more prone to deposit protein aggregates composed of the recombinant protein because the protein is usually produced at unnaturally high concentrations in recombinant animals or because the cell physiology of the recombinant animal is outside of the biophysical conditions of the source species (Tartaglia et al. 2007).

There are at least two potential, and opposing, impacts of the fear of transmission of a prion disease on the possibilities for biopharming in New Zealand – it could encourage the use of New Zealand-sourced animals both here and overseas, or it could discourage *any* use of animals such as sheep, cattle or goats or animal–derived tissues (cell cultures) to produce pharmaceuticals. The former would make New Zealand a source of disease-free animals, which could be cloned to further reduce the risk, as is under consideration by the FDA (see White 2005: 2-3). The latter would obviously have a negative impact on New Zealand's aspirations for a biopharmaceutical industry based on this capability. (This latter possibility was suggested to us by one of the scientists we interviewed; it was his view of the direction the FDA was likely to take.)

With regard to immunogenicity, some maintain that animal biopharming may not differ in this regard from other techniques already in use for the production of biopharmaceuticals, such as those using mammalian cell lines (for example, see Laible and Wells [2007]).

Other hazards, however, may be linked to the techniques used to produce transgenic animals. The use of the transgenesis technique of pronuclear microinjection can produce unpredictable changes in the resulting organism (Dyck et al. 2003: 397; Keefer et al. 2007: 2). For example, the milk produced by transgenic animals can have quite different characteristics from 'normal' milk. Laible and Wells (2007: 115), reporting on their attempts to change the casein content of bovine milk, note:

> Interestingly, the simple increase in gene dosage for two milk proteins resulted in complex changes including effects on the production of some other milk proteins, mineral balance and physical appearance. Although not

> necessarily unexpected, complex changes as a result of genetic modification are difficult to predict and can only be assessed in the transgenic animals once generated.

This example illustrates one of the important problems associated with the production of proteins from transgenics: how can non-obvious unanticipated changes be identified if one does not know what to look for?

*3.1.1.2. Drugs from biopharm plants*

Many have focused on the potential for drugs made with animal bioreactors to transmit disease; some argue that using plants as production platforms avoids this risk. Saint-Jore-Dupas et al. (2007) suggested that recent advances in the manipulation of plant glycosylation mean that what was regarded as a handicap in the use of plants as expression systems for the production of recombinant pharmaceutical proteins may turn into an advantage, as researchers have been able to humanise the plant-specific glycosylation processes. They see this as a way to overcome some of the difficulties associated with the use of mammalian cells and animal production systems, particularly the potential for the transmission of viruses and prion diseases.

However, as Elbehri (2005: 21) suggests, there is the potential for plants to pass on contaminants from soil fungi, bacteria and/or pesticides that would be new to the conventional drug production process. Moreover, compounds produced in plants can also cause allergenic or immunogenic responses and have the potential to adapt viral pathogens to humans.

Despite the apparent organismal differences between plants and animals, they share significant similarities at the cellular level, which is the level most relevant when considering the risk created by viruses and toxins. What differences there are may at times be overcome. There is informed speculation that "filoviruses [such as the Ebola virus] may be plant viruses, perhaps even involving transmission by arthropod vectors" (Swanepoel 1996: 321). While this remains speculative, to date the possibility has not been excluded (Peterson et al. 2004). There is solid evidence that in nature at least one plant virus was able to switch to an animal host through recombination with an animal virus (Gibbs and Weiller 1999).

This apparently unlikely combination of events implies that plant and animal viruses can infect multiple species even if they rarely cause symptoms in all species that they infect, or replicate to only very low numbers. Nevertheless, provided time or human assistance, they may eventually adapt to a new species and begin causing disease.

*3.1.1.3. Biopharm drugs in general*

A risk of using biological products sourced from any living organism is that they may not be sufficiently purified from other material that could cause harm in recipients. For example, the purification of antibiotics from the microorganisms that produce them

carries the demonstrated risk of transferring the antibiotic and the genes for antibiotic resistance simultaneously to patients, where the gene may be acquired by the bacteria in a patient (Heinemann 1999).

In considering the risk of pathogens accompanying the material being purified, it may be more useful to consider virus types rather than the species of the biofactory. This is because, first, some viruses have large host ranges and are therefore more capable of jumping species boundaries; and second, some viruses have a greater ability to adapt to a transmission route supported by human technologies (Heinemann 2007).

Another major issue relates to glycosylation, a type of post-translational modification of proteins. In terms of its impact on health risks, the glycosylation process is discussed as both an advantage and a risk of animal biopharming. Laible and Wells (2007: 113) point out that immune responses can occur "due to slightly varied glycosylation patterns compared with the native human equivalent". This is a concern for regulators because "although the transgene may code for a human protein, modifications may be made to the protein during its production in the transgenic animals" (Keefer et al 2007: 7). Moreover, "altered glycosylation patterns can affect the amount of time before a protein is cleared from a patient's system which can affect treatment protocols" (ibid.).

As noted above in connection with biosimilars, the context in which a protein is produced can have significant impacts on its functioning. These impacts can be difficult to detect.

> Even under the most stringently controlled culture conditions, proteins show a high degree of heterogeneity (e.g., in glycosylation or in folding). Often, *modifications occur as a result of abnormal processing because the recombinant proteins are unnatural products for the cellular expression system used.* Extraction and purification involves [*sic*] many steps that can also introduce protein modifications that influence biological activity or clinical properties….Production normally involves many hundreds of control steps, which involve numerous in-house standards. This complexity is the basis of the claim in pharmaceutical biotechnology that process is the product…. (Schellekens 2004: 1357; emphasis added)

It is possible, then, that different manufacturing platforms and processes will produce unexpected transformations in proteins, and these transformations may be harmful. For example, an Australian group found that the expression in peas of a protein normally produced in beans induced an immune response in mice, whereas the same protein produced in beans or in chickpeas did not (Prescott et al. 2005; Prescott and Hogan 2006). This difference in reaction was attributed to differences in glycosylation in bean and pea plants. The inducement of multiple modifications and the higher concentrations of the induced protein can be expected to increase the number of unintended effects on the modified organism.

The types of contaminants that must be removed are not always obvious even when they may be detectable. An example is provided by the manufacture of the common amino

acid tryptophan using genetically modified bacteria. In the late 1980s, the introduction of these bacteria was associated with 37 deaths in the United States and retrospectively associated with 97-100% of all cases of eosinophilia-myalgia syndrome. The change in the manufacturing process increased the concentration of otherwise low levels of hazardous compounds (Sustainability Council 2007; Schubert 2008).

The safety issues around biopharm drugs pose a challenge for drug regulators (i.e., Medsafe) in New Zealand regardless of whether New Zealand itself invests in biopharming. If New Zealand becomes a producer of such drugs, safety issues represent an economic risk as well.

### 3.1.2. Food contamination

Unlike other forms of drug production, biopharming poses the risk of contamination of the food supply. This is particularly the case if the drug is made in a food-producing platform (such as food-crop plants or cow, sheep or goat milk).

Biopharming involves processes of genetic modification (GM). There are those who argue that GM itself does not pose safety issues, that GM-derived material in food should not be policed or that some level of presence of such material in food should be considered acceptable. Regardless of these arguments, presumably all would agree that when GM is used to induce the organism to produce pharmaceuticals, contamination of the food supply poses a risk to human health. Such contamination has already occurred more than once in the U.S. (Ledford 2007), suggesting that the systems in place there are not, or at least have not been, adequate to protect against potential harms to human health through contamination of the food supply through large-scale biopharming activity. (For more evidence of inadequate systems and poor control of risks related to biopharming, see USDA Office of Inspector General, 2005.)

This also suggests that biopharming should trigger added scrutiny on the part of food safety regulators of imports from countries where biopharming occurs. Similarly, New Zealand can expect added scrutiny of its food exports if it should engage in biopharming using food-producing organisms.

As noted above, there have already been cases of biopharm products getting into the food supply. In 2002, Prodigene's "inadequately managed field trials" (Murphy 2007: 556) of biopharm corn resulted in crop contamination in the U.S. states of Nebraska and Iowa.

> In the Nebraska case, officials realized that some 500,000 bushels of harvested soybeans were contaminated with small amounts of GM corn, which had been grown during 2001 on the same plot, because the farmer did not weed "volunteer" plants from the field in which the soy was grown. In Iowa, federal officials required a local producer to destroy some 155 acres of corn because it could have been cross-pollinated by ProdiGene's engineered corn being raised in a nearby field. (Fox, 2003: 3)

From 2001 to 2003, the University of Illinois released 356 pigs, which were part of their biopharming experiments to produce pharmaceutical proteins in the milk of sows, to livestock dealers. The university argued that the pigs did not contain the genes of their parent stock nor were they old enough to be lactating; however, investigations by the FDA found that records were inadequately kept and they were unable to verify this (FDA 2003).

The potential pathways to food contamination are many and complex, including both biophysical and social components. Our interviews with practitioners highlighted a number of contextual factors that impact upon the likelihood of contamination.

*3.1.2.1. Plant biopharming vectors to food contamination*

One way of minimising the risk of food contamination would be to avoid using food plants in biopharming. Nonetheless, many developers of biopharm plants continue to use food plants as their production platforms, including maize, rice, barley, wheat, soybeans, oilseed crops, spinach, tomatoes, peas, carrots, lettuce, potatoes, alfalfa, and bananas (Murphy 2007; Morris et al. 2009: ch 1). Those with experience in the arable and seed-producing industries highlighted a number of areas relevant to their own production practices that shed light on possible pathways to contamination of the food supply.

*Cross-pollination*

It is widely recognised that, depending on the crop used, cross-pollination has the potential to transmit undesirable traits beyond the crop site. Vectors for cross-pollination include wind and animals (especially insects).

While isolation distances are used to avoid cross-pollination, the knowledge for setting isolation distances is not well developed. For example, while Oregon Seed Certification isolation distances for bentgrass were set at approximately 50-90 metres (depending on field size), research in 2004 on GM creeping bentgrass in Oregon showed that pollen could be transported much further than this by the wind, resulting in cross-pollination up to 21 kilometres away from the source plant.

> [Researchers from the U.S. EPA] collected seeds from wild grasses growing for tens of kilometres around the experimental plots, then grew the seeds in greenhouses and tested the growing grasses for transgenes and resistance to Roundup. They found extensive gene contamination up to 2 kilometres downwind of the experimental plots. Contaminated grass seeds also turned up across 310 square kilometres, with the most distant find 21 kilometres from the source. (Pearce 2004, citing Watrud et al. 2004)

The Seed Crop Isolation Distance (SCID) system, a voluntary crop registration system used by seed producers in New Zealand, stipulates isolation zones for out-crossing crops. Practitioners accepted those distances as good enough for their intended purpose. At the

same time, however, they believe that both wind (particularly Canterbury winds) and bees are capable of transporting pollen beyond the stipulated distances. For example:

> *[Is the isolation distance for carrots the same, is it 2km?]* Most crops, these out-crossing crops, we go one to two kms. Wind pollination. *[So it won't go any further than that. (He smiles – I say for the tape recorder!). In your experience is that enough?]* That's the industry standard, yes.

Practitioners pointed out that cross-pollination risks involve not only other growers but also weeds (particularly roadside weeds) and home gardens. These would require active policing and control. Currently seed production companies monitor fields and surrounding environments of the growers with whom they contract to produce high-value seed crops in order to identify and destroy sources of cross-pollination.

Brassicas, which include a wide range of vegetables such as swedes, turnips, radishes, cauliflower, broccoli, canola (rapeseed), kale and cabbage (including bok choi and pak choi), reproduce through wind or insect pollination and cross-pollinate widely within the brassica family. Brassicas are seen by those in the industry as presenting significant containment challenges for this and other reasons (see below). According to those in the industry, "[w]idespread canola planting in Europe has made growing vegetable seed there almost impossible and N[ew] Z[ealand] has become one of the few places in the world with enough 'uncontaminated' land to sustain the industry" (Fulton 2007). Because of this, the recent increase in canola plantings has caused concern within the industry. The increase is in response to a number of factors: demand for biofuel, including Solid Energy's biofuel-from-canola programme; farmers growing canola for their own diesel needs (Natural Systems Ltd 2008); and local growth in the edible oil processing industry (Federated Farmers 2008).

This has obvious implications for potential cross-pollination of biopharm crops in the brassica family, especially as there are concerns that some canola growers are not participating in the SCID system (see section 4.3.2 below).

*Seed persistence*

Seed persistence is another pathway to food contamination with biopharmed substances. The ability of seeds to persist in the soil and germinate long after the season in which they were sown varies markedly with type of seed. Here brassicas again are the standout risk crop. Growers recounted their experiences of brassica seeds persisting and germinating 20 years or more after being sown. Similar data have been reported in northern hemisphere oilseed rape fields (D'Hertefeldt et al. 2008; Messean et al. 2006).

*Seed dispersal*

There are various ways in which seeds themselves may move beyond their intended locations, including transport by animals, wind, water and human activity. Birds are an important vector, as seeds on which they feed may pass through them in a viable state

and be deposited at considerable distances from the source plant. Rodents and insects can also disperse seeds (Heinemann 2007). Some seeds are light enough to be dispersed by the wind. Seeds can also be moved through floods and runoff.

Human activity is another source of seed dispersal. People and machinery that enter crop paddocks can inadvertently carry seed out with them. Seed can be dispersed during transport or mixed with other seed if machinery and transport vehicles are not thoroughly cleaned. Removing every seed from harvesting machinery and transport vehicles can be difficult and time-consuming.

Seed cleaning may also result in seed dispersal. Some growers carry out seed cleaning on site; others send harvested seed to seed cleaning companies. In both cases, the resulting waste, which will contain viable seed, is dumped. Growers dump the residue on their own farms; seed cleaning companies may contract with a farmer to take it away (to be spread on paddocks as organic matter) or may pay to dump it in a landfill. Seed cleaning can generate considerable volumes of waste; we were told that every tonne of ryegrass seed harvested will result in approximately 200 kilos of waste. Disposal of this waste could, if not managed properly, be a vector for seed dispersal.

*

Seed dispersal, seed persistence and cross-pollination can all work together to produce complex vectors through which biopharmed substances may enter the food supply. While an answer to this problem might be to prevent flowering and seed set, the practicality and overall effectiveness of this solution are unclear. First, many biopharm plants have been developed to accumulate the pharmaceutical protein in seed or fruit, so preventing seed set will also render them unviable as production platforms. Second, not all plants being developed or considered for biopharming are propagated using seed. For example, potatoes and bananas are cultivated using propagules.

Third, using plants that do not accumulate the pharmaceutical product in seed or in which production of the pharmaceutical product could be induced, as in T-GURTs[3], would not eliminate the risk of pharmaceutical substances entering the food supply, as it would not protect against human error (for example, inadvertent admixtures of seeds and other materials could result in biopharm plants being inadvertently grown) and other contamination pathways. For example, insects, birds and small mammals that feed on the plant can be expected to accumulate quantities of the drug as they do the products of non-pharma plants (Harwood et al. 2005), and these animals may contaminate crops harvested for food (Thind and Clarke 2001).

[3] T-GURTS stands for trait-related genetic use restriction technologies. These are meant to prevent expression of particular engineered traits unless they are externally induced through, e.g., application of a particular chemical.

*Disposal of waste*

Whether biopharmaceuticals are extracted from seeds or from other plant material, extraction of the pharmaceutical compound will also result in significant quantities of residue. Methods of disposal of residue may also create pathways to contamination.

*3.1.2.2. Animal biopharming vectors to food contamination*

The use of large milk-producing animals as biopharm platforms is seen by some as inherently safer, because escapes of large animals are easy to detect. This will depend, in part, on the context of the operation, namely whether the biopharm operation is part of a larger dairy farm or is bordered by another farm containing the same type of animal. In addition to the movements of the animals themselves, the handling of the biopharm milk can also be a vector for contamination. Without a milking, storage, and transport infrastructure dedicated exclusively to the biopharming operation, it is difficult to see how segregation could be guaranteed.

A combination of economic incentives and the technical demands of producing biopharmaceutical milk may result in another pathway to contamination. As animals lactate in order to feed offspring, it is not possible to produce milk without the birth of new offspring. Transgenic animals will essentially be worthless if not needed for the herd and not welcome in the food chain. In the U.S. it is thought that biopharm operators may seek approval for excess animals to be permitted in human food or animal feed (U.S National Research Council, 2002: 54). There may be similar attempts to derive value from the milk of biopharm animals that is not required or suitable for pharmaceutical production. Regardless of the safety of the excess animals and milk as food, in light of the inevitability of human error, permitting such a practice would open a number of new potential pathways to contamination of the food supply with biopharmaceuticals.

*3.1.2.3. Aquaculture and food contamination*

The use of fish and other aquatic food species for biopharming, contrary to the discussion above, would pose significant risks of escape and food contamination unless fully contained and removed from wider marine and other aquatic environments. Containment in a marine environment is generally seen by practitioners as impossible. See Campbell et al. (2008) for a discussion of containment issues in marine environments.

### 3.1.3. Other risks to human health

If New Zealand becomes engaged in biopharming, it opens up further possibilities of harm to human health that can occur during, or as a result of, the food production process.

### *3.1.3.1. Pollen inhalation*

Containment of pollen for the purposes of preventing reproduction does not necessarily prevent the production of pollen. Even reproductively impotent grains of pollen can carry transgenes and pharmaceutical substances that may be inhaled by people and are potential allergens, immunogenic substances, or toxins. Compared to oral exposure, inhalation exposure can be many times more effective at sensitising a susceptible individual to an allergen (for example, see Kroghsbo et al. 2008). This risk will be particularly relevant to those who work with or near biopharm crops.

### *3.1.3.2. Resistant bacteria*

Biopharm plants and animals may significantly impact microbiota. For example, MoRST (2005: 70) has raised the possibility that biopharming could be a source of new classes of antibiotics that could overcome the growing problem of bacterial resistance to conventional antibiotics. However, the farming of plants modified to produce antibiotic substances could in fact aggravate the problem of antibiotic-resistant bacteria by encouraging resistance in populations of soil bacteria or gut bacteria in animals (particularly insects) that feed on these plants. The farming of animals modified to contain antibiotic substances in their blood, flesh or secretions could also aggravate the problem of antibiotic-resistant bacteria by encouraging resistance in populations of soil bacteria or bacteria that are the animal's natural commensals (which may often contaminate food produced from the animals). The degree to which this may be a problem will depend on the scale of the biopharming operations and the longevity of the biopharm organism. Importantly, many therapeutic compounds have antimicrobial properties in addition to their intended purpose (Heinemann et al. 2000). Recombinant human lactoferrin, one of the targets of the AgResearch programme, is one such compound.

### *3.1.3.3. Horizontal gene transfer*

The "generation of potentially pathogenic viruses by recombination between sequences of the vector used to introduce a transgene and related, but non-pathogenic, viruses that might be present in the same animal" (U.S. National Research Council, 2002: 52) is one possible outcome of horizontal gene transfer (HGT). It has been demonstrated in principle using tissue culture cells infected by a natural and a genetically modified vaccine virus that gave rise to different recombinant offspring viruses (Hansen et al. 2004). Interactions between "natural" viruses and the elements of transgenes are already well documented in plants, and there is no scientific basis for not expecting similar types of genetic interactions to occur in animals.

Once a transgene has been placed into a novel context in a new genome, it may have different opportunities for HGT. The plant or animal will be routinely infected by pathogens and parasites that may not have been encountered by the original source of the gene. Each of these pathogens and parasites may become a vector for further dissemination of the gene. Thus, consideration must be given both to a characterisation of

the potential hazards posed by the primary biopharm organism and its escape as well as to the potential hazards of other organisms that might acquire the transgene but are not part of the monitored agroecosystem.

## 3.2. Harm to ecosystems and animal welfare

### 3.2.1. Ecosystems

#### *3.2.1.1. Consumption by other organisms*

Biopharm plants grown in open fields create opportunities for a variety of animals to consume plant material containing pharmaceutical substances. Disposal of "waste" plant material, whether from cleaning equipment or after extraction of the compound, can also create opportunities for such consumption. The impact of this consumption will depend on the substance, the animal, and the ecosystem, and is unknown.

Animal biopharming also creates opportunities for impacts on ecosystems through consumption. Blood-sucking insects and parasites may be impacted in unknown ways by such exposure. Spreading biopharm milk on pasture presents further opportunities for wildlife to consume pharmaceutical compounds.

#### *3.2.1.2. Impact on microbiota*

"Soil-borne communities are dominated by microorganisms, which account for more than 80% of the total biomass in soil" (Icoz and Stotzky 2008: 563). This scale, both in terms of numbers of organisms and in terms of the degree of ignorance about the biology of soil microorganisms, makes monitoring impacts particularly challenging and creates a situation in which impacts may be easily underestimated. It is worth noting that most experiments performed to date examining the impacts of GM plants on soil microorganisms have been conducted at scales that would probably not have detected the impact of antibiotics in causing antibiotic resistance (Heinemann and Traavik 2004). We retrospectively understand the impact those anthropogenic agents have had on microbial communities, but our technology for monitoring has not significantly improved in this regard from that available in the 1950s (ibid: 2004).

#### *3.2.1.3. Impact on wild relatives*

The ecological risks of genetically modified organisms (GMOs) and other exotic organisms include the possibility that they will disrupt ecosystems by outcompeting wild relatives. This is particularly so in the case of plants because of the challenges of containment outlined above. Whether or not a biopharm plant would have a survival advantage over non-biopharm or wild plants depends on many factors (for a review of these factors see Heinemann [2007]), including selection, linkage and propagule pressure. Some oversimplify this risk analysis by reducing it to just a consideration of the selective advantage that the GM plant might have, with or without associated technologies in the

agroecosystem. While such selective advantage may be sufficient to achieve escape, it may not be necessary.

While for the most part, the ease (relative to plants) of preventing or reversing the escape of large terrestrial biopharm animals would mitigate the risks for wild relatives, this is not the case for marine organisms. As a way of addressing this, biotechnology is being used to attempt to effect forms of biological containment of, e.g., GM fish. This is done by inducing triploidy, which "involves manipulating newly fertilized embryos to have an extra pair of chromosomes by applying a temperature, pressure, or chemical shock" (Pew Initiative on Food and Biotechnology 2003: 27) and renders the fish sterile. According to Kapuscinski (2005: 316), this is "[t]he best developed and scientifically documented method for biological confinement of transgenic fish". However "[t]he weaknesses of this method include incomplete success in producing triploids and the fact that the degree of functional sterility in triploids varies depending on the species and sex" (ibid.). Moreover, plants and animals may adapt to these ploidy changes and regain fertility through mechanisms such as chromosome doubling (diploidisation). Diploidisation and sequence elimination are processes common among plants and may occur in animals as well (Eckardt 2001; Lu 2003; Wendel 2000).

While the degree of functional sterility can be increased in some species by also inducing all-female lines, "[t]he environmental entry of large numbers of triploid transgenic individuals on a recurring basis" could itself cause significant ecological harm through courtship/mating displacement of normal individuals and through heightened predation or competition arising from the possibility of sterile individuals growing beyond the normal lifespan (see Kapuscinski 2005: 316).

*3.2.1.4. Marine ecosystems*

The difficulty of containment of organisms in a marine environment and the extent of our ignorance of marine ecosystems mean that risks to marine ecosystems are both real and unknown.

According to Kapuscinski (2005: 316),

> Scientists are poorly equipped at present to provide decision-makers and other interested parties with the information needed for assessing and managing the biosafety of most genetically engineered fish and shellfish. Obstacles to providing this information include key gaps in the scientific knowledge about traits of aquatic GEOs [genetically engineered organisms], the ecology of natural environments these organisms might enter, and interactions between the two. These obstacles are sometimes compounded by a lack of understanding of the biology and ecological role of unmodified counterparts in the ecosystems that transgenic individuals might enter.

For more on this, see Campbell et al. (2008).

### 3.2.2. Animal welfare

#### *3.2.1.1. Target animals*

It is acknowledged that there are significant animal-welfare problems associated with the methods used to generate biopharm animals (Keefer et al. 2007; Laible and Wells 2007; PEW Initiative on Food and Biotechnology 2004; Dove 2000; Fiester 2005). Studies in a range of species have shown that "many clones display various abnormalities" (Laible and Wells 2007: 105). These abnormalities result in high mortality rates and can also result in health problems for surviving animals: "[a]berrations that occur early in embryonic, placental or foetal development may not necessarily prove lethal but may impair health in adulthood" (Ogura et al. 2002; Loi et al. 2006, both cited in Laible and Wells 2007). They can also generate health problems for the cloned animals' offspring (Wilmut et al. 2002 cited in Laible and Wells 2007), that is, the unintended pathological changes can be transgenerational. These aberrant patterns of gene expression in clones, say Laible and Wells (2007: 103), raise "animal welfare concerns that currently limit the acceptability and the applicability of the technology."

Many cloned and transgenic bovine foetuses suffer from "large calf syndrome", a developmental phenomenon that was first noted in nuclear transfer methods used in cattle (Dove 2000; Laible and Wells 2007; Fiester 2005). This syndrome causes dystocia, or difficult birth, for the incubating animal. If the calf is not delivered through caesarean section it can cause suffering and death for the cow and/or the calf. Cows giving birth to cloned calves also "generally show poor preparation for parturition and prolonged gestation" (Laible and Wells 2007: 106).

Also of concern is the much-increased tendency for cows to develop hydroallantois, or hydrops. This develops in the second half of gestation; it usually renders the calf non-viable and requires induced abortion to protect the cow. While hydrops occurs in around 0.02% of naturally occurring bovine pregnancies, 0.07% of artificial insemination cases and 5% of IVF cases, with clones the rate of hydrops occurrence is typically 25%. In response to this, efforts are underway to develop techniques for identifying non-viable pregnancies at an earlier stage (Laible and Wells 2007).

Cloned animals are more prone to musculoskeletal abnormalities and, perhaps particularly significant for biopharming, compromised immune systems. Abnormalities may not reveal themselves before the animal enters a production system, while some epigenetic aberrations may not show themselves in any obvious "external" or phenotypical way (Laible and Wells 2007). (On these and other animal welfare issues see also MoRST 2005; Fiester 2005; Dyck et al. 2003; and FDA 2007.)

Other animal-welfare problems can arise when animals are engineered to produce substances that may in themselves affect the animal.

> [C]ertain bioactive proteins produced in milk can have adverse effects on the animal's health. This is particularly true when they are produced at high

> concentrations and the protein can be reabsorbed. This limits the use of this type of recombinant protein production system [i.e., animal biopharming] to inactive or non-interfering proteins. (Dyck et al. 2003: 395; see also Echelard et al. 2006: 37)

*3.2.1.2. Non-target animals*

As noted above, both animal and plant biopharming provide opportunities for animals to be exposed to the pharmed compound. Such exposures, depending on the compound and the animal, may impact adversely on their welfare.

## 3.3. Economic harm

### 3.3.1. Economic impact of contamination

While food contamination has been discussed as a health issue above, it would also result in economic harms. Existing examples of accidental contamination of the food supply by GM crops may shed some light on the potential costs of such contamination. For example, in 2000 GM Starlink corn, which was not approved for human consumption, was detected in human foods in the United States.[4] It cost approximately US$1,000,000,000 to recall the contaminated food, clean the processing and storage facilities, and settle lawsuits (Smyth et. al. 2002). Japan temporarily ceased importing U.S. corn from October 27, 2000, until they were confident that testing procedures for Starlink were adequate. It has been estimated that the Starlink episode resulted in losses of between $26 and $288 million dollars for growers in the U.S. (Schubbert et al. 1997). [5]

Both the importance to New Zealand's economy of food exports and New Zealand producers' current access to markets seeking GM-free produce suggest that the economic impacts of biopharming on New Zealand could be significant. Engaging in biopharming can be expected to impact some export markets negatively because biopharming uses GM and/or because of the risk of contamination of the exported food with unwanted pharmaceutical compounds. According to an economic study for this project (Kaye-Blake et al. 2008), "[i]f consumers perceive that the potential for biopharming to 'contaminate' food crops is high, then the biopharm crop may have significant negative impacts on the wider agricultural sector." Should a contamination incident occur, this impact can be expected to increase.

Using the Lincoln Trade and Environment Model, Kaye-Blake et al. (2008) conclude:

[4] The Starlink gene Cry9C was found in a sample of Taco Bell shells on September 18, 2000 (Schubbert et al. 1997).. The gene was detected later in other foods.

[5] Mullholland et al. v. Aventis Crop Science USA Holding, Inc. was a case filed by non-Starlink corn growers who claimed damages from contamination. This involved loss of market value as well as storage and transportation costs resulting from contamination (Schmit et al. 2005: 392). The case was settled for $110 million in 2003.

> If … biopharming imposes costs on the agricultural sector or leads to negative consumer reactions …, then it would need to offset those costs in order to have a positive economic contribution overall. The size of the offset depends on the size of the production and consumption impacts. The modelling conducted for this research resulted in lost revenues to the agricultural sector of $133 to $3,352 million annually in current dollars.

This study also examined the impact of introducing GMOs more generally into the dairy sector:

> 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.

Our economic reports (Kaye-Blake et al. 2007; Kaye-Blake et al. 2008) focused primarily on impacts on the dairy sector. However, our interviews with those involved in the seed industry indicated that a contamination episode there could be devastating. The success of the seed industry is based on its ability to consistently produce seed with high levels of purity for elite markets. An interview with a representative of a seed production intermediary company (i.e., those who contract with growers on behalf of seed-company clients) spelled this out.

> There is a lot at stake if we get it wrong. … Contamination. If we got it wrong, we'd destroy our industry. [*So if there was one that got out…?*] And did something nasty. And our customers said 'that's it' – we're history. So whatever we do, we have to be very careful. And with these crops, a lot of these crops we're dealing with, as we've just been talking about, the contamination is potentially a big issue. From where we sit it's much more likely to happen than it is perhaps with a dairy cow. Because of the seed in the ground or the bee flying the pollen off somewhere else. So, it's: be very careful.

A grower also commented on this, extending it to GM production more widely:

> On my cropping programme at the moment, we are getting substantial premiums, and I mean substantial premiums, for being able to guarantee our GE-free status. And so that's why it's absolutely important that if we're talking biopharming …, then suddenly we are going to put pretty much the arable economy at risk. That's where I'm seeing it…. On the oilseed rape for argument's sake: the varieties that we're getting out from Europe – we've just had one of the guys over in Europe, and the Germans, the big breeding companies in there – because a lot of the oilseed rape for Europe is bred in Germany. And they have actually said: we're

> coming to New Zealand for the multiplication, to both get out of season, but [also because] we know we haven't got a cross pollination problem with GE. And at the moment if I grow oilseed rape for biofuel after pressing I can maybe achieve 80c a litre. If I'm growing GE-free and going for the culinary industry now, I'm over $2.

### 3.3.2. New Zealand "brand" damage

Regardless of what one may think of the accuracy of New Zealand's "clean, green" or "100% pure" brand, there is little doubt that damage to this brand is likely to have some negative impact on tourism and export markets.

> 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). … 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. (Kaye-Blake et al. 2007: 12)

Those in the aquaculture industry in particular emphasised the importance of the "clean, green" brand for their exports.

> The New Zealand aspect of our product is very important… New Zealand has a 'clean, green' type image, and the minute you bring GE into it then most of the industry will feel that that will destroy that image, particularly in Europe and The States.

### 3.3.3. Added costs for non-biopharm producers

Even if certain types of biopharming are found by New Zealand regulators to be low risk, and hence requiring minimal controls, overseas markets may force strict procedural standards to demonstrate freedom from contamination. This could mean that non-biopharm farmers in New Zealand are required to perform additional procedures or tests in order to ensure access to key export markets.

Recent events at CRI Plant and Food illustrate this. In the first year of its GM brassicas field trial, Plant and Food failed to remove all living GM brassica plant material at the end of the trial's growing season, and at least one GM brassica plant was permitted to

flower (Williams 2009). As a result, "the operators of the country's oldest organics unit fear it could risk losing its certification" (Radio New Zealand 2009a). There are concerns that "pollen from the flowering plant could have been spread to two certified organic properties which are within bee-flying range of the site" (*ibid.*).

> One of the properties, Lincoln University's Biological Husbandry unit, was growing brassicas, but it is not known whether the other, Heinz-Watties' Kowhai farm, had brassica crops at the time. The chair of the trust that leases the biological husbandry unit, Jon Manhire, says there is a risk the site could lose the organic status it has had since the 1970s. Mr Manhire said if organic certifiers are concerned they may require tests to be carried out to determine whether the crops have been contaminated, which would be expensive and disruptive. (Radio New Zealand 2009a)

### 3.3.4. Opportunity costs

Any calculation of the costs and benefits of using scarce capital in a particular way must take into account the alternative uses to which that capital could have been put. The quantification of such opportunity costs is well beyond the scope of this report. However, it is worth noting that scientists we interviewed were particularly aware of opportunities lost, especially those having what they considered to be more concrete and proven benefits. In addition, the focus of some public research organisations was seen to have been skewed by the "hype" around high-tech developments like biopharming and other biotechnologies to the disadvantage of New Zealand farmers and the New Zealand economy.

> I'll use a good example, actual example of the [CRI GM research programme]. That got huge publicity in the paper. Even if it comes off, it's 10 years before anybody's going to be able to get any value out of that at all. The chances of even getting ahead, starting it, are pretty small. And [the CRI] did a huge amount of publicity on that. Last week [there were] a couple of brassica field days in Southland. They actually forgot to advertise. I've never been in my life to a field days where no farmers turned up…. They were too busy advertising, too busy promoting all the bloody GM stuff. That's never, you know, it's not going to reach the light of day for years, and we had all this stuff which was really good, good stuff that could be taken up today and would benefit every farm in Southland but no farmer turned up because they forgot to advertise because they were too busy advertising this other stuff. Now, I think that that is a good example of not getting the basics right.

## 3.4. Social and cultural harm

Assessing the risk of social and cultural harms is particularly difficult. Social and cultural impacts extend beyond economic returns or employment opportunities to include such things as ability to engage in a valued way of life, community relations, the distribution of harms and benefits, and the socio-cultural implications of the intensified instrumentalisation of life forms. Exploring such harms was not the primary focus of much of our biopharming research. However, socio-cultural issues were strongly represented within the research on Māori assessments of biopharming in aquaculture. The key issues that emerged were the wider implications of damage to ecosystems, the impacts on cultural practices around mana moana and kaimoana, and implications of this for self-determination. The discussion below comes from two project reports, Cram et al. (2008) and Phillips (2008), which address aquaculture in general and as a venue for biopharming. Please see these reports for a more complete exposition.

Mana moana is the right of hapū or whānau to take resources from the ocean, accompanied by the responsibility to ensure the sustainability of those resources for future generations. An example of the wider socio-cultural implications of the marine environment for Māori was set out by Ngāti Kere. In their discussion of their connections with the moana, they note:

> [We] are renowned for our hospitality… We uphold our mana/reputation through the prestige of being able to provide Kaimoana for visitors to the hapü…. (Wakefield and Walker 2005)

Little is understood about the impact aquaculture may have on the values of local communities who have a vested interest in the species being farmed. And if such a species is genetically modified then there are potential impacts on the mauri of the species as well as the areas in which it is grown, as the inter-relatedness of our environment implies that "any mutilation, modification or unnatural desecration of any part affects the whole" by upsetting the balance of the mauri (Greensill 1999). And, as Morgan (2004: 5) writes, "Mauri is the binding force between the physical and the spiritual aspects. When the mauri is totally extinguished, this is associated with death."

Kaitiakitanga of the moana is linked closely to mana moana and is more than a duty of care for the coastal environment; it is about nurturing the inter-relationships between the people and the sea that are sourced within whakapapa in order to ensure that the mauri of the moana is sustained (Wakefield and Walker 2005). This fuller expression of kaitiakitanga is acknowledged by Te Puni Kökiri (2007a), and also by the Aquaculture Steering Group in their ideas about kaitiakitanga designed to seed discussion. These ideas include kaitiakitanga as: mahi tapu, founded in whakapapa, a web of obligations, and enabled through rangatiratanga (cited in Te Puni Kōkiri, 2007a: 22).

An illustration of the interrelatedness of the biophysical and the social is provided by Ngāti Kuri's approach to the environment. According to Ngāti Kuri, the key to reclaiming the physical environment is inextricably linked to the social. The environment impacts on

the people and the people impact on the environment. To halt the degradation and effect positive change, Ngāti Kuri have established Te Tai o Marokura and have implemented an environmental plan called *Te Pōhā o Tohu Raumati* (Te Runanga o Kaikoura 2005), which articulates Ngāti Kuri knowledge, values and practices. Through processes such as these, Ngāti Kuri are not just reclaiming the health of their environment they are also reclaiming their cultural traditions, knowledge and political structures.

*Te Pōhā o Tohu Raumati* is an articulation of Ngāti Kuri's mana whenua/mana moana status and outlines their kaitiaki responsibility which consists of a set of tikanga based policies to guide Ngāti Kuri in to the future – mo tatou, a, mo ka uri a muri ake nei. The Ngāti Kuri environmental plan outlines the core values of Ngāti Kuri, which include:

- Kaitiakitanga – ensuring the health and plentifulness of the environment for generations to come and in the process fulfilling manaaki obligations.
- Rangatiratanga and independence – the exercise of customary authority that enables manaakitanga
- Whakapapa and turangawaewae – establishing history and connection of the people which in turn gives practical expression to kaitiakitanga, whakapaparaNgā (which refers to the way different parts of the natural world speak to one another for example when the karaka trees are blooming it is said that the kina are calling, so it is a time to go diving), mauri and wairua. Values such as whakawhanaungatanga (building relationships) and whanaungatanga (family togetherness) are expressions of whakapapa and along with manaakitanga complete the link between people and the environment.
- Mana of tupuna – honouring the traditions and tikanga of tupuna
- Wellbeing of Ngāti Kuri whanui – includes taha wairua, taha tinana, taha hinengaro, and taha whānau.

Participation in commercial projects was seen by Ngāti Kuri as requiring consideration of more than just commercial returns, such as:

- Knowledge of the company, their ethical practices and procedures were seen as an important consideration when making a decision to participate or not.
- Ngāti Kuri sees the need to be informed about the research and research outcomes so that they can weigh up the benefits and risks of the technology.
- Co-ownership of the research and intellectual property was also considered a priority if it was to go ahead as are appropriate monitoring and managing mechanisms.

Such considerations are about the Hapū maintaining authority and control over anything that has to do with their whakapapa, knowledge and tikanga.

It is worth noting that, of the areas of relevant active research identified by New Zealand marine scientists, the most closely related to our original focus is what could be called non-GM biopharming: extracting naturally occurring compounds from marine organisms to be used for medicinal purposes. A New Zealand example of biopharming is the sea

sponge *Mycale hentscheli* from Pelorus Sound that has been found to have cancer fighting properties (peloruside A) and has potential as a pharmaceutical (Handley *et al*. 2006). As suggested by the discussion above, commodification and commercialisation of marine genetic resources cannot be extracted from issues of mana moana and kaitiakitanga.

# 4. Governance implications

## 4.1. Implications for ERMA

ERMA's role includes the evaluation of the risks posed by hazardous substances and new organisms. Key decisions include whether or not a risk is negligible, and, if it is not, whether or not it is outweighed by potential benefits.

### 4.1.1. Is the context safe enough?

Our research has confirmed that the (harmful and beneficial) effects of technologies cannot be understood independently of their contexts. It is often assumed that the dangers posed by contexts can be mitigated by procedural requirements or controls imposed on the use of the technology. However, our research also raises questions about whether it is practical to assume that mandated controls will be consistently implemented. This, too, will be a function of context, both social and biophysical.

*4.1.1.1. Social contexts*

Relevant elements of social context include: economic incentives and disincentives; ownership and management arrangements; individual assessments of and attitudes toward risks; quality of labour; and the inevitability of human error. These elements can be expected to interact.

*Economic (dis)incentives*

Biopharming for farmers would be an economic activity like any other. This creates a situation in which there may be economic incentives to flout requirements imposed by ERMA. It was suggested in our interviews with farmers that rules are most often ignored when there is an economic incentive not to follow them. A variety of possible developments could result in economic pressures on farmers. As with any product, increased market supply or reduced market demand may erode the profitability of the operation. In the case of biopharming, the existence of potentially competing production platforms could bring about sudden increases in supply (and reductions in price). Biopharm animals may become ill, rendering them an economic liability. Costs to farmers may increase unexpectedly and render the contract less profitable. Such pressures experienced by a farmer directly or through his/her employer could provide an incentive not to follow the rules.

A relevant example that emerged from interviews with dairy farmers of non-adherence to risk-management rules involves herds containing tuberculosis-infected cows. Infected animals must be made readily identifiable, and there are restrictions on their movement. However, our interviews indicated that some farmers flout these rules, moving the

infected herds without informing anyone. It was also noted that ear tags identifying such cows have on occasion been "helped to fall off".

An example in the arable sector pertains to the cleaning of machinery. Our participants in the arable sector acknowledged that it is difficult to ensure that a combine harvester is one hundred percent clean. Grower willingness to clean thoroughly depends on the financial returns:

> People importing combines from overseas, they have them spotlessly clean, but it takes them maybe two days because they're pulling panels out, water blasting things and blowing air out. So the practicalities of spending even eight hours cleaning a combine between crops – it would have to be a good margin and people aren't going to do it just for [pause]. It could be done. So, if the crop is lucrative and someone said 'This is the deal, this is the arrangement that we need to inspect your combine before and after you harvest this crop,' and they say 'Oh, I don't think so.' 'For $20 000 a hectare, would you do it?' 'No trouble at all!'".

However, growers also said that economic pressures might result in them not cleaning harvesters as well as they perhaps should:

> You've got this window of harvest that you can't just wait for weeks and weeks and weeks. Things need to happen quite promptly. And I think because of the present situation, that's where there's room for error and contamination. Cleaning the combine down, maybe a good job does take some hours, but an hour would look pretty good. Are you going to spend another three hours in the sunshine, you could be combining and the rain's forecast for the next day? Probably not. In practical terms, because people would say 'you're right, this combine will be cleaned', but when you think there's only so many days of harvest there…
> [*So people will be quite likely under various circumstances to push it a bit?*]
> I think they would. I can give you the PC answer, 'no, no, we signed the documents and we'll do that.' I think in practical terms corners get cut.

Such incentives are intertwined with ownership and management arrangements and with farmers' own assessments of and attitudes toward risks. Interviews with dairy farmers indicated that farmers are likely to be more meticulous with and committed to animals that they own. In their view, ownership of animals was associated with a higher level not only of care for the animal but also of attention to rules around managing the animals. Several interviewees regarded a scenario in which a manager would run the farm for a corporate owner as potentially risky for this reason. (However, whilst the majority of farmers interviewed agreed that ownership will affect attitude and in turn may affect willingness to follow rules, one farmer believed farm managers would be particularly capable of performing the proper procedures, because of the training and experience they must acquire before being employed as managers.)

Turnover of properties also provides economic incentives not to comply with risk-management protocols:

> They would also have to have some quite strict control protocols, because the farmer might say 'No, I'm not going to spray that. I just bought the farm.' You can see there's going to need to be a contractual arrangement, because a brassica crop could come up in 20 years. So if a farmer deep ploughs it, buries the seed very deep, and then leaves it there and 10 years later ploughs it up again, it will come to life because it's got the warmth and light. … So someone could say they'd check for two years, and there's no volunteers, no contaminants. Now, that would be a really stupid thing to do.

An eventuality that may raise compliance issues, as well as impose costs on government, is the economic failure of the biopharming company that has contracted with the farmer. (Economic failures among biopharming companies have not been unusual; two of this associated with New Zealand, PPL Therapeutics and Pharming, have gone into liquidation.). An example from the U.S. is also illustrative of some of the issues that may arise:

> [I]n 2002, Applicant E [a biopharm company] filed for bankruptcy and, according to a former employee, went out of business, during the postharvest monitoring period of a field test of a GE pharmaceutical crop. Applicant E never paid the cooperator [i.e., the contracted farmer] who was conducting the field test on the company's behalf, and APHIS [Animal and Plant Health Inspection Service] agreed that the cooperator was not legally responsible for monitoring the field for volunteers. Although the cooperator agreed to monitor the field, APHIS may not be able to obtain such assistance in all cases. (USDA Office of Inspector General, 2005)

The fact of economic influences on farmers' and other operators' behaviour has implications for how risk is assessed. Instead of treating the economic dimensions of a proposed activity or organism as a separate issue, quantifiable in terms of economic cost and benefit, they should instead be viewed as integral to environmental and health risks. The farmers' comments illustrate that economic factors may influence behaviour relevant to such risks, such as the ability or willingness to follow safety prescriptions.

*Attitudes toward risk*

Farmers' and other operators' own beliefs regarding the riskiness of an operation may also affect the likelihood that they will meticulously follow risk-management protocols. That is, if a protocol is felt to be arbitrary or out of proportion to the risk as the farmer understands it, it may not be followed. This implies that the effectiveness of controls is to a significant degree reliant on farmer discretion.

One example of this given in interviews with dairy farmers pertains to effluent disposal:

> They think 'oh, this will do'. You know, 'The rules are that strict, but if we do this and this, it might be all right'.

In the arable sector, the demands of production and farmers' confidence in their own abilities may shape attitudes toward following rules:

> Farmers tend – they're practical people cracking on with the job. So they're not looking at their ISO9000 quality control manual… It's not sloppiness or anything like that. But it's just the practical operation of things.

Extrapolating to biopharming, it was indicated that prescribed procedures in relation to escapes of biopharm animals from containment may not be followed. A farmer admitted that he would be unlikely to report any escape of biopharm cows onto his farm because he would not want to deal with red tape and potential monitoring requirements for an eventuality he did not believe was a risk. Thus, in the case of an animal escaping onto his farm, he would be likely to return it (or not) without reporting the escape, even if reporting were required by the risk-management protocols. The economic effects of the requirement to destroy potentially affected animals or terminate pregnancies may reinforce this tendency not to report some kinds of violations. These comments suggest that the effectiveness of containment protocols may depend not only on the biopharming farmer, but on his/her neighbours as well. In this example, protocols around managing escapes may be undermined by a reluctance of neighbouring farmers to comply.

In the arable sector, it was thought that a combination of economic incentives and individual attitude toward risks could provide a vector for the introduction of biopharming into the sector. Some of our interviewees assumed that, even if they would not do it themselves, someone would undertake biopharming despite the risks to the wider industry.

> There's farmers out there that would say 'Oh, there's nothing wrong with it, let's just get into it' without considering what effect that might have on their neighbouring farmers.

> You only need one clown. … The individual, less likely to be a company, but an individual who sees an opportunity. Stupid.

Presumably the same attitudes could also impact on the way an operation is conducted.

The Plant and Food GM brassicas field trial, mentioned above (section 3.3.3), illustrates the impact of attitude toward risk on compliance with risk-management protocols. According to Plant and Food's incident report, there was

> a serious error of judgment by the trial's manager not to follow correct procedures by digging out the plant's stem and roots to prevent re-growth after harvest. That led to serious non-compliance of the trial's consent conditions. (Radio New Zealand 2009b)

Farmers were also found to be resistant to the idea of clearly identifying any biopharm operation through signage. This was due partly to a different evaluation of the nature and degree of risk and partly to disagreement regarding the strategy for the management of risk. Some felt that signage may attract protesters or otherwise draw unwanted attention. On the other hand, lack of signage could create risks by denying relevant information to neighbours and others in the vicinity. Again, the Plant and Food GM brassicas trial is illustrative. In this case the significant compliance breaches were found not by the agency responsible for monitoring compliance, MAF, but by members of the public who were informally monitoring the site. This suggests that lack of signage could create risks by removing the ability of the public to monitor biopharming sites for breaches of risk-management protocols.

*Human error*

Interviews with farmers highlighted the ubiquity of human error and unexpected events. Interviewees could relate a litany of human error that occurs in everyday farming practice. In the dairy sector, interviewees cited the example of cows being milked that were not meant to be, simply through lack of communication or concentration. The milk of cows being treated with antibiotics, for example, is meant to be kept out of the milk sold off the farm, and these cows are marked to indicate this. However, our interviewees cited cases of such markings coming off or just being missed by the person responsible for milking. These errors occur *despite strong economic incentives to comply*: Fonterra and other dairy companies impose heavy financial penalties for farmers whose milk contains antibiotics.

This was less the case with arable farmers, who felt that the SCID system currently functioned well, but even there human error has had an impact.

> We had a case, a whole chapter of errors led to a crop being placed that nobody knew about, right between two of ours. And the only way we knew was when it started to flower, we started thinking: what's that? And what happened there, as I say, because of a whole set of errors, it wasn't picked up. At the end of the day that crop has been taken out, it has been completely destroyed. All the companies involved have had to chip in quite a bit of money to the farmer to say 'well, we've all mucked up. This is the only way out of it.' [*How did it happen?*] Pretty much a difference between an autumn sown crop and a spring sown crop. And I think the firm that placed the crop there were looking at is as an autumn crop. We were probably looking at the isolation as a spring crop, and the two didn't quite gel – I think, more human error than computer error. I think the computer was telling us the right things, but I don't think either party was sort of recognising it as being the right thing.

As with the case of antibiotics in milk, in the Plant and Food GM brassicas trial, the risk-management failures occurred despite a variety of presumably strong incentives to prevent them: the trial was a controversial activity that had received considerable public attention and could be expected to continue to receive public scrutiny; it represented an important component of a long-term, publicly funded research programme that presumably was important to the researchers responsible; and brassicas are associated with a high risk of cross-pollination and seed persistence (as noted in section 3.1.2.1).

Compliance and auditor reports from the AgResearch biopharming containment farm also point to the ubiquity of human error. For example, the auditor's reports show that some milk was sent to a destination that had not requested it, the number of embryos imported and used was not correctly recorded, and semen sent off site for processing into straws was not traced correctly. In addition, the staff training file had not been correctly updated and a new staff member had not been trained correctly about the keeping of lab records (Hale 2006: 46, 56; Operator 2005: 33). As these examples and the improper disposal of genetically engineered pigs at the University of Illinois-Urbana/Champaign

(FDA 2003) illustrate, mistakes are made even in a controlled situation such as a research facility with qualified staff. Many more opportunities for human error will be present on a full-scale commercial farm.

Risk assessment should take human error as given. A similar point is made by Marvier and Van Acker (2005) who list several examples of human error in the containment of corn to suggest that risk assessment should include the inevitability of human error. If, as they suggest, "smart, highly trained, and conscientious people make mistakes, and those mistakes may be repeated and go unnoticed for years" (ibid.: 102), it would seem advisable not only for risk managers but also for risk assessors to consider systematically the implications of human error.

*Labour conditions*

Since even highly trained and conscientious people tend to make mistakes, we can perhaps expect that the tendency for errors would be higher among those who lack appropriate training and/or are not particularly conscientious. Quality of labour, the number of workers employed and high staff turnover rates were all identified by dairy farmers as risk areas for animal biopharming. A 2002 report showed that although 76% of employees in the dairy farm industry had worked within the industry for over a year, only 28% had been in their present job for more than one season (Shearle 2002: 17). This indicates that a high staff turnover rate would be a particular problem that would need to be addressed by farmers, or pharmaceutical companies, who hire farm managers and farm workers.

Training will be a high priority in order to ensure the safety of biopharming, but the high level of turnover may make the implementation of training difficult and costly. Farmers or biopharm companies may not be able to secure staff that can be relied upon to understand and implement detailed controls. Furthermore, there may be little incentive for staff to gain skills that are specific to a biopharming operation since such skills will not be saleable elsewhere. In a situation of staff shortages, workloads and time pressure are likely to increase, making "short cuts" more likely. Alternatively, operators may be reluctant to pay the added costs of well-qualified labour.

The arable sector is also experiencing difficulties in attracting and maintaining good workers. While most arable farms are owner-operated, the trend is toward concentration, and there are also some extremely large corporate farms.

> The number of [seed] growers has declined in recent years, although those remaining are getting larger and more secure. There are concerns about the availability of people skilled in arable farming techniques and the implications for the next generation of arable farmers. A number of young arable farmers and machinery operators are choosing to work overseas where continued long term work can be achieved in comparison to New Zealand's strongly seasonal pattern of employment. Strong competition for labour between the agricultural sectors in Canterbury is also developing. Related concerns are that the arable industry is not

> "glamorous" enough, and there is no obvious career path such as there is in the dairy industry via sharemilking. (MAF 2008b)

All of this suggests that risk assessment may require a more detailed understanding of labour needs and supply and should take into account the likelihood of an operation hiring well-qualified staff.

*4.1.1.2. Biophysical contexts*

Our interviews with farmers highlighted several risk factors to do with the location of biopharms. Arable farmers identified opportunities for cross-pollination represented by strong winds, the presence of related crop plants or wild relatives, and animal and insect populations. Vulnerability to flooding and fire is also relevant. A dairy farmer described the level of disorganisation that occurs during a flood, in which normally controlled environments are disrupted, and animals from different farms may become mixed together. Flooding of a plant biopharm would create opportunities for dispersal of plant material. Interviewees in the dairy sector also emphasised the importance of soil characteristics. In order to minimise the impacts of biopharming on groundwater systems, soils should be deep and free-draining; in order to minimise impact on streams, clay soils, which result in greater run-off, should be avoided.

Those in the arable sector generally viewed complete containment in open field conditions as impossible due to the impacts of wind, insects, birds and other animals. However, even in greenhouse conditions, there is the possibility of escape:

> We have net houses…. And the net houses are translucent, fine mesh that we put over the trials, and put a beehive inside. Now everything inside is internally pollinated and there's no contamination. Now, when I say 'no', I'm sure when you open the flap, two or three smart-alec bees take off, and go and visit some flowers. So nothing's 100%.

As noted above, marine environments were seen as unsuitable for activities requiring containment.

Microbial communities, an element of biophysical context, may also limit the kinds of pharmaceutical substances that can, or should, be produced through biopharming. As noted above (section 3.1.3), biopharming may increase antibiotic-resistance among bacteria exposed to some types of biopharmed organisms.

### 4.1.2. Assessing benefit to New Zealand

Benefits claimed for scientific research not yet carried out are necessarily speculative to some degree. However, this does not mean that these claims should not be thoroughly scrutinised. As this research has shown, quite compelling prospective benefits may turn out, on closer examination, to be less convincing.

We note that in ERMA's 2002 decision to approve AgResearch's work with biopharm cattle, it argued:

> AgResearch is a reputable research institution and has invested considerable funds in this work. It would be unlikely to do so without some assurance of benefit. Because AgResearch is a CRI owned by the Government there is also some assurance that the benefits will accrue to New Zealand. (ERMA 2002)

We suggest that this reasoning is unsound and that, given the current structure of the science sector in New Zealand, it cannot be assumed that benefits to a CRI, even if these are realistically anticipated, equate to overall benefit to New Zealand (see Davenport and Bibby 2007).

### 4.1.3. Current risk-management protocols

#### *4.1.3.1. Monitoring for "volunteers"*

We note that ERMA's 2007 approval of the Crop and Food GM brassicas trial imposed, in addition to the controls whose violation was discussed above, a requirement "to monitor the field test site for one year after the last brassicas have been removed to look for any 'volunteer' GM plants" (ERMA 2007). We also note that Plant and Food, in its response to the discovery of breaches of the trial's operating conditions, "recommended its trial be closed down and the site monitored for a year to ensure no new genetically modified plants grow back" (Radio New Zealand 2009b). According to those with long experience in the arable sector whom we interviewed, brassica seeds can persist and remain viable in the soil for at least 20 years. We recommend that time periods during which operators are required to monitor for volunteers be revised to reflect this practical knowledge. We also recommend that risk assessments take into account the ability of some seeds to remain viable in the soil over extended periods of time.

#### *4.1.3.2. Monitoring for compliance*

The monitoring of operators for compliance with controls set by ERMA is the responsibility of the Ministry of Agriculture and Forestry (MAF). According to ERMA's *Guide to the Hazardous Substances and New Organisms Act 1996 for Enforcement Agencies* (ERMA 2001: s3): "The regime set up under the HSNO Act places a much greater emphasis on industry users of approved hazardous substances or new organisms and the community taking responsibility for their own actions." In the case of GM field trials, the regime is relatively prescriptive in its specification of operating procedures, but the monitoring process relies to a significant degree upon operator self-reporting. The findings presented in section 4.1.1. as well as the case of the Plant and Food GM brassica trial suggest that this approach may need to be reconsidered.

With regard to the Plant and Food trial, it is not clear why a MAF inspection was not made to check that the GM plant material had been removed as required at the end of the growing season. Biosecurity New Zealand's *Standard 154.03.01: Supervision of*

*Containment Facilities* (Biosecurity New Zealand 2005) stipulates with regard to field trials of annual plants that:

> On-site audits shall occur at a minimum frequency of three times within a 12 month period of the crop being planted in the field unless otherwise agreed with ERMA New Zealand and directed by Biosecurity New Zealand. Audits shall occur at an exact time of choosing by the inspector, during each of the following periods:
>
> - Planting/sowing/germination in the field;
> - Flowering (or as agreed with ERMA New Zealand where reproductive structures are removed in advance);
> - Harvest, final removal and destruction of reproductive plant material from the field test area.

In this case, the field trial site presumably was not inspected post-harvest; had it been, it would have been obvious that the operator had not complied with the requirement to remove all living GM plant material. ERMA's approval of the field trial included the following provisions:

> 6.2 The MAF Inspector may inspect and audit the field test site at any time to ensure the field test site is complying with this approval. The Operator shall arrange for inspection of the field test site and auditing of its operation to occur: (a) twice during the growing season, including at least once during the period when flowering could occur; and (b) once during the winter season if GM brassicas are planted in the field test site over the winter.

It is not clear why these terms were less prescriptive (with regard to the timing of on-site audits) than the generic terms contained in the *Standard*.

ERMA's approval of the field trial also stipulated that:

> At the end of each growing season, the entire field test site shall be monitored monthly to detect any GM volunteer plants. A log of these monitoring events shall be maintained and it shall record the date, details of any GM *Brassica* plants found and any action taken. Any volunteer GM plants found shall be removed and killed in accordance with control 1.12.

The decision to behead the plants rather than remove them together with the apparent weediness of the trial plot during this post-harvest monitoring period would have made it difficult to identify volunteers, if indeed these monthly inspections were carried out. Again, this would have been evident had an on-site inspection been carried out by MAF.

It is unclear to what extent inspectors' own evaluations of the risks and possible benefits of the field-trial activity can influence an inspection regime. According to ERMA's *Quick Guide to Enforcement and Compliance for New Organisms*:

> Enforcement officers will visit premises from time to time to check that controls on new organisms are being complied with. The frequency of inspections should reflect the risks involved – high risk situations should be checked often, while low risk situations may be visited on a less frequent basis. (ERMA n.d.)

This is consistent with the approach taken in the *Guide to the Hazardous Substances and New Organisms Act 1996 for Enforcement Agencies* (ERMA 2001), which makes it clear that enforcement agencies and their inspectors are expected to exercise their own judgement as to the intensity of monitoring and other enforcement activities.

> The level of enforcement should reflect potential risk to people and the environment if the Act is not complied with…
>
> Costs of enforcement should relate to the benefits of compliance. For cost-benefit reasons the level of inspection will never provide 100% coverage or the maximum possible intensity. However, the level of enforcement should ideally be such that the cost of enforcement should be balanced against the potential benefits of increased enforcement activity.

Guidance for inspection regimes for GM field trials (and commercial releases) may be more prescriptive than this; if it is not, we recommend that a more prescriptive approach be taken to on-site inspection, particularly in the case of biopharming activities.

### 4.1.4. AgResearch applications GMC07012, GMD07074, GMD08012, GMF07001

The research underpinning this report is directly relevant to the four concurrent AgResearch applications GMC07012, GMD07074, GMD08012, and GMF07001. Overall, our findings contest the applicant's assertion that risks can be assessed on a generic basis, without specification of the organism, the compound produced, the site of the activity or the ownership and management structure of the operation. As we have demonstrated above and in other reports in this series, our research has found that risks and benefits cannot be competently assessed independently of the specifics of the activity and of the context in which the activity will occur.

Further, the applicant claims an extraordinarily wide range of potential benefits. Because the scope of the applications is so broad and open-ended and ranges from basic research to commercial production, the claimed benefits can be considered to be within the scope of the applications. However, the applicant does not commit to any specific activity that would generate the benefits claimed. This means that, precisely because the applications are so open-ended and under-specified, the benefits are purely speculative and the likelihood that they will be attempted, let alone achieved, cannot be evaluated.

## 4.2. Implications for iwi governance

Ensuring appropriate mechanisms for safeguarding Māori cultural, environmental and developmental aspirations and enabling Māori engagement in biotechnological ventures such as in aquaculture cannot be understood outside of both collective and individual Māori cultural, social, political and environmental contexts. These contexts in turn are shaped by broader socio-political and legislative contexts such as the Treaty of Waitangi Act 1975, the Office of Treaty Settlements and the Fisheries Act. Our research indicates that the legislative parameters that iwi operate within, the relationships between iwi and hāpū, and the lived realities of whānau makes Māori involvement in aquaculture development and biopharming fraught. Of particular concern is the potential use of biotechnologies to advance aquaculture development and the impact (both positive and negative) that such technology may have on hāpū and iwi rights as mana whenua/mana moana to practice and fulfill kaitiakitanga obligations. Despite policies and legislation that promote Māori involvement in the aquaculture industry it is questionable whether hāpū and iwi are able to participate in ways that fulfil their cultural, environmental, and development aspirations.

Our research also calls attention to the question: 'who decides upon the issue that is to be consulted upon (or researched)?' While our initial focus in this part of the project was Māori assessment of marine biopharming, those with whom we spoke indicated that there were prior issues around Māori involvement in, and the impacts upon Māori of, aquaculture, as well as broader governance issues, that would first need to be addressed. This section of the report explicates some of those issues, which form a key part of the context for (marine) biopharming in New Zealand. Biopharming in this discussion includes the non-GM biopharming discussed in section 3.4.

### 4.2.1. Legislation and iwi governance structures

Traditionally hāpū were the central mechanisms for Māori political and social organisation; however, since colonial times there has been an ongoing shift to legislatively designed and defined governance structures. Moreover, according to Durie (1997) it is only in the last twenty years through the establishment of the Waitangi Tribunal and the settlement of claims that iwi governance has developed. These contemporary governance structures are based not on traditional governance structures but rather on legal-rational bureaucratic ones. Waymouth (2003) writes that "law appropriate to a liberal-democratic western society, and commercial practice to a corporation in a world of global corporations, have replaced the world of tradition and locality". The point to highlight here is that irrespective of the mechanism through which hāpū and iwi are governed, they have all become determined and controlled by government legislation. This in itself impacts on the ability of hāpū and iwi to determine and control their own resources, let alone futures. Since 1840 and up to the present day this struggle is well documented through Māori challenges and resistance over the appropriation of land, sea, cultural and intellectual property, and, of particular relevance to this research, over fisheries resources and knowledge. According to Dodd (2002) there

is a lack of cultural match between traditional authority and governance structures and western-centric models.

The main mechanisms through which hāpū and iwi are governed today include:

- Structures under the Te Ture Whenua Māori Act 1993, e.g., Ahu Whenua Trusts. While these have been established to halt further land fragmentation they are not fully representative of iwi and come under the control and scrutiny of the Māori Land Court.
- Māori Trust Boards under the Māori Trust Boards Act 1955, e.g., Te Runanga o Ngāti Awa. These have limited power and are accountable to the Minister of Māori Affairs rather than to beneficiaries.
- Incorporated Societies under the Incorporated Societies Act 1908, e.g., Te Kauhanganui o Waikato. Incorporated Societies are well known and understood but are not necessarily representative of iwi. Each beneficiary must register.
- Company Structures under the Companies Act 1993, e.g., Tainui Development Corporation Ltd and Ngai Tahu Development Corporation. These provide legal and commercial certainty but there is difficulty in identifying shareholders.
- Private Statutory bodies, e.g., Te Runanga o Ngai Tahu. These are established by special legislation which theoretically allows for iwi control. However they require government agreement with iwi needing to show they have approved mandating and governance structures in place.
- Trusts created (by Deed) under the Trustee Act 1956, e.g., Te Runanga o Ngāti Ruanui Trust. While there is flexibility in the deeds substance they are finite structures. Sources: Dodd (2002) and Royal and Stone (2003)

Whilst it is argued that the current governance models provide flexibility, clear rules, reporting and accountability within the context of individual shareholding and rights, they are unable to take into account Māori collective values and practices. This is problematic given that hāpū and iwi assets, including settlement proceeds, are collectively owned by virtue of whakapapa. Furthermore hāpū and iwi have multiple objectives that not only include maintaining the asset base but also ensuring representation, wealth redistribution and cultural objectives (Dodd 2002). This has particular implications in the post treaty settlement era.

One example of iwi becoming a corporate body through an act of parliament is Ngai Tahu with its governing body Te Runanga o Ngai Tahu Act 1996. Te Runanga o Ngai Tahu (TRONT), the central governing body, came into being to manage the assets and to distribute settlement benefits back to their people. In doing so, Ngai Tahu identity and belonging (to one of 18 papatipu runanga) has been shaped by the provisions in the Act. As the governing body TRONT ignores claims by the various hāpū to autonomous governance. In doing so, Waymouth (2003) argues, it represents a shift from whakapapa-based organisation to a legal corporate structure. This has led to tensions between hāpū and TRONT over some key issues, such as TRONT's economic imperative, the growth of legal-rational organisation, and its accountability back to local communities (Waymouth

2003; Phillips 2008). This has implications with regard to the nature of the relationship Crown agencies have with Māori communities and which communities they have relationships with. Legally the Crown is obliged to consult with and have relationships with iwi. However iwi are removed from hāpū and the everyday lives of their communities. This in turn impacts the very heart of Māori identity and belonging, privileging the political entity of iwi over hāpū and whānau authority.

### 4.2.2. Waitangi Tribunal

The Waitangi Tribunal, through the Treaty of Waitangi Act 1975, was established to hear claims brought by Māori of breaches to the Treaty of Waitangi. Initially the Tribunal was charged with hearing post- 1975claims, but in 1985 the Tribunal's jurisdiction was expanded to hear historical claims backdated to 1840. As of February 2008 1,430 claims had been lodged with the Tribunal (Waitangi Tribunal 2008). Whilst most claims are lodged by hāpū/iwi (some are by individuals or are pan-Māori in nature), the actual claimants are required to be individuals who claim on behalf of the collective group. Most importantly, Tribunal recommendations do not have any legal teeth. The Waitangi Tribunal only hears claims whereas the Office of Treaty Settlements, on behalf of the Crown, negotiates the terms and amount of redress.

The total amount of money set aside for settlements by the Crown was capped by the National government in 1995. This cap known as the 'fiscal envelope' was widely rejected by Māori, however successive governments have retained it. This has raised the issue of the equity of settlements. For example there has been an increase in the level of assets held by those iwi who have settled with the Crown that gives these iwi a head start in establishing their economic base.

Further, despite the Tribunal being a permanent commission of inquiry, the government has signaled a deadline for submitting claims. This possibly opens the way for further grievances given that it claims to be working within and giving effect to the principles of the Treaty, of which one is partnership. Yet the government continues to make unilateral decisions not just about the future of the Tribunal but also its outcomes.

Despite this the Tribunal remains an important mechanism for Māori, in which their grievances are heard and deliberated on. However, it is questionable as to how well it works for Māori given that (1) the Tribunal does not have teeth, (2) it operates within individualistic legal frameworks, and (3) its processes and outcomes, indeed its fate, are determined by government.

### 4.2.3. The Office of Treaty Settlements

The Office of Treaty Settlements (OTS) was established in 1995 within the Ministry of Justice to firstly, assess the mandating processes of iwi (Deed of Mandate) and ensure that iwi have appropriate governance structures in place to deal with settlement assets, and secondly, to negotiate and implement settlements (Deed of Settlement). They also advise the government on Treaty issues, including the government's overall strategy for

settling claims and the acquisition, management, transfer and disposal of Crown-owned land in settlements. Recently the Crown has enabled direct negotiations with iwi where there has been an acknowledged breach. Direct negotiations are made with OTS.

It is through the mandating process and the acceptance of an iwi's Deed of Mandate that an iwi claimant's geographic boundaries are determined, and the processes for mandating and accountability to the wider iwi are established. Within this framework it is clear that OTS and the Crown prefer to deal with iwi rather than hāpū (Office of Treaty Settlements 2002). Iwi representatives who are charged with obtaining the mandate from their members are accountable not only to the iwi but also to OTS with regard to ensuring that the agreed mandating processes are conducted and the monies given for mandating processes are correctly used.

The agreed redress between iwi and the Crown is contained in the Deed of Settlement. This reflects the quantum settlement that is agreed to along with the nature and scope of any other forms of redress, including cultural redress and the Crown's apology. The Deed of Settlement is required to be taken back to the wider iwi for ratification.

OTS also requires an iwi to establish a governance entity to hold and manage settlement assets. While the type of governance structure is left up to the iwi to determine, OTS nevertheless assesses them to ensure that they:

- adequately represent all members of the iwi;
- have transparent decision-making and dispute resolution procedures; and
- are accountable back to iwi members.

These governance structures are enshrined in legislation. Since 1989, 23 settlements have been legislated including the 1992 Commercial Fisheries settlement.

### 4.2.4. Fisheries Settlement and Te Ohu Kai Moana

Te Ohu Kai Moana Trustee Ltd (TOKM) was established by the Māori Fisheries Act 2004 to look after the assets arising out of the fisheries settlement until such time as iwi have met mandating and governance requirements to take over their share of the settlement. Prior to the Act TOKM existed as the Treaty of Waitangi Fisheries. TOKM currently comes under jurisdiction of the Ministry of Fisheries. Once iwi have received their share, TOKM will "continue to administer new quota … and supervise quota sales" (Te Ohu Kaimoana, nd.). TOKM's fisheries jurisdiction was expanded to include the aquaculture settlement arising out of the Māori Commercial Aquaculture Claims Settlement Act 2004. The Takutai Trust was established to administer the aquaculture settlement assets – that is, for receiving and allocating commercial settlements to iwi.

Under the legislation, iwi with coastal boundaries will receive 20% of new aquaculture space created after 1 January 2005. They will also receive 20% of pre-commencement space, that is, space created between 1992-2004 under the old legislation. Given the restrictions on existing space the allocation may be made up of additional new space, the

Crown buying existing farms or the Crown providing a cash equivalent. Any space should be of a size that is economically viable and "not have less than average productive capacity" (Te Puni Kōkiri, 2007a).

All space, both existing and new or farms that have been purchased or cash equivalents are held in trust by TOKM until such time as iwi satisfy certain conditions for the assets to be transferred to them. Iwi are required to establish a mandated Iwi Aquaculture Organisation (IAO). Despite this, assets are allocated on a regional rather than an iwi basis.

Iwi who have coastal boundaries are eligible to receive aquaculture assets. These iwi need to be one of the 57 that the government recognises. This in itself has been and continues to be challenged by hāpū and iwi. Established IAOs must act for the benefit of all their members and are responsible for establishing commercial entities to manage their allocated assets. However, because assets will be distributed regionally, iwi are required, where there are multiple iwi in a region, to come to an agreement on how their region's assets will be proportionally divided. Some iwi have taken a mana moana approach while others have taken a straight commercial settlement approach. If iwi cannot decide for themselves, then TOKM will determine the allocation based on iwi claims to coastline. Once this is determined, iwi then have to decide how the actual assets will be allocated.

There is tension in TOKM's dual role of being a trustee for Māori fishing interests on the one hand and answering to the Crown on the other. The potential for conflict also exists within TOKM due to its responsibility for advancing fishing as well as aquaculture interests. There is an inherent tension between aquaculture and commercial fishing because aquaculture takes up space where fishers already have the right to take fish. To that end fishermen argue that they have prior property rights. Commercial fishing and aquaculture are seen to be mutually exclusive activities. This has implications for the establishment of new aquaculture space given the undue adverse test that it has to undergo. According to TOKM, fishing interests have the upper hand as applications for new space have to get 90% of fishers'/quota owners' agreement. In effect they have the right of veto. TOKM is placed in a delicate position because it is charged with looking after fishing and aquaculture interests at the same time as "balancing the value of one against the other".

Adding to this tension is the differential value and commercial viability of fishing and aquaculture. Currently there is more value in fishing than there is in aquaculture with most of the aquaculture species currently being farmed having relatively low value compared to those that are fished. Therefore it is argued that the value of the fisheries settlement is higher than the value of the potential aquaculture settlement.

#### *4.2.4.1. Aquaculture Management Areas*

Regional Councils in consultation with community and interested parties are responsible for determining and establishing the Aquaculture Management Areas (AMA) within their

regions. The establishment of AMAs is a lengthy process. Firstly, AMAs must be specified in the regional council's coastal plan. These are either specified by the council itself or through a private plan. Secondly, while the creation of AMAs is provided for in the Resource Management Act 1991 (RMA), it is also required that they do not adversely affect customary, recreational or commercial fishing nor adversely impact on the environment. Thus they undergo a test (Undue Adverse Test), which is administered by the Ministry of Fisheries (MFish) (Ministry of Fisheries 2007). Finally, the plan requires the Ministry of Conservation's approval before it comes into being.

The establishment of AMAs has been slow. One reason for this is outlined above (see Section 4.2.4). In 2008 the Government consulted with Māori in order to progress aquaculture settlement. Māori are involved in both ends of this process. Not only are they required to be consulted under the RMA, they are also potential owners of the space.

### 4.2.5. Māori Engagement in Aquaculture

Underpinning the settlement of claims is the expectation by both the Crown and Māori that settlements will enable development by providing the necessary assets for that development. Relevant to this research is the expectation that the fisheries settlement provides Māori with the necessary resources to engage in aquaculture development. This is articulated in the government's push for the development of Māori participation in aquaculture (Ministry of Economic Development 2007) and the allocation of space in the aquaculture settlement. However, Māori participation remains problematic for a number of reasons. First even if iwi were keen to participate in aquaculture, the lack of space inhibits their participation. Second is the expense of establishing new aquaculture ventures with their high compliance and set-up costs and the expertise and experience required to profitably run them, notwithstanding the low returns for the species currently farmed and fluctuating market conditions. For those iwi who have not yet settled, the costs and lack of resources may make participation not just impracticable but also not a high priority. Third is the high cost in terms of time and resources in consultation with regional councils, industry and other government agencies such as ERMA.

There are real disparities of wealth and resources between iwi. There are also differences between iwi with regard to their level of political organisation and voice. Post-settlement iwi and those who are well organised and/or who are resource-wealthy have established plans and mechanisms for development, including environmental plans and in some instances specific aquaculture plans. This, in turn, enables their participation or potential participation in aquaculture development or in engagement on issues of cultural and ethical appropriateness of biotechnological development.

For many hāpū and iwi participation in aquaculture may mean partnering with industry (Te Puni Kōkiri 2007b). Such partnerships contain potential advantages for both industry and iwi. The New Zealand Aquaculture Strategy (Burrell and Meehan 2006: 14) states that "iwi have a range of interests as tangata whenua… [that] make them vitally important partners and allies in the regional development of aquaculture". Similarly the Government acknowledges the value of Māori knowledge of local fisheries to the

aquaculture industry. A key focus in the Government's *National Aquaculture Position Statement* is the importance of collaboration and relationship building to ensure the industry's growth, innovation and sustainability. While there may be benefits for both Māori and the industry it may also mean that Māori need to be wary of sharing their intellectual and cultural knowledge with those who may not value it other than for commercial purposes. This has implications for Māori safeguarding their taonga species that are potentially valuable because of their pharmaceutical and nutriceutical properties.

More importantly, and irrespective of whether or not iwi have settled, it is at the hāpū level that Māori are more likely to be politically and socially engaged and aligned. However, it is at the level of iwi that the Crown and government agencies are impelled to relate and consult. It cannot be assumed that iwi and hāpū have the same aspirations or ways of thinking about issues. There is a potential (and often real) disjunction between the outcome of consultation between the Crown and iwi, and the hāpū who are affected by the decisions. If the relationship between iwi and the Crown is fraught it can be argued that the relationship between hāpū and iwi is equally fraught.

In the context of this research it is the local and the traditional which hāpū *and* iwi have expressed as important and enduring in their sense of identity and fulfilling their kaitaikitanga responsibilities. Yet one of the primary responsibilities of contemporary governance structures is to look after tribal assets. Despite the prominence given to tribal values and tikanga, profits and economic development have tended to come first in the post-settlement iwi structures (Waymouth 2003). This has been driven by the economic imperative written into contemporary iwi governance legislation. As a result there is a cultural mismatch between hāpū and iwi aspirations and the governance structures put in place to advance those very aspirations. In the absence of cultural integrity, economic development and profitability is meaningless. Moreover iwi and their codification have been designed to meet government agendas rather than Māori ones (Maaka 1998).

### 4.2.6. Conclusion

The Crown has a duty to consult with Māori. Iwi (and hāpū) who have settled with the Crown have legislative constraints as to how they operate, yet iwi (and hāpū) are also governed by their collective knowledge and tikanga base. Legislative imperatives are not necessarily aligned to hāpū and iwi cultural imperatives. Nor are iwi and hāpū aspirations and practices necessarily the same.

While iwi and hāpū operate within tikanga and legislative constraints and directives, Māori private organisations and individuals face no such constraints to participate in aquaculture ventures or the development of biotechnologies. Thus it could be said that collective interests are controlled whereas individual interests, other than those that all New Zealanders face, are not. There is a tension between the fulfillment of collective aspirations of Māori and New Zealand's individualistic and bureaucratic political economy.

The Crown's aquaculture settlement process is focused solely on commercial aquaculture settlement. Customary aquaculture practice does not come under TOKM's jurisdiction. Currently no plans exist that allow iwi to develop aquaculture practice for customary purposes. Legislative change would be required to enable this to happen.

Dodd (2002) argues that successful iwi development is not about how much money an iwi has nor about where the development is located, rather it is about the type of organisations iwi build, the strategies they put in place and the kind of leadership that takes them into the future. Further, she argues that the true test of good governance is the extent to which it fulfils the civil, political, economic, social and cultural rights of iwi and their members. More importantly, she challenges the idea that the Crown enables Māori development through the capitalisation of treaty settlements, given the highly privatised and individualised outcome of the settlement process.

## 4.3. Implications for private governance systems

### 4.3.1. Audit systems

The 1990s saw the emergence of a new retailer strategy that achieved higher market share by promoting values like food safety and sustainability. What emerged was a form of food 'audit culture' that began to serve as a key market gateway into high-value markets like the ones serviced by many New Zealand food exporters. This audit culture in key export markets became most noticeable in New Zealand with the steady emergence in the 1990s of new private sector-derived forms of audit, Quality Assurance (QA) and other governance schemes in agricultural export chains (Wharfe and Manhire 2004; Le Heron 2003, 2005; Busch 2000; Busch and Bain 2004; Hatanaka et al. 2005). Some researchers have described this regulatory shift as emblematic of a wider power shift from agricultural exporting and production companies to food retail corporates (Burch and Lawrence 2005). This is manifested in an increasing sense that it is food retailers and not food producers who are now defining what is and isn't acceptable in terms of food production and management techniques (Campbell and Le Heron 2007; Codron et al. 2005; Fulponi 2006).

As a result, some New Zealand exporters began to experiment with alternative strategies of crop management (Campbell and Rosin 2008). For example, Zespri International Ltd encouraged growers into organic production between 1992 and 1997. By 2000, it had converted 5% of production into certified organic systems. Alongside Zespri, a similar process was taking place in the apple, processed vegetables, wine, and honey industries. In 1994, organic exports were valued at NZ$3 million. By 2007 they had exceeded NZ$120 million – almost all of which had grown up under the aegis of corporate exporters. In 2007, nearly 1000 producers were operating under certified organic systems (Grice et al. 2007).

Alongside organics, Integrated Pest Management (IPM) provided an alternative, more mainstream, pathway towards 'greener' food production. IPM provides a set of scientific

techniques to produce fruit with negligible chemical residues (Morris and Winter 1999). Eliminating hard sprays, it uses a combination of soft sprays and entomological science to manage pest thresholds on fruit with the intention of reducing pesticide residues on harvested fruit. In 1994, the kiwifruit industry developed an IPM system called KiwiGreen and by 1998, the entire kiwifruit industry was either KiwiGreen or organic.

The IPM system behind KiwiGreen has now evolved towards a much broader and heavily audited system of production, including soil, water, and energy audits in some sectors. Key industries, like kiwifruit and apples, have simultaneously integrated themselves with emerging new international environmental audit alliances like GLOBAL-GAP (formerly called EurepGAP), which is operated by the 30 largest supermarkets and cooperatives in Europe. GLOBAL-GAP protocols for sustainable production of fruit and vegetables are enormously dense and wide-ranging, yet provide the key to elite market access for food exporters. By 2003, GLOBAL-GAP had signed up over 200 companies as suppliers (including the entire kiwifruit and apple export industries in New Zealand) and has certified over 12,000 fruit and vegetable producers as fully compliant to the GLOBAL-GAP protocols (Campbell 2005; Campbell and Le Heron 2007).

While certified organic and Integrated Management via systems like GLOBAL-GAP have been influential around issues of environmental qualities in food exports, new forms of export governance around QA systems have proliferated among all export chains (Wharfe and Manhire 2004). For food export industries seeking to supply high-value markets, new forms of audit-based governance have become essential gatekeepers to market at multiple levels of the export chains. The question raised, then, is: how might exporters seeking access to high-value markets be affected by the participation of the New Zealand farming sector in biopharming?

Exporters now must prioritise issues of market access alongside other product attributes when developing new export products. Prior to the emergence of the new food audit culture, New Zealand's export products succeeded mainly through a combination of price competitiveness and particular quality attributes. Now, market access has become a third key criterion alongside these other two recognised attributes of export product success. Biopharmed products have the potential to raise three issues around the emerging necessity to preserve market access for exporters:

1. Biopharmed products themselves will be required to meet strict standards of safety and risk management in order to achieve market access.
2. Other non-biopharmed products produced by the same company will face increased scrutiny and risk of rejection, and companies will have to maintain strict protocols of containment.
3. Other companies exporting products will have to implement measures to ensure that there is no cross-contamination of products in the same ecosystem.

Of these three, different issues arise in the contexts of marine biopharming, dairy and seed industry applications. Dairy has relatively lower levels of concern over containment (although by no means absent) while marine and seed applications face major

containment problems. The problem of containment of biopharmed products in marine environments is already well established in this and previous reports. Hence, it is challenging to conceive of containment protocols and measures that would guarantee that non-biopharmed products were not compromised by the presence of biopharmed products in the same marine ecological zone. This would pose an important threat to market access for marine exporters should biopharmed products be introduced into important production platforms like the Marlborough Sounds.

Similarly, the seed industry is able to guarantee a very high level of seed purity, but, despite the application of SCID (see below), is not able to guarantee complete absence of contamination. Thus major challenges would emerge around managing the potential market impact of introducing biopharmed seeds into a key production region like Mid-Canterbury.

The greater likelihood of establishing containment around dairy facilities means that the export industry is more likely to face a less direct threat – that emerging from the increased cost and compliance requirements needed to guarantee risk management of products from the same company going into sensitive markets.

In all these three scenarios, the existence of complex gateways to market governing access to high value customers means that introduction of biopharmed products must be carefully evaluated in terms of the potential economic risks to both the companies producing such products and also to other exporters inhabiting the ecological production zone.

### 4.3.2. Seed Crop Isolation Distances (SCID) system

The SCID system was developed as an industry initiative to deal with problems emerging from the substantial increase in specialty vegetable seed production in the Canterbury region in the 1990s. Specifically it was developed "to maximise high value cruciferous and vegetable seed crop production by minimising the cross pollination risk when flowering" (AssureQuality website, n.d.).

The SCID system was a response to the absence of state regulation in this area.

> In fact the seed industry in New Zealand is – there's absolutely no legislation around it at all, other than biosecurity. So most countries around the world have pretty strict rules about what you can sell, what you can't sell, what you can do and what you can't do. But we're really laissez faire here, other than for biosecurity. (Interview, arable sector)

Or, as the Ministry of Agriculture and Forestry puts it: "In New Zealand the regulatory environment for seed is unique in that it has no laws specifically governing the domestic production, certification or marketing of seed" (MAF 2008b).

Participation in the SCID system is voluntary. Participants enter details of seed crops, including type of crop and location of planting, into a web-based programme that uses a GIS mapping system. The programme warns participants of potential crop isolation conflicts.

The following species are currently included in the SCID system:

| **Brassica** | **Species** |
|---|---|
| Campestris | Chinese Cabbage, Pak Choi, Choi Sum, Rape (Canola / Oil Seed Rape), Turnip Rape, Mustard, Turnip, Swede |
| Oleracea | Cabbage, Cauliflower, Brocolli, Brusselsprout, Chinese Kale, Forage Kale, Kohl rabi |
| Raphanus sativius | Radish |
| Juncea | Brown Mustard |
| Nigra | Black Mustard |
| | |
| **Other Families** | |
| Beet | Red Beet, Silver Beet, Sugar Beet |
| Sinapis alba | White Mustard |
| | Carrots, Celery, Lettuce, Onion, Parsley, Spinach |
| | Chrysanthemum |

Source: http://www.seedlab.co.nz/seed_news/seed_crop_isolation_distance_system.cfm

While those in the sector we interviewed approved of the SCID system, a number of problems that have implications for biopharming have arisen in connection with it. The first of these is the SCID system's voluntary nature. As noted above, growers believed there would always be individuals who would respond to individual economic incentives to plant a crop, regardless of the impact on the wider industry. Such a crop would not necessarily be registered in the SCID system.

Unregistered plantings of canola (or oil-seed rape, a brassica) are seen as a particular threat, given its ability to cross-pollinate with other brassicas over long distances and the long-term persistence of viable seed in the soil (see section 3.1.2.1). Solid Energy's Biodiesel New Zealand announced in 2007 that it would neither contract for canola crops in mid-Canterbury "to prevent rape seed straying into export vegetable-seed crops" nor buy spot crops or canola oil from non-contracted growers; it would also require its contracted crops to be registered with the SCID system (Cronshaw 2007). The New Zealand Grain and Seed Trade Association's response to these moves indicated ongoing concerns:

> We still have concerns that any biodiesel crops grown south of the Ashburton River are too close to those export vegetable seed crops and we would encourage Biodiesel New Zealand to look further south in Canterbury for their contracting farmers. It would be disastrous if rape seed contaminated other crops. (Grain and Seed Trade Association 2007).

In addition, not all new canola growers are growing for Solid Energy; there are also reports of farmers growing canola for their own diesel needs (Natural Systems Ltd 2008), while Federated Farmers expressed concerns that "livestock farmers diversifying into cropping may not be aware of the crop isolation requirements" (Radio New Zealand 2008).

A second emerging problem with SCID pertains to the accuracy of the data that are entered. In 2007, the Grains Council complained about false registrations on the SCID system.

> Companies are registering "phantom crops" on an arable database to create buffer zones for their product and safeguard future business. …[S]eed companies had been entering incorrect information on the SCID website to "pre-book" preferred crop sites, the grains council AGM in Ashburton heard last week. …In some cases, farms listed on the site may have grown export crops previously, or intend to, but SCID was designed only to record current crops. … [G]rain growers want an end to phantom crops being registered on SCID to protect business opportunities, or crops not being registered at all. … Grains council chairman Andrew Gillanders said SCID data needed to be more accurate and the scheme was not designed for "pre-booking" crops. (Fulton 2007)

The Grain & Seed Trade Association, which confirmed the practice of registering "phantom crops", also expressed dissatisfaction with the SCID system, saying it "firmly believes the industry needs a code of practice and [SCID] needs quite a lot of work done on it" (Fulton 2007).

These emerging issues indicate that the SCID system in its current voluntary, self-regulatory form cannot be relied upon to provide the kind of high-quality information that would be needed in order to determine the cross-pollination potential of a biopharm crop in any particular location.

## 4.4. The Resource Management Act

Interviewees expected that the Resource Management Act (RMA) would protect them from any potential negative impacts of a neighbouring biopharm. However, the degree to which residents are protected by the RMA is unclear, as is the ability of local government to use the RMA to ensure stricter standards of containment than ERMA has imposed. While the courts have ruled the precautionary principle to be inherent in the RMA, ERMA's use of the precautionary principle is optional (Terry 2004). Terry (2004)

suggests that the government has not yet explored the implications of these conflicting standards of precaution.

The potential for conflict between local government and ERMA rulings is also discussed by the Ministry for the Environment (MfE), which suggests that while it is possible for local governments to use the RMA to control the use of genetic modification (which would include biopharming) in their region, this would be very difficult to do. The Ministry's website states that the safety issues surrounding GM are "highly technical, meaning that councils are unlikely to have the skills to deal with these issues" (MfE n.d.). As ERMA is a specialised body designated to perform risk analysis, MfE suggests it will be difficult for local governments to offer any legitimate reasons for GM not to proceed if approved by ERMA.

Our research challenges this assumption. We have found that people who are unlikely to participate in ERMA's risk-assessment processes may have detailed knowledge of how biopharming could affect their particular local environment. Two conclusions may be drawn from this. The first is that, under certain conditions, local authorities may have better access to this knowledge than would ERMA, unless ERMA finds a way to elicit and utilise this knowledge in its assessment process. The second is that the relevance of this local knowledge of context is a strong argument in favour of publicly notifying any application (under ERMA or the RMA) to engage in biopharming activities.

These conclusions are relevant to the current reconsideration of the RMA and establishment of an Environmental Protection Agency.

# 5. Conclusion

Because technologies never operate outside a biophysical and social context, their potential effects cannot be assessed independently of those contexts. In order to evaluate the potential harms and benefits of a technology, we must know how it is likely to interact with its contexts.

Our research reinforced the importance of this observation. By exploring practices that characterise the contexts into which biopharming would be introduced, we identified a number of practice-related issues that are important to consider when assessing risks. These practices are also important nodes at which social and biophysical risk factors interact. By situating biopharming in its broader national and international social, economic and regulatory context, and by speaking with potential implementers in New Zealand, we also identified a range of issues relevant to assessing likely benefits to New Zealand of pursuing biopharming here. Our findings further demonstrate that people who are unfamiliar with the technology in question may nonetheless have knowledge of context that is highly relevant to assessing that technology.

This report has provided an overview and synthesis of our findings on the risk and governance implications of plant and animal biopharming. (Nutrigenomics has been treated separately, in Goven and Heinemann [2008].) More detailed discussions of these findings are available in Goven et al. (2008), Heinemann (2008), Morris et al. (2009), Campbell et al. (2008), Phillips (2008) and Cram et al. (2008).[6]

[6] To obtain these reports, please go to www.conversations.canterbury.ac.nz or email joanna.goven@canterbury.ac.nz

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