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Benefits of Rabbit Biocontrol in Australia

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Invasive Animals CRC


An Australian Government Initiative





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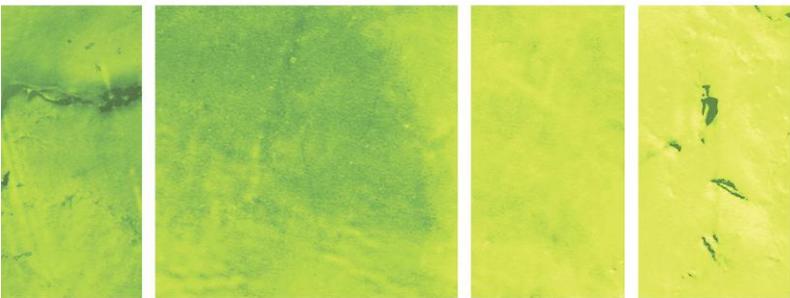
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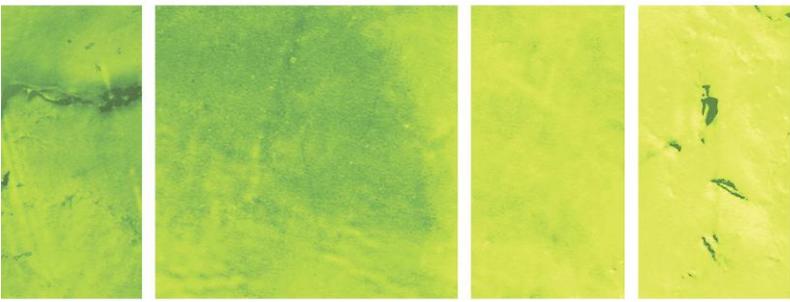
Contents

Executive Summary	1
Introduction.....	8
Project terms of reference	8
Overview of rabbit distribution, abundance and impacts	8
Benefits of current rabbit biocontrol technology ...	14
Environmental benefits	15
Social benefits	15
Economic benefits.....	15
General benefits of future rabbit biocontrol technology	16
Current rabbit biocontrol initiatives	18
RHD-Boost.....	18
<i>Strain selection</i>	<i>18</i>
<i>Overcoming immunity to existing RHDV strains</i>	<i>19</i>
<i>Interfering endemic non-pathogenic caliciviruses RCV-A1</i>	<i>20</i>
<i>Overcoming genetic resistance in wild rabbits</i>	<i>21</i>
<i>RHD-Boost Release and Performance Measurement</i>	<i>21</i>
<i>Measuring Impact</i>	<i>21</i>
<i>Integrating conventional control</i>	<i>21</i>
<i>Impact of RHD-Boost</i>	<i>22</i>
<i>Benefits of RHD-Boost</i>	<i>22</i>
RHD Resistance Model	22
RHD Accelerator	23
<i>Objective and rationale</i>	<i>23</i>
<i>Replicating natural selection</i>	<i>23</i>
<i>Impact of RHD Accelerator.....</i>	<i>24</i>
<i>Benefits of RHD Accelerator</i>	<i>24</i>
Bioprospecting	24
<i>Objective and rationale</i>	<i>24</i>
<i>Impact of Bioprospecting</i>	<i>25</i>
<i>Benefits of Bioprospecting.....</i>	<i>25</i>
Technology opportunity.....	25
Environmental and economic benefits of new biocontrol technologies	26



Image: Rabbit plague on Wardang Island in 1963
(Source: National Archives of Australia)

Reducing risks associated with future RHDV strain releases	27
RHD-Boost Release and Performance Measurement.	27
Maximising RHD Boost impact by optimising release of new RHDV strains when RCV-A1 prevalence is low..	27
Building and maintaining diagnostic capability to track biocontrol performance	27
Conclusions and recommendations	28
References	29
Appendix 1: Background information on rabbit biocontrol agents	32
Myxomatosis	32
Rabbit fleas	32
Rabbit haemorrhagic disease	32
Virally-vectored immunocontraception	33
Appendix 2: Diagrammatic representation of benefits from RHD Boost, RHD Accelerator, Bioprospecting and DSS/Rabbit Facilitator	34





Executive Summary

EUROPEAN RABBITS (*Oryctolagus cuniculus*) are a severe continental-scale threat to Australia’s globally important biodiversity and agriculture. The extreme sensitivity of many native plant species to rabbit damage - as few as one rabbit per hectare can impede natural regeneration - has resulted in 75 nationally threatened plant species and five threatened ecological communities being at risk from rabbit impacts. Rabbits are also Australian agriculture’s most costly vertebrate pest animal causing more than \$200 million in production losses each year.

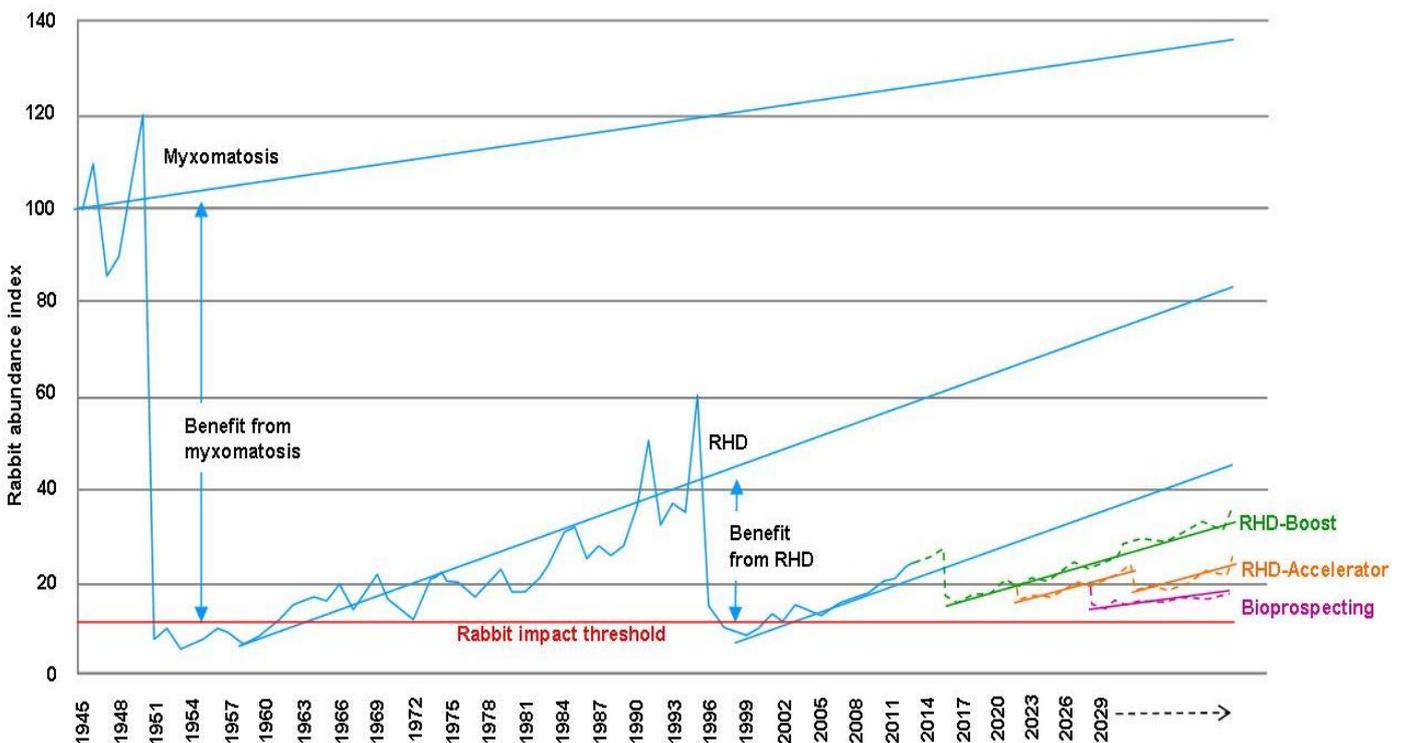
Without rabbit biocontrol agents, however, these impacts would be much worse: the combination of myxoma virus (MV) and rabbit haemorrhagic disease virus (RHDV) still limits rabbit numbers to about 15% of their potential numbers, and without them the cost for agriculture alone would be in excess of \$2 billion a year. The cumulative environmental benefits of the release of MV in 1950 and RHDV in 1995 includes landscape scale native vegetation regeneration, increased abundance of native plants and animals,

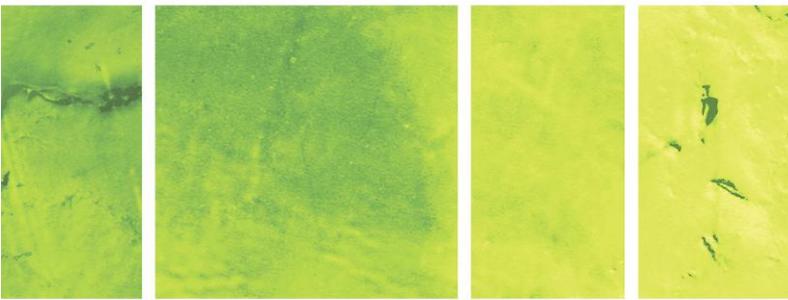
Myxomatosis - MV, a highly infectious poxvirus disease which causes severe generalised disease in European rabbits. It was introduced in to Australia in 1950 as a biocontrol agent for rabbits.

Rabbit Haemorrhagic Disease - RHD, a highly infectious disease specific to European rabbits caused by the calicivirus Rabbit Haemorrhagic Disease Virus (RHDV). It escaped quarantine in Australia in 1995 and was subsequently released as a biocontrol agent from 1996 to the present day.

continued persistence of many native threatened species, large scale carbon biosequestration, and improved landscape and ecosystem resilience. The cumulative economic benefits for agriculture alone from MV and RHDV over 60 years are estimated at \$70 Billion, or an average of \$1.17 billion per year.

To maintain these benefits and keep rabbit abundance below or near the rabbit impact threshold, strategic rabbit biocontrol research is critical to strengthen the effectiveness of existing rabbit biocontrol agents, and identify and evaluate new potential biocontrol agents. This is being partially progressed through three key





initiatives in the Invasive Animals CRC rabbit research program (2012-17):

1. **RHD Boost** - selection and evaluation of naturally occurring overseas RHDV strains shown to have improved effectiveness over the one endemic RHDV strain introduced in 1995,
2. **RHD Accelerator** - proof of concept for a platform technology to continuously develop new RHDV strains through accelerated natural selection, and
3. **Bioprospecting** - identify and assess feasibility of new potential biocontrol agents.

This research program has been designed to deliver strengthened RHDV strains from about 2015 to 2030, augmented by any new evaluated biocontrol agents from about 2030. The benefits of these three technologies are summarised below. The predicted impact of these technologies on rabbit abundance is outlined in four scenarios in the graph above:

Scenario 1: Business as usual shows an on-going increase in rabbit abundance that erodes all the gains from RHDV and leads to major increases in economic and environmental impacts over time.

Scenario 2: Release of new RHD-Boost RHDV strains regains most of the benefits of the original RHDV release, followed by a progressive increase in rabbit abundance

Scenario 3: Release of new RHD-Boost RHDV strains followed by new RHD-Accelerator RHDV strains which regain the benefits of the RHD-Boost release. Subsequent releases of RHD-Accelerator strains every 5-10 years see a repeated relative knockdown in rabbit numbers.

Scenario 4: Releases of new RHD-Boost RHDV strains followed by new RHD-Accelerator RHDV strains and a new biocontrol agent have the greatest impact on rabbit numbers.

While this balanced research portfolio aims to deliver a rabbit biocontrol technology pipeline in the short to medium term, there remain important gaps that create significant risk to the effectiveness of these research outputs and the seamless continuation of effective rabbit biocontrol. In the short term, knowledge gaps of the seasonal patterns of the endemic benign rabbit calicivirus (RCV-A1) remain, which is critical to ensure impacts from the release of RHD-Boost strains are maximised by knowing when the impeding RCV-A1 virus is least prevalent in a landscape. Additional resources also need to be secured to enable the performance and benefits of RHD Boost strains to be quantitatively measured in various landscapes.

Rabbit Calicivirus Australia-1 - RCV-A1, a pre-existing benign calicivirus which causes no disease and offers rabbit's partial protection to infection by the introduced pathogenic calicivirus RHDV. RCV-A1 is mainly found in the cool-wet regions of Australia with > 400mm annual rainfall.

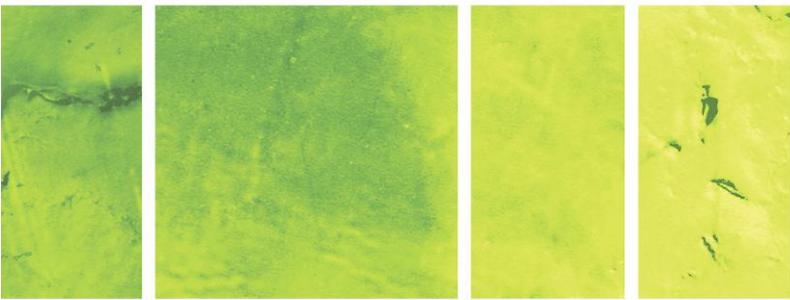
In the medium term, there is an urgent need to develop a coordinated program of rabbit disease monitoring and surveillance across the various climatic regions of the Australian continent to understand prevalence, seasonal fluctuations and interactions of rabbit pathogens such as RHDV, MV and the interfering benign calicivirus RCV-A1. Understanding these mechanisms is critical to identifying the factors that define the success of potential biocontrol/biocide releases. An integral component of this is to ensure availability of state-of-the-art differential diagnostic tools and epidemiological modelling. Capabilities in these areas need to be increased and maintained.

In the longer term it is essential to ensure that applied biocontrol research can continue. If successful in their proof of concept stages, the *RHD-Accelerator* and the *Bioprospecting* projects will need ongoing support to be further developed to the product stage. In addition, scientific research needs to continue to increase our understanding of the long term effects of evolution and genetic resistance development, as well as cumulative or neutralising effects that may arise from co-occurring pathogens. The latter is of particular importance as more and more pathogens and viral variants are added to the environment. This need is reinforced by the *National Biosecurity Research and Development Capability Audit* commissioned by the National Biosecurity Committee, which suggested that Australia should invest more heavily in the long term funding of biological control programs, including monitoring of field effectiveness.

The imperative for strategic rabbit biocontrol research is based on four facts: rabbits are becoming increasingly resistant to existing rabbit biocontrol agents, in good seasons rabbit populations can increase 7-10 fold, rural populations and labour continues to decrease, and the cost of rural labour continues to increase. Proactive investment in strategic rabbit biocontrol research will ensure rabbit abundance can be kept near the rabbit impact threshold which is less than one rabbit per hectare.



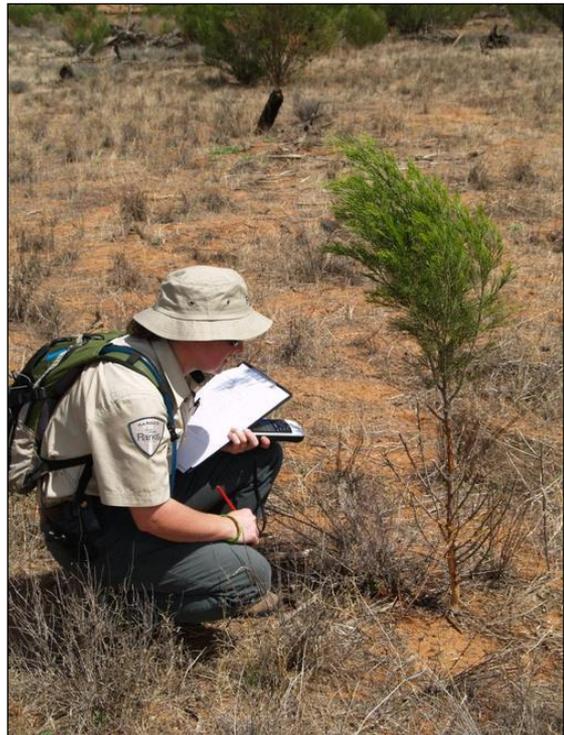
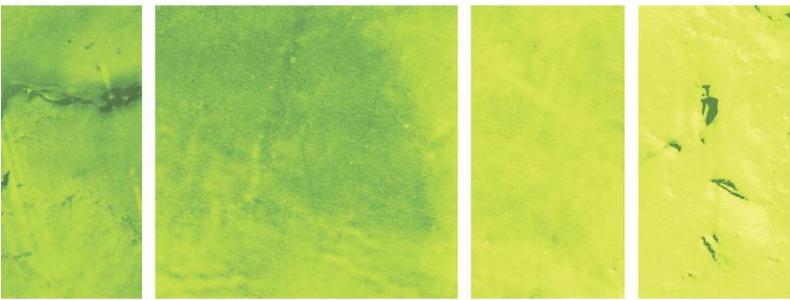
Improved RHDV effectiveness	Objective	Benefits
RHD Boost rollout	Identify, seek approval, release and selectively measure the performance of new naturally occurring overseas RHDV strains found to be superior to the one existing RHDV strain in Australia	<p>Net Present Value: \$1.4 Billion over 15 years made up of \$840 million of agricultural benefits and \$560 million in carbon sequestration benefits.</p> <p>Benefit Cost Ratio: 563 to 1</p> <p>Internal Rate of Return: 217%</p> <p>Biodiversity benefits: increased regeneration of native vegetation, and in longer term increase in abundance of many threatened species</p> <p>Carbon benefits: increase in standing biomass via regeneration</p> <p>Soil benefits: reduced soil erosion and land degradation</p> <p>Assumes selection and release about 2015</p>
RHD Accelerator platform technology	Develop a platform technology for on-going laboratory based selection of superior RHDV strains	<p>Net Present Value: \$79 million over 15 yrs and \$300 million over 30 years (60% are agricultural benefits, 40% carbon sequestration benefits)</p> <p>Benefit cost Ratio: 48 to 1 over 15 yrs</p> <p>Internal Rate of Return: 38%</p> <p>Biodiversity benefits: increased regeneration of native vegetation, and in longer term increase in abundance of many threatened species</p> <p>Carbon benefits: increase in standing biomass via regeneration</p> <p>Soil benefits: reduced soil erosion and land degradation</p> <p>Assumes new RHDV strains able to sustain the benefits delivered by RHD Boost</p>
Comprehensive RHD resistance model	Understanding the nature and geographical distribution of rabbit genetic resistance, to develop a framework for the optimisation of additional virus releases	Improves effectiveness of RHD Boost and RHD Accelerator technologies
New biocontrol agents assessed		
Assessment and prospecting for potential new biocontrol agents	Assess the feasibility of new potential rabbit biocontrol agents and establish an international alert network	<p>Net Present Value: \$28 million over 30 years</p> <p>Benefit Cost Ratio: 115 to 1</p> <p>Internal Rate of Return: 21.5%</p> <p>Assumes additional research of new biocontrol agent to enable release from 2030.</p>



Native grass regeneration post RHDV arrival and rabbit control on Thackaringa Station, Broken Hill. The regeneration occurred during a period of drought (Images: David Lord).



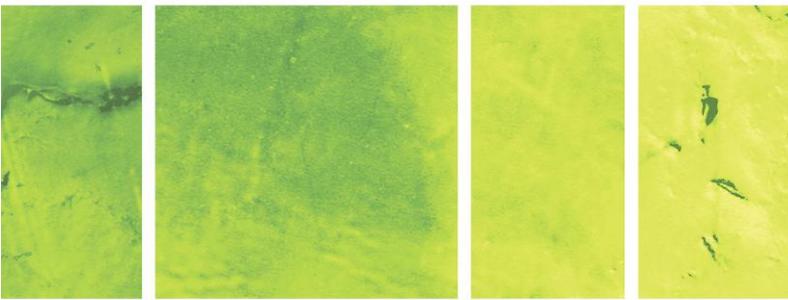
Exclusion fencing showing the change in vegetation structure due to rabbits on Macquarie Island (top) and in Coorong, SA (bottom) (Images: Brian Cooke).



Native plants which are especially susceptible to browsing by rabbits, even at low rabbit densities. Top left: *Myoporum insulare*, Boobiala, Coorong SA; Top right: *Acacia ligulata*, Sandhill wattle, Hattah-Kulkyne National Park, VIC; Bottom left: rabbit damage to tree guard and sheoak; Bottom right and left: rabbit damage to *Allocasuarina* and *Callitris* sp., Hattah-Kulkyne National Park, VIC. (Images: Brian Cooke).



This *Melaleuca lanceolata* grew during a period of rabbit relief after the spread of MV. Note the lack of understory and the browsing at rabbit height. Increases in rabbit numbers are winding back any gains made by the releases of MV and RHDV (Image: Brian Cooke).



Introduction

The 2009-10 Caring for our Country business plan included a priority outcome to reduce rabbit impacts with the following key target:

to suppress rabbit populations over the next three years to densities that are low enough to allow regeneration and recovery of critically endangered and endangered species and communities in identified priority areas.

To achieve this outcome, the investment portfolio included \$1.5 million of the \$2.7 million required for the RHD-Boost project. The RHD-Boost project aimed to identify and evaluate new naturally occurring overseas strains of rabbit haemorrhagic disease virus (RHDV) - the causative agent of rabbit haemorrhagic disease (RHD) - which were suitable for release into Australian rabbit populations and which sought to overcome the developing acquired immunity and genetic resistance to the current Czech 351 RHDV strain, and the impact of the benign calicivirus Rabbit Calicivirus Australia 1 (RCV-A1) which offers partial protection to infection by pathogenic RHDV.

This report reviews previous biological control efforts for rabbits in Australia, the likely economic and environmental benefits of the release of a new strain/s of RHDV (RHD-Boost), and the benefits of investing in future areas of rabbit biocontrol research such as the development of a performance management framework (RHD-Boost Release and Performance Measurement), the ongoing selection of improved RHDV strains (RHD-Accelerator), the continued search for new biocontrol agents (Bioprospecting) and It also describes current knowledge about the distribution of rabbits, and benign rabbit calicivirus (RCV-A1).

Project terms of reference

This project's statement of work required Invasive Animals Ltd to undertake a desk top evaluation of a successful release of an additional effective rabbit biocontrol agent. The evaluation was to include the likely benefits to production and the environment based on a literature review, historical information about the 1990's release of RHD, and current knowledge about the distribution of rabbits and the



benign and lethal varieties of RHD and myxomatosis (MV).

Overview of rabbit distribution, abundance and impacts

Wild rabbits were successfully introduced into Australia in 1859 and within 70 years had spread to inhabit 70% of Australia's landmass (5.3 million km²) (Figures 1 and 2). They are widespread throughout most locations where they are found (NLWRA and IACRC 2008).

Rabbits feeding habits include removing vegetation to ground level and digging for roots which can result in significant soil destabilisation and erosion, leading to the desertification of heavily impacted areas. Such damage is added to through the excavation of warren systems - often extensive and in ecologically sensitive areas. Rabbits are also prolific breeders. In good seasons populations can increase 7-10 fold. Rabbits impact 75 Commonwealth *Environment Protection and Biodiversity Conservation Act 1999* listed threatened plant species and five threatened ecological communities (Figure 3) and are the most costly pest animal to agricultural production: the annual cost exceeding \$200 million (Gong *et al.* 2009).

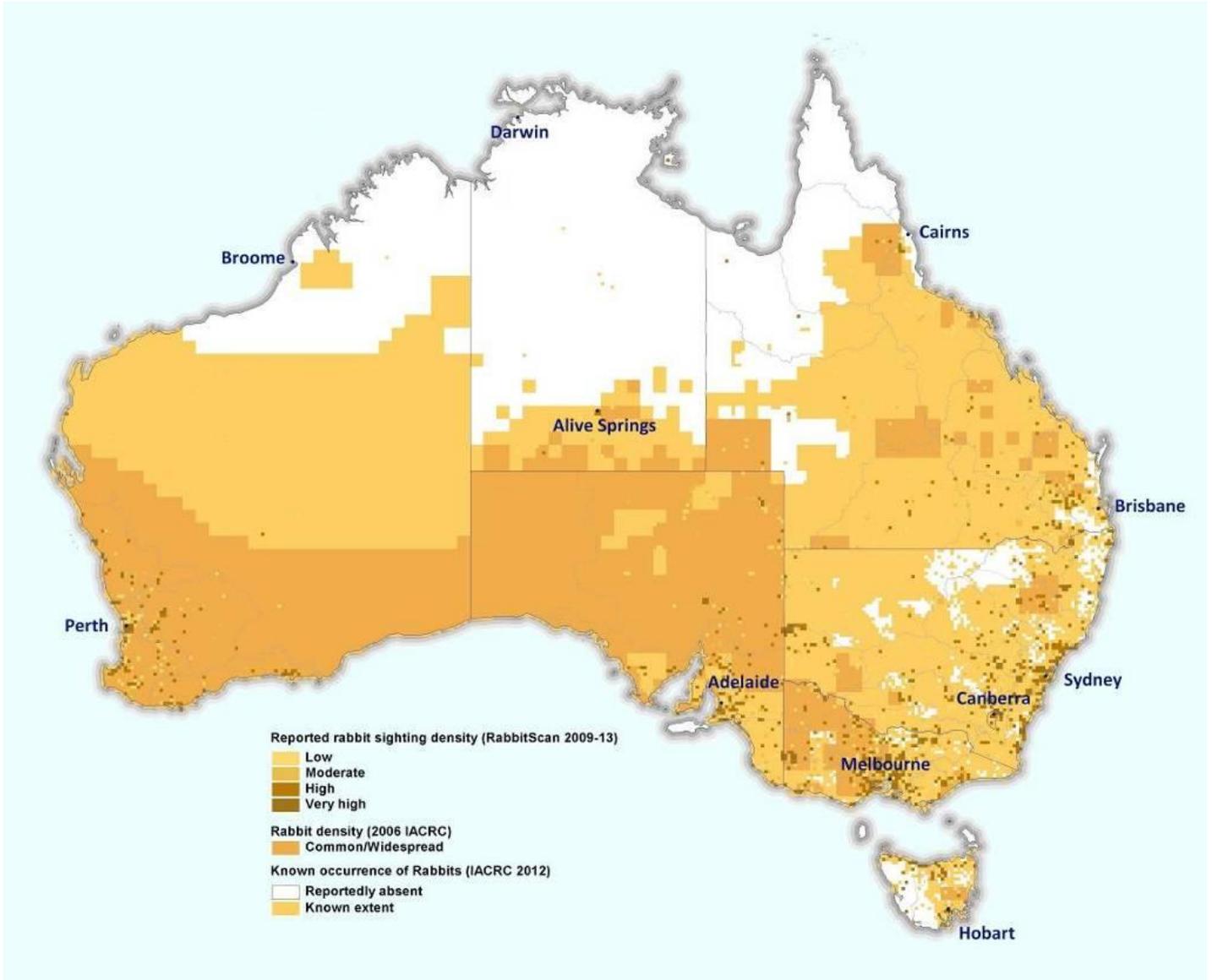


Figure 1: Reported abundance of European rabbits (*Oryctolagus cuniculus*) across Australia (Source data: Invasive Animals CRC, RabbitScan, and NLWRA and IACRC 2008).

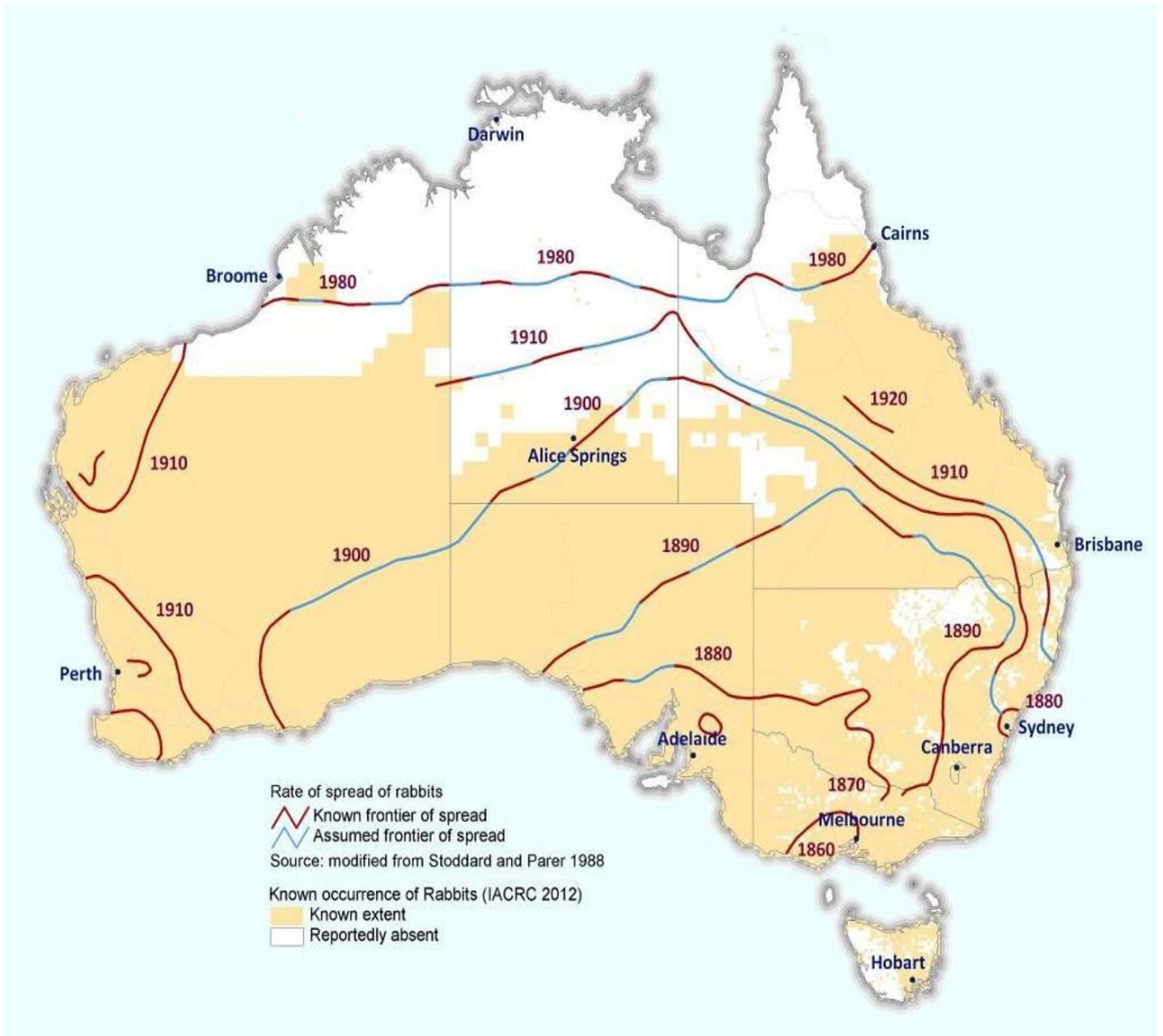
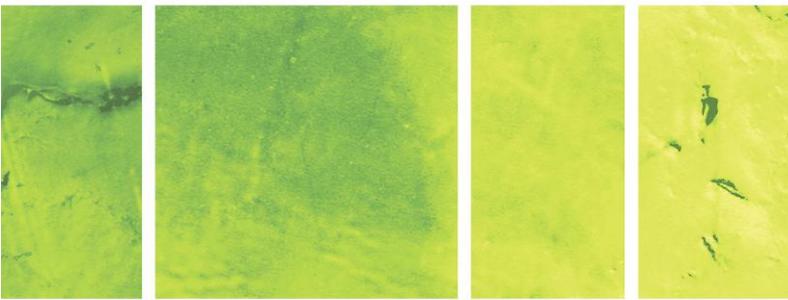


Figure 2: Rate of spread of wild rabbits since their introduction to Geelong, Victoria in 1859 to their current known distribution (Source data: Invasive Animals CRC, Stoddard and Parer 1988).

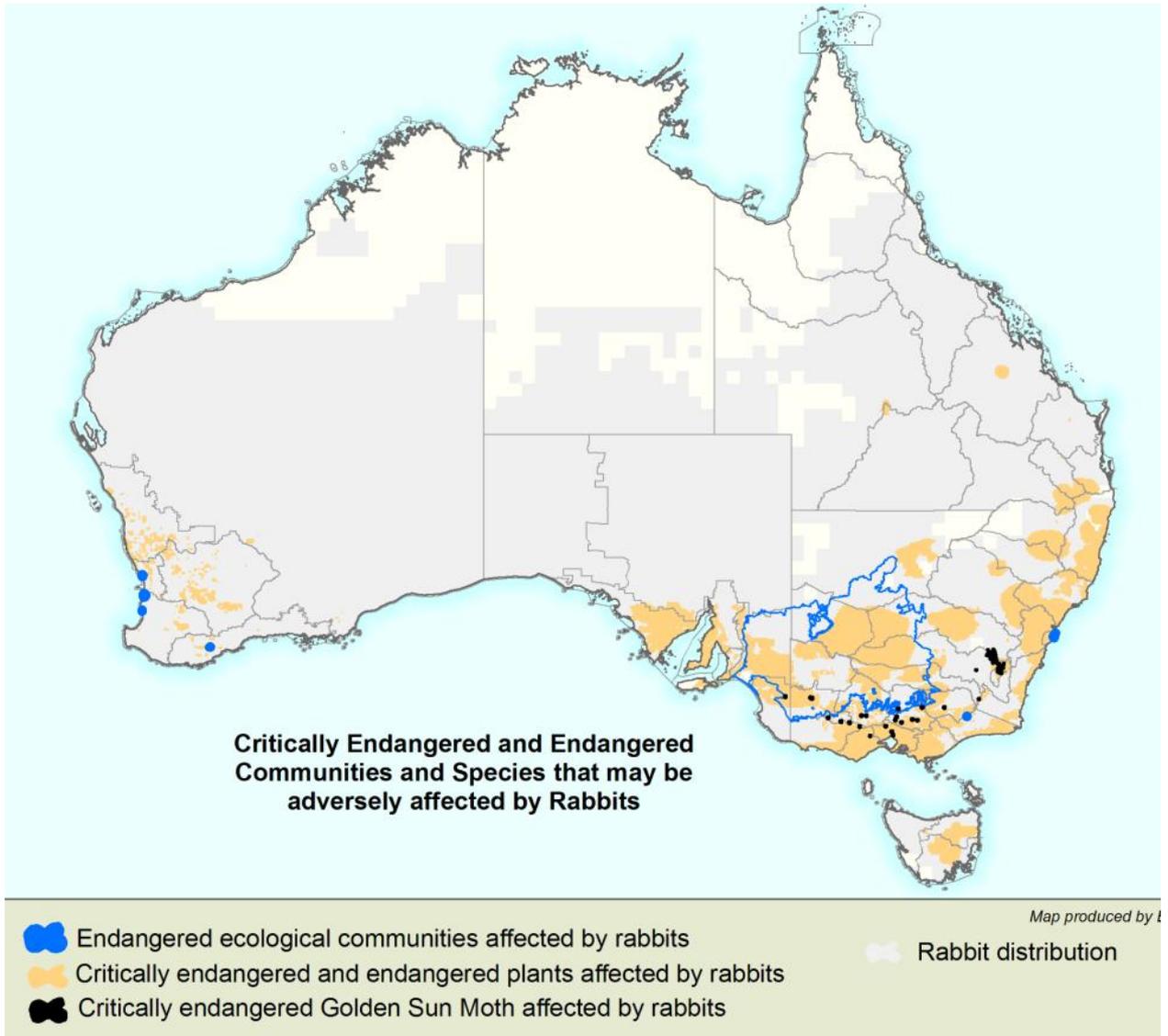
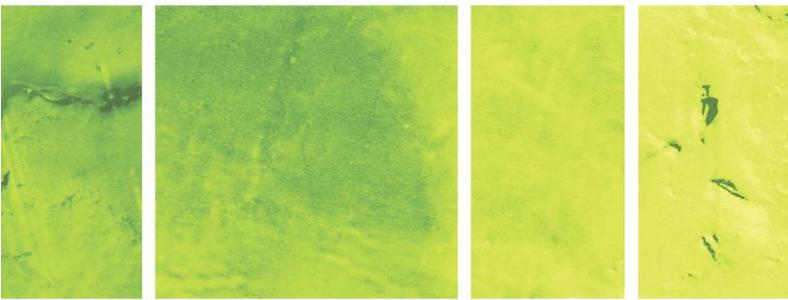


Figure 3: Locations of critically endangered and endangered communities and species that may be adversely affected by rabbits (Commonwealth of Australia 2008).



Brief history of rabbit invasion and rabbit biocontrol pipeline

(adapted from Department of Environment and Primary Industries 2011)

- 1859** 24 wild rabbits released at Barwon Park near Geelong, Vic, for hunting become established. Invasion across Australia at about 130 km per year. Some farms abandoned as early as 1881
- 1926** Estimated 10 billion rabbits in Australia with 70% of continent invaded
- 1950** World's first vertebrate pest biocontrol - myxoma virus (MV) - released and kills 99.8% of infected rabbits
- 1969** Rabbit flea species (*Spilopsyllus cuniculi*) approved for release to act as an improved vector to spread MV in areas low in mosquitoes
- 1990** Rabbit population about 600 million
- 1993** Spanish rabbit flea (*Xenopsylla cunicularis*) adapted for arid conditions approved for release and improves transmission of MV
- 1995** Rabbit haemorrhagic disease virus (RHDV) introduced and kills up to 98% of rabbits in arid areas
- 2000s** Rabbits begin to develop resistance to RHDV infection. Increasing resistance and increasing food availability as drought breaks results in observed increasing rabbit numbers
- 2009** Benign endemic rabbit calicivirus (RCV-A1) that confers partial protection to rabbits discovered and characterised
- 2009+** New naturally occurring overseas RHDV strains that have observed increased lethality to rabbits are imported from Europe and Asia and evaluated as part RHD Boost project co-funded through Caring for our Country Program
- 2012** Successful Invasive Animals CRC extension includes strategic rabbit biocontrol research program to boost effectiveness of RHDV, assess feasibility of new potential rabbit biocontrol candidates, and increased capabilities to promote regional integrated rabbit control

Recent research conducted by the Invasive Animals Cooperative Research Centre (IA CRC) has shown that Australian native vegetation is very sensitive to rabbit damage. A specific example is Mulga (*Acacia aneura*) which occurs across vast areas of central Australia. Recruitment of seedlings for this species is greatly impacted upon by rabbit densities as low as 1 rabbit/km² (Mutze *et al.* 2008). This greatly impedes natural regeneration. Similar stories can be told for a variety of palatable trees and shrubs across much of the distribution of the rabbit (Sandell 2002, Murdoch 2005, DEWHA 2008, Bird *et al.* 2012, Cooke 2012).

While the direct impact of rabbits on vegetation is obvious, their impact on native animals via competition is less so. For example, both kangaroo (*Macropus rufus*, *M. fuliginosus* & *M. robustus*) and wombat (*Vombatus ursinus*) numbers increased following native vegetation regeneration after the release of RHDV, suggesting that high populations of rabbits may restrict these species (Mutze *et al.* 2008; Bird *et al.* 2012).

Rabbit impact on native pastures affects a variety of other species, including endangered or critically endangered species such as the plains-wanderer (*Pedionomus torquatus*) (Baker-Gabb 2002) and the golden sun moth (*Synemon plana*) (Clarke and O'Dwyer 2000). Competition and land degradation by rabbits is listed as a Key Threatening Process under the Commonwealth *Environmental Protection and Biodiversity Conservation Act 1999*.

The general trend in rabbit abundance across Australia is upward. Figure 4 summarises information available on changes in rabbit numbers in the arid pastoral area of north-eastern South Australia associated with the introduction of MV, then RHDV in an area where other control measures, such as poisoning and warren ripping were not often applied. In that region, where mosquitoes were scarce, the release of European rabbit fleas (*Spilipsyllus cuniculus*) in 1969 enhanced the spread of MV. Importantly, it shows a marked increase in rabbit abundance since the early 2000s.

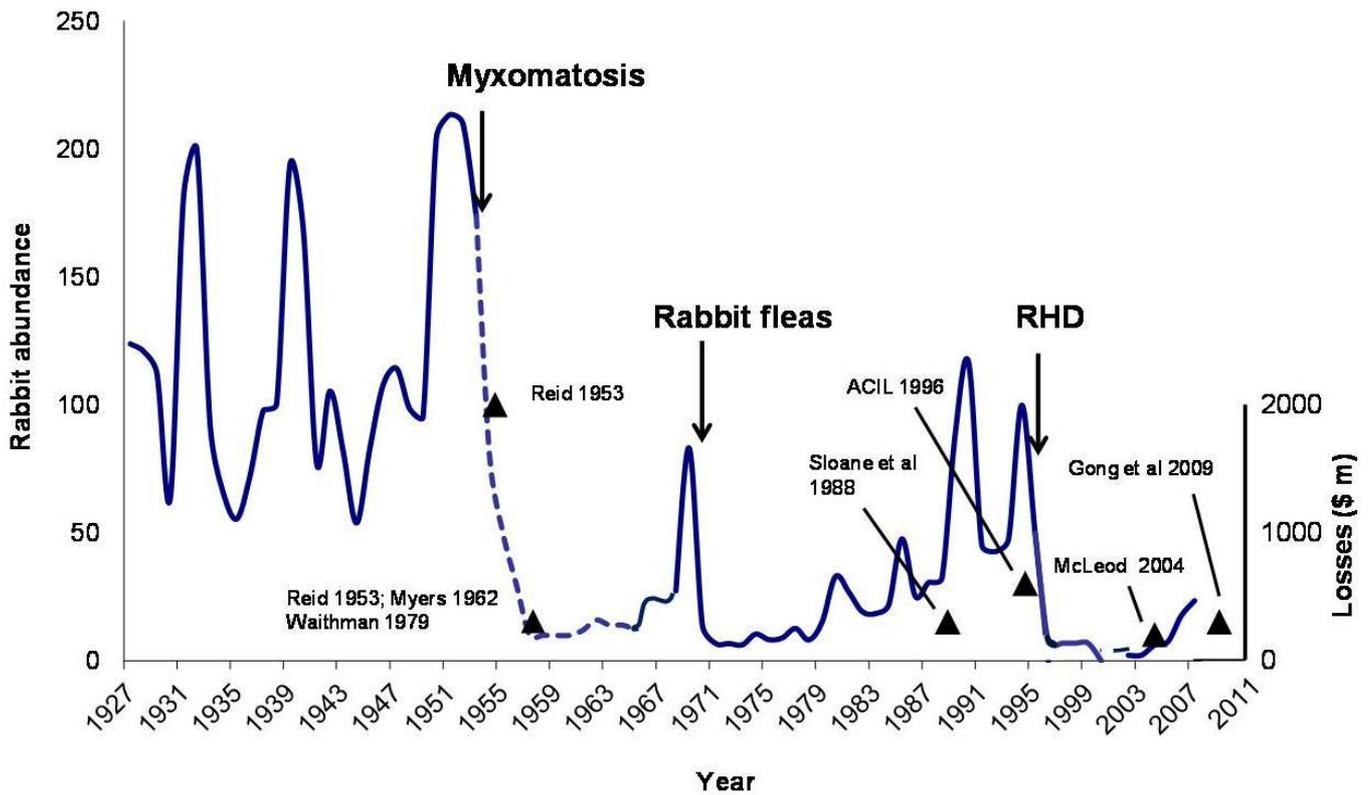
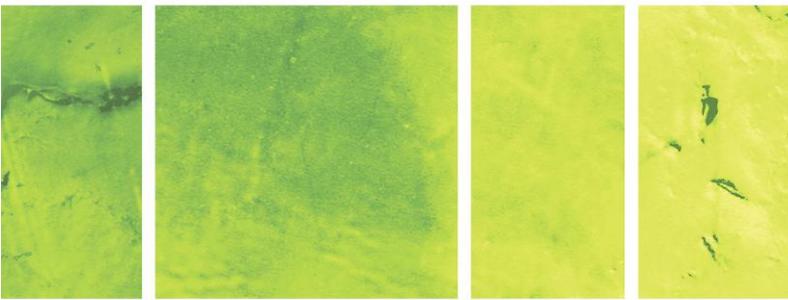


Figure 4: Diagram showing how rabbit abundance in semi-arid South Australia has varied through time in response to the release of biological control agents and the estimated Australia-wide economic losses to rabbits (black triangles). Scale for losses shown on right-hand side of figure (Cooke *et al.* 2013).



Benefits of current rabbit biocontrol technology

By far the most successful method of reducing rabbit impacts in Australia has been the use of biological control agents. At times these have reduced rabbit numbers in some areas by as much as 99 per cent. Their impact has allowed land managers to apply complementary conventional control techniques (e.g. warren ripping, baiting and fumigation) in a more cost efficient and effective manner. The continued suppression of recovering and/or reinvading populations with biocontrol agents post conventional control has also been of benefit, greatly improving the value of applied conventional control. Australia has introduced four biocontrol agents for rabbits over the last 60 years: two viral diseases and two insect vectors to aid their transmission, and undertaken extensive research into another: virally-vectored immuno-contraception (Hardy *et al* 2006, Saunders *et al* 2010). Background information is provided in Appendix 1.

The benefits of rabbit biocontrol are not uniform across Australia. This is particularly the case for RHDV, which was generally more effective in drier, lower rainfall areas (Figure 5). Monitoring of rabbit abundance showed an average decrease by two-thirds (67.3%) in low rainfall areas, and only a quarter (27.5%) in high rainfall areas.

The application of biocontrol agents has a number of benefits, particularly when applied to large-scale pest problems such as that presented by the European rabbit in Australia. The benefits of using biocontrol can be counted in environmental, social and economic terms and, in the case of biocontrol for rabbits, is the most cost effective way of managing a pest species.

Average decline in Rabbit populations at monitoring sites following RHD arrival and release across rainfall zones of Australia

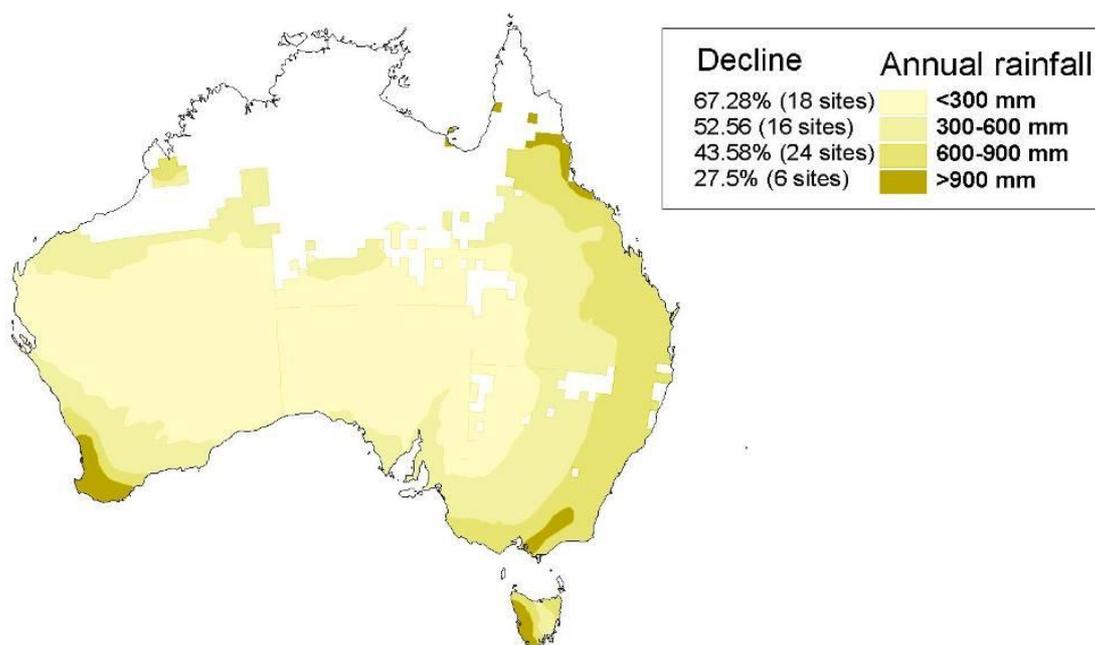


Figure 5: The decline in rabbit populations by rainfall zone after the arrival of RHDV.



Environmental benefits

The environmental benefits of RHDV were high, especially in semi-arid areas where significant regeneration of native vegetation occurred, despite below average rainfall (Sandell 2002, Murdoch 2005, Mutze *et al.* 2008, Bird *et al.* 2012, Figure 5). After the introduction of RHDV, studies have shown that populations of native animals also increased.

Populations of Spinifex hopping mice (*Notomys alexis*) and plains mice (*Pseudomys australis*) (Read 2003), common wombats (*Vombatus ursinus*), red kangaroos (*Macropus rufus*) and western grey kangaroos (*M. fuliginosus*) (Mutze *et al.* 2008) all showed signs of recovery post RHDV introduction. Fox and feral cat numbers decreased in the Flinders Ranges National Park after the rabbit population was reduced by 85% (Holden and Mutze 2002). The most notable impact was on feral cats with their body condition falling by 17%.

Social benefits

There has been very little systematic research into the social impacts of rabbits or any other vertebrate pests in Australia (Fitzgerald and Wilkinson 2009). It is likely that the effects of pest animals, for the most part, are economic and environmental, but there are flow-on social impacts. A collection of personal stories (Quealy 2011) recounts that prior to the introduction of MV many farmers and their families were forced to walk away from their properties because of the rabbit. Many talk of the psychological distress at having to make a new life away from the farm. Similarly, competing interests lead to conflict between those prospering from high rabbit numbers e.g. commercial harvesters, and those suffering because of the rabbit.

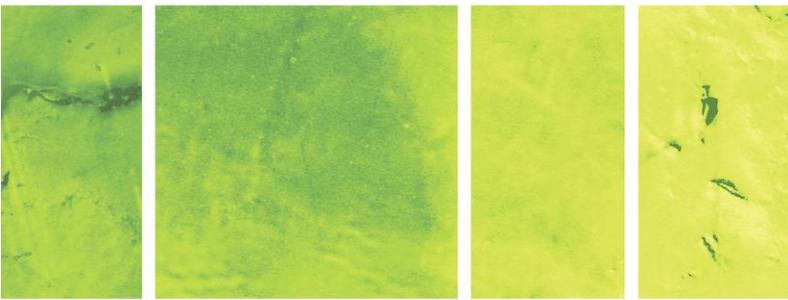
A case study of the social impacts of rabbits in the Hunter Valley region of NSW in 2009 highlighted that residents in this area were more concerned with the impact of rabbits on mine rehabilitation sites, damage to grape vines and the risk of injury to horses due the presence of warrens (Fitzgerald and Wilkinson 2009). While this region is not necessarily representative of the attitudes of the whole of the area of Australia where rabbits occur, it does highlight the shift in attitude, by some, from a concern about the impacts of rabbits on making a living, to a concern about the impacts of rabbits on their living amenity.

One negative social impact of effective rabbit biocontrol is that rabbits have lost some of their public profile as a major pest species. An increasing percentage of both the urban and rural population do not remember pre-RHDV or pre-MV rabbit numbers and damage. This has reduced the general awareness of rabbits as a problem, which in turn often results in diminished public support for ongoing rabbit research and control.

Economic benefits

Recent estimates value the cumulative benefit of MV and RHDV to Australia's pastoral industries at approximately AU\$70 billion over the last 60 years (Cooke *et al.* 2013). In the period immediately after its release, MV resulted in AU\$68 million in increased production (AU\$48 million in increased wool clips and AU\$20 million in increased sheep and lamb meat) (Sobey 1981). The economic savings generated by RHDV are estimated to be in excess of AU\$350 million annually, indicating that in the 17 years since its release RHDV has generated benefits of almost AU\$6 billion to the rural industries alone (Cooke *et al.* 2013). Considering that government and industry investment for the introduction of RHDV was in the order of AU\$12 million (Cooke *et al.* 2013) this return on investment is unmatched by any other investments in rabbit control research, or perhaps any other area of government investment, in the last 50 years.

When MV was first released it provided an estimated \$1.4 billion p.a. benefit (2011 A\$) (Cooke *et al.* 2013). MV and RHDV combined reduce rabbit numbers by 85% compared to their potential numbers, a benefit that would be lost if there was no biocontrol. If the initial myxo knockdown is used as a baseline, the current benefit of biocontrol is 85% of \$1.4 billion or some \$1.19 billion p.a. This equates with the average estimated annual benefit of \$1.17 billion derived from the calculated \$70 Billion benefit over 60 years from MV and RHDV (Cooke *et al.* 2013). In comparison, without rabbit biocontrol, the estimated national impact of some 10 billion rabbits caused livestock production losses of \$2 billion/yr (Department of Environment and Primary Industries 2011, Cooke *et al.* 2013).



General benefits of future rabbit biocontrol technology

Rabbit control is costly, especially in pastoral areas, and many pastoralists believe that investment in conventional controls such as rabbit warren ripping is not feasible (e.g. in sand hill country) and gains in production are unlikely to meet costs. There is therefore a continuing demand for the persistent use of biological control agents as the only plausible solution to current residual rabbit problems in arid areas. Furthermore, biological control agents are usually the only means of limiting rabbit damage in conservation areas because of the high cost and the potential damaging impact of conventional control.

Biological control research is high risk in that potential new pathogens would need to be discovered first and then imported into Australia under strict regulatory requirements. However the benefits can be extremely high as demonstrated by the economic returns. The principal benefits of continuous investment into biocontrol research are (Agtrans Research 2009):

- Increased pasture biomass for animal production;
- Decreased effort and cost associated with traditional rabbit control measures;
- Increased ground cover leading to decreased soil erosion;
- Improved native vegetation and associated habitats;
- Increased carbon sequestration, and
- Improved biodiversity.

The introduction of new and/or additional biocontrol agents to control vertebrate pests is the most cost effective way of conserving biodiversity when analysed against all other mechanisms (Morton et al. 2002, Possingham et al. 2002). New or additional agents would supplement existing agents (MV, rabbit fleas and RHDV) and avoid serious resurgence of rabbits in a timely way. The Threat Abatement Plan for Competition and Land Degradation by Rabbits (TAP) (Department of the Environment, Water, Heritage and the Arts (DEWHA) 2008) lists the improvement of efficacy, target specificity, integration and humanness

of rabbit control as one of its objectives. The conduct of research to maximise the effectiveness of existing biocontrols, and the investigation of new biocontrols, is a high priority, long term action under the TAP.

While investment risk in the Bioprospecting model depends on the chance of finding another pathogen or agent, Australia is well placed in that rabbits are an introduced species, unrelated to any other domestic or native species, and in that context the risk of harming non-target species by a rabbit pathogen are reduced. In terms of RHD-Accelerator, the development of a platform technology to sustainably address the rabbit problem can be expected to greatly enhance profitability and ecological sustainability in the long term. The current RHD-boost project if successful will provide a net present value of over \$1.4 billion over a 15 year period (Agtrans Research 2009). This value is likely to be an underestimation as the benefits to biodiversity were not valued.

The impact of biocontrol on rabbit populations in Australia has been significant. Continued investment in biocontrol and the roll-out of variations of existing agents or the release of new agents is expected to capitalise on previous gains made by MV and RHDV (Figure 6). If no further investment in biocontrol is made, then rabbit numbers will continue to increase and all gains from RHDV will be eroded. The release of additional strain of RHDV are expected to reduce rabbit numbers close to where they were following the original RHDV release; however rabbit numbers will eventually begin to increase again. Investment in the RHD-Accelerator project will see the release of strains that will regain the benefits seen by the release of RHD-Boost. The impact of the release of a new biocontrol agent in conjunction with these other efforts will ensure maximum impact on rabbit numbers.

Continued investment in biocontrol agents will have benefits to the environment through increased standing biomass and therefore an increase in carbon sequestration (Fitzgerald and Wilkinson 2009). While



there is currently no specific published research on assessing the carbon sequestration benefits of rabbit control, estimations are available. A 70% reduction in rabbit numbers could see a benefit of up to \$34 million in carbon sequestration based on the government carbon price of \$20 per tonne (Table 1). This could increase to \$45 million if an 85% reduction was achieved (Agtrans Research 2009). The impact this

increase in biomass would have on the wildlife ecology in these areas is not quantified.

Without continued investment in rabbit biocontrol, it is expected that the subsequent increase in rabbit numbers will result in an increase in the biodiversity impacts of rabbits, along with a reduction in carbon sequestration as the regeneration of woody perennials declines (Fitzgerald and Wilkinson 2009).

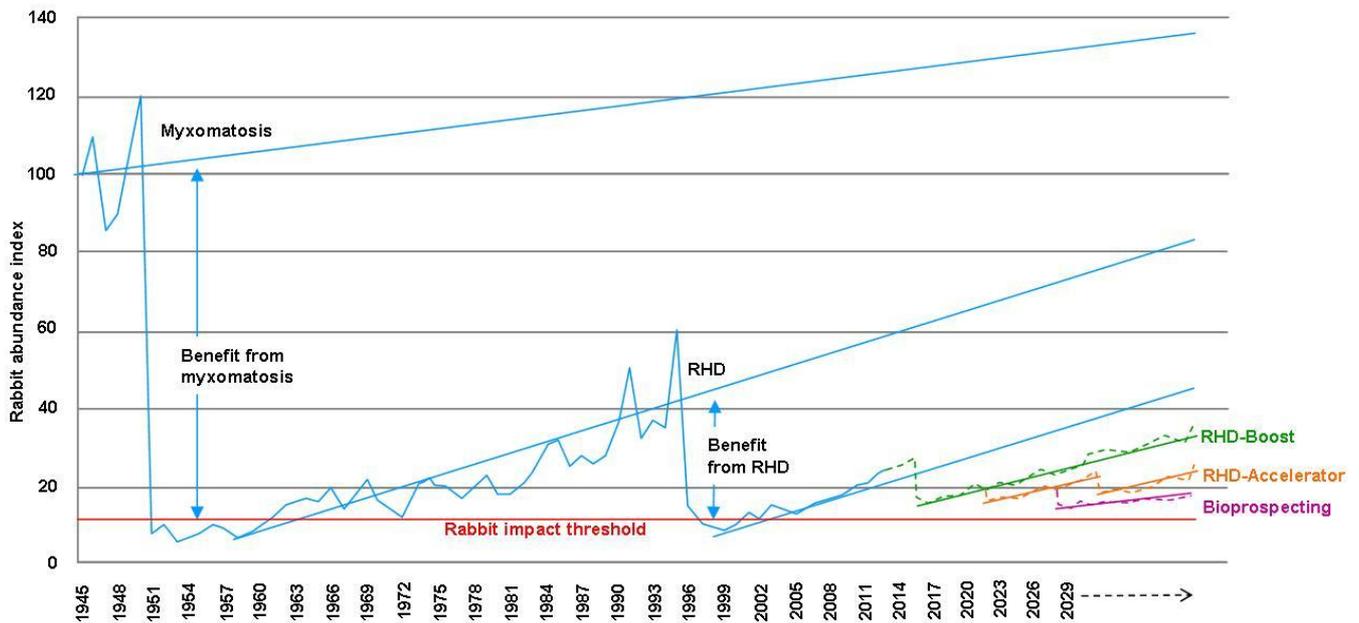
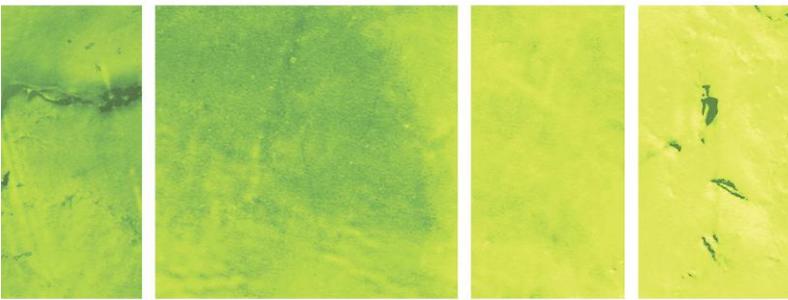


Figure 6: General trends in rabbit numbers since the release of myxomatosis in (1950) and projected benefits of future releases of biocontrol agents into the Australian rabbit population. The abundance baseline was arbitrarily set at an index level of 100 prior to myxomatosis. Pre-RHD figures are based on spotlight counts and established relationships between rainfall and rabbit abundance, and an average 90% reduction due to the initial impact of myxomatosis.

Table 1: Assumed impacts of a reduction in rabbit numbers on carbon sequestration (Agtrans Research 2009).

% Rabbit removal	Assumption of tonne/ha saved with rabbit reduction	Area of sequestration	Valued CO ₂ equivalent at \$20 per tonne
85	0.14	1.5 million km ²	\$42 million
70	0.115	1.5 million km ²	\$34.5 million



Current rabbit biocontrol initiatives

Rabbits are a key species of interest of the new Invasive Animals CRC (2012-17). The IA CRC strategic rabbit biocontrol technology pipeline is focussed on two objectives: 1. Increasing the effectiveness of RHDV, and 2. Identifying feasible new biocontrol agents that warrant further investment.

The three rabbit biocontrol technology projects specifically aimed at improving the biological control of rabbits in Australia are:

- RHD Boost and RHD Boost Release and Performance Measurement
- RHD Accelerator
- Bioprospecting for a new potential rabbit biocontrol agent.

The impact of the IA CRCs rabbit portfolio will increase over time and vary across climatic regions (Table 2). The objective, prospective benefits and technology opportunities for the three biocontrol technologies is discussed below and a diagrammatic representation of the benefits of each of the projects can be found in Appendix 2.

RHD-Boost

The RHD-Boost project was developed to address increasing evidence that rabbit numbers are building up again after the 15 year long respite provided by the initial release of RHDV. The follow on RHD-Boost Release and Performance Measurement project builds on the work undertaken in the RHD-Boost project and is designed to undertake a performance management evaluation of how differing strains of RHDV interact in the environment.

Strain selection

RHD Boost aims to identify new RHDV strains with high lethality to rabbits immune due to the endemic RCV-A1 and rabbits that are genetically resistant to infection with Czech 351 derived RHDV strains.

To select the most appropriate strain for release in Australia, a number of overseas strains of RHDV were evaluated. The overseas strains had to show evidence of high mortality in the field and the ability to outcompete existing field strains and the benign RCV-A1. More than 10 of these candidate strains, including antigenic varieties (RHDVa), were imported into Australia for evaluation under quarantine conditions.

Table 2: Estimates of changing impacts in future by climatic zones with the IA CRC investment (Agtrans Research 2011).

	High rainfall	Wheat Sheep Zone	Pastoral Zone
Reduction in Rabbit Impact	50% in 2014/15 compared to impacts assumed for 2013/14 in the counterfactual scenario	50% in 2014/15 compared to impacts assumed for 2013/14 in the counterfactual scenario	70% in 2014/15 compared to impacts assumed for 2013/14 in the counterfactual scenario
Impact level at which reduction stabilises	50% of 2013/14 impact level held for eight years and then impacts increase again at 5% per annum thereafter to a maximum of 150% of 2008/09 impact levels	50% of 2013/14 impact level held for eight years and then impacts increase again at 5% per annum thereafter to a maximum of 150% of 2008/09 impact levels	70% of 2013/14 impact level held for eight years and then impacts increase again at 10% per annum thereafter to a maximum of 150% of 2008/09 impact levels



These strains were genetically compared to the Czech 351 strain to ensure that the most successful and most genetically distinct strain/s would be selected for further testing. Five strains were selected for further testing, including a prototype strain, several antigenic variants and a highly virulent recent Australian field isolate.

The project is premised on the following facts:

- Australia has only one RHDV strain (Czech 351 or CZ351),
- In some areas Australian rabbits are beginning to develop genetic resistance to the original Czech strain
- Australia's one RHD strain has limited effectiveness in cooler, wetter environments, that coincide with prime agricultural regions and many threatened ecological communities and species, due to presence of RCV-A1
- In Europe, a greater variety of RHDV strains is circulating. European wild rabbit numbers have been suppressed for much longer than in Australia despite attempts to aid their recovery, and similar influences on RHD impact such as genetic resistance to infection and the presence of non-pathogenic viruses.

The European experience, in particular, shows that additional variants of RHDV and new sub-strains like RHDVa are likely to compete better against the pre-existing RCV-A1 recently isolated in Australia. RCV-A1 is almost certainly the cause of limited effectiveness of Czech 351 in cooler wetter parts of Australia. In contrast, in Europe new variants of RHDV are continuing to suppress wild rabbit populations in wetter, cooler regions, despite the presence of benign viruses similar to RCV-A1. In addition, the resistance to infection due to altered carbohydrate structures on the mucosal surfaces of some European rabbit populations can be overcome by different virus variants that bind slightly different carbohydrate receptor structures (Nystrom *et al.* 2011)

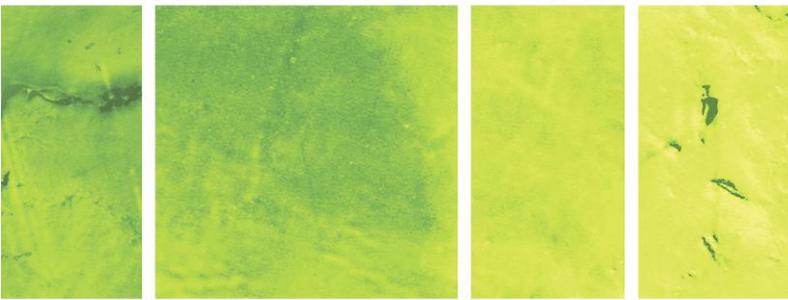
The selected strains are currently being evaluated for their competitive advantage, their ability to overcome both genetic resistance and acquired immunity and their effectiveness against animals previously infected with the benign virus RCV-A1. The results of these trials should be reported by December 2013 (after the

inclusion of two new promising strains that were identified late 2012) and it is expected that recommendations for the release of additional strains will be made based on the results of this study. As different properties of a putative new strain may be required to overcome each of the three problems listed above, it is feasible that different strains may be recommended to combat the different issues underlying RHDV-mediated biocontrol.

Overcoming immunity to existing RHDV strains

A rabbit that survives infection with RHDV will be immune to lethal RHD for the rest of its life. Re-infection can occur, but will only result in a boost in immunity. Virtually every rabbit population on the Australian continent has been exposed to RHDV at some stage since its release, and in most populations natural outbreaks occur regularly, albeit with varying frequency. Rabbit kittens generally do not die from RHDV until they are 3-4 weeks old; thereafter they become gradually more susceptible to infection and less likely to survive viral challenge until 12 weeks of age, and if first infected beyond that age most rabbits will die (Cooke 2002; Robinson *et al.* 2002). Young rabbits that become infected but do not die will develop antibodies to RHDV that will make them immune for the rest of their life, and these rabbits are likely to be recruited into the immune breeding population. Maternal antibodies from immune female rabbits are passed on to their offspring and may prevent infection. These younger rabbits in turn can receive their first RHDV infection at a later age, closer to when they become susceptible to lethal infection (Robinson *et al.* 2002). In some situations, maternal antibodies may not prevent infection but may slow the course of disease in the infected individuals and reduce mortality rates (Cooke 2002).

Depending on regional rainfall patterns, most rabbit kittens are born in late winter/spring. Consequently, RHD epizootics are most effective in the autumn/early winter period when susceptible sub-adult rabbits are challenged, before the breeding season, when young rabbits are present (Cooke 2003, Kerr and Strive 2012). However, spring is the usual time of RHD outbreaks in many populations across the country, as this is the time when young rabbits reach the susceptible age and enough individuals are present to carry an epidemic. At



the same time there are still enough young rabbits that will survive the outbreak with resulting immunity. In addition, areas with more homogenous rainfall patterns allow low level rabbit breeding throughout the year and thus constant availability of unsusceptible rabbits, further diminishing the impact of RHD outbreaks in these areas.

The RHD-Boost project is addressing this problem by investigating naturally occurring antigenic variants of RHDV, also referred to as RHDVa. There is evidence that RHDVa can partially overcome vaccination with the prototype virus (Schirmer *et al.* 1999), and there is also evidence that RHDVa strains are replacing the prototype strain in wild rabbit populations in Europe. Furthermore, a recent report from China describes a further variant ('RHDVb') that can partially overcome immunity to RHDVa (Wang *et al.* 2012), indicating that antigenic differences can be advantageous in the field.

Interfering endemic non-pathogenic caliciviruses - RCV-A1

When RHDV was first released in Australia it noticeably caused lower rabbit mortality in the temperate, high

rainfall areas than it did the arid, semi-arid areas of Australia (Mutze *et al.* 1998, Saunders *et al.* 1999, Henzell *et al.* 2002). This patchy efficacy of RHD has been attributed to the partial cross-protection of RCV-A1, a benign calicivirus which prevents infection with the pathogenic RHDV (Nagesha *et al.* 2000, Cooke *et al.* 2002, Robinson *et al.* 2002). This virus was recently identified and confirmed to provide partial and transient protection to lethal RHDV infection (Strive *et al.* 2009, Strive *et al.* 2010, Strive *et al.* 2013). This virus is most prevalent in the cool/temperate-wet regions of Australia and probably arrived in Australia with the first wild rabbits in 1859 (Jahnke *et al.* 2010). Recent work (Liu *et al.*, in preparation) has shown that the distribution of RCV-A1 is closely linked to those cool/temperate-wet areas where RHDV has traditionally had limited or patchy impact, and that encompass both Australia's high production areas and the areas where rabbits cause serious ecological damage (Figure 7).

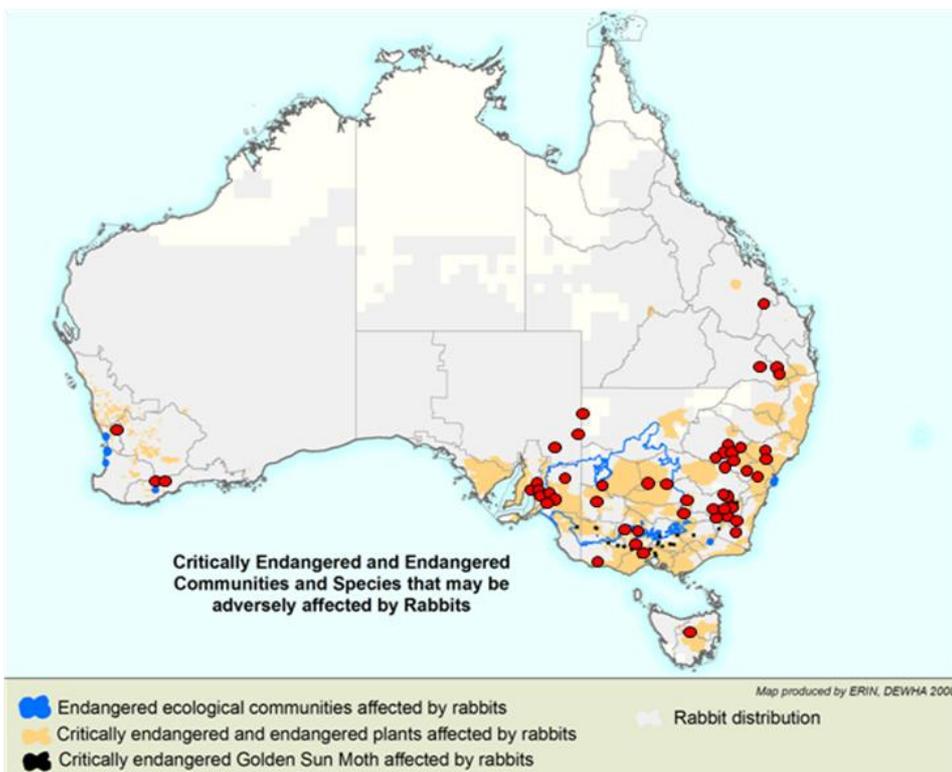


Figure 7: Distribution of the benign endemic calicivirus RCV-A1 in Australia. Red dots indicate current and historical sites that have tested positive for RCV-A1. (Commonwealth of Australia 2008, RCV-A1 data from Liu *et al.*, in preparation).



Overcoming genetic resistance in wild rabbits

A recently published study links the initiation of RHD resistance in Australia's wild rabbits to low dose infection with the originally released strain. These genetically resistant populations were mainly located in the more arid areas of Australia (Elsworth *et al.* 2012). The exact mechanisms for this resistance are unknown at this stage. However, one of the genetically resistant populations identified in the Hattah region of Victoria (Nystrom *et al.* 2011) has been shown to have a higher proportion of rabbits that lack the carbohydrate structures on the mucosal surfaces that are likely to facilitate the uptake of RHDV. Notably, despite this reported genetic resistance to infection, serological studies at this site reveal a very high prevalence of RHDV antibodies in the population (Tarnya Cox, unpublished).

RHD-Boost Release and Performance Measurement

The RHD-Boost Release and Performance Measurement project will address fundamental questions about the release of a new strain of RHDV into the Australian rabbit population. What impacts do these new strains have on rabbits? What do those impacts mean for the Australian environment? How will native wildlife recover? Can these new strains provide a respite for the recovery of threatened or endangered species? Will the new strain/s reduce rabbit numbers to a level to allow native vegetation regeneration? What impact will this have on carbon sequestration? Answers to these questions are of vital importance if we are to continue to use strains of RHDV as biocontrol agents into the future.

This research also has far reaching consequences. Populations of rabbits declined greatly following the spread of RHDV across their original home range on the Iberian Peninsula. The rabbit is listed as near threatened in its natural range by the World Conservation Union (IUCN) and vulnerable in Spain. The decline in populations of rabbits on the Iberian Peninsula have impacted on populations of their highly dependent predators the Iberian lynx (*Lynx pardinus*, critically endangered) (Ward 2004) and the Spanish Imperial eagle (*Aquila adalberti*, vulnerable) (Margalida *et al.* 2007). Research into the interaction and impact of additional strains of RHDV on rabbits, as well as the interaction of multiple RHDV variants and

MV may be of considerable benefit to rabbit conservation efforts in Europe. Australia is in the fortunate position of having only one variant of RHDV, unlike Europe, and as such, can evaluate the impact of additional strains on rabbit populations.

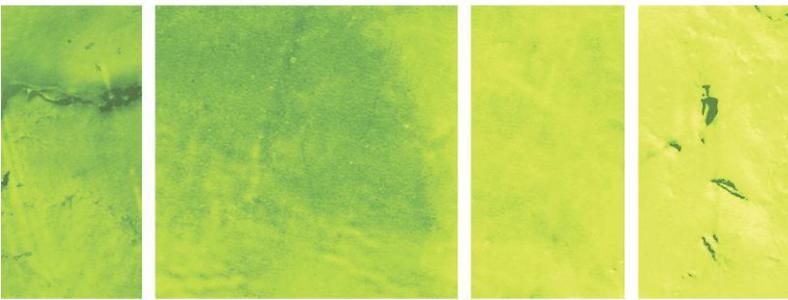
Measuring impact

The release of any new strains will not have the same impact as the initial release of RHDV had on completely naïve populations in the 1990s, and the effects will be more subtle and difficult to measure. As such, the RHD-Boost Release and Performance Measurement project will require a number of sites to be intensively monitored, both before and after the release of any new RHDV strain, to accurately assess its impact. Both treatment and control sites will need to be established across a range of climate and habitat types. Specific diagnostic tests will need to be implemented to determine which strain is present during an outbreak, and multiple samples will need to be collected from multiple sites before the true impact of any new strains can be known.

While the effects can be expected to be more subtle than the initial release of RHDV into a naïve population, the aim of the project is to slow down the recovery of rabbit populations by maintaining the significant benefits that RHDV has provided over the last 15 years. In addition, introducing a new strain of RHDV may also increase the genetic diversity of the virus and therefore provide opportunity for the virus to more quickly adapt to any acquired immunity or genetic resistance developed by the rabbit. This project will also provide a framework for investigation and performance management of releases of any new biocontrol agents for rabbits and/or other vertebrate pest species in Australia.

Integrating conventional control

Improving our understanding of virus interactions in the field will better inform current conventional control practices. Improved understanding of the impact of additional virus strains on rabbit populations under a variety of landscape and climatic conditions will lead to the improved application of conventional control techniques to maximise the impact of biocontrol agents. The National Rabbit Facilitator position (established through the IA CRC and due to start in



mid-2013) will draw on the information obtained from the RHD-Boost Release and Performance Measurement project to ensure best practice management is applied across the landscape. Conventional control needs to be applied in conjunction with the use of biocontrol agents for maximum impact. The National Rabbit Facilitator will encourage this combination of conventional control and biocontrol techniques, as well as advice on the appropriate variant of RHDV for release, based on information gathered during the RHD-Boost Roll-out.

Impact of RHD-Boost

The probability of impact of the RHD-Boost project given usage is 80%. The expected impacts of the usages of the outputs produced by the investment are:

- Observed spread of the released strains so that they are endemic throughout Australia within three years.
- The virus is effective in killing rabbits in the field and rabbit numbers decrease in most regions of Australia over the first three year period. This likely impact is supported by recent experience in France (Le Gall-Recule *et al.* 2011)
- Costs of rabbit control using traditional methods fall.
- The new strains are effective in those areas where the strain introduced in 1995 was ineffective and antibodies produced from RCV-A1 are no longer effective in protecting rabbits from RHDV.
- Individual commercial grazing animal productivity is observed to increase as a result of the release of the new strains.
- Greater shrub and tree natural establishment (including some threatened ecological communities) is observed due to the decline in rabbit numbers and there is an observed secondary biodiversity impact via reduced rabbit predators such as foxes and/or wild cats.

The increase in standing vegetation from improved regeneration acts as a carbon sink.

Benefits of RHD-Boost

The RHD Boost output will initially be released in strategic sites throughout the rabbits range using the IA CRC's freeze-dried RHDV bait technology. Like the

previously released strain of RHDV, it is assumed that it will then spread naturally throughout the rabbits range, augmented by further intentional releases at strategic sites. As such, usage of this output is assumed to be 100% provided it will occur over the rabbit's entire range. Usage, however, should not be confused with effectiveness as this will vary between climatic regions (Agrans Research 2009). The release of new RHDV strains has the potential to suppress rabbit populations over 5.33 million square kilometres (entire rabbit range) (West 2008).

Risk factors for not achieving some of the outputs and outcomes have been included in the estimates made of the expected benefits. Results show that, for a discount rate of 5%, the present value of the anticipated R&D investment of \$2.6 million (2008/09 terms) will provide a large return on investment.

Investment criteria are a net present value of over \$1.4 billion over a fifteen year period and a net present value of over \$1.8 billion if a 30 year planning period is assumed. For the fifteen year period, the industry benefits dominate at 60% of the total benefits, with the carbon sequestration benefits contributing 40% based on the government carbon price of \$20 per tonne. The benefit cost ratios are 563 to 1 and 708 to 1 for each of the 15 and 30 year periods. The internal rate of return is 217% for the 15 year period and similar for the 30 year period (Agrans Research 2009).

The biodiversity benefits include the regeneration of five endangered ecological communities and the regeneration of the 75 listed critically endangered and endangered plant species (excluding off-shore islands) listed in the rabbit Threat Abatement Plan.

RHD Resistance Model

Collection and genetic sequencing of RHDV recovered from rabbits around Australia has shown that since the initial introduction and spread of the Czech351 strain into Australia, the virus has undergone a process of gradual genetic changes. Three distinct genetic groups, each containing a range of genetically distinct variants, have evolved in separate but overlapping regions of the country (Kovaliski *et al.* 2011). Three RHDV variants, collected from outbreaks in different years at Turretfield in South Australia, have been shown to cause different mortality rates in wild-type rabbits,



with associated different times to death (Elsworth *et al.* in prep.). Of these, the most recent viruses were the most lethal and all were more lethal than the original Czech strain. Taken together with the evidence of emerging genetic resistance to infection in Australian rabbit populations (Elsworth *et al.* 2012), this indicates that both genetic resistance in rabbits and RHDV virulence are co-evolving in a complex, ongoing manner. We need to understand how these processes are interacting to aid selection of appropriate RHD Boost variants for release. The RHD resistance project will use results from laboratory challenge studies and field epidemiology to develop a statistical model of RHD resistance that can be used to project the likely benefit of RHD Boost candidates with different epidemiological characteristics.

RHD Accelerator

Objective and rationale

The RHDV accelerator strategy takes the RHDV Boost project to the next level. While RHD-Boost can be expected to deliver one or several additional virus

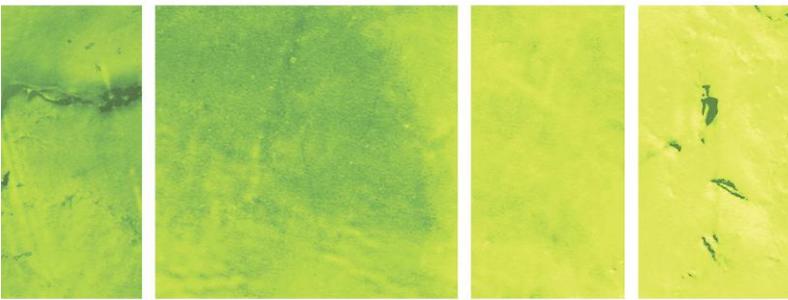
strains that will hopefully extend RHDV-derived benefits for several more years, co-evolution of host and virus is likely to again lead to genetic resistance development. Similarly, widespread immunity will develop once the new strains have become endemic in rabbit populations. In contrast, the RHD Accelerator project aims at developing a platform technology that will allow the ongoing selection of tailored RHDV strains able to better overcome immunity to existing field strains of RHDV and RCV-A1, by exploiting the principles of natural selection.

Replicating natural selection

RNA viruses such as RHDV have naturally very high mutation rates. During replication, virus genes are not replicated exactly, producing a mixture of progeny viruses that are all slightly different (Domingo *et al.* 2001). Some of these viruses will have altered surface structures that may not be neutralised by antibodies specific to the original strain. These variants are slowly selected for in natural infections, as RHDV often kills the animals too quickly for these selection processes to occur. The Accelerator project aims at

Table 3: Summary of the economic, environmental and social benefits from the RHD Accelerator Investment (Agtrans Research 2011).

Economic	Environmental	Social
<ul style="list-style-type: none"> Higher level of grazing productivity translated into additional farm profits in each of the three rainfall zones Reduced costs of rabbit control costs by governments and landholders Reduced damage to crops 	<ul style="list-style-type: none"> Increased regeneration of native vegetation and habitats, and in the long term improved biodiversity of fauna and flora Increase in standing biomass via regeneration leading to absorption of carbon dioxide. Greater ability to capitalise on summer rains as native grasses re-establish Improved biodiversity from reduced numbers of feral cats and foxes A possible cost in the potential increase in greenhouse gas emissions if ruminant livestock numbers increase Reduced soil erosion and land degradation 	<ul style="list-style-type: none"> Continuance of a more humane method for limiting rabbit numbers and reduced externalities from poisoning control methods Stronger rural communities from 'drought proofing' and enhancing the continuing viability of some pastoral properties. Improved landscape amenities



developing experimental systems that will allow accelerated evolution and targeted selection for such virus variants. This will exploit the natural high mutation rate that normally enables the virus to rapidly adapt to changing circumstances. If successful, the RHD-Accelerator platform technology can be used to commence selection of the subsequent strains as soon as a new strain is released, such that once any released strain again loses its initial efficiency the next one is ready to be released, thereby maintaining the impacts of RHDV biocontrol sustainably.

Impact of RHD Accelerator

The probability of impact of the RHD Accelerator project given usage is 90%. The expected impacts of the usages of the outputs produced by the investment are:

- Continuity of reduced rabbit populations Australia wide.
- Maintenance of productivity and profitability improvements due to less competition for pasture feed in grazing industries.
- Maintenance of increased ground cover with natural resource management implications.
- Maintenance of reduced cost of rabbit control (private and public).
- Continuing positive impacts on biodiversity and threatened and endangered plants and indirect positive impacts on native mammals by strengthening vegetation.
- Continuation of the decreased predation pressure through indirect removal of foxes.
- Maintenance of more humane control methods of rabbits when compared to toxins/fumigants (rabbit welfare).

Benefits of RHD Accelerator

This is a strategic long-term investment and carries considerable risk. However, even allowing for uncertain outputs and usage the investment provides positive returns. The analysis has indicated that if the investment commenced in 2012/13, and allowing for the lag period for the project to produce proof of concept as well as implementation, it is assumed that there would be no positive impact until the 2022/23

year. However, thereafter there would be considerable savings in the impact and control of rabbits. Given the assumptions made, this result is robust whether or not RHD Boost is successful (Agtrans Research 2011).

The expected net present value of the investment is estimated at \$79 million for the 15 year benefit period and over \$300 million for the 30 year period. The benefit cost ratio for the 15 year benefit period is 48 to 1 (Agtrans Research 2011). The principal potential benefits derived from the impacts described above are the continuation of the productivity gains for livestock from more effective rabbit control due to RHD Boost as well as the continuation of the reduced cost of rabbit control. A summary of the prospective benefits (and costs) from investment in the Accelerator Project is included in Table 3.

Bioprospecting

Objective and rationale

Experience from the use of MV, and more recently RHDV, has shown that their effectiveness in controlling rabbits throughout Australia will eventually wane. This process, due to host-pathogen co-evolution, can be addressed through the RHD Accelerator project. However, we cannot rely solely on the positive outcomes from the RHD Accelerator project and an international search for potential new biocontrol agents should be undertaken to ensure the best possible toolset is available for efficient, long-term biocontrol of rabbits.

Past experience shows that when a candidate biocontrol agent for rabbits has been identified, it takes a decade or more to assess them thoroughly and bring them to the point of release in Australia. This means that even if a new agent was identified now, it would be unlikely to be released before 2020. It is therefore essential that an initial assessment of currently known biocontrol candidates is carried out, complemented by the establishment of an international alert mechanism to quickly identify new diseases which may emerge in rabbit populations (domestic and free-living) that may have potential as future biological control agents in Australia.

The aims of the Bioprospecting project are:



- Assess currently known rabbit pathogens and identify any feasible agents that warrant further examination as potential new biocontrol agents.
- Establish an international search network to detect potentially new biological control agents.

Impact of Bioprospecting

The probability of impact of the Bioprospecting project given usage is 90%. The expected impacts of the usages of the outputs produced by the investment are:

- Maintenance of productivity and profitability improvements due to less competition for pasture feed in grazing industries.
- Maintenance of reduced cost of rabbit control (private and public).
- Maintenance of increased ground cover with natural resource management implications.
- Continuing positive impacts on biodiversity and threatened and endangered plants and indirect positive impacts on native mammals by strengthening vegetation.
- Continuation of the decreased predation pressure through indirect removal of foxes.
- Maintenance of more humane control methods of rabbits when compared to toxins/fumigants (rabbit welfare).

Benefits of Bioprospecting

The investment of the Assessment and Prospecting project has been analysed with the counterfactual scenario of both RHD Boost and RHD Accelerator being successful. Hence a potential new biological control agent is assumed to reduce by 25 per cent the residual rabbit productivity impacts and control costs after 2031/32, with a lesser proportionate increase in carbon sequestration in the pastoral zone (Agtrans Research 2011).

If a 30 year time frame is assumed, the investment criteria are positive with a net present value estimated at \$28 million, a benefit cost ratio of 115 to 1 and an internal rate of return of over 21% (Agtrans Research 2011).

The principal potential benefits derived from the impacts described above are the potential to capture productivity gains for livestock and reduced control

costs from more effective rabbit control. The key benefit is the potential for reducing the rabbit population to even lower levels than achieved given success of RHD Boost and/or Accelerator.

If RHD Boost and RHD Accelerator fail or are less effective than envisaged, the benefits from a successful Bioprospecting investment may be even greater than when the previous investments are successful.

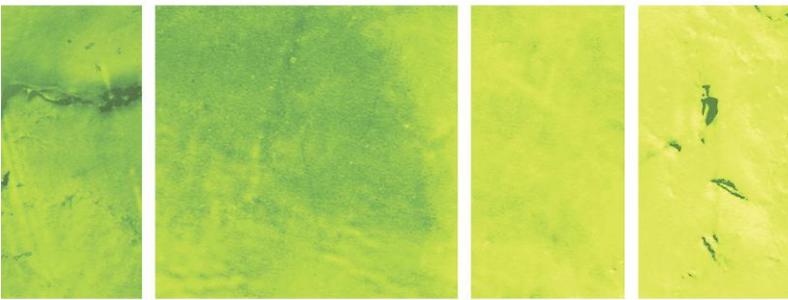
A summary of the prospective benefits (and costs) from investment in the Bioprospecting project is included in Table 4.

Technology opportunity

To mitigate the risk of relying on only two rabbit biocontrol agents, it is important to constantly search for potential new biological control agents as part of a strategic rabbit biocontrol research approach. As new biocontrol agents might already be circulating, or could become apparent at any time (as was the case for RHDV) it is essential to develop and maintain appropriate surveillance protocols.

Henzell *et al.* (2008) have suggested some potential biocontrol agents for rabbits that might be investigated for use in Australia and a strategy for prospecting for additional agents. In particular, new pathogens are likely to be detected by professional veterinary support in the international domestic rabbit industry, but may not come to notice of Australian authorities without a formal process to monitor disease notification in that industry. To put these ideas into effect, it is important to establish international networks that could allow information on potential agents to be assessed and to alert researchers and industry to new agents that may have application for wild rabbit control.

Alert mechanisms will include (amongst other things) the further development of existing international collaborative research relationships, cooperation and communication with existing wildlife disease networks (such as the Australian Wildlife Health Network and their associated organisations around the world) and alert mechanisms set up through domestic and international veterinary organisations.



Environmental and economic benefits of new biocontrol technologies

The objective of the RHD-Boost project and the subsequent rollout is to identify, seek approval, release and selectively measure the performance of new, naturally occurring overseas strains of RHDV. This project has a net present value of \$1.4 billion over 15 years, made up of \$840 million of agricultural benefits and \$560 million in carbon sequestration benefits (based on 2011 government carbon price of \$20/tonne). This is a benefit cost ratio of 563:1 and an internal rate of return of 217%. The biodiversity benefits include increased regeneration of native vegetation, and in the longer term, an increase in abundance of many threatened species. There will be a reduction in soil erosion and land degradation due to an increase in standing biomass via regeneration.

The RHD Accelerator project aims to develop a platform technology for ongoing laboratory-based selection of superior, naturally selected, RHDV strains. This project has a net present value of \$79 million over 30 years with a benefit cost ratios of 48:1 over 15 years and an internal rate of return of 38%. Biodiversity

benefits include increased regeneration of native vegetation, and in the longer term, an increase in abundance of many threatened species. There will be a reduction in soil erosion and land degradation due to an increase in standing biomass via regeneration. This project assumes that the new RHDV strains are able to sustain the benefits delivered by the RHD-Boost rollout.

The comprehensive RHD resistance model output is to develop a framework for assessing the likely success of RHDV variants with difference characteristics. This project will improve the effectiveness of the RHD-Boost and RHD Accelerator technologies.

Finally, the Bioprospecting project, aimed at assessing and prospecting for potential new biocontrol agents, will assess the feasibility of potential new rabbit biocontrol agents and establish an international alert network for new pathogens. This project has a net present value of \$28 million over 30 years with a benefit cost ration of 115:1 and in internal rate of return of 21.5%. This assumes that the additional research enables the release of a new biocontrol agent in 2030.

Table 4: Summary of the economic, environmental and social benefits from a potential new rabbit biocontrol agent (Agtrans Research 2011).

Economic	Environmental	Social
<ul style="list-style-type: none"> Higher level of grazing productivity translated into additional farm profits in each of the three rainfall zones Reduced costs of rabbit control costs by governments and landholders Reduced damage to crops 	<ul style="list-style-type: none"> Increased regeneration of native vegetation and habitats, and in the long term improved biodiversity of fauna and flora Increase in standing biomass via regeneration leading to absorption of carbon dioxide. Greater ability to capitalise on summer rains as native grasses re-establish Improved biodiversity from reduced numbers of feral cats and foxes A possible cost in the potential increase in greenhouse gas emissions if ruminant livestock numbers increase Reduced soil erosion and land degradation 	<ul style="list-style-type: none"> Possibility of a more humane method for limiting rabbit numbers and reduced externalities from poisoning control methods Stronger rural communities from 'drought proofing' and enhancing the continuing viability of some pastoral properties. Improved landscape amenities



Reducing risks associated with future RHDV strain releases

RHD-Boost Release and Performance Measurement

The RHD-Boost Release and Performance Measurement project commenced on 1 July 2012 and is in an early planning stage. However, it requires additional investment to ensure that there is an adequate number of monitoring and surveillance sites to robustly determine the national scale impact of any release of new RHDV strains. Without additional investment the project will not fully deliver on its aims, yet it is critically important for the successful delivery of the other biocontrol projects. Extensive monitoring and surveillance networks need to be established across Australia. These networks will evaluate the impact of newly released virus strains on rabbit population dynamics following virus release, as well as the resulting environmental and agricultural impacts. These are essential components for the development of a performance management framework, enabling a measurement of the success of additional rabbit control tools, and thus their return on current and previous investments in this area. It also provides guidance for the most effective means of delivering biocontrol agents in to Australian rabbit populations - opportunities that were not taken fully with the previous releases of MV and RHD.

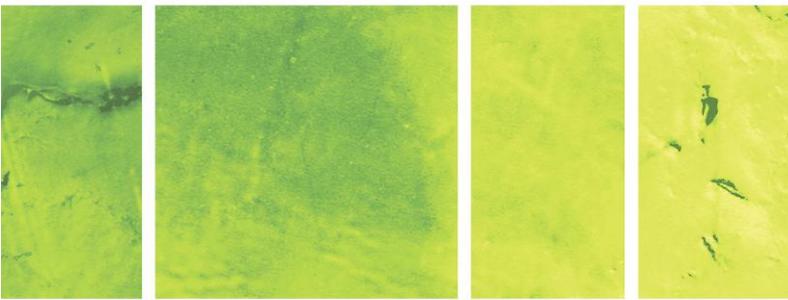
Maximising RHD Boost impact by optimising release of new RHDV strains when RCV-A1 prevalence is low

Recent studies show that the benign calicivirus RCV-A1 can cause protection rates of up to 50%. Fortunately, this protection is transient, and the effects wane after approximately two months (Strive *et al.* 2013), indicating that there may be a potential window of opportunity to apply RHDV biocontrol effectively, even in areas where RCV-A1 is present. While information about the distribution and prevalence of RCV-A1 in Australia is accumulating (Liu *et al.*, in preparation), little is known about the seasonal dynamics of this

benign virus in the different climatic zones of Australia. Preliminary data suggests that prevalence and seasonal occurrence of RCV-A1 may depend on a variety of factors, most importantly climate and the resulting changes in rabbit breeding patterns and population density. Frequent outbreaks of RCV-A1 throughout the year may have considerable negative impacts on rabbit mortality, despite the short-lived protection it provides. Studying the infection dynamics of RCV-A1 in different climatic zones is essential for determining the best timing of virus release to gain maximum benefit from new biocontrol agents in areas where RCV-A1 is prevalent.

Building and maintaining diagnostic capability to track biocontrol performance

Monitoring and surveillance of viral diseases relies on the availability of sensitive and specific molecular and serological tools. Current research efforts will result in an increase in the number of co-circulating rabbit pathogens in the environment. The very foundation for tracking the performance of any new biocontrol agent is the availability of tailored diagnostic tools that can differentiate between the co-occurring pathogens. There is currently a skills gap in this area and sustained investment is needed to build and maintain key capabilities to provide the ongoing development of these necessary tools.



Conclusions and recommendations

Rabbit biocontrol has been the most-cost effective approach to manage an established pest animal in Australia to date. The average benefits of RHDV alone are estimated to be in excess of \$350 million annually since its release in 1996, and the cumulative benefits of MV and RHDV are estimated at AU\$70 billion over the last 60 years. The combination of MV and RHDV still kills about 85% of rabbits born every year, with an average benefit of some \$1.19 billion a year. This high return on investment highlights the strong national interest in ensuring that scientific capability and capacity is maintained through stable, sustained investment in rabbit biocontrol research.

To maintain these major environmental and economic benefits, continued investment in strategic rabbit biocontrol research is critical. The current Invasive Animals CRC rabbit research program (2012-17) comprises three elements: 1.) improved RHDV impact through introduction of new more effective overseas RHDV strains (RHD Boost) and development of a platform technology to continuously develop new RHDV strains (RHD Accelerator), combined with strengthened knowledge of the mechanisms of rabbit resistance to RHDV; 2.) improved regional integrated control through decision support tools and improved facilitation; 3.) assessed feasibility of potential new biocontrol agents. It has been designed to deliver strengthened RHDV biocontrol agents from about 2015 to 2030, with future research initiated from the assessment delivering new biocontrol agents from about 2030 (Table 9).

If we are to continue to use RHDV as an effective biocontrol agent then we need to fully understand the impacts of releasing new strains into already exposed populations. This is a unique opportunity for Australia to understand the interactions of different pathogens at a landscape scale with controlled virus releases. The RHD-Boost Release and Performance Measurement project will enable us to further understand how more recently evolved RHDV strains interact with classic strains and co-occurring benign caliciviruses, and to gain further insight into establishing new viruses in the field. This last point is particularly important for the RHD-Accelerator and Bioprospecting projects.

In conjunction with these efforts, it is essential to build the capacity to conduct monitoring and surveillance of any additional pathogens. The coming years will see the release of one or several additional RHD-Boost strains, potentially followed later by RHD-Accelerator strains and, if discovered, additional rabbit pathogens. Any new release must be accompanied by extensive pre- and post-release monitoring, to determine their success and to better estimate the return on investment. This includes building capability to develop and conduct the differential diagnostic tests required, as well as providing adequate resources for the development and implementation of rabbit monitoring and surveillance plans. The RHD-Boost Release and Performance Measurement project is the critical first step in establishing an efficient performance management framework that can be rolled out across any future biocontrol agent releases.

Further investment into the rabbit biocontrol projects will allow for: better understanding of the disease ecology and interactions of the various rabbit pathogens in Australia; the ability to keep a watching brief so that Australia can quickly react should a new pathogen for rabbits appear; and the capability to take the RHD- Accelerator Platform technology to the production stage to ensure continuing development of effective, virulent and pathogenic strains of RHDV that are effective in the Australian environment.

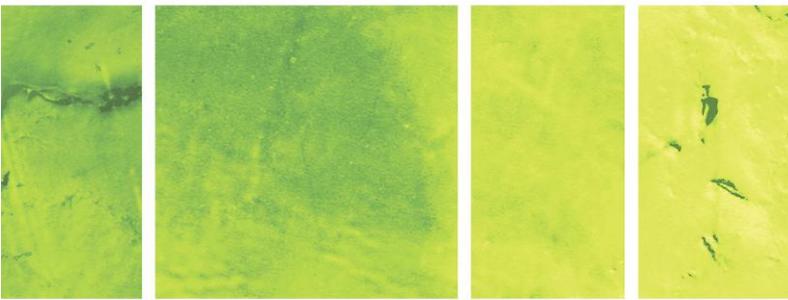
In the short term it is critical that additional resources are attracted to ensure robust measurement of the performance of any new RHDV strains released across a range of landscapes, knowledge about the seasonal patterns of RCV-A1 which impedes RHDV is gained, and diagnostic capabilities to track the performance of RHD-Boost are improved.

These conclusions are reinforced by the *National Biosecurity Research and Development Capability Audit* commissioned by the National Biosecurity Committee which suggested that Australia should invest more heavily in the long term funding of biological control programs, including monitoring of field effectiveness (Intergovernmental Agreement on Biosecurity 2012).



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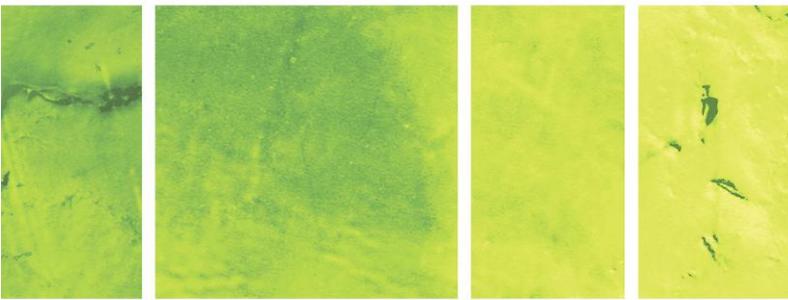
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Appendix 1: Background information on rabbit biocontrol agents

Myxomatosis

After the rabbit plague of the early 1900s, efforts were made to find a way to more effectively control rabbits on a large scale. In 1950 the myxoma virus (MV), a poxvirus (family: Poxviridae, genus: *Leporipoxvirus*) was released into the rabbit population in the higher rainfall areas of Australia (Myers 1954). In its natural host, the South American jungle rabbit (*Sylvilagus brasiliensis*), MV causes benign, localised fibromas. In the European rabbit however, MV causes myxomatosis, a pustule forming disease that affects the lymphoid tissue leading to profound immunosuppression and generalised systemic disease (Best and Kerr 2000a, b, Jeklova *et al.* 2008). Death can occur within 8-12 days in acute cases or 3-5 days after clinical signs develop. The impact of MV on the Australian rabbit population in the first year was dramatic: up to 99% reductions in some areas. However these declines were short lived, and host-virus co-evolution led to the emergence of less virulent field strains of MV as well as genetic resistance to myxomatosis in wild rabbits. Subsequent attempts to introduce new, more virulent strains of MV failed, as the new strains never became established in the field (Kerr 2012). Despite the loss of its initial virulence, MV is still an effective biocontrol agent, particularly in the wetter areas of Australia.

Rabbit fleas

The original natural spread of MV through the Australian rabbit population was facilitated by mosquitoes, particularly *Culex annulirostris*. However in areas where mosquito activity was low (such as arid areas, or areas with naturally low mosquito numbers), the impact of MV was also low (Williams *et al.* 1995). To boost the effect of MV, two species of fleas, *Spilopsyllus cuniculi* and *Xenopsylla cunicularis* were imported and released across the country. *S. cuniculi* is the main vector of MV in Britain and parts of Europe. Its introduction to Australia greatly increased the impact of myxomatosis in semi-arid and coastal areas where mosquitoes were scarce (Cooke 1983). However,

S. cuniculi did not survive in the more arid areas of Australia where the annual rainfall was < 200 mm (Cooke 1984). Native stickfast fleas (*Echidnophaga gillinaea*) are abundant in the arid zone and are capable of transmitting the disease, however they are poor vectors as they do not readily move from rabbit to rabbit but 'stick fast' to one individual. To facilitate the spread of MV in arid areas, the Spanish rabbit flea *X. cunicularis*, which is adapted to hot, arid conditions, was introduced (Cooke 1990). It is likely that the release of *X. cunicularis* into the Australian rabbit population boosted MV effectiveness in arid areas however research on the impact of this introduction was limited due to the escape of RHDV in 1995 and the dramatic reductions in arid zone rabbit populations before fleas became widely established.

Rabbit haemorrhagic disease

Even though MV was still an effective biocontrol agent and the introduction of the two rabbit fleas were aiding its spread, after almost ten years of good winter rainfall over most of Australia following the 1982 drought, rabbit numbers were once again on the increase. This prompted investigation into a recently emerged virus, RHDV. The highly virulent RHDV was first identified in China in 1984 where it killed 140 million domestic rabbits in less than 12 months (Liu *et al.* 1984, Xu 1991). The virus was later confirmed in rabbitries in Europe and soon spread to wild populations where it caused a major decline in wild rabbit numbers (Cooke and Fenner 2002). Investigation of the virus revealed it to be a calicivirus (family: Caliciviridae, genus: *Lagovirus*).

RHDV has been shown to be species specific and only infects European rabbits. It generally kills fewer young rabbits than adult rabbits. Young rabbits are innately resistant to lethal disease but can become infected, resulting in a comparatively mild infection of the liver and subsequent life-long immunity to RHDV. The reasons for this innate resistance to lethal disease are not completely understood, but it gradually wanes until



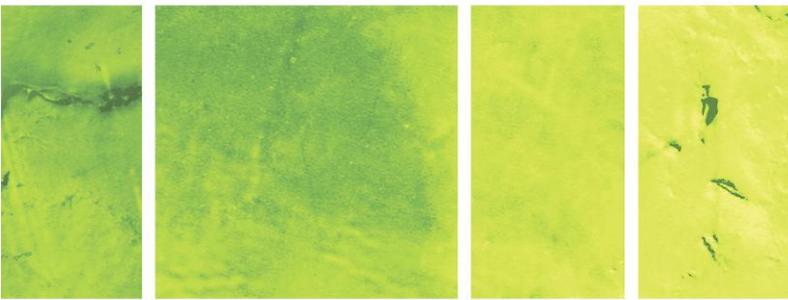
the rabbit becomes fully susceptible at approximately ten weeks of age (Robinson *et al.* 2002). Fully susceptible adult rabbits usually die within 72 hours following infection; however prolonged courses of the disease have also been reported (Kerr and Strive 2012). Rabbits with terminal RHD often develop fever, show lethargic behaviour and can die suddenly. Outwardly, animals that have died from RHDV appear healthy. The cause of death is usually liver failure due to a severe hepatitis and the formation of blood clots throughout the body.

RHDV was brought into Australia to assess its usefulness as a future biocontrol agent in 1993. Following host specificity testing in quarantine facilities at the Australian Animal Health Laboratories, RHDV escaped from an island research facility onto mainland Australia in October 1995. As with MV, RHDV had an immediate and devastating impact on the Australian rabbit population, particularly in the arid and semi-arid areas (Henzell *et al.* 2002), reducing the populations in these areas by as much as 98%. Notably unlike MV, RHDV did not attenuate rapidly but appeared to maintain its relative virulence. However, recent studies show that wild Australian rabbits are now beginning to develop some resistance to RHDV infection (Nystrom *et al.*

2011, Elsworth *et al.* 2012), a likely cause of the recently observed increase in rabbit numbers.

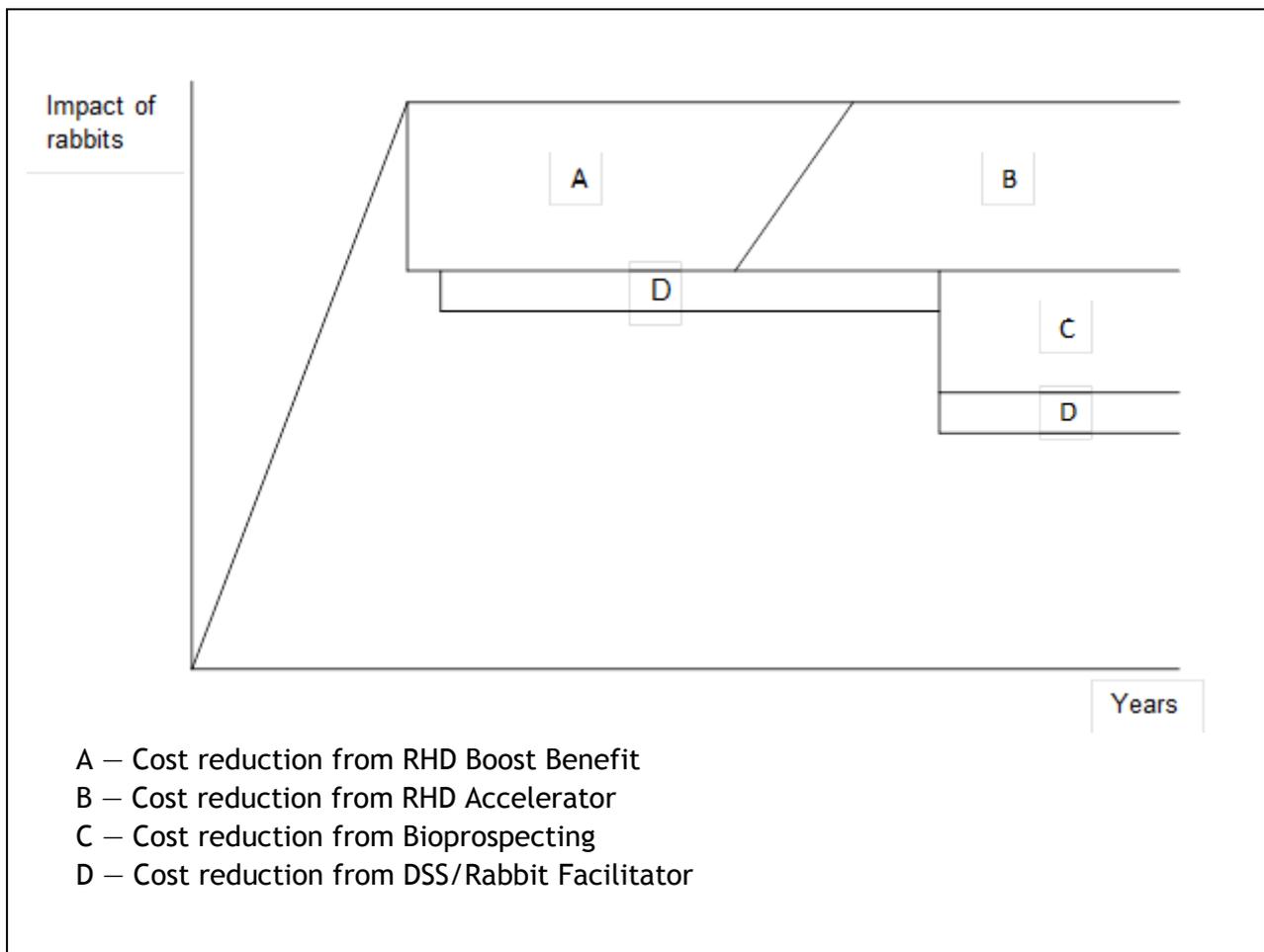
Virally-vectored immunocontraception

Between 1992 and 2005 research efforts of the Cooperative Research Centre for Biological Control of Vertebrate Pest Populations (predecessor of the Invasive Animals CRC) focussed on the development of non-lethal biocontrol options specifically aimed at reducing the fertility and fecundity of rabbits. Recombinant MVs were constructed that induced an auto-immune response to components of the reproductive tract, resulting in infertility. While the work succeeded in producing viruses that reduced the fertility of female rabbits by up to 100%, the approach was abandoned as high levels of infertility were not maintained in the long term (van Leeuwen and Kerr 2007). In addition, there was concern that a recombinant strain would disseminate insufficiently in the field, as it was unlikely to outcompete existing field strains of MV. There were also concerns about public acceptance regarding the release of a genetically modified virus into the environment (Henderson and Murphy 2006).



Appendix 2

Diagrammatic representation of benefits from RHD Boost, RHD Accelerator, Bioprospecting and DSS/Rabbit Facilitator (Agrans Research 2011).







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