FINAL

An Impact Assessment of FRDC Investment in 2014-729: Improving the palatability, bioavailability and efficacy of orally administered praziquantel for yellowtail kingfish with lipid nanoparticles and hybrid lipid carrier systems

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In submitting this report, the researcher has agreed to FRDC publishing this material in its edited form.

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Gavin Partridge, South Metropolitan TAFE (formerly Challenger Institute), Perth

Abbreviations

CBA	Cost-Benefit Analysis
CRRDC	Council of Research and Development Corporations
DAWR	Department of Agriculture and Water Resources
FRDC	Fisheries Research and Development Corporation
NSW	New South Wales
OCS	Office of the Chief Scientist
PZQ	Praziquantel
RD&E	Research, Development and Extension
UWA	University of Western Australia
WA	Western Australia
YTK	Yellowtail kingfish

Executive Summary

What the report is about

This report presents the results of an impact assessment of the Fisheries Research and Development Corporation (FRDC) investment in a project to improving the palatability, bioavailability and efficacy of orally administered praziquantel for yellowtail kingfish (YTK). The project was funded by FRDC in the three years ending 30th June 2015, 2016 and 2017.

Methodology

The investment in the project was analysed qualitatively within a logical framework that included activities/outputs, outcomes, and impacts. Identified impacts were then categorised into a triple bottom line framework. Principal impacts from those identified were considered for valuation.

Results/key findings

The prospective impacts of reduced production costs, or improved quality and volume of YTK produced, due to reduced impact of diseases on YTK production were not delivered. Also, the potential contribution to a reduced use of hydrogen peroxide leading to cost savings and a lowering of risks to aquaculture workers has not materialised.

Investment Criteria

Funding for the project over the three years totalled $0.37 million in present value terms. The FRDC investment costs were $0.22 million in present value terms. No quantifiable benefits were produced from the investment.

Conclusions

Apart from scientific knowledge that may be used in the future, it is evident that the project did not produce any industry impacts.

Keywords

Impact assessment, cost-benefit analysis, yellowtail kingfish, YTK, gill and skin fluke, parasites, praziquantel

Introduction

The Fisheries Research and Development Corporation (FRDC) required a series of impact assessments to be carried out annually on a number of investments in the FRDC research, development and extension (RD&E) portfolio. The assessments were required to meet the following FRDC evaluation reporting requirements:

- Reporting against the FRDC 2015-2020 RD&E Plan and the Evaluation Framework associated with FRDC's Statutory Funding Agreement with the Commonwealth Government.
- Annual Reporting to FRDC stakeholders.
- Reporting to the Council of Rural Research and Development Corporations (CRRDC).

The first series of impact assessments, that included 20 randomly selected FRDC investments, was completed in August of 2017. The published reports for the first series of evaluations can be found at: http://frdc.com.au/Research/Benefits-of-research/2017-Portfolio-Assessment

The second series of impact assessments also included 20 randomly selected FRDC investments. The investments were worth a total of approximately $5.62 million (nominal FRDC investment) and were selected from an overall population of 96 FRDC investments worth an estimated $21.32 million (nominal FRDC investment) where a final deliverable had been submitted in the 2016/17 financial year.

The 20 investments were selected through a stratified, random sampling process such that investments chosen spanned all five FRDC Programs (Environment, Industry, Communities, People and Adoption), represented approximately 26% of the total FRDC RD&E investment in the overall population (in nominal terms) and included a selection of small, medium and large FRDC investments.

Project 2014-729*: Improving the palatability, bioavailability and efficacy of orally administered praziquantel for yellowtail kingfish with lipid nanoparticles and hybrid lipid carrier systems* was selected as one of the 20 investments and was analysed in this report.

General Method

The impact assessments followed general evaluation guidelines that are now well entrenched within the Australian primary industry research sector including Research and Development Corporations, Cooperative Research Centres, State Departments of Agriculture, and some Universities. The approach includes both qualitative and quantitative descriptions that are in accord with the impact assessment guidelines of the CRRDC (CRRDC, 2014).

The evaluation process involved identifying and briefly describing project objectives, activities and outputs, outcomes, and impacts. The principal economic, environmental and social impacts were then summarised in a triple bottom line framework.

Some, but not all, of the impacts identified were then valued in monetary terms. Where impact valuation was exercised, the impact assessment uses Cost-Benefit Analysis (CBA) as its principal tool. The decision not to value certain impacts was due either to a shortage of necessary evidence/data, a high degree of uncertainty surrounding the potential impact, or the likely low relative significance of the impact compared to those that were valued. The impacts valued are therefore deemed to represent the principal benefits delivered by the project. However, as not all impacts were valued, the investment criteria reported for individual investments potentially represent an underestimate of the performance of that investment.

Background and Rationale

Both pests and diseases have a significant impact on production costs in Australian aquaculture. These costs are generally in the form of either prevention and treatment costs, or lost production due to pest and disease impact. There are also some concerns that the activity of aquaculture itself may lead to pest and disease problems in wild catch fisheries, through intensity of aquaculture production, or moving species outside of their natural habitat.

The farming of yellowtail kingfish (YTK) has been growing as an aquaculture industry in the past ten years, especially in South Australia, Western Australia (WA) and NSW. Fluke parasites have to be controlled in YTK farming in sea cages as parasites such as fluke can result in high mortality rates or slower growth if not treated. Current management procedures are to treat the fish with hydrogen peroxide; this treatment is costly and dangerous. Fluke also contribute to production costs in other fin-fish farming enterprises such as Southern Bluefin Tuna.

The project was primarily concerned with gill fluke (*Zeuxapta seriolae*) and skin fluke (*Benedenia seriolae* and Neobenedenia species) in yellowtail kingfish (Gavin Partridge, pers. comm., 2018).

The anthelmintic drug praziquantel (PZQ) has been shown to be efficacious for gill and skin fluke control. Previous research had shown that there was a need to achieve a critical known anthelmintic level within the blood plasma of treated fish. However, its take-up by YTK has been inhibited by its strong bitter taste. Flavour masking has not been successful to date.

As fluke impose a significant cost on the YTK industry, palatable PZQ at appropriate levels is required to reduce the costs and risks (to both fish and personnel).

Research on palatable PZQ has been conducted in WA since 2010 in collaboration with universities, research institutes and private companies The Wark Institute have technologies available to encapsulate poorly water-soluble drugs into nanopaticles; this process had been demonstrated to increase PZQ bioavailability in other animals and it was thought it would mask the bitterness of PZQ as well as increase its availability to YTK. The current project by the Challenger Institute of Technology and the Wark Institute to test the delivery of PZQ via nanoparticles was developed from previous work at the Challenger Institute in Perth.

Project Details

Summary

Project Code: 2014-729

Title: *Improving the palatability, bioavailability and efficacy of orally administered praziquantel for yellowtail kingfish with lipid nanoparticles and hybrid lipid carrier systems*

Research Organisation: South Metropolitan TAFE (formerly Challenger Institute)

Principal Investigator: Gavin Partridge

Period of Funding: July 2014 to June 2017

FRDC Program Allocation: Industry (100%)

Objectives

The objectives of the project were:

1. To produce nanoparticles with high loading rates and low burst release of praziquantel
2. To compare the palatability of optimised nanoparticles against pure praziquantel in yellowtail kingfish
3. To compare the bioavailability of praziquantel within optimised nanoparticles with pure praziquantel in yellowtail kingfish
4. To compare the efficacy of optimised nanoparticles against pure praziquantel in removing skin and gill flukes from yellowtail kingfish

Logical Framework

Table 1 provides a description of the project in a logical framework developed for the evaluation.

Table 1: Logical Framework for Project 2014-729

Activities and Outputs	• Palatability of diets containing nanoparticles was equal to or worse than those containing pure PZQ. • While success was achieved in preparing nanoparticles with the target loading rates of 10% demonstrating good release profiles in vitro, none of the nanoparticles tested showed an improvement in bioavailability. • It was hypothesised that the lack of improvement in bioavailability was derived from the lack of a transport mechanism in fish capable of taking up nanoparticles into the lymphatic system. • The lack of improvement in palatability of the diets containing the nanoparticles was unexpected; it was hypothesised that the loading rate of the nanoparticles may have contributed to this poor palatability. • The pharmokinetic data obtained on the wider range of fish sizes and water temperatures in this study compared with previous studies will be useful in the permitting process for PZQ and also for veterinarians in prescribing withholding periods when prescribing off-label use. • Success was also achieved in the application of a taste masking agent (garlic) to significantly improve the palatability of diets containing PZQ.

Outcomes	• The researchers will continue to investigate the application of a garlic extract to improve the oral delivery of PZQ to YTK (range of fish sizes and PZQ amounts). • Further studies that test the bioavailability of smaller nanoparticles will be useful to elucidate the mechanisms of improved bioavailability of PZQ-containing nanoparticles in different animals; however, even if bioavailability in YTK were improved using smaller nanoparticles, commercial application of nanoparticles to PZQ may be limited by their loading rate and the impact that such loading rates have on diet palatability. • As the project showed no benefit of bioavailability or palatability of the tested nanoparticles, the end users of the research (veterinary pharmaceutical companies and the YTK industry) are unlikely to continue pursuing nanoparticles for the oral delivery of PZQ to YTK.
Impacts	• The prospective impacts of reduced production costs, or improved quality and volume of YTK produced, due to reduced impact of diseases on YTK production were not delivered. • Also, the potential contribution to a reduced use of hydrogen peroxide leading to cost savings and a lowering of risks to aquaculture workers has not materialised. • Apart from scientific knowledge that may be used in the future, it is evident that the project did not produce any industry impacts.

Project personnel are currently collaborating informally with the pharmacy department at the University of Western Australia (UWA) testing their technology for masking bitterness in paediatric medications. Initially UWA prepared a number of different PZQ formulations in very small quantities which were assessed simply based on their smell (Gavin Partridge, pers. comm., 2018). Based on the outcome of these smell tests, UWA have recently made up some larger batches of the most promising formulations that will be tested with YTK. Investment by UWA and the project group has therefore been minimal but if the formulations prove successful then more investment may be sought (Gavin Partridge, pers. comm., 2018).

Whilst the garlic masking agent improved palatability a little, testing it commercially with industry demonstrated the improvement was insufficient to get the ingestion levels required to obtain an efficacious treatment (Gavin Partridge, pers. comm., 2018).

It can be concluded that this project to date has not yielded any industry applicable outcomes or impacts. As the project led to no prospective commercial applications, no intellectual property protection was sought for any of the findings.

Project Investment

Nominal Investment

Table 2 shows the annual investment made in Project 2014-729 by FRDC. There was no other funding organisation involved.

Table 2: Annual Investment in Project 2014-729 (nominal $)

Year ended 30 June	FRDC ($)	OTHER[(a)] ($)	TOTAL ($)
2015	50,000	64,250	114,250
2016	101,000	64,250	165,250
2017	20,000	0	20,000
Totals	**171,000**	**128,500**	**299,500**

Program Management Costs

For the FRDC investment, the cost of managing the FRDC funding was added to the FRDC contribution for the project via a management cost multiplier (1.122). This multiplier was estimated based on the share of 'employee benefits' and 'supplier' expenses in total FRDC expenditure reported in the FRDC's Cash Flow Statement (FRDC, 2013-2017). This multiplier then was applied to the nominal investment by FRDC shown in Table 2.

Real Investment and Extension Costs

For purposes of the investment analysis, the investment costs of all parties were expressed in 2017/18 dollar terms using the Implicit Price Deflator for Gross Domestic Product (ABS, 2018). No additional costs of extension were included as there was no substantive industry impact of the project.

Impacts

Table 3 provides a summary of the principal types of impacts expanded from those listed in Table 1 and categorised into economic, environmental and social impacts.

Table 3: Triple Bottom Line Categories of Principal Impacts from Project 2014-729

Economic	• The prospective impacts of reduced production costs, or improved quality and volume of YTK produced, due to reduced impact of diseases on YTK production were not delivered. • Also, the potential contribution to a reduced use of hydrogen peroxide leading to cost savings and a lowering of risks to aquaculture workers has not materialised.
Environmental	• Nil
Social	• Some scientific knowledge that may be used in the future to produce unspecified impacts.

Public versus Private Impacts

The direct beneficiaries of this project would have been the current and developing YTK industry participants in Australia.

Distribution of Private Impacts

Private benefits initially would have been captured in the first instance by the individual YTK producers. The final distribution of some of the benefits from the investment would have been distributed between participants along the commercial fish and fish product supply chains, including final consumers.

Impacts on other Australian Industries

It is assumed that there will not be any impacts on other Australian industries.

Impacts Overseas

No impacts on overseas parties are expected.

Match with National Priorities

The Australian Government's Science and Research Priorities and Rural Research, Development and Extension (RD&E) priorities are reproduced in Table 4. If potential impacts had been delivered n impacts would have contributed to Rural RD&E Priorities 1 and 2 and to Science and Research Priority 1.

Table 4: Australian Government Research Priorities

Australian Government	
Rural RD&E Priorities (est. 2015)	**Science and Research Priorities (est. 2015)**
1. Advanced technology 2. Biosecurity 3. Soil, water and managing natural resources 4. Adoption of R&D	1. Food 2. Soil and Water 3. Transport 4. Cybersecurity 5. Energy and Resources 6. Manufacturing 7. Environmental Change 8. Health

Sources: DAWR (2015) and OCS (2016)

Valuation of Impacts

Impacts Valued

The project did not produce any quantifiable impacts, so no quantitative evaluation processes were applied to estimate benefits.

Impacts not Valued

The impacts identified in Table 3 were not valued for the following reasons (Table 5):

Table 5: Reasons for Not Valuing Impacts

Impact/Potential Impact	**Reason why Impact Not Valued**
The prospective impacts of reduced production costs, or improved quality and volume of YTK produced, due to reduced impact of diseases on YTK production were not delivered.	A lack of evidence that any such improvements along the pathway to impact have been produced.
The potential contribution to a reduced use of hydrogen peroxide leading to cost savings and a lowering of risks to aquaculture workers has not materialised.	A lack of evidence that any such improvements along the pathway to impact have been produced.
Some scientific knowledge that may be used in the future to produce unspecified impacts.	The difficulty of placing a financial value on any contribution.

Results

All past costs were discounted to 2017/18 using a discount rate of 5%. All analyses ran for the length of the project investment period plus 30 years from the last year of investment in Project 2014-729 (2016/17).

Investment Criteria

Tables 6 and 7 show the investment criteria estimated for different periods of benefits and costs for the total investment and FRDC investment respectively. Note that, as no impacts were valued, the investment criteria reporting is restricted to the Present Value of Costs.

In the interests of consistency with other project analyses and reporting, the Present Value of Costs was reported for the length of the investment period plus for different periods up to 30 years from the last year of investment (2016/17).

Table 6: Investment Criteria for Total Investment in Project 2014-729

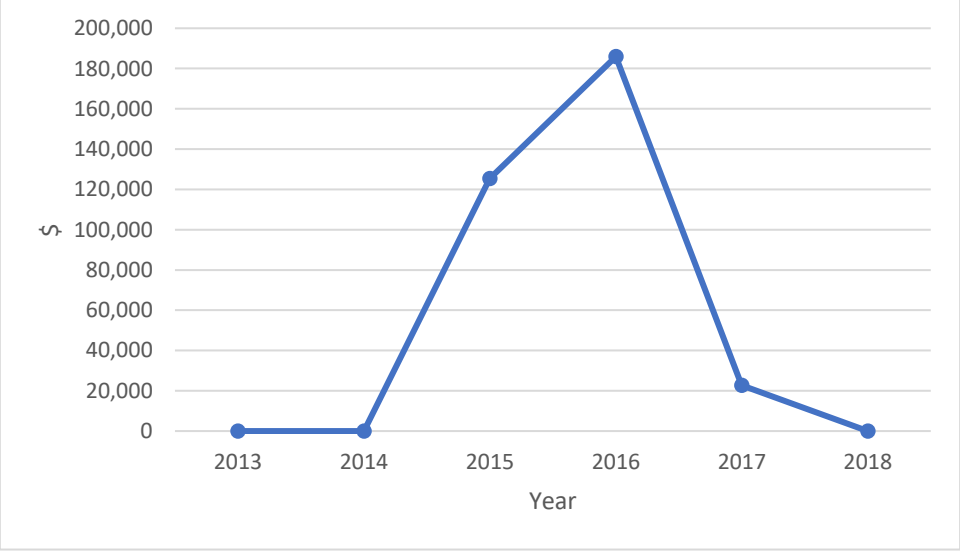
Investment criteria	**Number of years from year of last investment**						
	0	**5**	**10**	**15**	**20**	**25**	**30**
Present value of costs ($m)	0.37	0.37	0.37	0.37	0.37	0.37	0.37

Table 7: Investment Criteria for FRDC Investment in Project 2014-729

Investment criteria	**Number of years from year of last investment**						
	0	**5**	**10**	**15**	**20**	**25**	**30**
Present value of costs ($m)	0.22	0.22	0.22	0.22	0.22	0.22	0.22

The annual undiscounted cost cash flow for the total investment for the duration of investment period is shown in Figure 1.

Figure 1: Annual Cash Flow of Undiscounted Total Costs



Conclusions

Total funding for the investment over the three years totalled $0.37 million in present value terms. The FRDC investment costs were $0.22 million in present value terms. Apart from scientific knowledge that may be used in the future, it is evident that the project did not produce any industry impacts.

Glossary of Economic Terms

Cost-benefit analysis:	A conceptual framework for the economic evaluation of projects and programs in the public sector. It differs from a financial appraisal or evaluation in that it considers all gains (benefits) and losses (costs), regardless of to whom they accrue.
Benefit-cost ratio:	The ratio of the present value of investment benefits to the present value of investment costs.
Discounting:	The process of relating the costs and benefits of an investment to a base year using a stated discount rate.
Internal rate of return:	The discount rate at which an investment has a net present value of zero, i.e. where present value of benefits = present value of costs.
Investment criteria:	Measures of the economic worth of an investment such as Net Present Value, Benefit-Cost Ratio, and Internal Rate of Return.
Modified internal rate of return:	The internal rate of return of an investment that is modified so that the cash inflows from an investment are re-invested at the rate of the cost of capital (the re-investment rate).
Net present value:	The discounted value of the benefits of an investment less the discounted value of the investment costs, i.e. present value of benefits - present value of investment costs.
Present value of benefits:	The discounted value of benefits.
Present value of costs:	The discounted value of investment costs.

References

Australian Bureau of Statistics. (2018, January 31). 5204.0 - Australian System of National Accounts, 2016-17. Retrieved from Australian Bureau of Statistics: http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/5204.02016-17?OpenDocument

Council of Research and Development Corporations (CRRDC) (2014), Canberra. Accessed 19 June at: http://www.ruralrdc.com.au/wp-content/uploads/2016/04/CRRDC-Impact-Assessment-Guidelines-V.1-070514.pdf

DAWR (2015) Rural Research and Development Priorities, Department of Agriculture and Water Resources, Canberra, ACT, accessed January 2016 at: http://www.agriculture.gov.au/ag-farm-food/innovation/priorities

Fisheries Research and Development Corporation (2013-2017) Annual Reports, Canberra. Accessed May 2017 at: http://www.frdc.com.au/en/about-us/corporate-documents/annual-reports

OCS (2016) Science and Research Priorities, Office of the Chief Scientist, Department of Industry, Innovation and Science, Canberra, accessed 02 November 16 at: http://science.gov.au/scienceGov/ScienceAndResearchPriorities/Pages/default.aspx