KELLOGG RURAL LEADERSHIP PROGRAMME

Accelerating Crop Bioprotectant Development and Commercialisation from New Zealand

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And last - but not least - my family have been very tolerant and helpful as I have spent some weeks away from home and many a weekend researching and drafting this report. Thank you!

Author's comment

The views expressed in this report are my own and do not necessarily reflect the views of The New Zealand Institute for Plant and Food Research Limited.

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GLOSSARY

ACVM	Agricultural Chemicals and Veterinary Medicines (NZ)
AgRes	AgResearch (a CRI)
CAGR	Compound annual growth rate
CRI	Crown Research Institute
EC	European Commission
EPA	Environmental Protection Agency (NZ)
FAR	Foundation for Arable Research
HNZ-ALT	Horticulture NZ's 'A Lighter Touch' programme
IBMA	International Biocontrol Manufacturers Association
IP	Intellectual property
MWLR	Manaaki Whenua Landcare Research (a CRI)
PFR	Plant & Food Research (a CRI)
PPP	Public-private partnership
Psa	*Pseudomonas syringae pv actinideae* (a bacterial disease of kiwifruit)

EXECUTIVE SUMMARY AND RECOMMENDATIONS

The trend to towards the development and use of bioprotectants to control crop pests and disease is now in a surge mode, as evidenced by growth rates in bioprotectant sales (3x that of chemical protectants), start-up company formations, mergers and acquisitions, and multinational and venture capital investments. The stars are aligned in New Zealand for us to engage in this trend and indeed take a leadership position in it.

This report begins with some necessary background and context to this endeavour, followed by an assessment of market drivers and local and global opportunities that present themselves for bioprotectant development. An overview of New Zealand capabilities in public sector research institutions and their enviable track record bodes well for the ability to deliver on the goal of being a partner in bioprotectant development at a global level. Looking back at the factors that have promoted or constrained past product developments, and the nature of our commercial partnerships, then enables us to develop a strategy to achieve a more focussed, collective, engaged approach to new product development, resulting in clear benefits to all participants in the value chain of bioprotectant development, commercialisation and use.

A vision for 2030 could look like this:

- Fundamental science activity is adequately resourced to support product development
- There is a branded and collective ‘front door’ through which bioprotectant IP is channelled to commercial partners and thence the market
- Commercialisation and business development professionals are active from within this entity
- This entity also acts to promote awareness of NZ capabilities to attract investment and co-development partnerships
- Product developments are tied to clear market needs, especially global opportunities
- Product development is coordinated across key public sector institutions
- Commercial partnerships begin early in the development phase, are robust and enduring
- Several IP assignments or licenses are executed for bioprotectants every year
- The regulatory framework favours bioprotectant development and registration
- Revenue exceeds NZ$15m per annum and continues to grow
- The product brand is established and respected overseas.

Recommendations

Section 5 details a strategy to enhance bioprotectant development in New Zealand for global markets. In summary, the proposed actions encompass recommendations in the following categories:

Revenue sources

Private capital; redirection of internal funds; ‘A Lighter Touch’ programme engagement

Scientific Expertise

Postgrad and postdoc support; public-private research secondments and exchanges; sponsored senior research positions

Foundation science

Target biology and ecology; culture collections; new sources of accessions; biofermentation facilities; nanostring technology

Commercial partnerships

Earlier engagement models; strategic relationships are formalised; active relationship management

Prioritising product goals

Focus on global markets; greater rigour via new assessment tools applied early; new modes of action developed; semiochemical-based control products developed; targets agreed with commercial partners; microbial consortia; new markets (floriculture, postharvest); wider label claims on existing products;

Commercialisation

Patentability a key criterion; improved contractual conditions in testing with commercial partners; performance criteria in licenses

Regulatory reform

Broadening group standards; preferential review for bioprotectants; referencing overseas data

An incorporated entity

For collective IP and commercialisation activity from public sector organisations; branded

Sector engagement

More extensive engagement of public sector professionals in agrichemical/bioprotectant industry events and organisations

Validation of biocontrol

Post-market data and practices to validate technology; industry outreach programme for biocontrol;

Above all, focussed leadership and a collective mind-set from public and private organisations, and a vehicle for it, will be needed to bring this strategy to fruition.

INTRODUCTION

Research question

> *"How can the development of new bioprotectants from NZ public sector research organisations be accelerated to benefit all in the value chain?"*

Purpose

The purpose of this project is to identify strategies that will enhance the development of bioprotectants from New Zealand's public sector R&D providers, and facilitate the pathway to their commercial use locally and globally. The focus is on the *development* of bioprotectants by public sector R&D-intensive organisations, with consideration given to strategies that will enhance the targeted development of bioprotectants and productive connections with commercial entities to foster their development, registration, distribution and use.

As such, this theme dovetails well with Horticulture NZ's 'A Lighter Touch' programme whose interest commences with the current existence of near-market or in-market bioprotectants and concerns itself with getting these to market and employed usefully by the primary sector.

Scope

The focus for this report is on crop rather than animal bioprotectants, and primarily for commercial agriculture and horticulture. This report will be limited to microbial bioprotectants, semiochemicals and natural substances that can impact on pest and disease control.

Excluded from consideration are entomopathogenic nematodes, minerals (e.g. copper, sulphur) and mineral oils which act as bioprotectants. Similarly, biostimulants that act indirectly on pests and diseases through enhancement of plant growth are also excluded from consideration in this report.

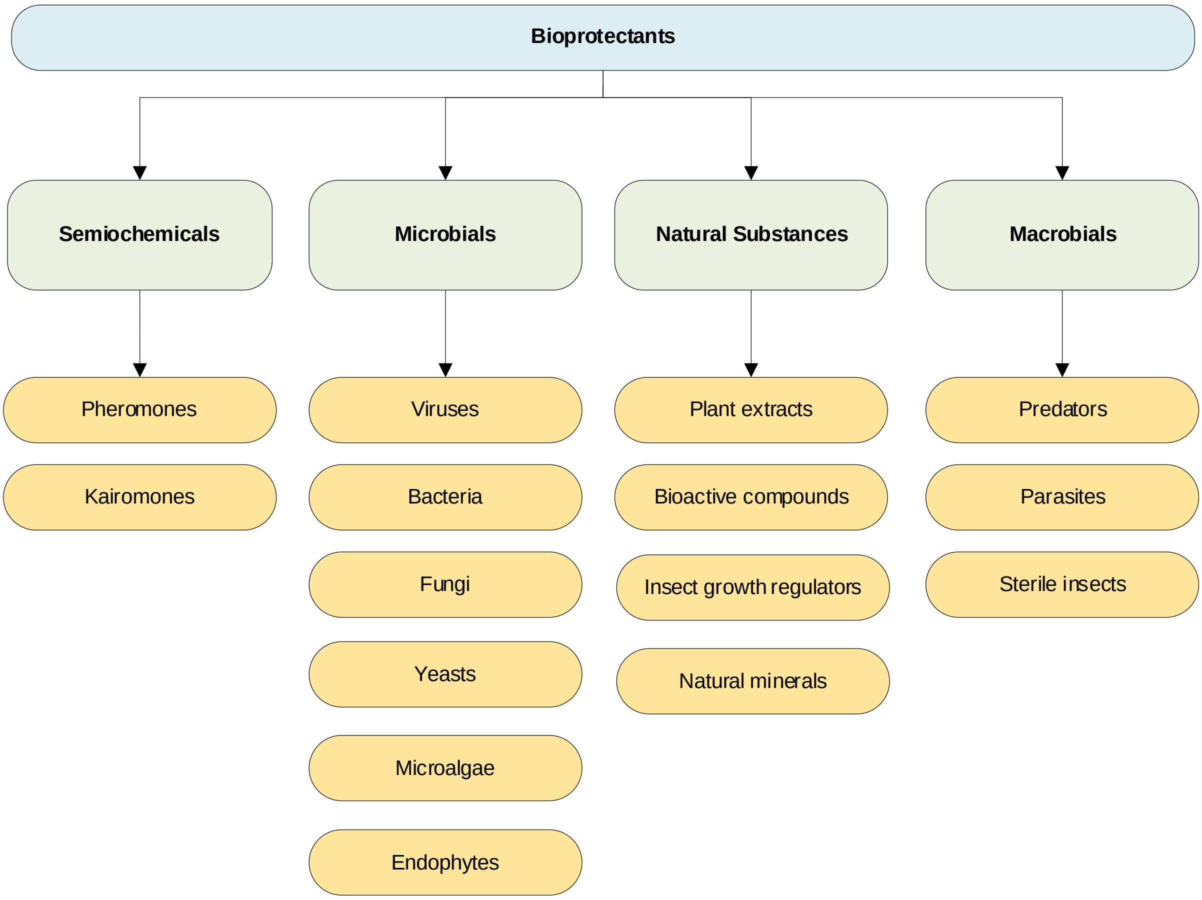
No consideration is given to the bioprotection of pests and diseases in the native estate, nor for biosecurity risks not yet present in New Zealand. Similarly, this report focuses primarily on bioprotectant development for the horticulture industry, with less reference to arable crops and pasture. This is not to say they are unimportant, or do not present opportunities, but I need some limitation to the scale of this report.

Definitions

Bioprotectants are defined here as those 'natural' products that can be applied to crop plants to control pests and diseases. The International Biocontrol Manufacturers Association (IBMA) identifies four categories of bioprotectants, with definitions and subcategories articulated by the author (Figure 1). This terminology will be used throughout this report.

'Agrichemical' is used herein to define synthetic chemistry developed and applied to crops for pest and disease control. By comparison, pheromones are produced for commercial use by synthetic organic chemistry but are nature-identical and their use augments the natural presence of the same compounds in nature.

Figure 1. Categories and terminology of bioprotectants used within the context of this study.



Bioprotectants do have their pros and cons compared to agrichemicals (Table 1). This report will deal with some of these factors and how we may address the weaknesses for improved market share.

Table 1. Strengths and weaknesses of bioprotectants.

Source: Adapted from Lew (2021)

Strengths	Weaknesses
Association with sustainable farming practices	Narrow target range
Safe for humans and environment	Efficacy levels lower and variable
Specific target range	Product price
Amenable to IPM and organic programmes	Manufacturing processes can be challenging
Little or no withholding period before harvest	Not systemic in host plant
Little or no worker re-entry period after application	Speed of kill may be slow
Compatible with natural enemies and pollinators	Short residual activity
Low risk of resistance	Sensitive to abiotic factors
	Storage life and conditions
	Application technology needs to be right
	Some incompatibility with agrichemicals
	Higher levels of knowledge needed for on-farm use
	Perceptions by end-users
	Regulatory environments may not account for type

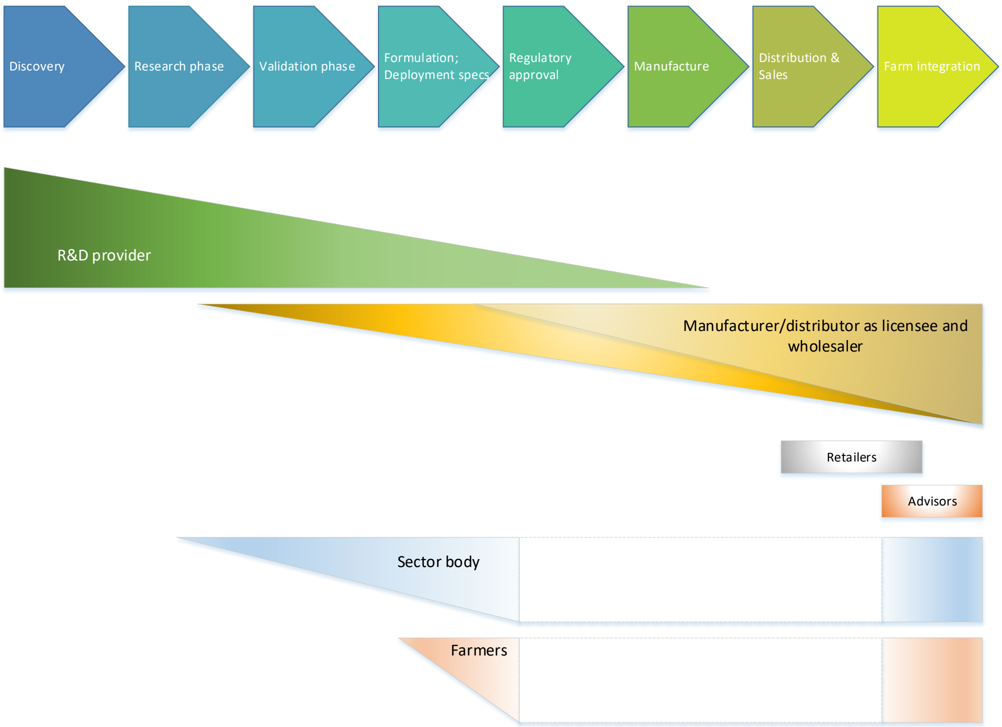
The bioprotectant development pathway

A schematic and simplified bioprotectant development chain is illustrated in Figure 2, showing the relative engagement of different stakeholders during these phases. This does vary among individuals within each type of stakeholder. For example, agrichemical companies vary in the point at which they start to truly engage, as evidenced by their commitment to funding or in-kind contributions. Sector bodies (e.g. NZ Apples & Pears, NZ Avocados, Zespri, Onions NZ, etc.) may fund R&D from an early discovery phases or commence their interest once a working prototype is available for field trials. Farmers may engage during the product validation or deployment specifications phase by offering their properties for experimentation.

Although these figures are simplified they represent the core of the development pathway of bioprotectants from discovery to a workable prototype stage. These diagrams ignore the essential activity that precedes the product development cycle shown (market assessment and drivers) and that follow market entry (integration, market monitoring and deployment refinement). While products may be licensed to commercial partners at the end of the development stage, there is still more R&D to do to make a saleable product. This would include deployment specifications, fit with IPM systems within which they would be deployed, registration-specific trials (e.g. bee toxicity, territorial testing), and off-target investigations. Genomic markers for the unique identification of a commercial strain of microbial bioprotectant are increasingly needed.

These figures also exclude other R&D necessary to develop effective products: mode of action studies and target pest/pathogen biology and ecology. These may precede or parallel the product development steps. The figures below also hide the activities needed for commercialisation, including IP protection, tendering processes, commercial partner relationship management, business relationship models and contracting processes.

Figure 2. Stakeholder engagement in the bioprotectant development chain.



For different classes of bioprotectants, the details differ. For microbial BCAs, the detail is better represented in Figure 3, and for semiochemicals in Figure 4.

Figure 3. Microbial bioprotectant development pathway.

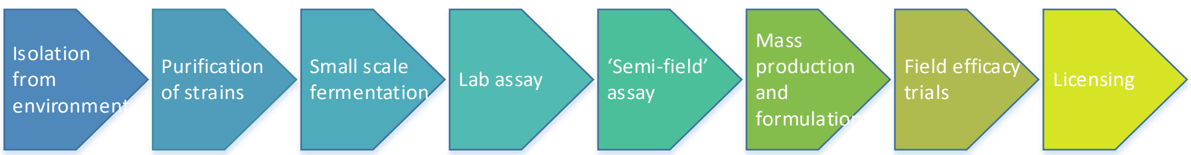
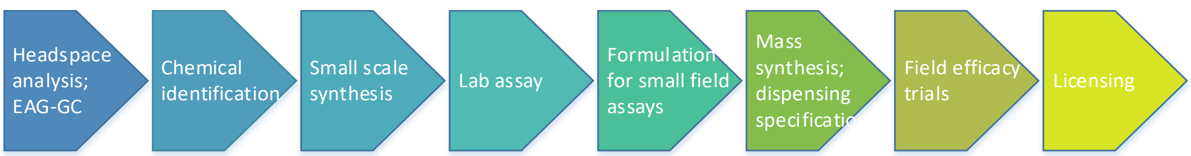


Figure 4. Semiochemical development pathway.



RESEARCH METHODS

A qualitative assessment of the capabilities of key research institutions with a history of bioprotectant development (Table 8) was done within each by key researchers and their colleagues.

Key researchers were interviewed to elicit information on the history of development of nine of the in-market products and 12 of the pre-market products currently in development in Table 2.

Table 2. Product development pathways reviewed.

Status	Semiochemicals	Microbials	Natural substances
In-market	Isomate® Avocado Desire™ Mealybug Lurem®	Aureo®Gold BlossomBless™ Botryzen® BioShield™	Armour-Zen® Midi-Zen®
In development	Pheromone 107 Kairomone 108 Pheromones 109-110	Microbial 204 Microbial 206 Microbial 207 Microbial 208 Microbial 209 Microbial 280 Microbial 281	Natural substance 303 Natural substance 304

Researchers, as key informants, were queried on the following characteristics of each bioprotectant development pathway:

Factors driving the initiation of development
Technical factors associated with development
R&D funding history
Intellectual property management
Licensing
Regulatory issues
Commercial partnerships and market entry

Key informants from agrichemical and biotech companies locally and internationally were also interviewed for their experiences with public sector bioprotectant developers, in the context of the partnerships they seek. Information from all of these semi-structured interviews were collated and anonymised to reveal the factors associated with either good progression of product development and commercialisation, or factors that created limitations in the path to market.

During 2020, a programme assessing market opportunities and constraints for a particular type of microbial as a bioprotectant was run under the direction of CreativeHQ (https://creativehq.co.nz/) as an 'Activate' accelerator programme. The author and three Plant & Food Research colleagues conducted structured interviews with five agrichemical companies, two viticulturalists and two sector bodies in the wine and strawberry industries. These interviews examined the problems to be addressed, solutions tried, desired outcomes and values for such bioprotectants. The scenario for study was for Botrytis control in wine grapes.

RESULTS AND DISCUSSION

1. BIOPROTECTANTS: TRENDS AND OPPORTUNITIES

GLOBAL TRENDS IN BIOCONTROL

A number of reports are released annually with global estimates of the bioprotectant market. Although they vary in their scope and inclusions, several facts remain consistent: the bioprotectant market is large, is growing rapidly, and growing much faster than that of chemical pesticides and fungicides (Table 3). This clearly represents an opportunity for those developing and commercialising bioprotectants.

Table 3. Global status and growth in the bioprotectant market (in red), compared to that of agrichemical options (in black).

Category	Baseline[1]	Projected[1]	CAGR[4]	Source
biofungicides	$1,767 m (2018)	$4,208 m (2024)	15.6 %	Modor (2021a)
	$2,340 m (2020)	$4,973 m (2025)	16.1 %	MarketsandMarkets (2020a)
biopesticides	$7,438 m (2020)	$16,730 m (2026)	14.5 %	Modor (2021b)
	$4,826 m (2020)	$10,824 m (2027)	12.4 %	ResearchandMarkets (2021)
fungicides[2]	$27,352 m (2019)	$35,836 m (2025)	4.6 %	MarketsandMarkets (2020b)
Pesticides[3]	$83,373 m (2019)	$129,916 m (2023)	5.7 %	ResearchandMarkets (2019)
TOTAL crop protection[2]	**$342,566m (2019)**	**$438,813m (2025)**		**Statista (2019)**

[1] NZD (converted from USD at 1.463) and presented in millions of dollars, with the applicable year referenced

[2] Inclusive of agrichemicals and bio-protectants

[3] Inclusive of agrichemical options only

[4] Compound annual growth rate

The sources referenced in Table 3 attribute the preferential growth of bioprotectants to several factors, including increasing demand for safer food and food security, increases in the ‘middle class’ in emerging markets, increased areas under organic production systems, environmental concerns, and regional regulatory regimes that favour bioprotectants and discriminate against chemical control. All of these factors are a consequence of market drivers that are pulled by the consumer (or their retail proxy) and combine with a push from the production sector. Despite this growth, bioprotectants only account for 5-10% of the crop protection market (Fenibo et al., 2020; Damalas & Koutroubas, 2018), a figure likely to increase given the trends outlined above.

An analysis of research publications in biocontrol over 25 years revealed a downwards trend in Google search hits from 2004, but increases in publications and international research collaboration (Brodeur et al., 2018; Damalas & Koutroubas, 2018). Although two thirds of these publications were targeted at biological control of pests, an increasing proportion were being aimed at crop pathogens – primarily field crops. Two thirds of the pest biocontrol papers were focussed on natural enemies. An apparent disconnect between research publication profiles and commercialised bioprotectant profiles suggests a need to re-prioritise R&D.

Symptomatic of this growth in bioprotectant development is the rise in start-up companies in this field. Table 4 lists but a few of these and show the range of new modes of action that should excite researchers in NZ. Grasslanz is the only public sector spin-out dedicated to bioprotectant development and commercialisation in NZ. The global interest in biocontrol is also evident in the mergers, acquisitions and investments happening globally[1]. Bayer's acquisition of AgroQuest in 2012 and Prophyta soon after, and Syngenta's acquisition of Valagro more recently, exemplify this trend. UPL has also announced the formation of a Natural Plant Protection business unit. Second tier multinationals (e.g. Certis, Lallemand) are also active in this space. Future acquisitions or divestments from the large multinational agrichemical companies will reflect their strategic intent in relation to biocontrol generally. There is an increasing trend in private investment in biocontrol due to increasingly philanthropic virtues and greater acceptance of longer times to exit or returns on investments (R. Gwyn, pers.comm). These could be 10-15 years.

Table 4. Examples of start-ups generated over the last 5-10 years in the broader crop pest and disease biocontrol space.

Company	Scope	Origins
BioLogic Insecticide	Natural product for stored products pests	USA
BioPhero	Biofermentation of pheromones	Denmark
Bee Vectoring Technologies	Bee vectoring of bioprotectants	Canada
Agrospheres	Controlled release encapsulation (inclusive of RNAi)	USA
Biotalys	Protein-based biocontrols	Denmark
Aphea.Bio	Row crop microbial biocontrols and biostimulants	Belgium
APS Biocontrol	Bacteriophages	Scotland
Novozymes	Enzymes and microbes	USA
Vestaron	Peptides	North Carolina, USA
Evolution Biotechnologies	Entomoviruses	UK
Biocontrol Technologies	Trichoderma	Spain
Terramera	Natural products	Vancouver, USA

[1] E.g. https://www.agribusinessglobal.com/tag/acquisition/

EC Green Deal

Europe has tended to lead the progression to safer food standards and climate change response through regulation. By means of example, the EC Green Deal[2] was established in late 2019 with the express goal of making EC's climate, energy, transport and taxation policies fit for reducing net greenhouse gas emissions by at least 55% by 2030, compared to 1990 levels. A new sustainable use directive is due which will more prescriptive and measurable. The Green Deal includes earlier directives relating to the Farm to Fork and Biodiversity strategies. In broad terms, its goals in relation to agriculture are[3]:

- to ensure food security in the face of climate change and biodiversity loss
- reduce the environmental and climate footprint of the EC food system
- strengthen the EC food system's resilience
- lead a global transition towards competitive sustainability from farm to fork

More specifically:

- 50% reduction in use and risk of chemical pesticides, particularly the more harmful pesticides by 2030
- 25% of agricultural land under organic systems
- 50% reduction of antimicrobials for farmed animals and aquaculture by 2030
- Reduce nutrient losses by 50%, and of fertilisers by 20%, by 2030
- Bring back at least 10% of agricultural land under high diversity landscape features by 2030

Specifically for pesticides, the EU Directive 2009/128/EU was introduced earlier to achieve a sustainable use of pesticides in the EU by reducing the risks and impacts of pesticide use on human health and the environment and promoting the use of Integrated Pest Management (IPM) and of alternative approaches or techniques, such as non-chemical alternatives to pesticides. National action plans required by 2012 included:

- training of users, advisors and distributors
- inspection of pesticide application equipment
- the prohibition of aerial spraying
- the protection of the aquatic environment and drinking water
- limitation of pesticide use in sensitive areas
- information and awareness raising about pesticide risks
- systems for gathering information on pesticide acute poisoning incidents, as well as chronic poisoning developments, where available

These targets are ambitious, and are driving agricultural practice in the EC and internationally in markets that supply the European community. The trend will no doubt be seen in NZ in some form at some time.

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[2] https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal_en

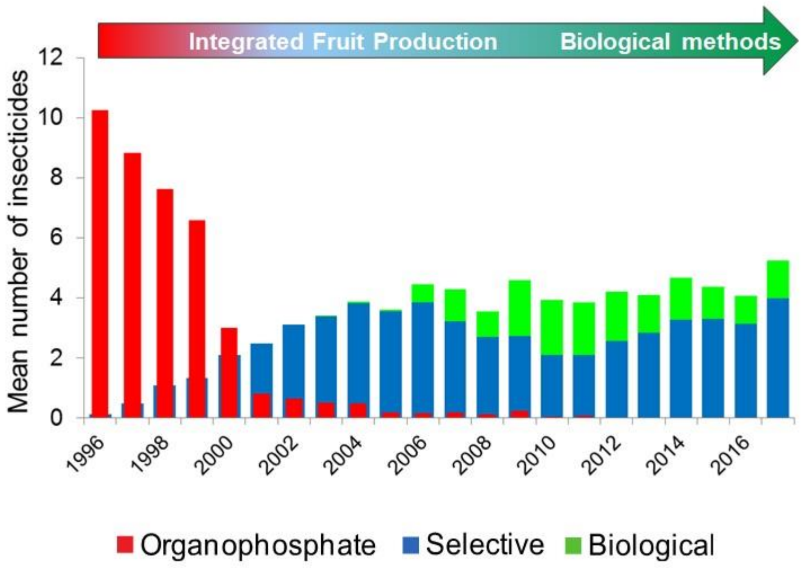
[3] https://ec.europa.eu/info/strategy/priorities-2019-2024/european-green-deal/agriculture-and-green-deal_en

In a review of progress to date on the sustainable use of pesticides, it was noted that the lack of viable alternatives to chemical pesticides was one of the main issues hindering the implementation of this goal (Ramboll 2021). The experiences of the companies registering bioprotectants in Europe is that even bioprotectants are expensive to register, the process takes a long time and are treated the same as chemical pesticides (e.g. Kiewnick, 2007). These experiences are relevant to NZ in that we often follow the initiatives brought into that market, in part because EC directives do influence food standards of those providing produce into that market.

By way of example, trade negotiations being held since 1999 between the EC and the Mercosur countries (South America – Argentina, Brazil, Paraguay, Uruguay) pact are now being put at risk by the latter's lack of adherence to EC Green Deal expectations – primarily over Amazon deforestation and scepticism about Brazil's current commitment to tackling climate change (Blenkinsop, 2021; Euronews, 2021). Thankfully, New Zealand has a good reputation for food safety in produce exported to the European market, compared to other food-producing nations. Our kiwifruit and apple industries in particular are exemplary in the use of IPM and in the reduction in the use of the more harmful pesticides, particularly broad spectrum organophosphates (Figure 5). Other NZ sector groups such as wine, avocados and summer fruit, all have explicit goals for greater sustainability. But New Zealand cannot afford to be complacent in relation to our trade negotiations with the EC – it must address our climate change goals, and agricultural practices are part of this and will be scrutinised.

Figure 5. Pesticide use in NZ apple production.

Changes in the use of insecticides and bioprotectants over 20 years in the NZ apple industry. (Source: J. Walker)



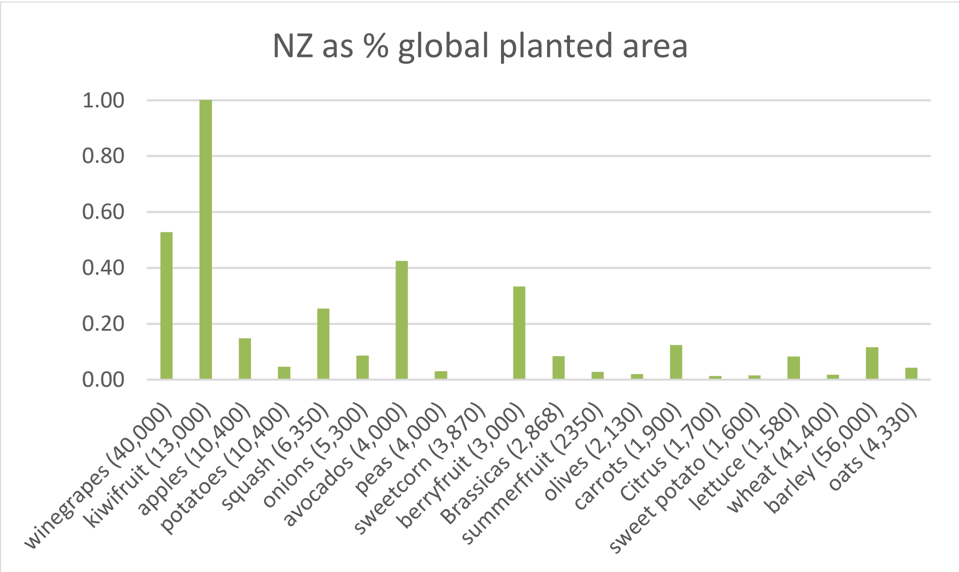
MARKET-LED DEVELOPMENT

While the New Zealand market demand for bioprotectants is clear for a local benefit to the food production and marketing value chain, the product developers have less to gain. For our public sector R&D institutions, developing bioprotectants for the NZ market fulfils a legislated (for the CRIs) and moral obligation for local primary sector benefit. Without Government investment for early stage and novel mode of action development the development pipeline will dry up, as seems to be happening now. With little or no revenue returned to the inventing institution because of low sales volumes of released bioprotectants, the public purse has effectively bankrolled previous developments and provided at least some return to the commercial sector. For the local and multinational agrichemical companies, the New Zealand market is small, to the point where the profits to be made from sales of a registered product may not justify the costs and timelines of registration for the local market. For all parties, therefore, global markets offer a more realistic opportunity to achieve significant returns on investment and to enable re-investment.

With the exception of kiwifruit, NZ planted area for our key horticultural and arable crops (above 1,000 ha) is less than 0.5% of global planted area (Figure 6). While this may demonstrate broadly the potential opportunities for bioprotectants internationally, it is tempered significantly by the occurrence of target pests and diseases in other territories, the economic status of those and the availability of competitive bioprotectants. Therefore, developing bioprotectants for NZ agriculture may provide opportunities into greater global markets under certain conditions. Similarly, developing bioprotectants primarily for global markets may have a spin-off benefit to NZ agriculture. Whether the primary driver is local or international will determine the nature and timing of research and commercial collaborations, third party resourcing and research intensity.

Figure 6. NZ planted area as a percentage of global planted area.

Note that the kiwifruit data exceeds the scale, at 3.1%. The NZ planted area (in hectares) is included in the x-axis labels. Source: FAO (2021)[4], Aitkin & Warrington (2020).



[4] http://www.fao.org/faostat/en/#data accessed January 2021

Loss of chemistry

As mentioned earlier, the loss of essential agrichemicals (chemical pesticides/fungicides) is a current and key driver for the development of bioprotectant options. By way of example, loss of wheat yield in France was estimated to be 5-13% due to a regulated 50% reduction in pesticide use (Hossard et al., 2014) – without suitable replacement. What is contributing to the loss of agrichemicals is:

1. Pest/pathogen resistance to the pesticide/fungicide
2. Market forces restricting to their use (e.g. for food residue or environmental reasons)
3. Associated regulatory pressure in the territory of food production or sale
4. The natural life cycle of products due to profitability or improved replacements

Single site of action fungicides in particular have consistently shown development of resistance in their target pathogens (e.g. Rovral). Chlorpyrifos products (e.g. Lorsban, a broad spectrum organophosphate insecticide) is no longer being manufactured and was removed from the NZ market because of its toxicity.

Mancozeb (an extensively-used broad spectrum fungicide relied on by many crops such as potatoes, tomatoes, winegrapes and apples (Gullino et al. 2010)) is destined to be removed from use in Europe by 2024 due to concerns of environmental and human toxicity. NZ will no doubt follow although it is not on the EPA's list of chemicals currently under review[5]. Mancozeb has been in use for over 50 years with its popularity secured by good efficacy, broad-spectrum use, crop safety, low resistance risk, and low cost. Loss of Mancozeb would cause increases in costs to the farmer (e.g. 'Canadian potato farmers react'[6]) and significant yield loss[7] (Wynn 2014). Should Mancozeb be lost, single site-of-action alternative fungicides risk the development of additional fungicide resistance, creating a double-edged sword. With increasing pressure to restrict the use of alternative fungicide chemistries the range of options becomes more limited - pathogen-resistant cultivar breeding and bioprotectant development are viable alternatives.

Prioritising bioprotectant opportunities therefore needs to factor in:

- Which class of chemicals will be lost?
- When they will be lost?
- What crops currently depend on their use, and are therefore more at risk?

Answering these questions will determine the urgency and target crop that needs to be addressed. Given the timescale of bioprotectant development, some crops will be at significant risk of economic losses because of the gap between agrichemical unavailability and bioprotectant availability. The development of bioprotectants for these New Zealand markets must therefore be of higher priority.

[5] https://www.epa.govt.nz/industry-areas/hazardous-substances/chemical-reassessment-programme/current-reassessments/
[6] https://spudsmart.com/going-without-mancozeb/
[7] https://www.fwi.co.uk/arable/crop-management/disease-management/mancozeb-why-the-potato-industry-must-prepare-for-its-loss

TARGET PRIORITISATION

A comprehensive list of target pests and pathogen of economic significance compiled by PFR researchers, and relevant to both local and international markets across multiple sectors, is detailed in Tables 5 and 6, along with an assessment score for the opportunity. This will help frame prioritisation for development. This overlaps the targets listed in Bellamy et al. (2020) which was developed by and for the sector groups co-investing in Horticulture NZ's 'A Lighter Touch' ('HNZ-ALT') programme[8]. It is worth noting that the HNZ-ALT co-investing sector groups are a subset of NZ horticultural and arable industries, with the notable absence of the apple and avocado sectors. Some sectors in the HNZ-ALT programme are small by NZ standards and even smaller internationally (e.g. boysenberries, persimmons, passionfruit, feijoa). The HNZ-ALT objectives are nonetheless worthy. It is hoped that for their constituent sectors that bioprotectant registrations can proceed for those sectors that would otherwise not justify such investment from commercial companies.

[8] Programme Partners – A Lighter Touch (a-lighter-touch.co.nz)

Table 5. Target pests of interest in NZ and globally.

Source: N. Mauchline.

'-' represents no opportunity, through to '+++' for a significant opportunity, based largely on the global opportunity.

Common name	Taxonomic spp.	NZ host crops	Global host crops	Rationale	Opportunity score
Thrips	*Thrips tabaci* *Heliothrips haemorrhoidalis*	Onion, leek and garlic, cabbage, cauliflower and broccoli, asparagus, sugarbeet, melon, pumpkin, marrow and cucumber, strawberry, potato and many fruiting and ornamental plants	Onion, leek and garlic, cabbage, cauliflower and broccoli, asparagus, sugarbeet, melon, pumpkin, marrow and cucumber, strawberry, potato, tobacco, cotton and many fruiting and ornamental plants	Old chemistry, banned or imminent withdrawal Vector of plant viruses	+++
Aphids	*Myzus persicae*	Tomato, capsicum, cucumber, brassicas Anything and everything!	Tomato, capsicum, cucumber, brassicas Anything and everything!	Old chemistry, banned or imminent withdrawal Vector of plant viruses Insecticide resistance	+++
Armoured scale	*Hemiberlesia lataniae* *Hemiberlesia rapax* *Aspidiotus neri* *Aonidiella aurantii* *Quadraspidiotus perniciosus*	Apples, kiwifruit, citrus, avocados, tea, ornamentals	Apples, kiwifruit, citrus, avocados, tea, ornamentals	Old chemistry, banned or imminent withdrawal	+++
PVH (SLF proxy)	*Scolypopa australis*	Kiwifruit, avocado, cherry, grape, passionfruit, peach, pumpkin, rhubarb, squash	Kiwifruit, avocado, cherry, grape, passionfruit, peach, pumpkin, rhubarb, squash, fig, sunflowers	Old chemistry, banned or imminent withdrawal	+
Mites	*Tetranychus urticae* *Eotetranychus sexmaculatus*	Anything and everything	Anything and everything	Old chemistry, banned or imminent withdrawal Resistance	+++
Psyllid	*Bactericera cockerelli*	Solanaceae (potato family), Convolvulaceae (kumara and bindweed family)	Solanaceae (potato family), Convolvulaceae (kumara and bindweed family)	Bacterial transmission	++

Rice weevil	*Sitophilus oryzae*	Wheat, rice, and maize	Wheat, rice, and maize	Re-infestation risk	+++
Whitefly	*Trialeurodes vaporariorum* *Aleyrodes proletella*	Tomato, capsicum, cucumber, brassicas Anything and everything!	Tomato, capsicum, cucumber, brassicas Anything and everything!	Old chemistry, banned or imminent withdrawal Vector of plant viruses Insecticide resistance	++
GVB (BMSB proxy)	*Nezara viridula*	Vegetables, cucurbits, maize and macadamias	Vegetables, cucurbits, maize, barley, oats, rye, wheat, soybeans, maize, peas, cassava	Change in insecticide use. Change in effectiveness of biological control.	++
Chorus cicada	*Amphipsalta zelandica*	Kiwifruit, avocados	Not applicable	Old chemistry, banned or imminent withdrawal	+

Table 6. Target pathogens of interest in NZ and globally

Source: P. Elmer

'-' represents no opportunity, through to '+++' for a significant opportunity, based largely on the global opportunity.

Common name	Taxonomic spp.	NZ Host crops	Global host crops	Rationale	Opportunity score
Downy mildew	*Bremia lactucae* *Peronospora destructor* *Hyaloperonospora brassicae* *Peronospora farinose* *Peronospora sparsa* *Plasmopara viticola*	Lettuce Onions, spring onions, garlic Vegetables brassicas Spinach Boysenberries Grapes	Lettuce Onions, spring onions, garlic Vegetables brassicas Spinach Boysenberries Grapes	Old chemistry banned or imminent withdrawal Resistance development to older chemistries	+++
Botrytis	*Botrytis cinerea* *Botrytis pseudocinerea*	causing grey mold on **more than 1400 known hosts**, in 586 plant genera and 152 botanical families, including high-value crops such as grapevine and tomato	causing grey mold on **more than 1400 known hosts**, in 586 plant genera and 152 botanical families, including high-value crops such as grapevine and tomato	Increasing global residue restrictions Old chemistry banned or imminent withdrawal Rapid resistance development to new chemistry – lack of effective alternatives overseas **but not in NZ**	+++
Blue and green molds	*P. expansum* *P. digitatum* *P. italicum*	All citrus crops, apples, high value mushrooms	All citrus crops, apples, high value mushrooms	Increasing global residue restrictions Old chemistry banned or imminent withdrawal Rapid resistance development to new chemistry – lack of effective alternatives overseas and NZ	++
Anthracnose	*Colletotrichum acutatum* complex *C. gloeosporioides* complex *Colletotrichum* sp.	Avocadoes, blueberries, apples, Cereals, legumes, vegetables, chilli, Strawberries, Feijoas, buttercup squash, persimmons Subtropicals - Guava Papaya Mango Passionfruit	Avocadoes, blueberries, apples, Cereals, legumes, vegetables, chilli, Strawberries, Feijoas, buttercup squash, persimmons Subtropicals - Guava Papaya Mango Passionfruit	Increasing global residue restrictions and negative public perceptions about copper use and copper accumulation in soil Old chemistry banned or imminent withdrawal Rapid resistance development to new chemistry – lack of effective alternatives overseas and NZ	+++

Canker and shoot die-back	*Botryosphaeria* sp. *Neofusicoccum* sp.	Avocadoes, blueberries, grape vines High value ornamentals	Avocadoes, blueberries, grape vines High value ornamentals	Increasing global residue restrictions Old chemistry banned or imminent withdrawal – lack of effective alternatives overseas and NZ	++
Sooty mold	Sooty molds are a large group of fungi, most of which are nonparasitic, non-pathogenic colonizers of leaves of a single growing season or may extend for several seasons. Commonly *Cladosporium* sp. and *Alternaria* sp.	Natives species especially *Nothofagus* sp. Kiwifruit Avocados Citrus	Kiwifruit Avocados Citrus	Control of sap sucking insect pests is the best treatment	+
Alternaria	*Alternaria dauci* *Alternaria radicina* *Alternaria brassicae* *Alternaria brissicicola* *Alternaria alternata*	Carrot Carrots Brassicas Tomatoes Capsicums Passionfruit Potatoes	Potatoes Tomatoes Capsicums	Increasing global residue restrictions Old chemistry banned or imminent withdrawal – lack of effective alternatives overseas and NZ	+++
Fusarium	*Fusarium avenaceum* *Fusarium oxysporum* *Fusarium redolens* *Fusarium graminearum*	Peas	Peas	Increasing global residue restrictions Old chemistry banned or imminent withdrawal – lack of effective alternatives overseas and NZ	+++
	Fusarium graminearum *Fusarium culmorum* *Fusarium avenaceum*	Wheat	Wheat		
	Fusarium oxysporum	Cucurbits Boysenberry	Cucurbits Boysenberry		
	Fusarium oxysporum *Fusarium passiflorae*	Passionfruit	Passionfruit		
	Fusarium proliferatum *Fusarium verticollioides* *Fusarium meridionale*	Maize	Maize		

	Fusarium spp.	Barley, Beans	Barley, Beans		
Rhizoctonia root rot	The most common species that infects plants is *Rhizoctonia solani*.	With a wide host range, Rhizoctonia can cause a variety of diseases including stem rot, root rot, damping-off in seedlings and aerial blight of leaves. It is often the cause of rot in cuttings, especially those under mist. Potatoes Tomatoes Turf grasses	With a wide host range, Rhizoctonia can cause a variety of diseases including stem rot, root rot, damping-off in seedlings and aerial blight of leaves. It is often the cause of rot in cuttings, especially those under mist. Potatoes Tomatoes Turf grasses	Increasing global residue restrictions Old chemistry banned or imminent withdrawal Lack of effective alternatives overseas and NZ	+++
Late blight	*Phytophthora infestans*	Potatoes tomatoes	Potatoes tomatoes	Increasing global residue restrictions Old chemistry banned or imminent withdrawal Rapid resistance development Lack of effective alternatives overseas and NZ	+++
Mycosphaerella leaf spot	*Mycosphaerella brassicicola*. *Mycosphaerella fragariae* *Mycosphaerella graminicola*	Vegetable brassicas Strawberries Wheat	Vegetable brassicas Strawberries	Old chemistry banned or imminent withdrawal Lack of effective alternatives overseas and NZ	+++
Rusts	*Puccinia hordei* *Puccinia sorghi* *Puccinia sorghi* *Puccinia triticina* *Transchelia spp.* *Transchelia spp.* *Transchelia spp.* *Transchellia discolor* *Transchellia discolor*	Barley maize Sweet corn Wheat Nectarine Peach Plum Apricot Cherry	Barley maize Sweet corn Wheat Nectarine Peach Plum Apricot Cherry	Rapid resistance development Lack of effective alternatives overseas and NZ	+++
Bacterial blast Over 48 different *Pseudomonas*	*Pseudomonas syringae* pv. *syringae*	All stone fruits incl. almonds Mango	All stone fruits incl. almonds Mango	Increasing global residue restrictions Old chemistry banned or imminent withdrawal	+++

syringae pathovars	*Pseudomonas syringae* pv. *tomato*	Tomato	Tomato	Copper resistance up to 80% in some NZ orchards Copper dependence – lack of effective alternatives overseas and NZ	
Bacterial spots in a wide range of tree, vegetable and fodder crops	*Xanthomonas arboricola pv. pruni* *Xanthomonas arboricola pv. juglandis* *Xanthomonas campestris pv. campestris* *Xanthomonas citri pv. citri*	All stone fruits incl. almonds Walnuts Wide range of cruciferous vegetables citrus	All stone fruits incl. almonds Walnuts Wide range of cruciferous vegetables citrus	Increasing global residue restrictions Old chemistry banned or imminent withdrawal Copper dependence and negative public copper-based perceptions – lack of effective alternatives overseas and NZ	+++
Fire blight	*Erwinia amylovora*	Apples and Pears	Apples and Pears	Increasing global residue restrictions Old chemistry banned or imminent withdrawal Rapid resistance development to anti-biotics – lack of effective alternatives overseas and NZ	+++
Soft rots	*Dickeya* sp. *Pectobacterium* sp.	Wide host range incl. – potatoes, sweet potato, kumara, cabbage, leeks onions, bulb crops celery, Chinese cabbage, artichoke, carrot, parsley, sugar beet,	Wide host range incl. – potatoes, sweet potato, kumara, cabbage, leeks onions, bulb crops celery, Chinese cabbage, artichoke, carrot, parsley, sugar beet,	Increasing global residue restrictions Old chemistry banned or imminent withdrawal – lack of effective alternatives overseas and NZ	+++
Liberobacter	*Candidatus liberibacter solanacearum*	Capsicums, Carrots, Celery, Parsley, Potatoes and tomatoes. renders French fries or potato crisps unmarketable	Capsicums, Carrots, Celery, Parsley, Potatoes and tomatoes. renders French fries or potato crisps unmarketable	Vectored by the potato and tomato psyllid *Bactericerca cockerelli* to potato and tomato	++

A number of bioprotectants are currently in development at PFR. They key activities required to advance them through to commercialisation are listed in Table 7, along with indications of market opportunity. The driver for their development has largely been the need from the NZ kiwifruit, wine and apple sectors, with two exceptions. Some of these products address some of the targets listed in Tables 5 and 6.

Table 7. Strategies for PFR products currently in development and their market opportunity.

'-' represents no opportunity, through to '+++' for a significant opportunity, assuming no broader control than a species-specific target.

ID#	Development strategy up to licensing	NZ market	Global market	Market driver
107	Formulation finalised Field specifications validated	+	-	Market access for NZ produce
108	Market opportunities quantified Preliminary data package shared with potential licensee	-	++	Multiple pest monitoring
109-110	Discovery phase still in progress Concurrently: develop dispensing technology options	++	++	Environmental pest control
204	Currently undergoing NZ registration Test combination product with research partner	+	-	Pathogen causing crop loss
206	Increase biofermentation yields Counter-seasonal trials on multiple targets Secure commercial partner	+	+++	Multiple pest control
207	Test for efficacy on related targets Secure commercial partner	+	-	Single pest control
208	Test for efficacy on related targets Secure commercial partner	++	++	Single pest control
209	Establish biofermentation protocols In vivo tests Secure commercial partner	+	+++	New mode of action

MARKET VIEWS OF BIOPROTECTANTS

Plant & Food Research has been investigating the opportunity to develop a type of microbial bioprotectant that infect and limit crop plant pathogens. Interviews of industry professionals conducted in the CreativeHQ Activate programme in 2020 uncovered common themes of interest to the future development of these in the NZ market context. Although focussed on the market opportunity for this type of bioprotectant for the wine industry, most comments were made in relation to bioprotectants generally. There was a lot of commonality in the responses of near-market stakeholders (agchem companies, growers, sector representative bodies) which indicates an intimate level of knowledge of their sectors and market. Cost-benefit, efficacy and sustainability goals were consistently the most important goals for bioprotectants, given awareness of their current status.

The voice of industry: Interviewee responses

Below are the specific responses received in these interviews.

Economics

- The cost-benefit has to be there
- Bioprotectants are generally more expensive than chemistry, but impressions of the product price depend on whether the target crop is high-return or not - there was variation on the acceptability of higher price points among different crops
- Most viticulturalists have a target ceiling for pest and disease control so product price point in comparison to alternatives is very important

Efficacy

- Expectations are for efficacy levels at or near current chemical fungicides. Currently, field experience shows that bioprotectants are less effective than chemistry, particularly in high disease-pressure times (within or between seasons). Growers can be more forgiving of bioprotectant efficacy given the other attributes they bring.
- Perception of less efficacy was also cultured by over-promising from sellers
- Variability in performance is also of great concern.
- Small gains in efficacy can be important
- Efficacy of sold product reflects on the credibility of the product merchant
- Broad efficacy across multiple pathogens is ideal, and across territories
- Need to set expectations with growers with good quality data
- Balance needed between product price, efficacy and acceptable levels of crop loss

Sustainability

- Desired reputation for sustainability, with special impact for organic systems
- Bioprotectants do solve the residue issue, enabling (or not limiting) market access for our produce in an export-oriented sector such as that of New Zealand's

- Health and safety of product applicators is important and will aid in market penetration of bioprotectants, but there is a lessening gap in health and safety requirements between bioprotectants and agrichemical options nowadays
- Brand value for sustainable crop protection is increasingly important to agrichemical companies – the environmental and social license is of less concern than the brand value for safe food
- There is inconsistency in perceptions of 'organics' as the term can be used somewhat fraudulently by uncertified suppliers – this is contributing to some 'snake oil' reputations across the bioprotectant market
- There is little accountability for companies selling 'snake oil' products of little effect – therefore compromising grower returns
- Growers genuinely want to spray less

Product attributes

- Recognition that a systems approach is needed for pathogen control in vineyards and that a bioprotectant can be part – but not all – of that. Agrichemical companies prefer to offer a full suite of (their) pest/disease control options, inclusive of crop management practices and biostimulants so that growers are buying a programme to achieve the outcomes. The systems approach is often driven by the industry body more than the grower.
- Ability for bioprotectants to be applied with agrichemical options is an important step towards less use of agrichemical control options – they should 'co-habitate'. Could they be somewhat immune from co-sprayed fungicides? Tank mixing option desirable.
- A shorter shelf life is 'expected' from bioprotectants because of their perceived and real reputation. Short shelf life for bioprotectants that are not used in low disease-pressure years will leave stock on the shelf unable to be sold – will be discarded and a loss.
- Handling is more difficult than agrichemical options – storage temperatures, application procedures, distribution
- Timing: They can fill a gap in the season where fungicides may not be able to be applied because of residue issues. They tend to fill a niche.
- Growers place a higher premium on the bioactives produced by live bioprotectants, compared to the live organism, because they are easier to handle
- Off-target impacts may be of concern if unknown
- Potential for mutation and what this may cause (that is different to the planned impact) may be of concern
- Bioprotectants needed particularly for late season control when residues and withholding periods limit the use of chemical options
- Microbial bioprotectants in the market tend to be prophylactic rather than curative
- New modes of action is very exciting, but proof is needed
- Lack of resistance development is a key attribute for bioprotectants

Market presence and drivers

- Agrichemical companies tend to work to maximise their market share for any product type, and are currently putting significant effort into bioprotectants (generally) to do so

- The NZ market alone is not big enough to justify bioprotectant development – larger overseas markets are necessary to justify development. Large agrichemical decisions are based on planted area for a target crop.
- Organics alone will not justify product development – not enough of any market
- Growers have long memories – failure in one year is remembered and can limit subsequent sales.
- Trust in the market is very important for a merchant
- 'First to market' is important
- Protected cultivation systems will become more important – these will increase pest and disease pressure. Need to develop bioprotectants for indoor use
- Retailers are the key sources of advice for an end-user (grower). They often promote some products over others. Data is important to a grower to justify product use.
- New entrants into the wine industry are bringing fresh perspectives and are more willing to try new products

Consumer demand

- A dichotomy exists where consumers want perfect food but made with 'soft' pest/pathogen control options, which the latter may not be able to deliver currently. Food quality expectations may need to be lowered to achieve improvements in sustainable systems.
- Supermarkets critical as drivers as the proxy for consumers. They need to educate consumers to accept less-than-perfect produce.
- There is little knowledge of the attributes of chemical protectants by the public – they may only know about the ones in the public eye (e.g. glyphosate).

Education

- There is a need for, and growing activity in, education for handling bioprotectants from product owners, resellers and growers
- Such product support is vital to get the best out of bioprotectants
- Manage expectations with end-users (growers)

Regulatory

- Bioprotectants can be more difficult and expensive than chemical protectants to get through registration processes, and therefore require a bigger market size to justify investment in development
- EC market requirements – and the supermarket's interpretation of these – are driving which protectants can be used in NZ, if that product is not registered for field use in the EC
- In NZ, expect 5 years from a formulated product to sales to go through registration and scale up phases
- Bioprotectants should be getting MRL exception (unless it is the metabolite from the live organism that is identified as the key active – in which case a chemistry route is needed for regulatory approval)

Intellectual property

- The more protection the better
- Microbial bioprotectants are harder to protect by a patent
- Protection of ACVM data on a product is an important means of market dominance
- 'Fingerprinting' is desirable to protect a product from third party exploitation

Product development

- Need to have 3-4 products in development to get at least one successfully through to market, as well as a continuing release schedule
- Formulation is often where technical hurdles may be experienced
- Commercial scale manufacturing is a challenge even if pilot/research methods may be OK
- Local manufacturing gives better control of product quality
- Multinational agrichemical companies are more likely to pick up a product further down the development pathway (i.e. nearer market-ready) than a smaller or local company would?
- Products more difficult to register for organic markets as formulations are less able to be tweaked and still meet organic requirements
- Experimental trials of bioprotectants should be compared against non-chemical standards as comparison against established agrichemical options is unfair
- There are more variables in the use of bioprotectants in experimental trials (e.g. what was in the spray tank beforehand, what other treatments were applied to the crop before and after the trial bioprotectant, what were the environmental conditions when it was applied, what was the level of disease pressure, was coverage sufficient to impact on the target pest/disease (e.g. if direct contact is required), was the spray equipment calibrated, what was the water rate, etc.)

It is pleasing to see that the wine industry has an overt commitment to sustainable practices through voluntary membership of Sustainable Winegrowing NZ[9] (SWNZ), an entity established in 1995.

New markets

NZ science providers are well placed to drive the development of new modes of action. They represent considerable opportunities for the science providers given that commercial partners are always looking for new and exclusive opportunities and may be more willing to partner early. New technologies would include new modes of delivery as well as new active ingredients.

Given PFR's reach into developing markets overseas to assist with horticultural developments, thought should be given to using this presence to develop or test bioprotectants there. This is not without challenges in entering markets that have traditionally been reliant on agrichemicals, as well as being comprised largely of smallholdings and potentially the lower margins that may not justify bioprotectant use.

[9] https://www.nzwine.com/en/sustainability/swnz

2. NZ PUBLIC SECTOR BIOPROTECTANT DEVELOPMENT

CAPABILITIES

The R&D capabilities for bioprotectant development from NZ public sector R&D organisations are described in Table 8. This tables is limited to those organisations that have had a primary role in developing bioprotectants to market but it should be noted that other NZ CRIs, universities and Government agencies contain concentrations of relevant specific expertise, such as MWLR, Callaghan Innovation, University of Otago, University of Auckland and Massey University, and these groups have engaged with product developments led by the organisations in Table 8.

Collectively, NZ's public sector R&D institutions have comprehensive capabilities for the full range of bioprotectant development for a wide range of agricultural sector groups. Facilities are generally adequate to do the job, although biofermentation and formulation facilities are somewhat limited for larger scale field trials. Sector coverage is good across pastoral, horticultural, arable and forage crops, but more limited in floriculture. There is also engagement in new industries such as medicinal cannabis and plant proteins.

Table 8. Self-reported bioprotectant R&D capabilities in New Zealand's key public sector R&D organisations active in bioprotectant commercialisation.

A. Microbials

Capability	PFR	AgRes[1]	Scion	Lincoln
Biodiscovery and isolation	+++	+++[2]	++	++
BCA culture collection	++	++	+	++
Microbial taxonomy	++	+++	+++	+++
Target pest colonies and pathogen collections	++	+	++	++
Target pest/disease biology and ecology	+++	+++	+++	+++
Laboratory assays	++	+++	++	++
Glasshouse assays	+++	++	+++	++
Field assays	+++	+++	++	+++
Mode of action studies	++	+++[2]	+	++
Microbial genomics	+++	+++	+++	++
Microbial proteomics	+++	+++	-	+
Microbial metabolomics and metabolite ID	+++	+++	+++	+
Biofermentation – liquid	++	++	+	++
Biofermentation – solid state	+	++	+++	++
Product formulation	+	+++	+++	+
Bioinformatics	+++	+++	++	+
Residue analysis	+++	++	+++	++
Bacteriophage and viroid biology	++	++	+	+
Host plant endophytes	-	+++[2]	-	+++
Elicitor development	++	-	+	+
Natural product development	+	-	+	+

[1] Includes expertise from its wholly-owned subsidiary Grasslanz

[2] World-leading expertise

B. Semiochemicals

Capability	PFR	AgRes	Scion	Lincoln
Target pest biology and ecology	+++	+	+++	+
Headspace volatiles analysis	+++	-	+++	++
Gas chromatography-Electroantennograms	+++	-	+++	-
Chemical structure elucidation	+++	-	+++	+
Chemical synthesis methodology	+++	-	++	+
Olfactometer testing for response	+++	-	++	+
Formulation for testing	+++	-	+++	+
Field assays	+++	-	+++	++
Commercial synthesis methods	++	-	-	+
Commercial formulation	+++	-	-	-
Active space, lure longevity	+++	-	+++	+
Deployment specification	+++	-	+++	++
Monitoring technologies	+++	-	++	++
Control technologies	+++	-	++	++
Mating disruption	+++	-	+	+
Lure and kill	+++	-	+++	++
Biotremology	+	-	-	-

C. Supporting expertise

Capability	PFR	AgRes[1]	Scion	Lincoln
Market assessment, business cases	++	+	+++	+++
Regulatory conditions	+	+++	+	+
IP management	+++	++	+++	++
Commercialisation (strategy, licensing)	+++	++	+++	++
Licensee relations	+++	++	+++	++
Target crop sector relations	+++	+++	+++	++
Integration into IPM programmes	+++	++	++	++
Containment facilities	++	++	+++	+++
Modelling	++	++	+++	++
Agricultural economics	+	++	+++	+++
Insect rearing facilities	++	+	++	++
Host plant propagation	+++	+	+++	+++

[1] Includes expertise from its wholly-owned subsidiary Grasslanz

PUBLIC SECTOR-DERIVED PRODUCTS

Table 9 lists the bioprotectants originating from New Zealand public sector R&D institutions with current label claims for use in-market[10]. The list includes pheromone products - which do not require ACVM registration. These organisations have clearly been productive in generating bioprotectants for the NZ market, albeit with little impact in primary sectors overseas. Twenty-eight pheromone products, 10 microbial bioprotectants, 10 endophytes and two natural products have been released to the market. Of these, only a minority have patents granted or under examination (three semiochemicals, two microbials, one natural product).

Development times have varied considerably among this group. Some have been very quick: Isomate® Avocado took five years because of pre-existing pheromone technology being available; Aureo®Gold development was rapid and from a standing start, due to industry pressure for a solution. Others have been slow: The Desire™ Mealybug pheromone patent was submitted locally in 2009 but the product got to market in early 2021, due largely to the need to incorporate another mealybug species pheromone; Lurem® had a slower lead up before commercial development truly kicked off.

[10] Source: https://eatsafe.nzfsa.govt.nz/web/public/acvm-register

Table 9. Bioprotectants of NZ public sector origin.

The following are products registered and in-market which a NZ CRI or University have developed, or played a role in establishing in NZ.

A. Semiochemicals for pest monitoring and control

Product	Target	Host crop	Active ingredient	R&D Origin	Agent/Distributor
Lurem®	Thrips spp.	Fruit, vegetables, flowers	methyl isonicotinate	PFR	Pherobank, Koppert
Isomate® Avocado[1]	Leafrollers	Avocado	4 pheromones	PFR	UPL
Isomate® 4PlayMax	Leafrollers	Apples	4 pheromones	PFR	UPL
Isomate® 3NZ Leafroller	Leafrollers	Apples	3 pheromones	PFR	UPL
Isomate® LBAM	LBAM (*Epiphyas postvittana*)	Apples	1 pheromone	PFR	UPL
Isomate® CPlus	Codling moth (*Cydia pomonella*)	Apples, pears	1 pheromone	Shin-Etsu[3]	UPL
Isomate® CTT	Codling moth (*Cydia pomonella*)	Apples, pears	1 pheromone	Shin-Etsu[3]	UPL
Isomate® OFM Rosso	Oriental fruit moth	Stonefruit	1 pheromone	Shin-Etsu[3]	UPL
Desire™ Mealybug[2]	Mealybugs	Grapes	2 pheromones	PFR	UPL
Desire™ LBAM	LBAM (*Epiphyas postvittana*)	Apples	1 pheromone	PFR	UPL
Desire™ Octo	*Planotortrix octo*	Apples	1 pheromone	PFR	UPL
Desire™ Pex	*Planotortrix excessana*	Apples	1 pheromone	PFR	UPL
Desire™ Cob	*Ctenopseustis obliquana*	Apples	1 pheromone	PFR	UPL
Desire™ Herana	*Ctenopseustis herana*	Apples	1 pheromone	PFR	UPL

[1] Isomate®-branded products are used as a mating disruption tool for pest control and are manufactured by Shin-Etsu Fine Chemicals in Japan.

[2] Desire™-branded products are used for monitoring only. Twenty target pest species are covered by Desire™ lures with the above 6 shown by means of example. For some products, the pheromone was discovered by PFR or its predecessor organisations (DSIR, HortResearch).

[3] Product was developed overseas but specifications for NZ commercial use were tested and developed in NZ by PFR.

B. Microbial bioprotectants for the management of crop pests and pathogens

Product	Target	Host crop	Active ingredient	R&D Origin	Agent/Distributor
BioShield®	Grass grub	Pasture	*Serratia entomophila*	AgResearch	BioStart
Blossom Bless™ (NZ) Pomavita® (Europe)	Fireblight	Pipfruit	*Pantoea agglomerans* P10c	PFR	Grochem (NZ) Agrifutur (global)
Aureo®Gold	Psa	Kiwifruit	*Aureobasidium pullulans YBCA5 (CG163)*	PFR	UPL
BOTRY-Zen® WP (NZ) BotryStop™ (USA)	Botrytis; Psa; Botrytis, Sclerotinia	Grapes, blackcurrants, ornamentals; Kiwifruit; Kiwifruit	*Ulocladium oudemansii*	PFR	Botryzen (NZ); BioWorks (USA)
Tenet®	While rot Fusarium basal rot	Onion/Allium spp.	*Trichoderma atroviride LU132*	Lincoln Univ	Agrimm
Sentinel®	Botrytis	Grapes, tomatoes	*Trichoderma atroviride LU132*	Lincoln Univ	Agrimm
LettuceMate™	Improvement in transplant shock	Lettuce	*Trichoderma hamatum LU132*	Lincoln Univ	Agrimm
Kiwivax™	Psa	Kiwifruit	*Trichoderma atroviride LU297, LU668* *Trichoderma virens LU753*	Lincoln Univ	Agrimm

C. Endophytes embodied in cultivars registered under NZ Plant Variety Rights

Product	Target	Host crop	Active ingredient	R&D Origin	Agent/Distributor
AR1	Argentine stem weevil, pasture mealy bug	Ryegrass	Obligate endophyte (*Epichloë*)	AgRes	Grasslanz[1] / seed companies
AR37	Argentine stem weevil, porina, African black beetle, root aphid, pasture mealy bug	Ryegrass	Obligate endophyte (*Epichloë*)	AgRes	Grasslanz/ PGWS/ Barenbrug
Endo5	Argentine stem weevil, African black beetle, pasture mealy bug	Ryegrass	Obligate endophyte (*Epichloë*)	AgRes	Grasslanz/ PGWS (only marketed in Australia)

Edge	Argentine stem weevil	Ryegrass	Obligate endophyte (*Epichloë*)	DLF Seeds	Grasslanz[3] / PGWS
Happe	Still to be confirmed - Argentine stem weevil, African black beetle, root aphid, grass grub	Ryegrass	Obligate endophyte (*Epichloë*)	DLF Seeds	Grasslanz[3] / PGWS
GrubOut® U2	Argentine stem weevil, pasture mealy bug, African black beetle, root aphid, porina, grass grub, crickets	Festulolium	Obligate endophyte (*Epichloë*)	Cropmark[2]	Cropmark
MaxP (AR542) - MaxQ in USA)	Argentine stem weevil, African black beetle, root aphid, grass grub, crickets	Tall fescue	Obligate endophyte (*Epichloë*)	AgRes	Grasslanz/ PGWS/ Pennington Seeds
MaxP (AR584) – MaxQII in USA	Argentine stem weevil, African black beetle, root aphid, grass grub, crickets	Tall fescue	Obligate endophyte (*Epichloë*)	AgRes	Grasslanz/ PGWS/ Pennington Seeds
Protek (E647)	African black beetle	Tall fescue	Obligate endophyte (*Epichloë*)	Aarhus University, Denmark	Grasslanz/ PGWS/DLF
MaxR (AR1017)	Argentine stem weevil, African black beetle, root aphid, grass grub, crickets	Meadow fescue	Obligate endophyte (*Epichloë*)	AgRes	Grasslanz/ PGWS

[1] Grasslanz is a wholly-owned subsidiary of AgResearch

[2] Cropmark is a wholly-owned subsidiary of Plant & Food Research

[3] Moved into the Grasslanz portfolio since the purchase of PGWS by DLF Seeds

D. Natural products of public sector origin for crop pathogen control

Product	Target	Host crop	Active ingredient	R&D Origin	Agent/Distributor
MIDI-Zen®	Botrytis, Sclerotinia	Grapes	Soybean oil	PFR	Botryzen
ARMOUR-Zen®	Botrytis, Sclerotinia	Grapes, ornamentals, cut flowers	Chitosan	PFR	Botryzen

NZ REGISTERED BIOPROTECTANTS OF COMMERCIAL ORIGIN

Table 10 lists those bioprotectants that are registered by ACVM for use in NZ and are from commercial sources and not of NZ public sector origin.

Table 10. Bioprotectants of commercial origin registered in NZ.

A. Semiochemicals

Product	Target	Host crop	Active	Registrant/Agent
[1]NoMate 3 species	LBAM, green- and brown-headed leafrollers	Apples	3 pheromones	Grochem
[1]NoMate CM spirals	Codling moth	Apples	1 pheromone	Grochem
[1]NoMate OFM spirals	Oriental fruit moth (*Grapholita molesta*)	Stonefruit	1 pheromone	Grochem
[1]NoMate Quattro	Codling moth, LBAM, green- and brown-headed leafrollers	Apples	4 pheromones	Grochem
Codling moth lure	Codling moth	Apples	1 pheromone	Grochem
Oriental Fruit moth lure	Oriental Fruit moth	Stonefruit	1 pheromone	Grochem
LBAM lure	Light brown apple moth	Apples	1 pheromone	Grochem
Green headed leafroller lure	Green headed leaf roller	Apples	1 pheromone	Grochem
Brown headed leafroller lure	Brown headed leaf roller	Apples	1 pheromone	Grochem
Citrus flower moth lure	Citrus flower moth	Citrus	1 pheromone	Grochem

[1] Used for mating disruption

B. Microbial and natural product bioprotectants targeting pests (entomopathogens)

Product	Target	Host crop	Active	Registrant/Agent
Agree® WDG	Leafrollers White butterfly, diamond back moth, soybean looper caterpillars	Kiwifruit Brassicas	*Bacillus thuringensis* var. *azawai/kurstaki*	Hilado Pty Ltd.
Bactercide WG	caterpillars	Apples, kiwifruit, avocados, grapes, Citrus, berryfruit, vegetables, Brassicas, tomatoes	*Bacillus thuringensis subsp kurstaki serotype 3a, 3b, strain SA 11*	Grochem
Bactur	Leafroller caterpillars, other Lepidopteran larvae	Fruit and vegetables	*Bacillus thuringensis* subsp *kurstaki* serotype 3a, 3b, strain HD 263	Grosafe Chemicals
Beaublast	Aphids, psyllids, thrips aphids and whitefly	multiple	*Beauveria bassiana* strain K4B3	Ecolibrium Biologicals Ltd
Beaugenic	Thrips, aphids, whitefly	multiple	*Beauveria bassiana* strain K4B1	Ecolibrium Biologicals Ltd
Biobit® DF	Caterpillars	multiple	*Bacillus thuringensis* subsp *kurstaki* serotype 3a, 3b, strain ABTS 351	Valent Biosciences LLC Via Grochem
BMP™ 48 LC	Lepidopterous larvae	Fruit crops, tomatoes, Brassicas	*Bacillus thuringensis* subsp *kurstaki* serotype H3a, 3b, strain HD 263	Agrenz Ltd
Contego BB	Two-spotted spider mite, Western flower thrips, Green peach aphid, Silverleaf whitefly	Field crops, vegetables, fruit trees, vines, turf and ornamentals	*Beauveria bassiana* strain ATCC 74040	Biological Solutions Ltd
CYD-X	Codling moth	Apples	Granulosis virus	Hilado Pty Ltd
Delfin®	Leafrollers Tomato fruitworm White butterfly, diamond back moth	Apples, avocados, berryfruit, Citrus, grapes, kiwifruit Tomatoes Brassicas	*Bacillus thuringensis* subsp *kurstaki* serotype 3a, 3b, strain SA 11	Hilado Pty Ltd

Dipel® ES, DF	Leafroller caterpillars	Avocados, kiwifruit and other fruit, vegetable and ornamental crops	*Bacillus thuringensis* subsp *kurstaki* serotype H3a, 3b, strain ABTS-351	Valent Biosciences LLC
eNtoblast	Thrips, whitefly, green peach aphid, carrot aphids, mealybug, psyllid, passion vine hopper	Vegetable crops	*Lecanicillium lecanii* strain K4V2	Ecolibrium Biologicals Ltd
eNtokill	Thrips, whitefly, green peach aphid, carrot aphids, mealybug, psyllid, passion vine hopper	Vegetable crops	*Lecanicillium lecanii* strains K4V1 and K4V2	Ecolibrium Biologicals Ltd
Foray® 48B	Lepidopterous larvae	Multiple	*Bacillus thuringensis* subsp *kurstaki* strain ABTS-351	Valent Biosciences LLC
Grandevo® WDG	Mealybugs	Grapes	*Chromobactyerium subtsugae* strain PRAA4-1T	Nufarm
Madex	Codling moth	Apples	Granulosis virus	Key Industries Ltd
Organic Caterpillar	Caterpillars	Fruit, vegetables, ornamentals	*Bacillus thuringensis* subsp *kurstaki*	Kiwicare Corporation Ltd
Poncho® VOTiVO®	Nematodes, black beetle, greasy cutworm, Argentine stem weevil	Maize/sweetcorn	*Bacillus firmus* I-1582 (with clothianidin)	BASF
Sincocin	nematodes	Multiple	Plant extract from Quercus falcate, Opuntia lindheimen, Rhus aromatic and Rhizophona mangle	Agriganics Ltd
Virex	Codling moth	Apples	Granulosis virus	Grochem
Xentari® WG	Diamond back moth and white butterfly caterpillars	Brassicas	*Bacillus thuringensis* subspp *aizawai* Abbott strain 1857	Valent BioSciences LLC

C. Microbial bioprotectants targeting pathogens

Product	Target	Host crop	Active	Registrant/Agent
Bacstar™	Botrytis powdery mildew, sour rot Downy mildew Fireblight Anthracnose Greasy spot, Melanose Sclerotinia minor Brown patch, dollar spot, rust	Grapes, berryfruit, kiwifruit, Citrus, persimmons, onions, ornamentals Grapes Onions Apples, pears Avocados, Citrus, turf Citrus Lettuce Turf	*Bacillus subtilis* var. *amyloliquefaciens* strain D747	UPL
Botector®	Botrytis	Grapes	*Aureobasidium pullulans* DSM 14940 and 14941	Nufarm
Clarity®	Botrytis Powdery mildew, sour rot Anthracnose, greasy spot, melanose *Sclerotinia minor* Downy mildew	Grapes, berryfruit, kiwifruit, onions, Citrus, ornamentals Grapes, ornamentals, turf Grapes Citrus Lettuce Onions	*Bacillus amyloliquefaciens* strain MBI 600	BASF via Grochem

	Rust, Dollar spot, brown patch, Anthracnose	Turf		
Companion® Gold	Powdery mildew Botrytis Sour rot	Grapes, ornamentals Grapes, ornamentals Grapes	*Bacillus subtilis* strain GB03, plus nutrients	Lonza
Contego BSub	Botrytis, powdery mildew and other fungal pathogens	Grapes, fruit crops, potatoes, ornamentals and vegetables	*Bacilluis subtilis* strain ATCC 6051	Biological Solutions Ltd
Contego ST	Root rot, damping-off fungi, foliar fungal pathogens	Agricultural and horticultural crops	*Streptomyces lydicus* Strain ATCC 55445	Biological Solutions Ltd
Donaghys FoliActive	Botrytis, powdery mildew	Grapes	*Bacillus subtilis* KTSB	Donaghys
Dygall	Crown gall	Nursery plants	*Agrobacterium radiobacter*	Agbioresearch
Integral®	Soil-borne damping off fungi	Multiple	*Bacillus amyloliquefaciens* strain MBI 600	BASF
Integralis™	Botrytis Powdery mildew, sour rot Anthracnose, greasy spot, melanose *Sclerotinia minor* Downy mildew Rust, Dollar spot, brown patch, Anthracnose	Grapes, berryfruit, kiwifruit, onions, Citrus, ornamentals Grapes, ornamentals, turf Grapes Citrus Lettuce Onions Turf	*Bacillus amyloliquefaciens* strain MBI 600	Praegressus Ltd

Serenade® Optimum/Max	Botrytis Downy mildew Powdery mildew, sour rot Fireblight Anthracnose Greasy spot, melanose *Sclerotinia* minor Brown patch, dollar spot, rust, powdery mildew	Grapes, berryfruit, kiwifruit, persimmons, onions, ornamentals Onions Grapes Apples, pears Avocados, Citrus, turf Citrus lettuce turf	*Bacillus subtilis* QST 713	Bayer
Timorex® Gold	Powdery mildew Sclerotinia	Grapes Kiwifruit	Tea tree oil	Syngenta
TripleX™	Botrytis Sooty mould	Grapes, stone fruit, avocado, persimmons, vegetables kiwifruit	*Bacillus amyloliquefaciens* BS1b	Bio-Start

D. Endophytes of commercial origin registered under NZ Plant Variety Rights.

Product	Target	Host crop	Active ingredient	Agent/Distributor
NEA 2 (mix of NEA 2 and NEA 6)	Argentine stem weevil, pasture mealy bug, African black beetle, root aphid	Ryegrass	Obligate endophyte (*Epichloë*)	Barenbrug
NEA (NEA 2)	Pasture mealy bug, African black beetle	Ryegrass	Obligate endophyte (*Epichloë*)	Barenbrug
NEA 4 (mix of NEA 2 and NEA 3)	Argentine stem weevil, pasture mealy bug, African black beetle, root aphid	Ryegrass	Obligate endophyte (*Epichloë*)	Barenbrug

Notable by their absence from the preceding tables are non-endophytic bioprotectants of use in pasture, amenity horticulture, row crops (e.g. corn, wheat, barley, seed crops) and fodder crops. The traditional view of this gap is that the economics of crop production do not support the use of these more expensive bioprotectants, and these industries have tended to habituate agrichemical use. This habituation is not a practice exclusive to these sectors though – it is still apparent in some fruit and vegetable crops.

Entomopathogens represent less than 10% of the New Zealand-registered pesticides (Glare & O'Callaghan, 2019). The commercial microbial products used for pest control have come from a narrow range of organisms, primarily *Bacillus thuringensis* and *B. firmus*. Other microbials registered for pests include *Baeuvaria bassiana* and *Chromobactyerium subtsugae. Yersinia entomophaga* is showing promise against diamondback moth, especially given its effect on strains showing resistance to *Bacillus thuringensis* and the pesticide Spinosad (Hurst el al., 2019).

For pathogen control, most products are based on *Bacillus subtilis* and *B. amyloliquefaciens*, with less common use of *Agrobacterium radiobacter, Streptomyces lydicus* and *Aureobasidium pullulans.* With the exception of *Aureobasidium pullulans* (Aureo®Gold), the NZ-derived bioprotectants source a different range of microbial bioprotectants. The narrow range of commercialised microbial bioprotectant species does not reflect the range (157 species of potential bioprotectants) that has been researched and published historically, with *Bacillus subtilis*, *Trichoderma* and *Pseudomonas fluorescens* having the broadest target spectrum and 118 species described for efficacy against only one target (Nicot et al., 2012).

For some target pathogens the market is seemingly crowded with biocontrol products – particularly Botrytis and powdery mildew. While this suggests that pursuing products for this target would not be worthwhile because of intense competition, there are nuances to this opportunity. The value proposition for a new bioprotectant for Botrytis should therefore be a significant gain in efficacy in most applications, or a new mode of action for efficacy, filling a seasonal gap, ease of use or price, assuming other bioprotectants have otherwise equivalent properties.

Suckling (2012, Table 1) lists 28 pests for which their pheromone-based products were produced or sold in New Zealand at that time, many of which were discovered and developed by NZ scientists, and the remainder of which had the refinement of the pheromone blend and/or deployment specifications developed by local chemical ecologists and applied entomologists for application to local industries or for our biosecurity interests. This collective set of scientific expertise, along with close connection to biosecurity and orchard management practices, has led to the success of pheromone-based pest control in NZ, and continues to create impact today as more products are developed.

Many pheromone products are applied to NZ's commercial apple orchards, and these products – along with their integration into a wider IPM programme – have contributed to fewer synthetic insecticide applications (Figure 5), lower pesticide residues, exclusive access to high value Asian markets, and consistent ranking of NZ's apple industry as the most competitive in the world – despite its size (Belrose, 2018; Suckling et al., 2015).

NZ INSTITUTIONS AS DEVELOPERS OF BIOPROTECTANTS

It is apparent from the preceding information that NZ public sector institutions have a comprehensive array of expertise and facilities to develop bioprotectants for local and overseas markets. This comprehensiveness places NZ well as a provider of early development to commercial partners with local and global reach to those markets. Furthermore, NZ public sector R&D providers have a good track record in getting bioprotectants to market. This is earned from a strong science base, together with capabilities and facilities in applied field research – including developing IPM programmes – and productive commercial partnerships to take bioprotectants to market.

Our location is both a benefit and a hindrance. We are able to offer an off-season location for northern hemisphere field work, doubling the speed at which such work can progress in collaboration with commercial or research partners. This has occurred for a number of semiochemicals in development or released, and is currently the case for Microbial #201 as additional label claims are sought. In contrast, there will be some limitations for joint work because of phytosanitary or biosecurity barriers to pests, diseases or microbial bioprotectants in different territories.

New Zealand's local institutions can and do act collaboratively with each other with relative ease. The R&D community is small and most researchers are aware of relevant colleagues in other institutions. The administrative burden varies within and between universities and CRIs given some different approaches to IP, legal review turnaround and internal versus market motivations. For some bioprotectants, collaboration has enabled product development to progress (e.g. Aureo®Gold, microbials 204, 206 and 207, pheromones 109-110).

The NZ CRIs and universities differ from all but the largest commercial entities in that they have a broad and deep base of discipline-specific expertise in entomology, pathology, physiology, biochemistry and crop science to the most fundamental level. This provides a science capability of use to commercial partners in that we are able to develop bioprotectants based on novel mechanisms of action, describe mechanisms of action to genomic and metabolomic levels, describe target pest/pathogen biology and ecology, and integrate bioprotectants into IPM programmes.

There are few public sector R&D providers internationally who individually have such a range of discipline-specific capabilities that are coordinated to bring bioprotectants to market. This is enhanced further when one considers the collective expertise of NZ public sector R&D providers who are active in bioprotectant development (PFR, AgResearch, Scion, Lincoln University) are bolstered by pockets of other relevant expertise such as those in MWLR, DoC, MPI and other universities.

Currently, there is no common gateway to NZ's collective expertise for bioprotectant development. This is exacerbated for those commercial entities that have limited insight into NZs expertise. Generally, the intent to collaborate among public institutions is strong - and the major public R&D funding mechanisms in NZ encourage collaboration through their allocations.

3. SUCCESS FACTORS AND CHALLENGES

SUCCESS FACTORS

Factors that have facilitated the development and commercialisation of bioprotectants from New Zealand public R&D institutions to date include:

1. Market-driven needs from industry bodies were dominant in initiating development.
2. R&D providers have been supporting bioprotectant science and development for decades, building up significant expertise and reputation across the bioprotectant development pipeline, as well as foundation facilities such as culture collections.
3. Applied researchers have a good handle on target pests and diseases and their importance within each crop sector, and are connected directly to end-users in each industry.
4. Commercial partners have a direct line to researchers.
5. There are innovation leaders in the end-user farming community who readily take up new bioprotectants and lead their introduction into their sector.
6. Strong IP positions being attractive to commercial partners
7. Co-innovation across CRIs and universities
    a. Base funding mechanisms (e.g. MBIE's Next Generation Biopesticide programme 2013-2019)
    b. Complementarity of skill sets and business objectives.
8. Awareness of public sector bioprotectant developments by the commercial sector, driven by proactive outreach to them by research and/or business development personnel.

Examples

Five of the nine products currently in market have patent positions secured or under examination. While this is not essential for success, it has been a strong driver for commercial interest.

Isomate® Avocado (pheromone-based mating disruption of 4 leafroller pests)

Development was very rapid due largely to having the four active ingredients in existence (formulated individually and validated in other products), a proven dispensing system for mating disruption (Isomate® 'ropes'), an existing commercial partner contracted to receive such a product as a licensee, and comprehensive scientific expertise before development began. Avocado industry engagement and co-funding then leveraged commercial, Government and PFR internal funding. The development phase to licensing was a mere five years and consisted primarily of field-based testing and formulation refinement, as well as deployment characteristics.

Post-market development was not without its challenges though. More efficient deployment of the product into avocado trees, greater acceptance by the farmers and a stronger drive from their sector body is needed to speed up market penetration (this is their sector's first pheromone-based product), and further development of a non-plastic biodegradable dispenser would enhance this, and related, opportunities.

Aureo®Gold (microbial bioprotectant to control Psa on kiwifruit)

The development cycle was a surprisingly fast at 6 years given that discovery and development started from scratch. There was a culture collection in existence that could be screened to provide candidates for a bioprotectant, but the crisis in the kiwifruit industry that arose in late 2010 led to a significant mobilisation of resources in the research, sector and agrichemical community, with adequate funding (estimated $3.2m in total). Concurrent with product development was the need to understand the target pathogen's ecology and biology which was previously unknown in the NZ context, being a recent invasive pathogen. The lack of 'green' pathogen control alternatives – for an industry keen to build on this reputation – was also a contributing driver.

Aureo®Gold development happened at pace despite two rounds of acquisition of the commercial partner in 2018 and 2019. Since market entry in 2018, Aureo®Gold is now being tested for other pathogen targets on other crops in other territories. This represents a significant revenue opportunity for all involved should this global opportunity is realised.

CHALLENGES AND CONSTRAINTS

In a retrospective review of the development of 20 in- and pre-market bioprotectants (Table 1) developed at public sector institutions in New Zealand, a number of factors were identified as contributing to slower or less effective development and commercialisation of these. The most common and impactful factors hindering bioprotectant development were the timing, nature, consistency and extent of commercial partnerships, the lack of Government/internal funding for direct or foundational R&D to support early development, fatal technical flaws (see point 5 below) and an overestimated market opportunity (sometimes because of product competition).

One microbial bioprotectant (Microbial #210) did not reach the market after several years of development because of a mix of recorded opportunistic human pathogenicity of the same species elsewhere, compromised IP, variable efficacy against the target pathogen and a lack of commercial management along the whole development cycle. All of these factors could have been forecast or addressed earlier. Natural product #303 failed at a late hurdle due to product residues above the level of detection, thus requiring MRLs to be put in place in all export markets. The cost of this did not warrant further development.

In more detail:

Drivers and market forces

1. Historically, most product developments have been led by 'researcher push' rather than 'industry-driven demand' (although this is changing). Speed of development seems proportional to sector and commercial partner engagement.
    a. One product currently in development had 100% researcher push but no market pull
2. Product goals have largely been driven by New Zealand needs, thus limiting the value of the products to commercial partners and the inventing R&D partner, unless NZ represents a starting point for larger global markets. While a NZ crop sector may wish for a bioprotectant, if a commercial agrichemical company does not wish to take the product on there will be no supply of it.

3. Bioprotectant development opportunities to date have been initiated on an opportunistic, case-by-case basis rather than from a more strategic portfolio approach. This has limited the development of underpinning resources and left the pipeline open to the risk of running dry.
4. Negative perceptions of bioprotectant efficacy relative to chemical options are alive and well in most crop sectors. Only by necessity (e.g. loss of alternative options) or through effective education will bioprotectants attract strong interest and acceptance.

Forecasting technical or market hurdles

5. Low efficacy, limited storage life, regulatory barriers (e.g. human pathogenicity), handling challenges (e.g. cool storage requirements, light sensitivity) and low fermentation yields can be fatal to product development and should be tested earlier in the development cycle.
6. Some technical hurdles were able to be forecast (e.g. commercial supplies of co-formulants stopped).

Product competition

7. Some products are going into markets where there are already a number of pest/pathogen control options. Competition and market uptake may be limited but can be forecast.
8. Generally, the R&D organisations are aware of market gaps and competing products before embarking on new product development, but the realities of market opportunity require commercial partner input from the beginning. This is nuanced by the portfolios of each commercial partner and their competitive positions in the market. This may encourage multiple product development from the public sector for the same target, licensing these through competing partners but achieving greater market share for the R&D institution.

R&D Expertise and resourcing

9. Most product developments were researcher-driven, recognising though that researchers do generally have a good understanding of market need. Most researchers though were acting alone or with little internal collaboration so the research intensity was low and led to longer development timeframes than desired.
10. There is competition for any researcher’s time between short term fee-generating client services and long term product development revenue
11. Collaboration among R&D providers requires joint funding applications and multiple contracting, increasing the administrative burden of joint activity.
12. Funding limitations:
    a. Foundation culture collections or core competencies are not overtly funded
    b. No underpinning R&D (e.g. pest and disease life cycles and ecology) is done because it is funded neither by third party public good funders nor commercial interests
    c. Funding cycles are shorter than development timelines

Intellectual property

13. Intellectual property (IP) positions are often weak
    a. Although there are no examples in NZ of reverse engineering or copying of products
    b. Significant time elapses negotiating IP arrangements, including that due to exits of partners.

c. Exits of commercial partners during development may include subsequent restrictions on trade for the R&D partner, further delaying development through alternative commercial partners.
d. Third party IP may pose some constraints (formulation, territory opportunities)

Development disruptors

14. The Psa crisis of the 2010s did direct PFR resources away from other bioprotectant developments for several years
15. There has been high turnover of business or commercialisation support personnel in some places within the public sector

Commercial partnerships

16. Commercial partners do go through natural life cycles, including acquisitions, that may disrupt engagement in bioprotectant development
17. The product may have been developed to a very advanced formulation before commercial interest kicked in
18. Commercial partner selection
    a. Some may have been selected because they were 'on the spot' rather than sought out
    b. BCAs may not be core business for the commercial partner, or their revised strategy subsequently excludes this interest
    c. Not enough due diligence done by the R&D institution of potential commercial partners
19. Commercial co-development
    a. The public-private partnerships vary considerably with respect to the nature and extent of engagement with commercial entities. There may be little engagement after licensing (e.g. in formulation improvements), despite a wealth of relevant experience in researchers that would be of assistance
20. Licensee performance in market
    b. Licensees can and do underperform at times, in terms of market penetration and sales. There can be many reasons for this but without performance criteria in license agreements there is little the licensor can do to redirect licenses.
    c. On rare occasions the licensee is a manufacturer rather than distributor, thereby limiting their ability to develop and penetrate markets.

Market entry

21. Regulatory processes
    a. Despite Government goals for the environment and agriculture, regulatory processes do not preferentially hasten the introduction of sustainable biocontrol products (over that of agrichemicals).
22. Technology transfer
    a. Technical staff in the commercial partners, downstream retailers and sector bodies may be limited in their understanding of bioprotectants and how to use them
    b. There can be a business driver (e.g. profitability, competition, client/end-user familiarities) that favours the sale of products other than bioprotectants

   c. Market share underperformance due to lack of technology transfer intensity.

23. End-user demand for bioprotectants is still limited by historic perceptions
    a. Economic benefits have not been quantified and shared with end-users in order to promote their value and generate demand

The New Zealand regulatory environment

There is no doubt that a robust regulatory framework is necessary for crop protectants in order to minimise risk to humans and the environment and ensure food is safe to eat and can be exported to discerning consumer markets. With political will, New Zealand has a great opportunity to foster the use of sustainable bioprotection products for agriculture through preferential processing through our regulatory pathways.

Interviews with industry participants sought real-life experiences with the registration process in New Zealand. Many of these issues are reflected in other territories (e.g. Damalas & Koutroubas, 2018; Kerr & Bullard, 2020).

Semiochemicals developed here or imported for use in New Zealand are exempt from registration under the ACVM Act, but require registration under the HSNO Act. There is a group standard for Straight Chain Lepidopteran Pheromones ('SCLP') that covers approvals for all such pheromones, such that these do not require individual approval (Boyd-Wilson et al., 2012). This is the case whether the pheromone products are used for monitoring or control, but the SCLP only allows for passive dispersal of the pheromone. If a pheromone product is dispersed by more active means (e.g. puffer sprays) or contains other products such as insecticides for a lure and kill application, EPA and ACVM approval is required. Some current requirements for registration are not applicable e.g. buffer zones for pheromones, and the size of buffer zones in relation to typical orchard or farm size. Pheromones do have to be entered into the EPA's Chemical Classification and Information Database (CCID). Some data required for this is almost impossible to generate, such as the volumes of pheromone and extraordinary costs needed for toxicity tests.

The HSNO Act does not cover any specifics relevant to microbial bioprotectants – they are reviewed using the same criteria as those for agrichemicals despite clear differences in their nature and modes of action. Microbial bioprotectants do not need EPA approval if the organism is sourced from local environments (i.e. is demonstrably already present in the wild here), but in any case must be registered through ACVM. The Microbial Agricultural Chemicals guidelines from MPI outlines the criteria and requirements for this process (Ministry for Primary Industries, 2016). As with all registration requests, they are reviewed in the order received. Review and registration of the same product in other territories are not officially recognised in NZ review, even though some of the data is equally applicable (e.g. bee and human toxicity data). It is common to have sequential review through EPA and ACVM last up to 6 years. Data protection legislation under the ACVM Act is only valid if submission to ACVM is done first followed by application to EPA once the ACVM application is accepted. This adds considerably to the time frame to get to market.

Biostimulants that have no claim for pest and disease control but may enhance general growth and wellbeing of a crop plant, do not require ACVM registration.

Gerard & Barratt (2021) point to some of the issues that complicate registration, including that the information required may not always be available. Ehlers et al. (2020) pointed to the dilemmas of funding and benefit to different stakeholders that often apply to biocontrol development and registration. Difficult, expensive and long term registration processes are not unique to NZ nor new (Gregg et al., 2010; Kerr & Bullard, 2020).

In summary, the regulatory environment – while absolutely necessary – does not *preferentially* favour the introduction of bioprotectants despite a groundswell of support locally and internationally to shift the balance of pest and disease control from chemical options to the more sustainable bioprotectant option. This hinders the opportunity to develop NZ as a counter-seasonal territory for the development of bioprotectants for local and international markets. A more favourable and quicker regulatory system will also create greater preparedness for biosecurity incursions where a rapid response is needed.

There are multiple entities of relevance to this outcome. The Primary Sector Council, GIA, MPI, MfE, organics groups, regional councils, AGCARM and agrichemical companies with bioprotectant interests all have a vested interest in positive change. Coordinated leadership for this goal is needed.

4. Co-innovation for impact

Quote from Adrian Percy, Chief Technology Officer, UPL[11]:

> *"Our food production systems need a shakeup," said Percy. "Agriculture is in dire need of transformation, and today's painfully slow rate of technology innovation and on-farm deployment simply can't continue. Our OpenAg purpose is tearing down limits and borders to create partnerships that will transform agriculture by delivering broad value across the entire food production network."*

Co-innovation within the public sector

The R&D community relating to bioprotectants is relatively small in New Zealand – most researchers know each other and are generally willing to collaborate. Section 2 revealed some degree of complementarity – and some overlap – in skill sets between institutes. A number of goal-specific funded projects have brought together individual researchers from different institutions to good effect, not only from the key CRIs and universities but also the Department of Conservation, Ministry for Primary Industries, Manaaki Whenua Landcare Research and others.

The larger and longer-term MBIE-funded programmes (e.g. the 2013-2019 Next Generation Biopesticides programme involving several institutes working across several sectors) have been the catalyst for NZ-wide collaboration with clear purpose, and has resourced relevant fundamental research in tune with commercial objectives. MBIE rated this programme very highly after its conclusion but re-applications to MBIE all failed. This has caused a retreat of researchers into their own institutions (i.e. less collaboration) and a stalling of progress in bioprotectant science and product development.

Bioprotection Aotearoa (hosted by Lincoln University) has been in existence since the Centres of Research Excellence were launched in 2002. Bioprotection Aotearoa is a partnership of 11 NZ universities and CRIs that exists to train the next generation of bioprotection researchers and to deliver world-class research that protects the productive and natural landscapes of Aotearoa New Zealand and the Pacific. It has just been granted another 7-year extension in 2021. It is not overtly focussed on supporting bioprotectant development as a primary focus.

Co-innovation between the public and private sectors

Generally, a minority of bioprotectant development outside of multinational companies emanates from public R&D institutions (R.Gwyn, pers.comm.) although the track record in NZ suggests otherwise (Section 2). Conversely, start-ups – whether from public institutions or de novo - are more common overseas but can fail if commercial rigour is not applied early. In NZ there are few private companies who have developed bioprotectants of their own accord locally (e.g. Agrimm, BioStart) and none started as a spin-out from a NZ public institution.

Multinational agrichemical companies acquire bioprotectant technologies through a range of avenues. Aside from their large scale acquisitions, their awareness of new technologies and products

[11] https://www.wraltechwire.com/2020/08/14/multinational-firm-upl-is-looking-for-rd-partners-adding-jobs-at-new-rtp-hub/

comes from a range of interactions such as common networking opportunities for scientists from both parties, scientists moving from public to private employers, ongoing relationships with public institutions including the funding of postgraduate student research, online portals for technology submissions (‘open innovation platforms’), and ‘cold’ direct approaches from institutions. They also have scouts for this purpose.

Some multinationals have systems in place for their internal review of external opportunities. Contributed ideas and opportunities often fall into two categories: earlier stage platform opportunities and well developed pre-market products. Each is treated differently. Consideration of early stage technologies relies initially on a review of supplied *in planta* data dossiers (preferably to greenhouse or field tests) and relevant known properties (e.g. toxicity, production), fit with the multinational’s product portfolio, competitive space, and expectations of intellectual property protection (freedom to operate; potential, applied for or granted patents), all under a non-disclosure agreement. Subsequently, agreements would be put in place and sufficient product supplied in a timely manner for the multinational to test in house the prototype product. Some multinationals prefer to own the technology (e.g. full assignment of patents) as it gives them a clear and simple position to work from. Only a small minority of early stage technologies would be taken on by a multinational, especially if the technology is a new microbial species or a new mode of action. The timing of interest in new technologies is a balance between its novelty, stage of development and level of data available.

Acquisition of an external party’s technology need not mean the relationship is exited; the interaction can continue if there is a complementary fit of expertise between the parties, and the product pipeline may continue to be filled. The partnership may be based on a formal or casual ‘first rights’ understanding.

Caution should be exercised from the research institutions in external assessment of their developmental bioprotectants. The researchers who know the product best should be engaged in third party protocol development - comparing bioprotectants against an agrichemical framework can be misleading and may downplay their opportunity. The timing, placement and duration of treatments are different and rely on an intimate knowledge of the target pest/disease biology, phenology and ecology as well as the bioprotectant. For example, the value proposition for a bioprotectant will not rely solely on yield or target pest/disease incidence – other parameters should be measured, and expectations of efficacy of 80% efficacy need not be the goal. Managing the conversation and setting appropriate expectations with the third party are essential.

Institutional researchers also need to meet the market demands of potential commercial partners. Engaging earlier, handing over products (and earlier), engaging collaboratively with those partners, closing down unfruitful opportunities earlier and responding to commercially-driven targets would add to reputations and outcomes.

Public sector developers of commercial bioprotectants often have an additional role as independent sources of expertise to test the bioprotectants or agrichemicals of other parties – often involving the same researchers. There is therefore the potential for a perceived conflict of interest in conducting those independent trials. It is also conceivable that the institution may compete with itself in the same market with its own products, as well as with existing licensees and commercial products.

Case study

A successful partnership worth highlighting is that which has developed between PFR and UPL NZ Ltd for the development of semiochemicals.

Up until 2010 HortResearch (the successor to DSIR and predecessor of PFR) was manufacturing pheromone lures for the NZ market as there were no commercial suppliers locally. This included the Isomate® mating disruption products (manufactured By Shin-Etsu in Japan) and the Desire™ monitoring lures. This business was not a good fit for a Government-owned research institute so in 2010 HortResearch sold that business to ETEC Crop Solutions, a local company. The relationship continued in semiochemicals thereafter as they worked to further develop pheromone products for the NZ market, licensing new products through ETEC as they arose.

In 2019 this relationship was formalised in a heads of agreement for semiochemical development, based on a first rights principle for both parties for development and commercialisation. This still allows the opportunity for PFR to develop semiochemical products independently as directed by any other client. Annual investment and priority setting is conducted under this relationship and managed by a joint R&D Committee. Despite two rounds of acquisition of ETEC in the late 2010s – first by Arysta LifeSciences and then by UPL, the operation of the collaborative activity has not wavered. Since then two new semiochemical products have entered the market.

The NZ branch of UPL was instrumental in introducing PFR to UPL global managers at the ABIM conference in Basel, Switzerland in late 2019. This has led to a global reach for PFR now, with access to international markets and opportunities.

The relationship is enduring, the engagement is weekly, and the relationship is actively managed from both parties. They have also celebrated milestones and successes with appropriate occasions.

The future contribution of NZ public institutions

The local institutions with a track record in bioprotectant commercialisation (PFR, AgResearch, Scion and Lincoln University) are positioned well to co-innovate with commercial partners for local and global markets. Collectively they have a full complement of specialist expertise that ranges from fundamental disciple-based experience through to applied integrated pest management successes.

Additionally, there are other supporting pockets of scientific expertise from other NZ public R&D institutions that add value when needed. Furthermore, business and research staff have close relationships with crop sector bodies, agrichemical companies and end-users (farmers) and thus have a sound knowledge of commercial drives.

The CRI Act of 1992 mandates that CRIs provide impact to industry, and their Statements of Core Purpose define the sectors they serve, thereby minimising competition and overlap. CRIs are able to form appropriate business entities, with demonstrable success in setting up spin-out companies, joint ventures, business partnerships and research collaborations. Our southern hemisphere location facilitates counter-seasonal activity to accelerate product development, and this isolation offers some degree of secrecy of activity from international eyes. CRIs are also well resourced in having research farms across the country as well as suitable access to commercial properties for research trials. Our institutions also have business and commercialisation professionals and strong IP mandates.

There would be few such institutions internationally that offer this breadth of capability and the intent and ability to do business locally and globally. New Zealand is therefore well placed to act as early stage developers of commercial bioprotectants.

5. Strategy for accelerating growth

Given the market opportunities and experiences with past and current bioprotectant developments, we can now develop strategies and a *modus operandi* to facilitate bioprotectant development from public sector R&D organisations for local and global markets. It is interesting to note that some of these recommendations were highlighted in 2012 (Glare et al., 2012), suggesting progress has been slow. There is therefore a need for fresh approaches to ensure these recommendations have impact.

Goal

A vision for 2030 could look like this:

- Fundamental science activity is adequately resourced to support product development
- There is a branded and collective 'front door' through which bioprotectant IP is channelled to commercial partners and thence the market
- Commercialisation and business development professionals are active from within this entity
- This entity also acts to promote awareness of NZ capabilities to attract investment and co-development partnerships
- Product developments are tied to clear market needs, especially global opportunities
- Product development is coordinated across key public sector institutions
- Commercial partnerships begin early in the development phase, are robust and enduring
- Several IP assignments or licenses are executed for bioprotectants every year
- The regulatory framework favours bioprotectant development and registration
- Revenue exceeds NZ$15m per annum and continues to grow
- The product brand is established and respected overseas.

Actions

Revenue sources

Despite an extremely successful MBIE programme from 2013-19, funding from them has evaporated since despite further applications. We could consider re-application with a different focus and mandate, but this will not guarantee success.

An earnest discussion among the 4 key institutions is warranted to consider whether SSIF and PBRF revenue could be concentrated into a consortium for bioprotectant development. Investment from these institutions can be formularised with returns from commercialised products shared on that basis. Allocations from this centralised fund can be made on a project basis, commensurate with market opportunity.

Bioprotection Aotearoa and the B3 programme, both of which engage multiple public institutions, each play a key role in the wider bioprotection space. Closer integration with the proposed bioprotectant consortium proposed here would be warranted.

PSAF funding via Kiwinet is appropriate as it leverages commercial investment in later stages of development that has some history of public sector investment. It should certainly be applied for when there is a greater consortium of products within the proposed entity described later. On their own, each product may not have the market value and resident commercial partner that drives PSAF investment decisions.

Absent from current revenue sources is private venture capital. Public R&D institutions, given their Government ownership model, cannot attract such funds directly. Should the IP associated with bioprotectants be assigned into a new legal entity, this funding option opens up. Given the evidence of global investment trends outlined in Section 1, the timing would be right for this. Even locally in NZ, we know there is an appetite for investment in primary sector initiatives and primary sector private investors with money to invest. There is also a general willingness to invest over longer time frames than previously – this is needed for bioprotectants.

Scientific expertise

NZ is currently well-served with expertise for bioprotectant development. Funding is needed to engage postgraduate students and postdocs to ensure there is succession planning in place for this expertise. Long term commercially sponsored senior positions in NZ institutions can assist with this. Our distance from the R&D-intensive seats of multinational commercial companies need not hinder the opportunity for bilateral scientific exchanges (travel permitting), with appropriate protection of commercial sensitivities in place. Government funded exchange programmes do exist, and Horticulture NZ's 'A Lighter Touch' programme could also support this endeavour.

Foundation science and facilities

Most institutions would benefit from an internal commitment to foundation science programmes and resources to fill the development pipeline further. These areas have traditionally not been overtly supported well, but are vital for product development.

-Omics studies

Complementing more applied research is the opportunity to use genomic, proteomic and metabolomic research to identify modes of action and potentially devise *in vitro* screening tools for microbial selection. Hurst et al.'s (2016) analysis of the genome of the entomopathogen *Yersinia entomophaga* is an example of the lead in to this.

Target biology and ecology

Essential to the rapid development of a bioprotectant is a thorough knowledge of the biology and ecology of the target pest and disease. Biocontrol development without this is a 'stab in the dark' and likely to delay development. This R&D has been difficult to fund in the past, and would require additional foundation funding. Both CRIs and universities in New Zealand have access to suitable 'in house' funding (SSIF, CoRE and PBRF) that can be used to this end and requires only internal decisions to be used for this purpose.

Efficacy enhancement

It is recognised that bioprotectants have some reputation for variable efficacy in real world systems (Heydari & Pessarakli, 2010). Further research is required in novel formulations to increase efficacy in variable microclimates in the field (and for enhanced storage life of microbial bioprotectants), understanding microbial bioprotectant response to environmental parameters, and methods for mass propagation (biofermentation) and formulation. Lessons learnt can be applied across multiple bioprotectants.

Culture collections

Collections of beneficial microorganisms are the engine room of microbial biocontrol development. Sadly, these have been maintained at variable levels and in uncoordinated ways within most of the CRIs and universities hosting them. With pipelines of product development potentially running dry, and posing limitations to candidates as future bioprotectants, it is imperative that these collections continue to be added to and that they are stored and recorded for quick access. For most institutes their microbial culture collections are poorly curated, only moderately characterised, opportunistic in content and not shared. All four aspects need to be improved if future product development is to succeed to a larger and quicker scale.

There is an opportunity to increase collections of microbials from wild sources (e.g. the conservation estate) as potential bioprotectants – a largely unexplored area but with current evidence of this opportunity (Table 9; Stott & Taylor, 2015). The engagement of local Maori is essential, and they too should be beneficiaries of this. Care needs to be exercised if such microbes are intended to be exploited overseas, not only needing the blessing of iwi as kaitiaki but with respect to biosecurity issues across borders. Both the local (Wai 262) and international (Convention on Biological Diversity, Nagoya Protocol) environments pose significant issues to the exploitation of and trade in such indigenous resources. Potential semiochemicals from native plants pose another opportunity that should be explored.

Our institutions are also well placed to provide deep science to determine modes of action of bioprotectants as well as agrichemicals. This opens up a fee-for-service opportunity to commercial companies, at least in part.

There are small scale scattered facilities for biofermentation and formulation across locations and institutions. The developing opportunity from the BioSouth initiative in Canterbury is exciting and should play a key role connected to our institutions for bioprotectant development for the purposes of product development.

The recent introduction of nanostring technology and equipment into PFR could be a game changer for the early development phase of bioprotectant development, enabling more extensive and rapid screening of microbial candidates. This technology should be supported and applied across the participating public institutions.

Commercial partnerships and business models

'The earlier the better'

Most of the in-market bioprotectants developed in New Zealand have been driven by the needs of target crop sector bodies, for example Zespri, NZ Apples & Pears, FAR, etc., with commercial (manufacturing and distribution) partners engaged further along, or even late in, the development pathway. As noted before, researchers have initiated bioprotectant development on their own accord with an understanding of a market need, or have done so in concert with the relevant sector body.

It is recommended that agrichemical partners are consulted when estimating the market opportunity for a proposed bioprotectant, as well as raising at that time the risk factors that could arise during product manufacturing, registration and market uptake.

It is recommended that public sector R&D providers extend their relationships with commercial partners through strategic relationships. The PFR-UPL relationship with respect to semiochemical development detailed earlier is a good example of a productive PPP environment for bioprotectant development.

1. Heads of agreements pre-empt and lock in commercialisation partnerships (e.g. licensing for manufacturing and distribution) rather than needing to secure these later in the development process
2. Some formality to joint decision-making on product opportunities
3. A dedicated fund that supports annual investment into new product development, even if covering only some of the costs. At the very least, this funding can provide leverage for third party funding
4. The commercial partner provides more direct insight into the new product opportunity and can drive the intensity of this from the beginning
5. The commercial partner brings a strong and early focus on the economic opportunity for the proposed bioprotectant

The downside to such an arrangement is that there is less freedom for the R&D entity to secure competitive licensing arrangements. It is possible to mitigate this by identifying the limits to distribution rights for the foundation commercial partner (e.g. for different territories or applications) in order to secure additional licensees.

As with any business partnerships, relationship management is key. A client relationship manager (CRM) is important, as is an open line from the commercial company to the researchers. The opportunity for a joint media presence and celebratory events should not be forgotten. A mature business relationship should be able to be identified, and seen, as 'intimate'.

Consideration should be given to a range of product commercialisation models, including:

- Licensing through a single commercial partner has been the common model for commercialisation of NZ public sector-generated bioprotectants. This has been successful in many cases, but the vagaries of commercial parties can work against this
- 'Open access' is one model but this requires development to a later stage (perhaps even market registration) and would be more applicable to products with local or limited market opportunity and poor IP protection. Ensuring equity among contributory partners requires care, but royalties could be applied differentially according to prior contributions.
- Spin outs can be done and there are precedents internationally in the biocontrol space. Independent start-ups can and do succeed.
- Partnerships such as joint ventures with equity investment
- Packaging product with services for a subscription-like model direct to end-users

Prioritising product goals

Greater rigour is needed at the early stages of product development to identify market drivers, product competition, product performance, IP, and development and commercial pathways. A new scoring system is proposed that will assist in this (Appendix 1). A definition of addressable markets is also provided below to make comparative assessments of market opportunity. Target pest and diseases are itemised in this report with particular note on those opportunities that extend to global markets. Prioritisation within these, and business cases with quantified market analyses, now rests with each institution in partnership with commercial entities.

Assessing market opportunities

To provide some rigour to initiating new product development, a 5-point scoring system is introduced that focuses on six domains, each with multiple criteria (Appendix 1):

1. Target market (as drivers, and the scale thereof)
2. Product competition in the market
3. Expectations of new product performance
4. New product development pathway
5. Intellectual property
6. Commercial pathway

This tool provides a suitable means to assess the opportunity for a new product into an open or competitive market, whether to pursue more label claims for an existing bioprotectant, identify current and future risks, and whether to continue or discontinue with development. It also helps to decide on a patenting strategy. This tool is applied to several products in development (Appendix 2).

The tool also enables input from a number of stakeholders, and/or at different times, with the variations in scoring of additional interest and debate. It is a useful structure to flesh out a business case when warranted. Many characteristics are embodied in the Multiple Criteria Decision Making model of Lizzaraldi et al (2016) and the criteria of Cho & Lee (2013).

Addressable market

The total addressable market (TAM), serviceable available market (SAM) and serviceable obtainable market (SOM) are three parameters often used to determine market opportunities in different sectors (https://en.wikipedia.org/wiki/Total_addressable_market). For bioprotectants, the following factors will help to identify these parameters to estimate the market opportunity for any one particular bioprotectant.

Table 11**.** Definition of TAM, SAM and SOM in relation to bioprotectants.

	Definition	Assumptions
TAM	Total global acreage of crops that could host the **type of target** pest/disease for which the bioprotectant is being developed **AND** the pest/disease is recognised as being present in each territory **AND** is an economic pest/disease	That the proposed bioprotectant could be efficacious against species closely related to the specific target; Qualitative judgement of economic impact of the target
SAM	As for TAM but applied to the **specific** target pest/disease for which the bioprotectant is being developed	
SOM	As for SAM, **AND** limited to the **realistic market share**	Importance and value proposition of existing competitive products used in conjunction with, or instead of, the bioprotectant (e.g. efficacy, price, period of application)

Although the unit of measurement above is based on planted area (hectares), the value can be estimated by using a multiplier based on the unit wholesale or retail price and the number of units applied per hectare. A further percentage could be applied if royalty returns alone were of interest.

For cosmopolitan pests these parameters may be difficult to quantify given the wide host range, and it is difficult to determine whether a pest/disease is an economic issue to the crop grower, as opposed to just being recorded as present on the crop but requiring no control.

Opportunities

Global market opportunities should be a priority, with NZ benefit an added bonus. There will be some instances where only a local market opportunity is targeted but may be justified for reasons other than a return on investment on the product alone. It is recognised that other consequential benefits may accrue, including market access for NZ produce, and brand value in production systems (e.g. for sustainable, low residue produce).

The greatest business opportunity for bioprotectants will rest with the development of new modes of action. Some are underway but progressing too slowly (from a commercial and IP perspective), others require a focus onto bioprotection. Efforts towards known microbial BCAs struggle to attract commercial attention (e.g. “we don’t want another *Bacillus*”).

Semiochemicals

For semiochemicals, prioritisation of future effort should lie with control applications and new modes of and technologies for deployment. The latter includes biodegradable dispensing systems but efforts are likely already underway commercially to this end.

Cheaper stereo-pure sources of pheromone precursors from harvested plant material has been used to effect (Birkitt & Pickett, 2003). Initiatives using genetically modified plants to manufacture pheromones have been reported in the scientific literature (Ding et al., 2014; Petkevicius et al., 2020; Holkenbrink et al 2020) and are underway commercially (e.g. Biophero, BioTrend, Novagrica). NZ has the expertise to reach into this technology locally and for overseas markets despite the regulatory and political environment not enabling commercial use here.

Microbial bioprotectants

Given that a key limitation for market share of microbials is their perceived lack of or inconsistent efficacy, the following approaches are warranted:

- Sourcing microbes from suitably challenging environments
- Screening for abiotic tolerance early
- Screening against different host crop plant cultivars
- Consider microbial consortia as a single product
- Fundamental research to enhance their physiology for better efficacy (using –omics approaches)
- Fundamental research on the bioprotectant-target-host relationship to identify where improvements can be made (using –omics approaches)
- A more generic approach to new formulation options
- Measuring the efficiency of bee vectoring for flowering-relevant microbials within orchard systems
- Earlier screening for biofermentation yield
- Earlier quantification of shelf life
- Development and application of elicitors that complement the mechanism of action of microbial bioprotectants when used in combination
- Packaging the product with crop husbandry practices to optimise their impact

For microbial BCAs, the concept of consortia of microbes as bioprotectants is gaining interest in the research and commercial domains (Czajkowski et al. 2020; Parnell et al., 2016, Syed-Ab-Rahman et al., 2018). A start up from the USA (BoostBiomes) features in this area and has received Series A investment.

While the horticultural market is better served with bioprotectants than the arable sector, the floriculture sector is less well served. Floriculture industries worldwide are a stand-out opportunity as some of them are higher margin crops and some already use bioprotectants (e.g. natural enemies, semiochemical-based pest monitoring). Those sectors have traditionally not been strong investors or leaders in R&D in NZ, which remains a challenge for bioprotectant development. But as a non-food industry, agrichemicals offer a better economic option for growers. Only those wishing to claim a higher ground based on sustainable farming would call for bioprotectants.

Increasing the returns from commercialised bioprotectants can be achieved by increasing the label claims for each product (additional pest/disease targets, additional crops, additional territories). Given that the majority of the development costs have already been incurred, adding new label claims – while not cheap necessarily – does provide for better returns on the additional investment.

Other types of biocontrols such as mycoviruses and bacteriophages also hold promise and should be pursued.

The postharvest market should not be ignored either. PFR currently has some of its commercialised and pre-market products being tested for postharvest application, albeit in a small way. Some are showing efficacy in assays. More thought should be given to control of postharvest pests and pathogens with pre- and/or post-harvest bioprotectant applications (Droby et al., 2016).

Lastly, bioprotectants have to fit into integrated pest management programmes, where the interplay of agrichemicals, crop husbandry, microclimate, soils, other bioprotectants, harvesting, residues and many other factors all need coordination to ensure optimal yields and quality. Developing a single bioprotectant is at the start, rather than end, of this process and necessarily engages those involved in food production and distribution. An entire value-chain approach will ensure good bioprotectants are developed, commercialised and taken up by farmers (Tabassum et al., 2017).

Commercialisation

IP protection opportunities or limitations should rank higher and earlier in the prioritisation process. The patent is the gold standard for maximising commercial opportunities, but early analysis of the patent literature will also reveal any issues related to freedom to operate.

Stronger patent positions should rank higher in product prioritisation processes. Multiple patents in new modes of action should be targeted with greater vigour, and patent protection of individual bioprotectants should be assessed early. It is noted that territories vary in their approach to patent protection of microbial bioprotectant strains, with the USA being the strongest.

The experiences of NZ-origin bioprotectant commercialisation has been variable. In order to reduce the risk of unfavourable experiences, some contractual remedies with commercial partners should be imposed, such as:

- Performance criteria for product sales, with associated consequences
- Time limits on testing and commitment to commercialisation
- Very limited restrictions (in time and scope) on data sharing if the commercialisation option is declined

Regulatory reform

There are process changes that could be made in the current EPA and ACVM regulatory systems that should prioritise the development, commercialisation and application of bioprotectants, without needing changes in statutes. These should be implemented with a constructive and positive intent through industry-wide representation, political will, an R&D voice, and third party funding.

An environment for preferential or fast-tracked registration of bioprotectants is encouraged through the following actions.

- Engaging political forces to lead positive regulatory change for more sustainable agricultural systems
- Broadening the SCLP Group Standard to include pheromones for non-Lepidopteran species
- Developing a group standard for microbial bioprotectants
- Preferential ranking for the review of bioprotectant applications (‘jumping the queue’)
- Enabling data protection for registrants without sequential application to ACVM first, then to EPA
- Referencing overseas registrations for the same product to focus only on additional NZ-specific issues for local registration
- Harmonise regulations between EPA and ACVM, and with other jurisdictions
- Engaging Horticulture NZ’s ‘A Lighter Touch’ programme and resources to co-fund registrations
- Engaging Horticulture NZ’s ‘A Lighter Touch’ programme and resources to co-fund the development of group standards.

The impact of such changes will be seen in bioprotectants coming to market in more numbers and quicker, and ahead of some losses in agrichemicals. This will help to minimise crop losses on agrichemical loss and support the transition of numerous agriculture sectors towards more sustainable practices.

An incorporated entity to channel public sector bioprotectants

Consideration should be given to the establishment of an incorporated entity that coalesces the interests of the four key public institutions for a focus on bioprotectant development and commercialisation. This entity should not employ science staff but should include business and commercialisation staff. It would require a commitment to assign IP into this entity and to sharing the benefits arising from commercialisation.

The existing capacity and experience of business development and commercialisation expertise - from PFR and Grasslanz especially but inclusive of the other institutions’ experts - can then be focussed and applied across the portfolio. Grasslanz and PFR are complementary in their connection to different commercial entities and the sectors they serve.

Such an entity then creates the opportunity to provide a single branded interface locally and internationally for investment and commercialisation. As an incorporated entity it is amenable to external investment. The entity would, on its inception, have a portfolio of products assigned into it. Naturally, agreements and expectations would be in place contractually with each constituent partner for the flow of IP, benefits and contracted science activity. Legal and other services should be contracted out privately to ensure responsiveness.

PFR has recently developed a new trademark (Bioprotia™) for its bioprotection products and this could be used across the portfolio. It could even be the entity’s trading or legal name. The domain name has already been reserved.

The proposed entity could also serve as a portal for international interest in counter-seasonal trials in NZ, acting as a broker for this as needed. However, the regulatory environment – at least for experimental work – would need to be improved in order for NZ to be seen as a welcoming and easier environment for this activity compared to other territories. Once past this point, the reputation gained in one territory can enhance opportunities in others (Gregg et al., 2010).

The proposed entity could also have a secondary role in supporting bioprotectant use in industry (compare Gowda et al., 2016), a role that neither science professional bodies (e.g. NZ Plant Protection Society), sector bodies (e.g. NZ Apples & Pears), science providers, agricultural bodies (e.g. AGCARM) nor agrichemical companies have the focussed mandate to do, but which all play their part. It is apparent that knowledge transfer does face losses and misinterpretations as it moves from researcher to licensee (wholesale distributor) to reseller (retail distributor) to end-user (farmer). Overt separation of the technology transfer and commercial product sales functions would be needed.

The proposed entity would have the commercial freedom to partner with commercial entities for bioprotectant development and commercialisation – in any form and without necessary reference to their parent institutions. It therefore also takes on all the risk. Public-private partnerships (PPPs) such as those supported in CGIAR institutes provide good examples we could follow (e.g. Spielman et al., 2007; ICRISAT's Hybrid Parents Research Consortia, Gowda 2016). Multiple commercial engagement in this model increases competition, reduces prices and enhances access to products, none of which is preferred by commercial partners. Thought therefore needs to be given to the most appropriate PPP model to avoid failure.

Sector engagement

The public sector institutions seem to play an almost invisible role with agrichemical industry events and organisations, with little apparent voice. AGCARM events and membership, and ABIM attendance are some examples. A better profile through such events and entities would contribute to the presence and reputation of bioprotectant capabilities of our public institutions.

Industry and public validation of biocontrol

As seen earlier from the evidence of growers, there are perceptions that bioprotectants "don't work as well" as agrichemicals. Our public institutions have a role to play to disprove this, and can do so in various ways:

- Gathering data of scientific quality that demonstrate economic and intangible benefits on a commercial level (such programmes have been initiated for the Isomate® Avocado and Desire™ Mealybug pheromone products for at least 3 years post market entry).
- As part of the technology transfer process to industry, developing comprehensive husbandry practices to fit in with bioprotectant use
- Direct education of growers on the peculiarities and handling requirements of bioprotectants (part of Grosafe courses?)
- Providing more comprehensive resources (online and printed) for the handling of bioprotectants
- Publishing sound data in industry journals and sector body publications to demonstrate commercial value

- Exhibition stands and speaking opportunities at industry events to showcase available bioprotectants and their integration into IPM programmes

CONCLUSIONS

Section 5 has articulated a number of recommendations that have been drawn from the market data, product development history analysis and sector-wide interviews conducted for this study. The need for environmentally friendly alternatives to agrichemicals has never been stronger, to the point that some crops may be at risk of significant losses unless bioprotectants are introduced beforehand.

The timing is right to consider a step change in the development of bioprotectants from New Zealand public sector R&D institutions. The constraints that were experienced in the past that influenced the extent and timing of product development can be overcome with a new strategy across several fronts:

1. Prioritisation of products with global market potential
2. Early assessment of the market opportunity and risk factors to successful commercialisation through to market
3. More emphasis on new technologies that have new modes of action for pest and disease control
4. Broaden applications of bioprotectants to floriculture and postharvest, and increase label claims on existing products
5. Prioritise products that demonstrate patent protection opportunities
6. Overtly resource the underpinning science needed to bring bioprotectants to market (target biology and ecology, culture collections and facilities, including biofermentation and nanostring technology, integration into IPM programmes)
7. Greater exchange of scientific expertise with commercial entities, including support for postgrads/postdocs
8. Earlier and more strategic partnerships with commercial entities as potential distributors
9. Enhance the processes within the regulatory approval systems to prioritise bioprotectants and their speed to market
10. Consideration of a new incorporated entity to coalesce the outputs from the four key institutions with a record of bioprotectant development, license the bioprotectants under a common brand, and attract private sector funds that leverage internal investments
11. Engage widely and deeply to promote bioprotectant use in industry to improve product performance and therefore uptake.

With a collective, engaged and refocussed effort we can look forward to greater impact in more territories, to the benefit of all stakeholders in the bioprotectant value chain.

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APPENDIX 1. BIOPROTECTANT DEVELOPMENT ASSESSMENT TOOL

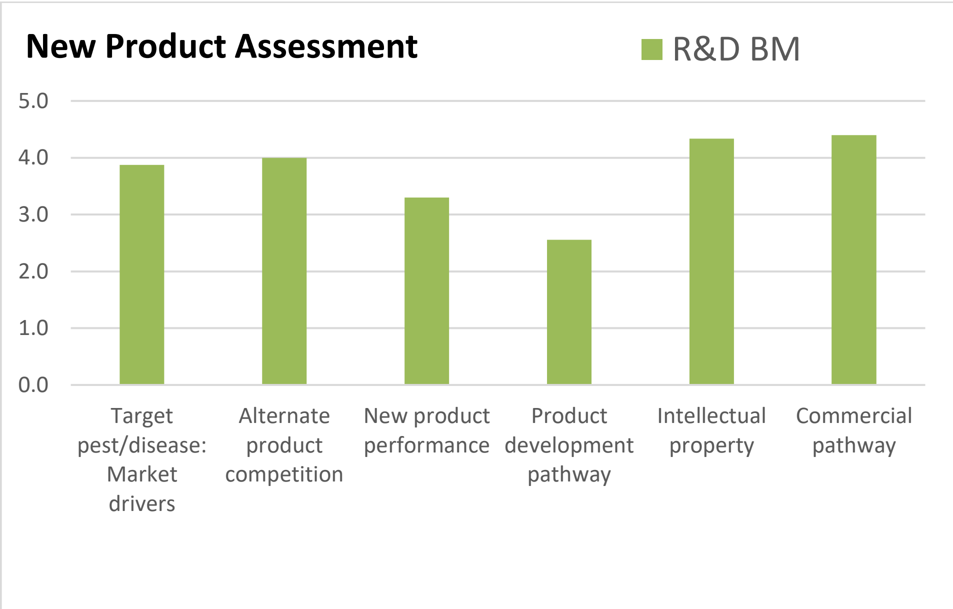
A. Domains and criteria

Domain	Criterion
Target pest/disease: Market drivers	Economic impact of pest/dis
	Biosecurity threat to NZ
	Phytosanitary/market access
	Organics opportunity
	Current Residue issue
	Host crop hectares
	Market growing?
Alternate product competition	# alternatives
	# BCAs
	Multiple MoAs available?
	Available now
	Available in foreseeable future
	Seasonal gaps for use available?
	Efficacy/control experience
	Pricing
	Market share possible
New product performance	Achievable efficacy
	Multiple targets possible?
	Platform or single product?
	Food residues expected
	Toxicity (env, human, host)
	Storage life expected
	Tank mix possible
	Mass production potential
	Component costs
	IPM compatibility
	Regulatory approval issues
Product development pathway	MoA
	Assays exist?
	Pre-screening needed?
	PFR has the expertise
	NZ location for R&D
	Development timeline
	Fit with PFR product range
	Funding req'mts
	Target biology known/needed?
Intellectual property	Level of protection

	Patent RoI potential Freedom to operate
Commercial pathway	Prior commitment exists Partner product fit Partner's market reach is relevant Partner investment timing Partner distribution network

B. Graphical representation of scoring data

A Business Manager assessment of Aureo®Gold at the very beginning of its development in 2011 is modelled here.



Scores higher than 4.0 indicate very strong market drivers for new bioprotectant development, above 3.5 indicate moderate to strong drivers. Scores below 3 represent some risks. Noting that variation in scoring from different stakeholders is expected and acceptable.

The R&D Business Manager analysis alone showed that:

- Market drivers are sufficiently strong
- There is little product competition
- Expectations of product performance are moderate
- There are some risks evident along the product development pathway
- There is a strong IP position
- The commercial pathway is reasonably secure

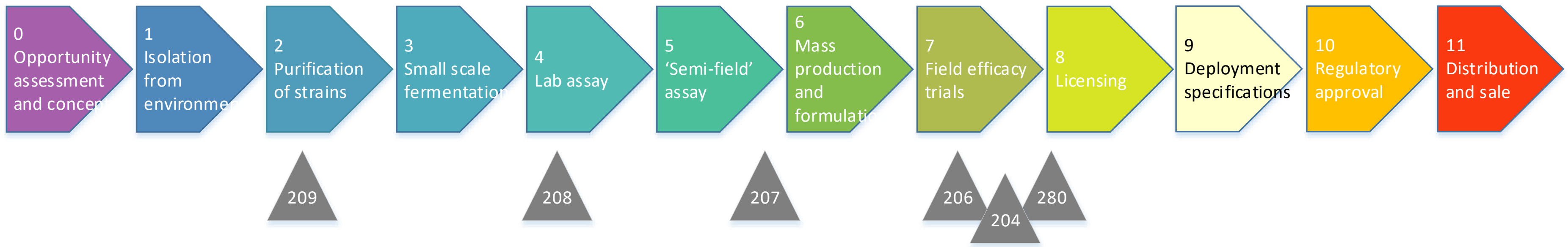
C. Example of scoring in use

Note that only the first three domains are shown. This example is an assessment of the potential for a microbial bioprotectant for the bacterial disease Psa on kiwifruit, assessed soon after the crisis hit in 2010. Such a product eventually entered the market in November 2018 as Aureo®Gold.

Assessment Date:	Target/Product:	avg score/5	Bioprotia#		Purpose				Bioprotectant type:	MoA:
25-Jan-11	Psa	3.6	201		NPD to an open market				microbial BCA	Prophylactic
			SCORES							
Domain	**Criterion**	**avg score/5**	**R&D BM**	**R&D res'r**	**role 3**	**role 4**	**role 5**	**role 6**	**Quantified**	**Notes**
Target pest/disease: Market drivers	Economic impact of pest/dis		5	5						
	Biosecurity threat to NZ		5	5						
	Phytosanitary/market access		4	2						
	Organics opportunity		4	4						
	Current Residue issue		4	4						
	Host crop hectares		2	1						
	Market growing?		2	4						
		3.64	3.71	3.57	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!		
Alternate product competition	# alternatives		4	5						
	# BCAs		5	5						
	Multiple MoAs available?		5	3						
	Available now		4	5						
	Available in foreseeable future		3	3						
	Seasonal gaps for use available?		4	4						
	Efficacy/control experience		4	2						
	Pricing		3	3						
	Market share possible		4	3						
		3.83	4.00	3.67	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!		
New product performance	Achievable efficacy		2	3						
	Multiple targets possible?		unknown	2						
	Platform or single product?		2	3						
	Food residues expected		5	4						
	Toxicity (env, human, host)		4	4						
	Storage life expected		3	3						
	Tank mix possible		2	4						
	Mass production potential		4	4						
	Component costs		3	3						
	IPM compatibility		5	4						
	Regulatory approval issues		3	3						
		3.33	3.30	3.36	#DIV/0!	#DIV/0!	#DIV/0!	#DIV/0!		

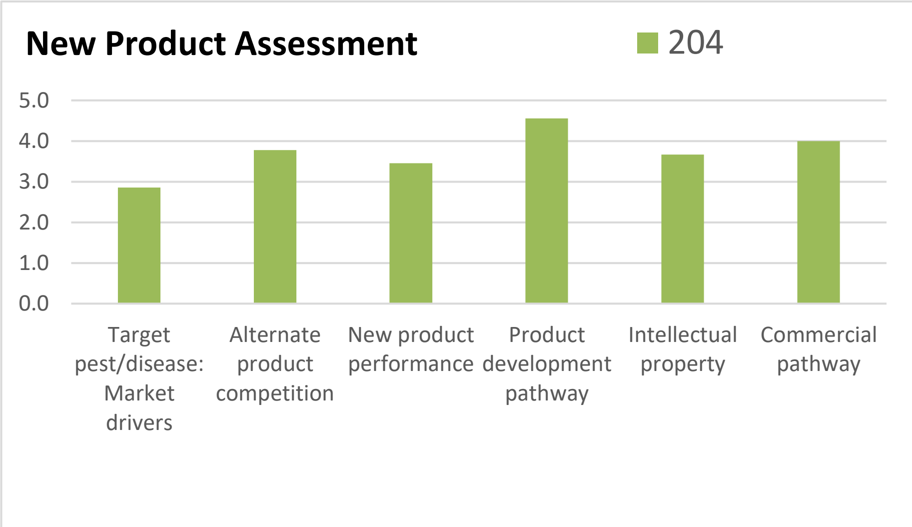
APPENDIX 2. DEVELOPMENTAL BIOPROTECTANTS REVIEWED

A. Microbials



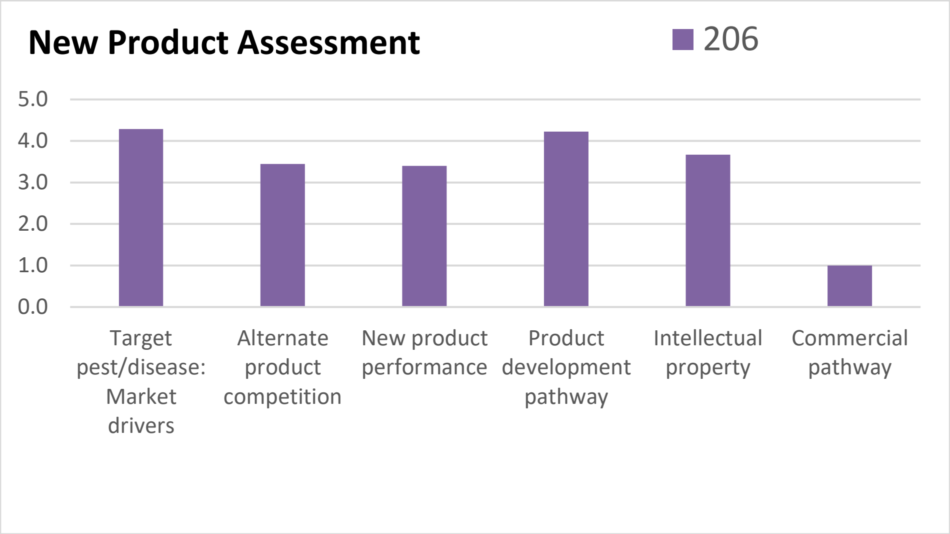
Product 204:

1. Market drivers are weak (based largely on market size)
2. There is some product competition
3. Expectations of product performance are moderate
4. There is very good chance of success along the product development pathway
5. There is a moderate IP position
6. The commercial pathway is secure



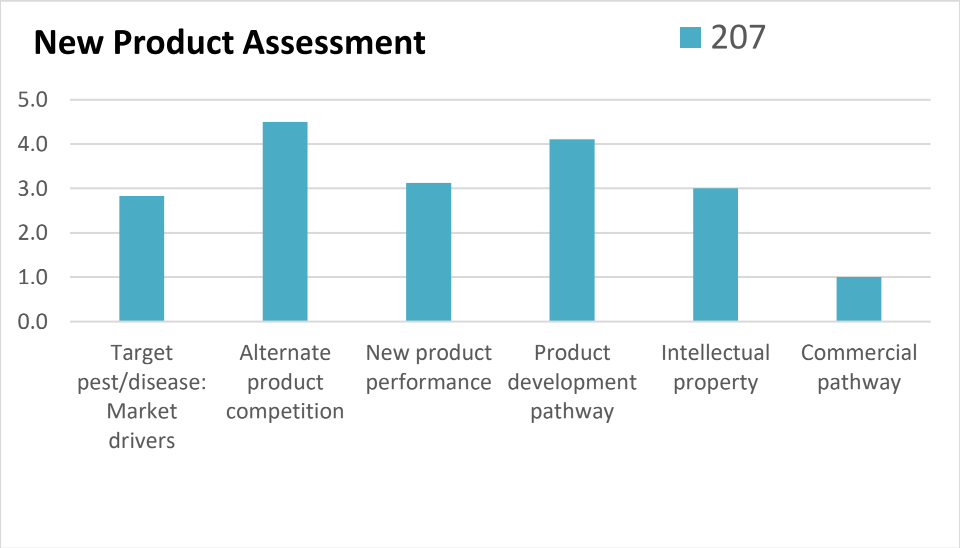
Product 206:

1. Market drivers are quite strong
2. There is moderate product competition
3. Expectations of product performance are moderate
4. There is very good chance of success along the product development pathway
5. There is a moderate IP position
6. The commercial pathway is insecure as no partners are currently engaged



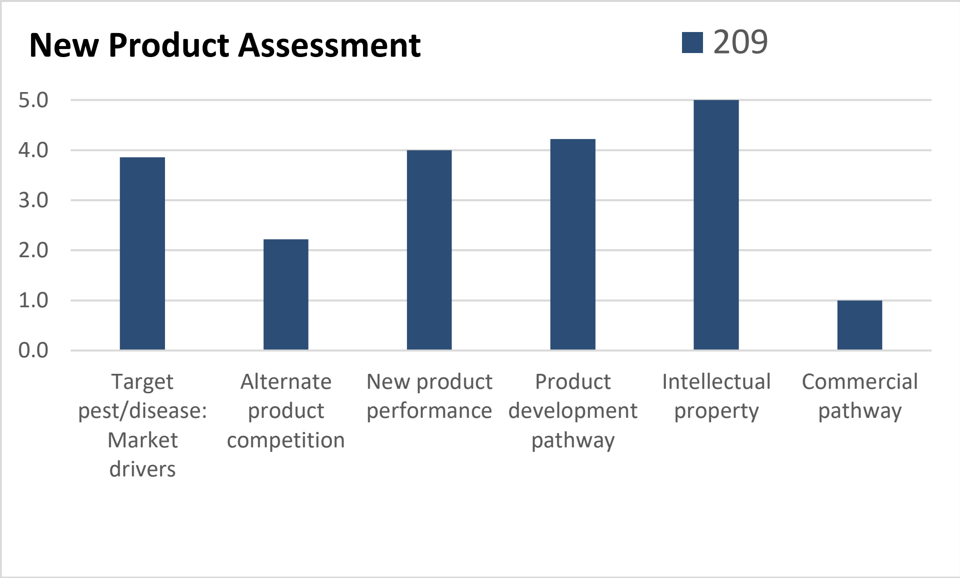
Product 207:

1. Market drivers are relatively weak
2. There is unknown level of competition
3. Expectations of product performance are moderate
4. There is very good chance of success along the product development pathway
5. There is an average IP position
6. The commercial pathway is insecure as no partners are currently engaged

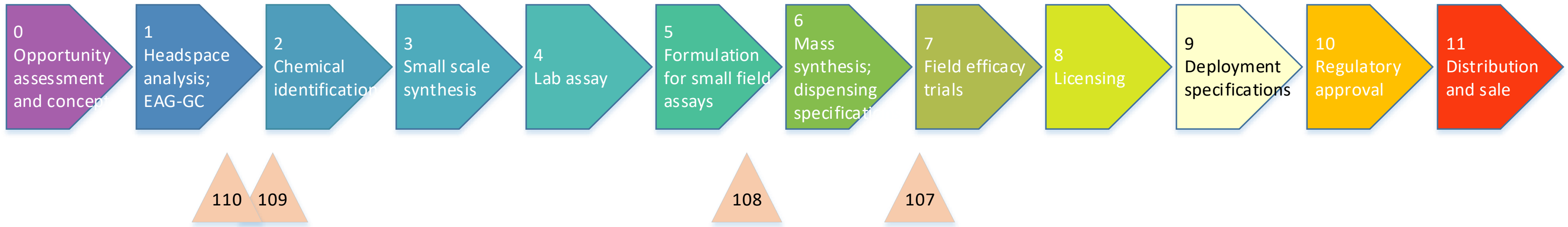


Product 209:

1. Market drivers are reasonably strong
2. There is strong level of competition
3. Expectations of product performance are moderate-high
4. There is very good chance of success along the product development pathway
5. There is a strong IP position possible
6. The commercial pathway is insecure as no partners are currently engaged

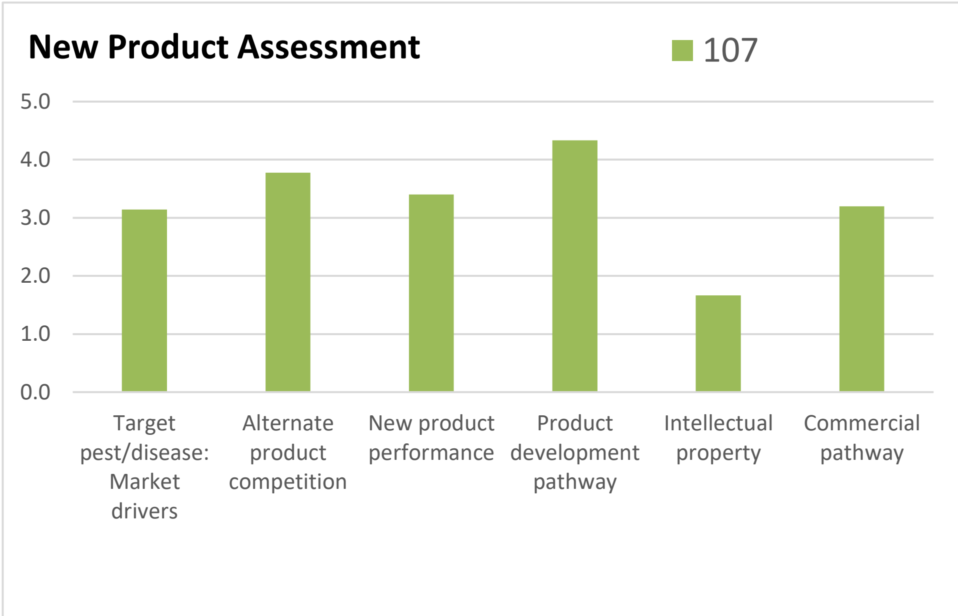


B. Semiochemicals



Product 107:

1. Market drivers are moderate (due largely to small/local market size)
2. There is a moderate level of competition
3. Expectations of product performance are moderate
4. There is very good chance of success along the product development pathway
5. There is an poor IP position (third party IP with a license to use expected)
6. The commercial pathway is moderately secure with a committed partner



Product 109/10:

1. Market drivers are strong
2. There is moderate level of competition with poor efficacy
3. Expectations of product performance are moderately optimistic
4. There is moderate chance of success along the product development pathway (in early development still)
5. There is strong IP position potentially
6. The commercial pathway is secure with a committed partner