

**Whai Hua Primary Growth Partnership (PGP) Programme
New Dairy Products and Value Chains**

Final Summary Report

April 2017

Executive Summary

- **Investment.** The PGP programme “New Dairy Products and Value Chains” was approved in April 2013 and completed in December 2016. A total investment of \$4,130,000 was approved and actual expenditure was:

Whai Hua Partners	MPI	Total
\$2,081,000	\$2,036,000	\$4,117,000

- **Outcome.** The outcome that the Whai Hua partners sought was the production of new differentiated milk products that would enhance the immune status and health of target customers.
- **Product A¹.** A herd of 500 cows with naturally high levels of the target product was established during the 2013-14 and 2014-15 milking seasons and subsequently maintained with replacement cows. For the target product, the seasonal pattern and repeatability of production between years is understood, as is the genetic heritability of the production trait. A Standard Operating Procedure manual has been prepared for use in the expansion and maintenance of these specialist herds.
- **Product B.** The initiative to produce milk containing target products that would promote the activity of probiotic products achieved mixed results. A new vaccine adjuvant was used and while animal reactions to vaccination were acceptable, the immune response in producing specific antibodies was irregular and weak.
- **Product processing.** Processing studies showed that the target product was very sensitive to heat during processing. Following further process development, recent commercial validation runs using a prototype pasteurizer have achieved 70% activity retention of the target product. A Standard Operating Procedure manual has been prepared for the production of Skim Milk Powder (SMP) containing Product A and a provisional patent for the processing method has been lodged.
- **Product functionality.** Approximately 35% of the programme’s investment went to researching the function and efficacy of the target product. Significant findings were that the target product in bovine milk binds to pathogenic, commensal and probiotic bacteria in a similar way and level as for human milk; and Skim Milk Powder with elevated levels of the target product dampen down the infection levels of pathogenic bacteria in the gut of mice. The results of this research have been published in independently reviewed international journals to ensure robustness and credibility to the marketing messages.
- **Market Development.** The approach used in market development has been to segment the target markets and to then prioritise potential customers on the basis of scale, early adoption, ingredient use and branding opportunities. To-date, direct engagement has occurred with 18 potential customers and from these, 5 target customers have been identified to supply further information and/or test samples to them.
- **Short Term Outcomes.** During the four years of the programme, the large majority of intended outcomes were achieved across a broad range of farm production, milk processing, marketing and efficacy research and development. The area of work where this did not occur

¹ Product A and Product B are the names given to the two products under development in this programme. The actual names for each have been removed due to commercial sensitivity.

relates to the immunisation work where we were unable to develop a multi-antigen vaccine containing an adjuvant that provided acceptable animal welfare and immune response levels.

- **Future Commercialisation.** The direction and rate of commercialisation will be strongly guided by the success of future marketing initiatives. The initial intent of the programme was to develop an ingredient Skim Milk Powder with elevated levels of the target product based on specially selected herds. This has been achieved, but importantly the programme has also provided a significant spin-off in the form of a new processing method. Market development initiatives that will be under-taken by Miraka during 2017 have been identified.
- **Net Economic Benefits and Spill-Over Benefits.** Expected net economic benefits to New Zealand vary depending on which product-market combinations are successful and the interactions between bioactive levels, product volume and value margin. Over the next five years, the combined estimates of net economic benefits per year for the various product-market options range from \$5.0 m to \$16.4 m per year; and there is considerable upside on these estimates if these options occur concurrently. An additional spill-over benefit of the programme is a stronger ongoing link between the Maori business partners, innovation and R&D institutions.

Context

The New Dairy Products and Value Chains PGP programme is a partnership between MPI and Whai Hua. The Whai Hua commercial partners include Wairarapa Moana Incorporation, Miraka Ltd and Kanemastu NZ. The programme has provided the investment and resources to research and develop the production and processing of milk with elevated levels of the target Product; to understand the function and efficacy of milk containing the target product; and to engage with potential customers. The outcome that the Whai Hua partners sought was the production of new differentiated milk products that would enhance the immune status and health of target customers.

The initial PGP contract with MPI (\$3,518,000 total funding from all partners) was scheduled for July 2013 to December 2015, although a Go-Early agreement allowed work to commence in April 2013. Following a mid-term progress review, an extension to the programme until June 2016 was approved (+\$376,000). Finally, to complete processing and market development work, a second extension until December 2016 was approved (+\$236,000). In total, \$4,130,000 was made available to the programme of work. Note that investment in this second extension was a 60:40 split between Whai Hua and MPI, to reflect changes in PGP funding criteria whereas the previous investments were a 50:50 split.

The following table summarises the actual expenditure for the programme.

Whai Hua Partners	MPI	Total
\$2,081,000	\$2,036,000	\$4,117,000

Objectives and Milestone Delivery

There were five objectives within the programme of work that remain unchanged from the original business plan:

- **Product A.** Optimise selection of herds containing naturally high levels of the target product (i.e. understanding the determinants of Product A production and then develop specialist

herds without severely compromising other production traits). These herds will form the basis of the naturally high Product concept.

- **Product B.** Develop effective and safe multi-antigen immunisation (i.e. determining the compatibility of the immunisation protocols and multi-antigen vaccines) leading to vaccine registration. An acceptable protocol will underpin the Product B concept.
- **Product Processing.** Identify suitable milk processing parameters (i.e. developing and testing a process that will ensure the retention of at least 95% of product activity). Supplying safe product with consistently high functional activity will be essential to gaining market confidence.
- **Product Functionality.** Provide evidence of biological functionality (i.e. demonstrating that bovine Product performs in a similar manner to its human counterpart in human model systems). This evidence is essential for the purpose of functionality claims and engagement with in-market partners.
- **Market Development.** Develop market intelligence and new markets (i.e. desk research and early market engagement to understand market sizes, values and expectations for Product dairy ingredients in Asia and New Zealand). Market development will require strong business relationships with in-market partners that operate in the immune health sector.

The majority of the delivery milestones were those that were planned in the original Business Case and initial contract. The major exceptions were:

- More product functionality work was undertaken as a result of the mid-term progress review. This focused on dose responses and product comparisons in mice trials.
- Modified Product B work that resulted from unacceptable site reactions to vaccination. A new adjuvant had to be found and then test for site reaction and immune response levels.
- Product processing work identified that significant losses of product activity occurred during processing. An alternative, new pasteurisation prototype was needed to be developed and tested.

Of the milestones that were annually contracted, all were completed. In some cases, final delivery was carried over into the following year with the approval of the Programme Steering Group. The total investment for each objective is provided in the following Table 1.

Table1. Total investment into each of the programme objectives and management.

Product A	592,000
Product B	668,000
Product Processing	956,000
Product Functionality	1,417,000
Market Development	222,000
Programme Management	262,000
Total	\$ 4,117,000

Key Achievements

Product A Herd

Based on phenotypic screening of approximately 5,000 WMI cows, a herd of 500 cows with naturally high levels of the target Product was established during the 2013-14 and 2014-15 milking seasons. This herd has been maintained for the subsequent two seasons using second calving replacements. The knowledge gained from the development of this herd has been used to produce a Standard Operating Procedure manual for use in the expansion and maintenance of a Product A herd.

Product B

This objective aimed to produce milk containing specific Product B that would promote the activity of probiotic products. It was based on a vaccination procedure patented by AgResearch and involved two commensal bacteria species. Unfortunately, results from this work have been mixed. In the early studies, the reaction of cows to vaccination was unacceptable from an animal welfare perspective. The cause of these reactions was identified as the adjuvant that used in the vaccine. Therefore, the programme had to be redesigned to identify an alternative adjuvant that was acceptable from an animal welfare and immune response perspective.

A new vaccine adjuvant was identified and while animal reactions to vaccination were acceptable, the immune response in producing specific Product B was irregular and weak. Further work indicated that this weak response was the result of the new adjuvant used, not the antigens.

Product Processing

The work in this area has been challenging, yet very rewarding. The first significant finding was that Product integrity was very sensitive to heat during processing. Lab-based studies determined optimum processing conditions. Based on these studies, specifications for processing Skim Milk Powder (SMP) were developed. Early trial runs gave disappointing results of <20% activity retention. The problem resided with the configuration of the plant, so alternative processes were developed and tested.

- Recent commercial validation runs using the alternative process and milk from the Product A herd have achieved approximately 70% activity retention of the target product in Skim Milk Powder. Test samples of this product have been supplied to potential customers.

A Standard Operating Procedure (SOP) manual has been prepared for the production of SMP using a new processing method. Product levels in SMP far exceeds product levels in standard SMP using this method.

- A provisional patent has been lodged for the processing method. The opportunity for significant spill over benefits from this new method are also exciting.

Further research looked at the impact of secondary processing of SMP on product retention given the expectation that the product will be used as ingredients in foods and/or drinks.

- Of greatest interest was the benefit of associated additives in retaining product activity, with the best retention occurring in a model infant formula. These results have been very useful in discussions with potential customers.

Product Functionality

Understanding the function and efficacy of bovine Product A was considered to be very important in supporting future marketing activities. Feedback from the market place was that potential customers and consumers of the product had little awareness, nor understanding of this milk product. Consequently, approximately 35% of the programme's investment went to this area of work. The key findings are:

- Bovine Product A binds to pathogenic, commensal and probiotic bacteria in a similar way and level as human Product.
- SMP with elevated levels of Product A has dampened down the infection levels of pathogenic bacteria in the gut of mice. [Note that this does not necessarily demonstrate a product effect.]
- The recovery of gut biota in mice that have been administered antibiotics is different when they have been feed SMP Product A.

The results of this research have been published in independently reviewed international journals to ensure robustness and credibility to the marketing messages. The results of the above work have been used in preparing marketing collateral.

Market Development

Market development has involved two stages – the first being desk-based studies and more recently direct engagement with potential customers. The initial work identified that there was a unique opportunity and story to tell about Product A, but it would be difficult and expensive to make specific health claims. The focus for market development with specific product opportunities for each segment has been identified for future commercialisation. It was identified that more functionality /efficacy information would be needed to support any marketing initiatives in the product areas.

The second stage of this work has been to segment the market and then prioritise potential customers on the basis of scale, early adoption, ingredient use and branding opportunities.

- To date, direct engagement has occurred with 18 customers and from these, 5 target customers have been identified to supply further information and/or test samples.
- Whai Hua has signed a collaborative agreement with a major international company to test SMP Product A in its product evaluation programme. Other target customers are also evaluating the opportunities.

These customers have been provided marketing collateral that contains the information resulting from the previously described product functionality and processing work.

Short Term Outcomes

The intended short term outcomes arising from the contracted work were identified in a logic map at the outset of the programme. During the four years of the programme the large majority of intended outcomes were achieved across a broad range of farm production, milk processing, marketing and efficacy research and development. The area of work where this did not occur relates to Product B where we were unable to develop a multi-antigen vaccine containing an adjuvant that provided acceptable animal welfare and specific Product levels. A summary of the short term outcomes is as follows:

- **Product A and Product B are developed and capable of being produced:** A Product A herd has been operative at WMI for four years and processing specifications now result in approximately 70% retention in the final SMP product. Product B has not progressed to a product.
- **Evidence of product function in supporting immunity is established:** Bovine Product A binds to bacteria in a similar way to human Product; and Product A SMP dampens gut infection of pathogenic bacteria in mice. Three peer reviewed scientific papers have been published. A further two papers have been submitted for publication.
- **Whai Hua partners have the confidence to consistently produce high quality products:** Two commercial runs have produced approved SMP product with activity retention of approximately 70%. Test samples have been provided to four potential customers. An SOP has been produced for producing Product A SMP.
- **Market knowledge is increased and likely in-market partners have been identified:** A market strategy/plan and supporting collateral has been developed. Five target customers have been identified and product information and/or test samples provided.

Intellectual Property Status

Significant intellectual property has been generated from the programme. This is being managed as follows:

- Where novelty in IP exists a provisional patent has been taken;
- where IP is not patentable the approach of trade secret has been used (ie: Standard Operating Procedures);
- and where the IP is required for marketing purposes, it has been made public through scientific publication.

Future Steps to Commercialisation

Given the results/outputs that have been achieved in the programme, commercialisation activities will concentrate on Product A opportunities. The direction and rate of this commercialisation will be strongly guided by the success of future marketing initiatives. These initiatives will build on the marketing strategy and customer engagement that has been developed during the programme.

The initial intent of the programme was to develop an ingredient Skim Milk Powder with elevated Product A levels based on specially selected herds. This has been achieved, but importantly the programme has also provided significant spin-off opportunities in the form of a new processing method.

Potential product-market combinations have been identified for future commercialisation work. Two of the Whai Hua partners will lead on this commercialisation work and these companies are investing in further research work and additional market development resources to further develop the opportunities which have emerged as a result of this PGP programme.

Economic & Spill-Over Benefits

In the original Business Case, the net economic benefits were predicted to eventually be \$5.0 m/year for the Product A concept and \$3.5 m/year for the Product B concept. These predictions are no longer valid, given the developments that has been achieved during the programme and the market knowledge that has been gained through more recent customer engagement. The net economic benefits will vary depending on which product-market combinations are successful and the interactions between Product/bioactive levels, product volume and value margin.

- During the next 5 years the combined estimates of net economic benefits per year for the various product-market combinations are estimated to range from \$5.0 million to \$16.6 million per year.

As noted in the original Business Case, higher value margins from milk products can provide the opportunity to pay milk premiums to growers and thereby, sustain the business of dairy farmers who need to de-intensify in environmentally sensitive catchments. One further spill-over benefit of the PGP programme is the stronger link between the Maori business partners and R&D services.

Post PGP Reporting

A contractual requirement of the PGP programme is that Whai Hua will report annually (2017-2022) to MPI on progress with the commercialisation outcomes from the programme.

Appendix 1: Short Term Outcomes

Short Term Outcome	Initial Target	Actual Achievement
Product A and Product B are developed and capable of being produced.	<p>Processing protocol which retains Product at >95% successfully developed and documented.</p> <p>Best practice manual for Product A herd protocols and procedures.</p> <p>Product A herd of at least 500 cows established.</p> <p>Vaccination of multi-antigens is safe for animals and produces sufficient levels of specific Product antibodies.</p> <p>Samples of both Product A and Product B powders are produced for marketing purposes.</p>	<p>Based on lab experiments, processing specifications to retain 85% have been developed and documented.</p> <p>SOP manual has been developed and is managed as a trade secret.</p> <p>Product A herd is operative.</p> <p>The vaccine that used a new adjuvant was acceptable from an animal welfare perspective, but produced low levels of specific antibodies.</p> <p>Commercial test samples of Product A SMP have been supplied to potential customers.</p>
<p>Evidence of product function in supporting immunity is established.</p> <p>Whai Hua partners have the confidence to consistently produce high quality products.</p>	<p>Peer reviewed paper comparing effects of human and bovine Product on pathogens.</p> <p>Two published papers on beneficial effects on Bovine Product in animal models</p> <p>Published paper on efficacy and dose response of Product A SMP and WPC in animal models</p> <p>Report on immune responses to specific probiotic vaccine.</p> <p>Protocol for production of Product A SMP which retains at least 70% Product activity validated at commercial scale.</p>	<p>Paper published on bacteria binding.</p> <p>One paper published on gut biota recovery of mice after the use of antibiotics.</p> <p>One paper redrafted for publication on the effects of Product A on the establishment of a gut pathogenic bacteria in mice.</p> <p>Confidential report completed.</p> <p>Two commercial runs have produced approved SMP product with activity retention exceeding 70%.</p>

	Standard Operating Procedures for commercial production of Product A SMP documented.	An SOP has been produced for producing Product A SMP.
Market knowledge is increased and likely in-market partners have been identified.	Marketing plan and supporting collateral for customer engagement completed for Product A. EOI from at least 4 potential customers.	A market strategy/plan and supporting collateral has been developed. EOI and follow-up information and test sample activities have occurred with five targeted customers. Commercialisation of Product B has not proceeded.