DECISION AND IMPLEMENTATION FRAMEWORK FOR

INVESTMENT IN GENETIC BIOCONTROL OF VERTEBRATE PEST SPECIES IN AUSTRALIA

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COLLABORATION INNOVATION IMPACT

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1 SUMMARY

Genetic biocontrol is a species-specific tool using genetic technologies to modify the development of offspring leading to sterility or biasing sex ratio towards one sex, with the aim of population decline of the targeted pest species. There are many different approaches, some of which build on naturally occurring self-propagating genetic elements or use a range of synthetic CRISPR-based genetic technologies (e.g. RNA-guided gene drives). Development of genetic biocontrol for vertebrate pests requires a solid basis for investment decisions, which not only includes a 'proof of concept' in a vertebrate model species, but parallel ecological, social and economic investigations into the implementation environment to prepare a foundation for further investment in genetic biocontrol.

In Australia, invasive vertebrate pests are the greatest threat causing native biodiversity loss. In addition, their substantial direct and indirect impacts on agriculture production continue, largely unabated in the absence of any effective, landscape-scale control methods for the majority of species. This report reviews key vertebrate pests in Australia (including rodents, rabbits, carp, cane toads, cats, foxes, pigs, birds, and others), and their estimated economic impacts on agriculture and the environment. It considers the limitations of current control strategies, and the potential value provided by recent technologies. The management of vertebrate pests in Australia is governed by several legislative and policy instruments and is overseen by various committees. The development of vertebrate control methods needs to be cognisant of these legislative and governance processes and market forces driving implementation, including potential impacts on international trade. In particular, the development of genetic biocontrol technologies needs to consider the implementation environment for proposed technologies, particularly factors associated with social acceptance and risk.

Targeted engagement with key stakeholders highlighted important factors that influenced their level of support for genetic biocontrol technologies Demonstrating the safety and efficacy of genetic biocontrol technologies (e.g. ability to contain a release, species-specificity), will require extrapolation and modelling of data from laboratory studies of model vertebrate species. Learning from and incorporating international research findings, will further help to build both stakeholder and public confidence in the safety and efficacy of the technologies within Australia.

Public engagement and the communication of genetic biocontrol technology science should commence immediately and continue throughout the duration of all phases of genetic biocontrol research, development and implementation. Such programs should recognise that public 'acceptance' itself may not be the ultimate end goal and that pursuing outcomes that more broadly reflect public tolerability towards innovative solutions, or seeking to genuinely engage affected groups in dialogue, are more likely to build trusted relationships with various segments of society.

Successful development of genetic biocontrol technology will inevitably lead to the animals being classified as genetically modified organisms (or living modified organisms). As such, appropriate regulation, licencing and risk assessment will be brought to bear and must be addressed before any release of modified animals into the wild. Importantly, post-deployment monitoring of the modified animals and any associated genetic biocontrol technology contaminants, will be necessary to assure Australia's trade security.

Whilst the case for vastly improving vertebrate pest management in Australia is strong, new advances including genetic biocontrol technology, must have clear advantages over existing technologies. Currently, the level of interest and support for genetic biocontrol research and development favours the pursuit of ongoing collaborations across a variety of disciplines (e.g. genetics, ecology, social science, communication, policy and regulation). Co-ordination of this multi-disciplinary work would benefit from the formation of a centralised system. Such a system, a 'Community of Practice', could provide an independent source of governance and knowledge.

Australia has an enviable environment for the development of genetic biocontrol technologies that provides a clear advantage for significant progress in coordinated and integrated advancement of this technology. We have excellent scientific and technical capability, an established risk assessment community, a society able to be engaged, and strong demand for applications given the scale of vertebrate pest impacts. The establishment of a decision and implementation framework with agreed approaches to further develop and strong investment in a science roadmap, will realise these current advantages and unlock the significant potential for major advances in genetic biocontrol technologies for vertebrate pest management. This will ultimately deliver substantial economic, environmental and social benefits to Australia.

2 PURPOSE

This report outlines an approach for a decision framework for investment into research for genetic biocontrol of invasive vertebrate pest species in Australia. The approach builds on two workshops and consultations with a diverse range of stakeholders via a project funded through the Centre for Invasive Species Solutions. For most established vertebrate pests, broadscale control options are currently lacking, and the use of some current techniques are increasingly challenged on animal welfare grounds. The extent of impacts from vertebrate pests on agriculture and the environment means new or improved control methods are required. Any new technology, including genetic biocontrol, needs to have clear advantages over existing technologies and have minimal negative environmental, societal and/or economic consequences.

3 SCOPE

The intent of the document is to provide a context for the proposed development of genetic biocontrol technologies for vertebrate pest management in Australia; present an overview of the discussions with multiple stakeholders; identify themes of concern; and identify a pathway for the development of a decision-making framework for investment.

4 DRIVERS FOR NEW PEST ANIMAL CONTROL TECHNOLOGIES

4.1 Vertebrate Pests in Australia

The economic cost of the impacts and management of invasive species in Australia has amounted to at least AU$389.6 billion since 1960 and now costs around $24.5b per annum or, an average of 1.26% of the GDP (Bradshaw et al. 2021). The costliest taxonomic classes of invasive species across all of Australia are vertebrate pests with cats, rodents (mice Mus musculus and rats Rattus spp.), pigs, rabbits and foxes accounting for 95% of costs for mammals ($26 billion, 1960–2017, Bradshaw et al. 2021). Invasive species cost Australia's primary producers in excess of $750 million per annum and are the primary driving force behind the decimation of Australia's unique fauna and flora (Kearney et al. 2018).

Established vertebrate pests are a significant social, economic and environmental burden for Australia (see https://pestsmart.org.au/ for information on key vertebrate pest animals in Australia). They can affect productivity, access to export markets, public health, and the conservation of biodiversity in both natural and built environments. These effects can lead to increased production costs, loss of or restrictions to export trade, reduced tourism, loss of biodiversity, greater public health costs and reduced public amenity.

Extensive research is conducted to reduce the impacts of these species. In many instances, refinement of existing practices or the development of new control strategies are required to add to the management toolbox. The knowledge that comes from research and development (R&D) is critical for the implementation of evidence-based management. In many cases, substantial advances in invasive species management will require the development of new techniques and the further acquisition of knowledge. The resources directed to R&D need to be proportional to the size and scope of the program that it underpins; at present there are clearly unmet needs.

Genetic biocontrol is just one of these promising recent transformational technologies that could help manage invasive species. However, it may not be appropriate for all species, and where suitable, will still take many years to develop.

4.2 Impacts — Economic impacts on Agriculture

Combining study estimates on the economic impact of the seven most prominent established pest animals have indicated that the combined production losses and ongoing control costs by landholders and local governments exceed $609 million annually (Tables 1 and 2; McLeod 2004, McLeod 2016).

Table 1: Estimated Annual Production Impact ($) by Pest Animals across Australia, 2013-14 for Low, Average and High Production Loss Scenarios across seven vertebrate pest species. From McLeod (2004) 1 otherwise McLeod (2016)

SPECIES	LOW $M	MEDIUM $M	HIGH $M
Rabbits	108.31	216.63	250.57
Goats	5.3	6.79	8.48
Pigs	12.73	14.4	15.64
Fox	26.74	28.4	34.59
Dogs	64.39	89.33	111.21
Introduced birds (starlings)	49.98	68.57	146.93
House Mice		35.61	
Total	**267.45**	**459.72**	**567.42**

Table 2: Estimated Annual Economic Impact and Government Expenditure ($M) by Production Industry, for Low, Average and High Production Loss Scenarios (2013/14). From McLeod (2016).

INDUSTRY	LOW $M	MEAN $M	HIGH $M
Wool Production Loss	62.99	94.45	98.06
Sheep-meat Production Loss	36.04	50.46	60.67
Beef Production Loss	113.52	204.03	221.22
Broadacre Cropping Industry Loss	4.96	6.60	40.54
Viticulture Loss	48.98	68.57	146.93
Subtotal Production Losses	**266.45**	**424.1**	**567.41**
Vertebrate Pest Management Costs			
Broadacre and Livestock Farm	34.59	46.13	57.66
Viticulture Farm	19.67	19.67	19.67
Commonwealth Expenditure	14.74	14.74	14.74
State and Territory Expenditure	69.58	69.58	93.11
Subtotal Pest Management	**138.58**	**150.11**	**185.18**
Total	**405.03**	**574.21**	**752.60**

These costs are averaged out to annual estimates at various impact levels in Tables 1 and 2, because for many pest species, especially the smaller and faster breeding ones, the impacts can be episodic and patchy. For instance, house mouse plagues may occur every one in four- to- seven years, depending on geographic location (Brown and Singleton 2001). The 1993 mouse plague that ravished South Australia and Victoria was estimated to have caused $64.5M (in 1993) worth of damage to cereal crops (Caughley et al. 1994) and off-farm costs (reflecting mouse damage to infrastructure, produce, and the cost of cleaning up) were conservatively estimated to be $1M (Caughley et al. 1994). The 2011 mouse plague reportedly caused over $200M in-crop damage alone (S. Humphry 2011, Invasive Animals Co-operative Research Centre, (https://www.smh.com.au/environment/conservation/farmers-bane-returns-20111022-1mdgf.html) and the current 2021 plague has similar projections.

Production losses attributed to pest animals are estimated from the net losses in outputs borne by wool, sheep-meat, beef, viticulture and broadacre cropping enterprises across Australia. Key losses include, reduced wool and meat production as a result of grazing competition with rabbits and goats; predation of production animals by wild dogs, foxes and feral pigs; crop damage by feral pigs; and, viticulture damage from introduced birds. Annual losses estimated for wool, sheep-meat, beef and grain industries for the 2013–14 year, along with data on the expenditures by governments and farmers are shown in Table 2.

4.3 Impacts — Environmental Impacts

Invasive species are the primary threat facing Australia's unique fauna and flora (Kearney et al. 2018). Conservation International identifies Australia as one of 17 megadiverse countries comprising 566,398 species of animals and plants, many of which are endemic (Chapman 2009). One hundred species have become extinct since European colonisation in 1788 (Woinarski et al. 2019), with another 1,770 currently listed as Threatened. Many interacting factors contribute to species' extinctions and ongoing declines, including competition with introduced herbivores (Legge et al. 2011), habitat loss and climate change. However, predation by introduced predators, notably the feral cat and European red fox, is regarded as the greatest threat currently facing Australia's native mammals and the key driver of many extinctions (Woinarski et al. 2015).

Numerous introduced vertebrate pests are listed by the Commonwealth as key threatening processes under the Environment Protection and Biodiversity Conservation Act 1999 (EPBC Act 1999). These key threatening processes include:

- Predation by feral cat
- Competition and land degradation by rabbits
- Predation by the European red fox
- Predation, habitat degradation, competition and disease transmission by feral pigs
- Predation by exotic rats on Australian offshore islands of less than 1000 km2
- Aggressive exclusion of birds from potential woodland and forest habitat by over-abundant noisy miners
- Competition and land degradation by unmanaged goats
- Novel biota and their impact on biodiversity
- The biological effects, including lethal toxic ingestion, caused by cane toads.

The reintroduction of threatened mammals to islands or fenced areas from which introduced predators have been eradicated, is a conservation method increasingly used throughout Australia (Legge et al. 2018), at least until landscape-wide solutions are found (Woinarski et al. 2014). The establishment of additional introduced predator-free areas is one of the four key approaches of the Australian Government's Threatened Species Strategy (Australian Government 2016).

The monetary costs to the environment and society as a result of pest animal species are difficult to quantify and are not commonly reported (but see Bradshaw et al. 2021). However, McLeod (2004) provides an estimate of the environmental impacts of foxes ($190 million per annum), feral cats ($144 million per annum) and carp ($11.8 million per annum). More recently a National Carp Control Plan (NCCP) project determined a range of market and non-market impact cost data that could be used to estimate the impact costs of carp in Australian waterways. These estimates ranged up to $3b using a Willingness -To-Pay method but were dependent on the extent of environmental recovery following carp control. However, until the relationship between carp biomass and 'key environmental attributes' is known, a credible estimate of the total impact costs of carp cannot be calculated (Hardaker et al. 2020).

4.4 Current Control

Depending on the species, location and extent of the incursion, a combination of techniques is typically required to achieve sustained control of vertebrate pests at levels acceptable to management. Very rarely is total eradication of a vertebrate pest animal feasible, with some island eradications being notable exceptions (see Veitch and Clout 2002). There is an ongoing drive towards developing effective control tools and methods that also deliver improved welfare outcomes for both target and non-target animals. Conventional methods of control currently include fencing, trapping, baiting, shooting and biological control and have differing relative efficiencies.

Fencing

Exclusion fencing, initially for the protection of livestock and primary production industries, has a long history in Australia with the introduction of netting fences for rabbit and dog exclusion commencing in the early 1900s. Specialised fencing to exclude other vertebrate pests, such as foxes and feral cats, is more recent and is only viable where the area to be enclosed is relatively small. Specialised fences designed to exclude vertebrate pests are more costly than conventional stock fences, making it impractical to exclude vertebrate pests from very large tracts of land. Additional, ongoing investment is required to inspect and maintain exclusion fencing, and linear barriers throughout the landscape may also impact dispersal and ranging behaviour for both target and non-target species (Moseby et al. 2020, Smith et al. 2020). As such, fencing costs can be as high as $40,000/km with pest eradication (and proof of eradication) inside exclosures adding additional costs of up to $2500/km2 (Ruykys and Carter 2019).

Trapping

A variety of traps are used for vertebrate pest control, including conventional cage traps, soft-catch traps, lure cages, aluminium box traps and yards. Trapping is labour intensive and by default is not efficient at the landscape level. Consideration needs to be given to the welfare of both target and non-target animals, and to the accessibility of trapping locations for frequent monitoring. Advances in artificial intelligence and camera monitoring of traps may improve the efficiency of some vertebrate pest trapping programs.

Baiting

Several vertebrate pest animal pesticides are registered by the Australian Pesticides and Veterinary Medicines Authority (APVMA). Sodium fluoroacetate (1080), baits are commonly used to control large feral herbivores (e.g. wild horses, feral camels, donkeys and goats) and other established vertebrate pests including wild dogs, foxes, feral cats, pigs and rabbits. Risk to non-target species can be addressed by several measures, including burying baits, dying baits or incorporating baits into a specialised 'lethal trap device', but none of these measures eliminate non-target risk entirely. No antidote exists for poisoning from 1080; therefore, much care is required in its use around native animals, and domestic animals, including livestock. Other pesticides such as PAPP (para- aminopropiophenone) and sodium nitrite are being trialled as complements to 1080 as they are considered more humane on welfare grounds (Eason et al. 2014) and may have more acceptable application in places where acquired tolerance to 1080 is low. Anticoagulants are used to control rabbits, and globally, are also the tool of choice for many rodent eradications on islands. Rodenticides are extensively used to control rats and mice in agricultural and urban/industrial settings. Australian grain growers routinely apply zinc phosphide baited wheat grains to minimise damage by mice to grain crops (Brown et al. 2010), especially during mouse plagues. The current mouse plague (2021) in eastern Australia has seen the APVMA issue Emergency Permits for its use, including at 3–5–times the labelled delivery rate (from 1 kg/ha to 5 kg/ha, PER90793, PER91133) vastly increasing the amount of toxin likely to be delivered into the environment.

Shooting

Shooting by experienced operators is one of the most humane ways of controlling vertebrate pest animals; however, used in isolation, this technique rarely achieves sustained control of pest populations (Braysher 2017). There are also further limitations and considerations placed on shooting as control method for vertebrate pests inhabiting urban and peri-urban environments. Shooting from an aerial platform can permit humane control of larger vertebrate pests such as wild horses, camels, donkeys, feral pigs, and goats over large, remote areas with often rugged terrain.

Classical biological control

Biological control is the control of pests by natural predators, parasites, disease-carrying bacteria, fungi and / or viruses. For vertebrate pests, a noted success was the release of the myxoma virus into rabbit populations in 1950. In the six months following the release, the virus was believed to have killed more than 90% of rabbits in the temperate regions of Australia. Despite this initial success, a lack of vectors in semi-arid regions and developing resistance of rabbits to the myxoma virus meant that rabbit numbers were able to recover throughout Australia. Consequently, research was undertaken to release a new form of biological control for rabbits and in 1995, rabbit haemorrhagic disease (RHD, also known as rabbit calicivirus disease) established itself in Australia and reduced rabbit numbers, especially in arid areas. Australia's various rabbit biocontrol initiatives are estimated to have delivered benefits of >$70 billion AUD over 60 years to Australia's agriculture (Cooke et al. 2013). Their ability to establish in Australian wild rabbit populations and cause repeated outbreaks without the need to regularly re-apply is the key factor accounting for the success of viral biocontrols towards long term suppression of rabbits at a landscape scale. However, inevitable co-evolution of viruses with their hosts can lead to a lessening of the initial effectiveness of biocontrols, necessitating further research and development into improved forms of biological control. Biological control programs, on average, provide very high rates of return on investment, with the added advantages of freedom from non-target impacts and ability to be effective in remote and difficult to access places. The current rabbit biocontrol program is based on many years of research into increasing the effectiveness of RHD and has a benefit:cost ratio estimated at between 2.5:1 and 36.3:1.

Synthetic biocontrol

Virally-vectored immunocontraceptives (VVIC) were extensively explored for use on European foxes, rabbits and house mice (and brush-tail possums in NZ). Proof of concept of this approach which uses a genetically modified virus to deliver a fertility control antigen into the target animal was carried out for mice and rabbits. However, due to insufficient duration of induced sterility, as well as ineffective transmission of the viral vector (and the sterilising effect), this approach did not result in a viable control product and most research in this area was discontinued in 2005 (Hardy et al. 2006).

Genetic options that have the ability to distort pest population sex ratios are attractive because in theory they have several intrinsic advantages over conventional biological control: (1) they can be very effective; (2) they are species-specific; (3) they can target one sex or a particular life-history stage in order to maximise efficacy or minimise damage to non-target species; (4) their effects are potentially reversible if something goes wrong; and (5) some recombinant approaches lend themselves to relatively quick and inexpensive modification to target different species, while retaining species-specificity for each (Teem et al. 2013). The last characteristic helps to spread the high cost of developing autocidal technology across many species, in stark contrast to conventional biological control programs that must target each new species individually. Modelling fish populations however has shown that Trojan Y chromosome and other autocidal approaches such as Daughterless Carp strategy are slow acting, and effective population control typically requires 10 generations or more (Thresher et al. 2014).

4.5 Social acceptability of novel genetic approaches to pest management

There is limited research that has examined public attitudes towards genetic biocontrol technologies including gene drives, however some research has been carried out in New Zealand. A national survey conducted by MacDonald and colleagues (2020) used choice modelling methodology to examine public attitudes towards gene drive. Participants supported gene drive (32%) the least when compared with the Trojan female technique (42%) and the pest-specific toxin (52%); results also showed that participants could be clustered into four distinct 'worldview' categories based on underlying worldview constructs. The four-segment model based on these worldview values was found to be more dominant in explaining support for gene drives than other explanatory factors such as scientific knowledge, political ideology and religiosity.

In Australia, a national survey was conducted by social scientists within CSIRO's Synthetic Biology Future Science Platform, to measure public attitudes towards the development of synthetic biology (synbio) tools for solving National challenges such as conservation and invasive species management. Synthetic biology is a new field of research that applies engineering principles to biology, enabling the development of biological parts and systems that will perform new functions. While not specifically related to the topic of gene drives, this survey examined public attitudes towards the use of genetic tools for invasive species control; participants were introduced to the technology concept through a visual storyboard. The storyboard explained that future synthetic biology technologies, using gene editing, can potentially be used to reduce numbers of invasive species, by slowing down or even halting population growth. It was explained that gene editing involves changing an organism's genetic code by deleting, replacing or inserting a DNA gene sequence, and that synthetic biology had the potential to modify a pest species' genes so that offspring are infertile or limited to a single sex (e.g. male-only offspring) thus reducing opportunities to reproduce. Over time, this would naturally reduce the population size of future pest generations and potentially limit the impacts of invasive animals on the Australian environment.

Results showed a high level of awareness that invasive pests are present in Australia, with most participants (89%) at least moderately aware that invasive pests were present in Australia; most also rated pest animals as a moderate to very big problem (94%). Approximately 60% of participants moderately or strongly supported the development of synbio technologies for invasive species management; and just over half of all participants also indicated that they would not be particularly bothered if their local land management authority used the technology to manage invasive pests in their area. Participants were asked to rate their level of support for the use of synbio technology in managing different types of invasive pests and results showed that support was highest for using synbio to manage cane toads. However, participants also stated support for using synbio to target other pest species, such as crown-of-thorns starfish, carp, feral cats, rabbits, rodents, wild pigs, wild dogs and foxes. Although support was generally favourable, many people (over 75%) still expressed concerns about unknown consequences and a desire for further information about the potential risks and risk management procedures surrounding the technology. A large proportion of the public indicated that they would be interested in being kept informed of the outcomes of such research and being given the opportunity to provide feedback and have a say over how the technology is developed and implemented. Specifically, 73% indicated at least a moderate amount of interest in receiving results of research on the technology (e.g. a summary report). Accessing information and providing feedback through social media also was viewed relatively positively with around 70% expressing at least moderate interest. Around half of participants were interested in making a formal contribution to decision-making and indicated an interest in participating in public information sessions.

Survey results summarised here are available in full at: A baseline survey of public attitudes towards synbio – Synthetic Biology Future Science Platform (csiro.au)

Overall, the social research in Australia examining invasive species management using genetic tools suggests that people express more positive than negative attitudes and emotions towards these novel approaches. However, support is conditional based upon social risk perceptions and unknown implications for humans, animals and the environment. Importantly, CSIRO's synbio research suggests that support for synbio is highest when there is: (1) a public health imperative, or (2) A pollution management/bioremediation goal. Support for novel genetic solutions using synbio has so far been driven by emotion, perceived benefits/relative advantage of technology over current solutions, efficacy of technology, trust in scientists and trust/confidence in governance (Carter and Mankad 2021, Carter et al. 2021, Mankad et al. 2020, Hobman et al. 2021).

4.6 Limitations of current 'established' pest management

The Victoria Government Invasive Plants and Animals Policy Framework (IPAPF) considers that eradication is the optimal outcome for managing high-risk invasive species that are established in an area. The fact that there are relatively few examples of eradication of invasive species being achieved at a state or regional scale reflects the high degree of sustained commitment and resources required in successful eradication programs.

Eradication has often been identified as an aspirational goal where it is highly unlikely to be achieved at a landscape level, or there is insufficient information to make a valid assessment of feasibility. Future identification of species as targets for eradication should be based on a rigorous analysis of feasibility and risk. The very large benefits resulting from eradication of high-threat invasive species justifies assessment of innovative techniques and technologies.

The principles of the invasion curve (Figure 1) highlight that economic return on investment in on-ground management of established, widespread vertebrate pests is generally low relative to prevention, eradication or containment (c.f. Leung et al. 2002, Yokomizo et al. 2009). Whilst targeted government investment for innovative advances in established vertebrate pest control can deliver positive benefit: cost ratios, sound management of public funds dictates governments must maximise return on investment. The argument against government investment in established pest or disease management is therefore not that there is no net public benefit in doing so, but that the return on investment is generally lower in comparison to other areas of biosecurity management (i.e., prevention and eradication). An exception to the generally low return on investment in managing widespread species is the high return on investment into biological control techniques. For example, an economic assessment for the Australian weed biological control effort since 1903 has indicated an overall return of approximately $23 for every dollar of investment (Page and Lacey 2005). However, biological control is currently only available for a small subset of invasive species, and only one pest mammal — the rabbit.

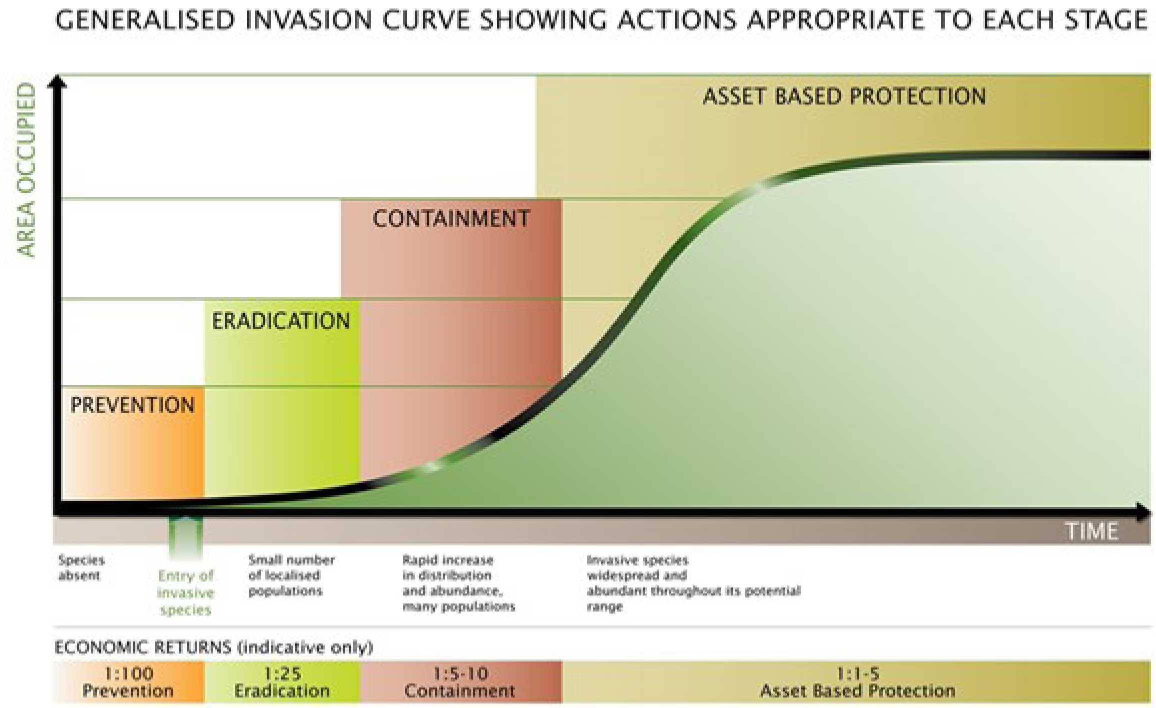

Figure 1: Victorian Government (2010) Invasive Plants and Animals Policy Framework, DPI Victoria, Melbourne. (https://agriculture.vic.gov.au/biosecurity/protecting-victoria/legislation-policy-and-permits/invasive-plants-and-animals-policy-framework)

Innovation is critical for ongoing sustainable management of established vertebrate pests. A clear pathway for the adoption of innovative research and development by both private and public practitioners is required, ensuring full consideration is given to associated costs, benefits and risks. In accordance with government investment principles, government investment in innovation will require practitioners to contribute in proportion to the benefits they receive.

4.7 National Biosecurity System (National and international requirements to control pests)

Governments at the National, state and territory levels; industry; non-government organisations and individual landholders all have a long history of investing both collaboratively and individually, in pest animal management. Managing biosecurity is critical to a sustainable and productive agricultural sector and healthy environment. Effective management of established pests also assists Australia to meet its international obligations with respect to international trade and prevention of further biodiversity loss. Given the shared responsibility for their management across multiple jurisdictions, the effective management of established vertebrate pests requires clarity of policy direction and prioritisation, and a defining and assigning of roles and responsibilities.

The goal of a national biosecurity system (Figure 2) is to minimise the impact of pests and diseases on Australia's economy, environment and the community. Resources are targeted to manage risk effectively across the incursion management continuum, while facilitating trade and the movement of animals, plants, people, goods, vectors and vessels to, from and within Australia.

The Intergovernmental Agreement on Biosecurity (IGAB) is signed by all jurisdictions in Australia. The agreement outlines national biosecurity goals and objectives and clarifies roles, responsibilities and governance arrangements. Key principals of the IGAB include:

- Biosecurity investment prioritises the allocation of resources to the areas of greatest return, in terms of risk mitigation and return on investment.
- Biosecurity activities are undertaken according to a cost-effective, science-based and risk-managed approach.
- Governments contribute to the cost of risk management measures in proportion to the public good accruing from them. Other system participants contribute in proportion to the risks created and/or benefits gained.

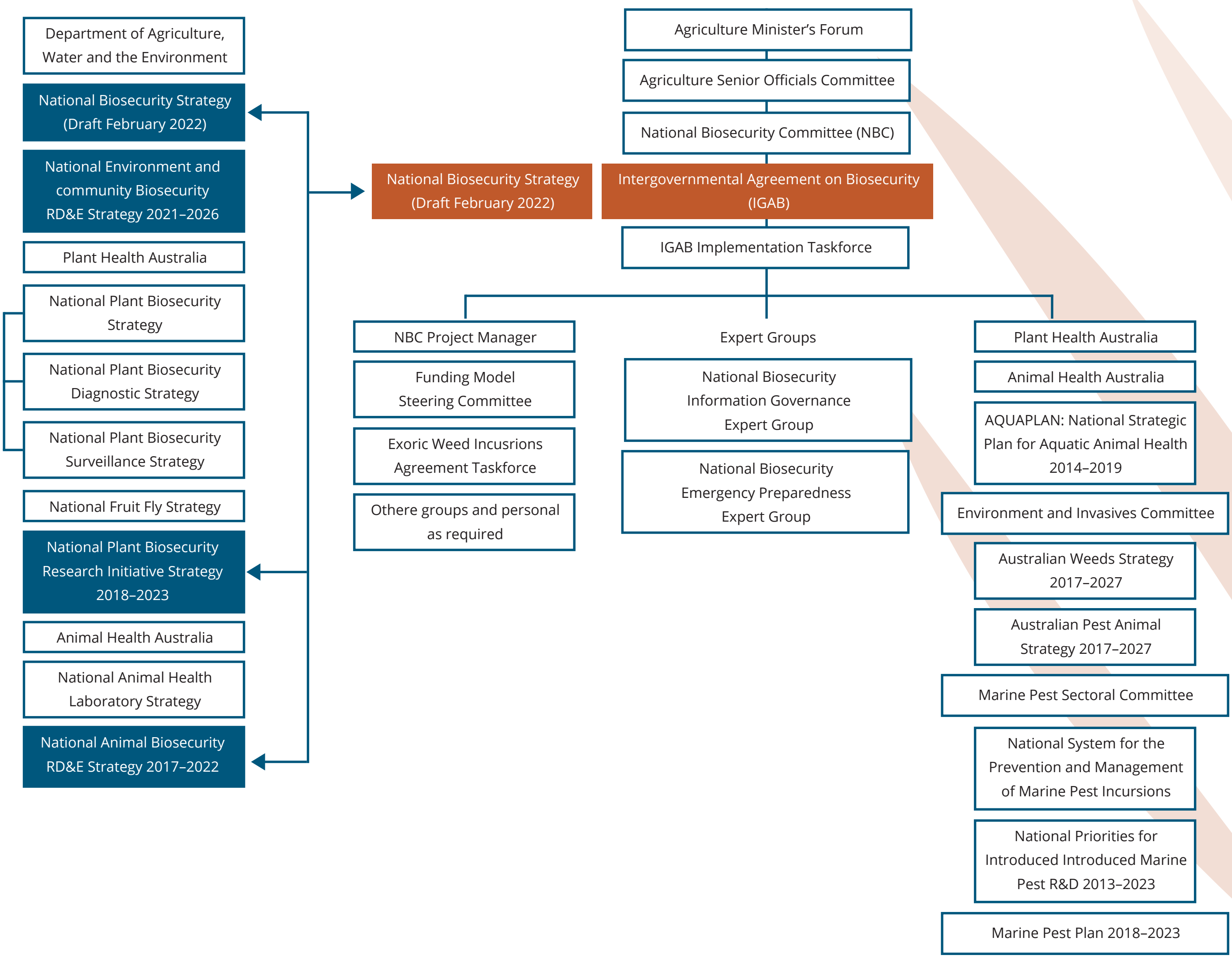

Figure 2: Schematic of Australia's current national biosecurity system taken directly from the National Environment and Community Biosecurity Research, Development and Extension Strategy 2016 to 2019 Department of Agriculture and Water Resources, Canberra (agriculture.gov.au/publications).

STRATEGIES AND AGREEMENTS

The Australian Pest Animal Strategy (APAS) is a strategic framework developed by the former Vertebrate Pests Committee (VPC) and revised in 2016 under the leadership of the Invasive Plants and Animals Committee (IPAC). While the APAS does not identify research, development and extension priorities, it does recognise the need to improve research coordination (Goal 1 — Provide leadership and coordination for management of pest animals; Objective 1.3), by specifically outlining the following: 'Produce a shared research and development plan to improve the development and adoption of best practice pest animal control methods and facilitate adoption of this plan by all stakeholders'

The APAS recognises that there is a need to both continually refine control techniques for vertebrate pests and to develop additional techniques. Specifically, the strategy recommends that research, development and extension programs:

- Address gaps in ecological knowledge for some organisms.
- Improve understanding of the social components of vertebrate pest management.
- Develop a vertebrate pest animal research and development plan.
- Identify current impediments to research and development and ways in which they could be overcome.
- Canvass approaches for more effective adoption of more effective control methods.

The APAS articulates that the Australian Government has responsibilities to coordinate national research in high priority areas. The APAS recommends that the Commonwealth provide leadership, co-ordination and resources for research and evaluation of vertebrate pest issues of national significance; while state and territory governments have the responsibility to provide leadership, coordination and resources for research, evaluation and advisory services about pest animals affecting their jurisdiction. Community and industry organisations have responsibility to contribute to the funding of research and development of improved pest control methods.

Overseeing these arrangements and strategies are a number of committees, including the National Biosecurity Committee, and the Environment and Invasives Committee.

Committees

The National Biosecurity Committee (NBC) was formally established under the IGAB, with a revised IGAB (IGAB2) coming into effect in January 2019. The Commonwealth and all states and territories are signatories to the IGAB2, which was developed in response to the recommendations of the Priorities for Australia's Biosecurity System Report (Craik et al. 2017).

The NBC is responsible for managing a national, strategic approach to biosecurity threats relating to plant and animal pests and diseases, marine and aquatic pests, and the impact of these on agricultural production, the environment, community well-being and social amenity. A core objective of the committee is to promote cooperation, coordination, consistency, and synergies across and between Australian governments. This includes exploring measures to:

- Provide assurance that the system is working,
- Better connect the biosecurity rationale to market access and trade,
- Increase visibility and engagement with sectoral committees,
- Engage, partner and communicate with relevant stakeholders as required,
- Coordinate biosecurity investment in the national interest.

The NBC provides advice to the Agriculture Senior Officials Committee on national biosecurity, and on progress in implementing the IGAB. The NBC is supported by four sectoral committees and a communications and engagement network. These provide policy, technical and scientific advice on matters affecting their sector, covering all pests and disease risks to terrestrial and aquatic (inland water and marine) animals and plants, and to the overall environment:

- Animal Health Committee
- Plant Health Committee
- Marine Pest Sectoral Committee
- Environment and Invasives Committee
- National Biosecurity Community and Engagement Network

The Environment and Invasives Committee (EIC) is responsible for providing national policy leadership on the identification, prevention and management of invasive plant, vertebrate and invertebrate species that adversely impact on the environment, economy, and community. The EIC provides a national mechanism for the identification and resolution of national priorities on freshwater aquatic and terrestrial invasive species and any other species where there is an environmental or community biosecurity impact where it is found not to be the responsibility of any other sectoral committee. The core objectives of the EIC include:

- Development and implementation of national strategies.
- Provision of clear governance structure for priority pest management; and
- Prioritisation of research, development and extension related to invasive species biosecurity.

4.8 Summary

Established vertebrate pests cause catastrophic impacts on Australia's unique biota and substantial economic impacts on primary production. Numerous vertebrate pests are widely established across multiple jurisdictions, causing further impact to social amenity and infrastructure. The effective management of established vertebrate pests over large landscape scales is fraught with difficulty and due consideration to welfare outcomes for both target and non-target species is essential.

The biosecurity system in Australia provides a governance framework for both the NBC and the EIC and is built around several key agreements and strategies. This governance framework advocates for the minimisation of impacts from vertebrate pests on Australia's economy, environment, and community. It also provides clarity around cost-sharing, roles and responsibilities and prioritisation of research programs.

Effective management of established vertebrate pests needs to be technically and legislatively feasible and be underpinned by appropriate socio-political support and cost-sharing arrangements. There is an imperative for innovative research to provide solutions that enable efficient, large-scale, humane control of established vertebrate pests. Where invasive species affect multiple industries and/or multiple jurisdictions, it becomes more difficult and costly for the private sector to provide effective management. Government may need to play a role in coordinating the actions of affected parties (Victorian Government 2010); with the EIC, for example, being responsible for providing national policy leadership for research and development prioritisation and the management of invasive pest animals.

The costs of Australia's vertebrate pests to production, trade and the environment is enormous and increasing at a rate that is outstripping the capacity of current management. For a high impact established pest of national significance, the absence of efficient management methods is considered grounds for coordinated research and development (The National Framework for the Management of Established Pests and Diseases of National Significance, NBC 2016). As such, this paper finds a clear case for government and industry support for investment in R&D into disruptive technologies such as genetic biocontrol technologies for vertebrate pets of significance.

5 DECISION AND IMPLEMENTATION FRAMEWORK FOR INVESTMENT IN GENETIC BIOCONTROL TECHNOLOGIES

Genetic biocontrol provides opportunities for the control and potential eradication of invasive species. The term 'genetic biocontrol' refers to techniques that alter the genes of an organism to control invasive species in the environment. Work is already underway to investigate advanced biotechnology applications for pest management and biodiversity conservation, all of which show a range of possibilities for addressing invasive species (Piaggio et al. 2016, Harvey-Samuel et al. 2017). CRISPR-Cas9 has been used to create synthetic gene drives in which acquisition of a trait and the CRISPR-Cas9 machinery are coupled to ensure rapid trait propagation through a population. This often occurs through the distortion of meiosis or gamete development (termed 'meiotic drive'), or by breakage and self-insertion into the homologous target sequence (termed 'homing-based drive'). The fundamental mechanism of a CRISPR–Cas9-mediated gene drive has now been demonstrated feasible in mice (Grunwald et al. 2019). If successful, this transformational technology could potentially be applied to a number of vertebrate pests, such as rabbits, feral cats and toads (Prowse et al. 2017, Tingley et al. 2017, Kachel 2018).

5.1 Background to Investment Decision Framework Development

The framework, the themes contained within the framework, and the recommendations for implementing the framework were generated from various data sources. These include: two Stakeholder Workshops (2020-2021); combined expert knowledge among team members (ecologists, geneticists, biologists, social scientists) and the relevant published literature.

Workshop 1 participants comprised largely of representatives from the broader pest and invasive species research community including CSIRO, University of Adelaide and Macquarie University. A small number of government representatives also participated in Workshop 1 and included attendees from state and federal government agencies and non-government organisations with an interest in this topic. Several civil society organisations were also invited to participate in discussions including the RSPCA. While participants were invited to attend the meeting to share their perspectives on using genetic biocontrol technologies and pest species prioritisation, the nature of engagement and participation in these forums cannot easily distinguish between personal and organisational views. It is likely that a mixture of personal, organisational and group-mediated views was offered during discussions. Thirty-six participants attended Workshop 1, excluding project staff. In general, stakeholders participating in our workshops were optimistic towards genetic biocontrol as a future possibility and that it could be transformative in pest control but acknowledged that it was not a silver bullet and was not appropriate for all pest species, and as such, investment required a cautious and integrated approach (Figure 3).

Figure 3: A Word Cloud from the first Stakeholder Workshop (Appendix 1) held where participants were asked what words best describe their interest/ passion for the topic: Genetic Biocontrol Technologies in Future Vertebrate Pest Management in Australia.

Workshop 2 was run as small online focus-group discussions comprised of potential investors of genetic biocontrol technologies and included industry representatives (e.g. GRDC, MLA), multijurisdictional government decision-makers and managers (e.g. DAWE; DAF, Qld; DPI, NSW; DPIRD, WA; ECODEV, Vic) and NGO representatives (e.g. Australian Wildlife Conservancy). Eighteen participants attended Workshop 2 spread across two half-day sessions. Participants in Workshop 2 discussed the broader investment decision-making environment and institutional appetite for investment in this space. The design, methods and detailed results of both workshops will be made available in a journal paper, currently in preparation.

This decision and implementation framework included information gathered during Workshop 2 and aligns with existing governance, institutional and social considerations and expectations with respect to responsible science in invasive species management (cf. Carter et al. 2020). The decision framework represents key themes revealed by group discussions designed to unpack the following:

- The current investment and management environment for organisations potentially funding, supporting or governing genetic biocontrol options,
- The critical conditions for investment in genetic biocontrol options, and
- The enabling conditions for investors to support, sponsor and/or fund genetic biocontrol initiatives.

This report discusses in detail the second cluster of themes identified by stakeholders and experts, namely, the conditions for investment in genetic biocontrol technologies. It is this component of the framework that is identified as essential to understand, plan and manage as to ensure trust and confidence are established among investors and stakeholders.

5.2 Themes and considerations for investment in genetic biocontrol technologies

Four themes were identified by stakeholders as conditions for investment in genetic biocontrol solutions in Australia:

- Safety and efficacy of control approaches
- Engagement of community stakeholders to enhance acceptance and manage perceptions of social risk
- Considerations of trade implications
- Articulation of the advantages of genetic biocontrol technologies over existing pest control technologies to provide strong drivers.

While the stakeholders who participated in our Workshops considered these themes to be critical to investment decisions (unpacked in more detail below), all four conditions are also known to be key components of effective and responsible science development (NASEM 2016, Teem et al. 2020). Additionally, Workshop 2 participants also considered investment opportunities to be diverse and potentially comprised of various modes including: knowledge and resource support and partnerships, advocacy and mobilisation, and financial and philanthropic support (Figure 4).

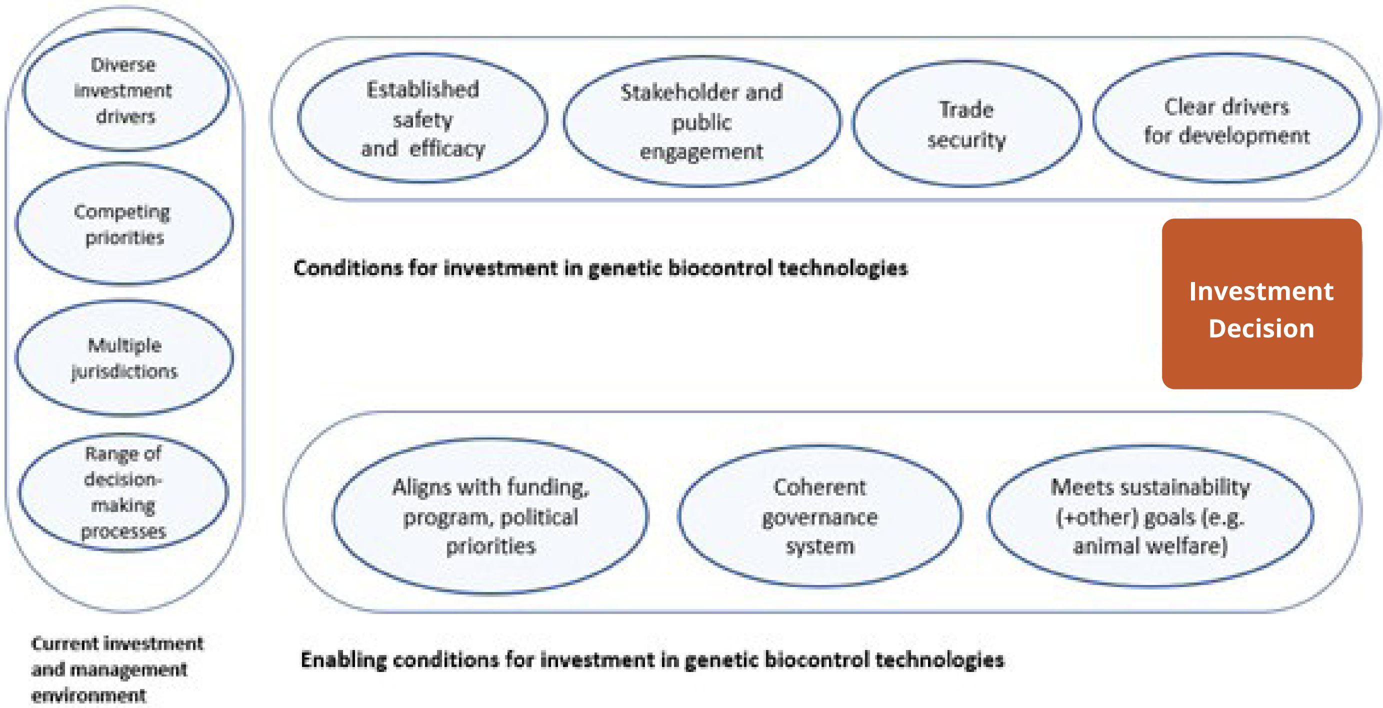

Figure 4: Themes emerging from discussions around investment decisions for genetic biocontrol of invasive and pest species in Australia (this figure first appeared in Carter et al. 2021, in prep).

5.2.1 Safety and efficacy

When considering conditions for investment in new genetic biocontrol technologies, established safety and efficacy was a recurring theme and in addition to conforming to existing safety regulations, workshop participants raised concerns about potential unintended consequences of genetic biocontrol technology deployment. These included unintended impacts on target species (especially charismatic ones), or broadscale 'escape' of genetic biocontrol technologies, organisms, or elements beyond targeted populations. Such events would carry an added risk due to potential negative effects on public confidence in genetic biocontrol technologies which has the potential to threaten future viability of such initiatives. Thus, safeguards (e.g. genetic, physical, ecological) to ensure target specificity are a key condition for investment.

5.2.2 Social license, stakeholder and public engagement, and public acceptability

The range of concepts that describe public engagement with science

While our Workshop participants (and indeed the broader research community) largely refer to concepts like 'social license' and 'social acceptance' as proxies to convey the implicitly understood importance of public support for the deployment of genetic biocontrol strategies, these terms are value-laden and originate from disparate contexts (Carter and Mankad 2021). They carry with them embedded historical and institutional meanings across various sectors and disciplines which require due consideration (cf. Moon and Blackman 2014). Concepts like 'social license' and 'public acceptance' should not be used independently from consideration of the broader goals of engagement efforts.

For example, it may be more constructive to consider public acceptance at different scales; specifically, social acceptability for the development of genetic tools for environment management and conservation, and place-based community acceptance for the local deployment of a genetic pest management tool (e.g. a gene drive; Shackleton et al. 2019). Importantly, the motivation for engaging with various publics must also be transparent. Use of terms like 'social license' in the pest context can be perceived as a permission-seeking tick-box exercise, rather than a more holistic approach where research and development programs give full consideration to the socio-political context within which they will be implemented (Carter et al. 2020).

Approaches to public and stakeholder engagement and governance

Social science research can reveal information about multiple facets of public and stakeholder acceptability including: public perceptions about using genetic biocontrol solutions to solve environmental problems; social risks of pest management; attitudes and emotions relating to the problem at hand, or the solutions proposed and the quality of trust relationships (Carter et al. 2020). Yet, information about public sentiment is not sufficient to secure public trust or support for genetic biocontrol interventions. An engagement process that goes beyond the creation of science outputs and includes open dialogue, including a transparent and inclusive process to express concerns and discuss alternatives is also required, especially for communities and stakeholders likely to be directly affected by genetic biocontrol strategies (Rowe and Frewer 2005). Science communicators, engagement practitioners, partnership and knowledge brokers, and facilitators, in collaboration with social and natural scientists, are examples of the types of professionals that can be valuable in the design and implementation of inclusive and deliberative engagement processes, whilst bridging the gaps at the science-policy interface (cf. Bielak et al. 2008, Duncan et al. 2020).

Stakeholder mapping and analysis for the purpose of invasive species governance is best achieved using structured methodological approaches (cf. Reed and Curzon 2015). Resisting the urge to perceive the public as a homogenous and static entity and instead identifying the various actors and groups, their interests and their perceptions of and attachment to the problem (and solution) will enable the science community to better understand the nuances between the full range of stakeholder groups. Avoiding transferring the findings from previous GM-related research to the invasion science context is also advised, especially given more recent research on public attitudes towards genetic solutions. In a national survey published by CSIRO in 2021, broad level 'curiosity' and 'hope' was found among Australians in relation to selected synthetic biology applications and their potential to help solve Australia's current environmental challenges .

Engagement with stakeholders is further strengthened by including the perspectives of immediate users of science (e.g. policy makers, land managers, regulators, other researchers). This is a critical step along the pathway towards successful deployment of genetic biocontrol strategies (cf. Stokes et al. 2006). It is those immediate users and brokers of science where traction in the governance of genetic biocontrol is likely to take shape. How both public-facing and the broader stakeholder engagement strategies are planned will influence the quality and transparency of information flow, the effectiveness of partnerships, and ultimately the levels of trust built among stakeholders.

In relation to understanding public engagement with science, there are multiple and inter-related areas of scientific and professional enquiry possible. These span social scientific enquiry (i.e. public attitudes and perceptions of risk, drivers for technology acceptance and uptake, bioethics, institutional arrangements) to understand the broader context of the technology implementation environment; public engagement (e.g. consulting with and working with the public to listen and acknowledge concerns and provide feedback); and science communication (e.g. providing information about new technologies to keep the public informed). While these can overlap, their intentions and goals require careful consideration.

Our workshops (2020–2021) revealed key information gaps for decision makers about social acceptability and public engagement; some of these themes are discussed below.

Ethical considerations relating to genetic biocontrol

The consideration of ethical issues relating to genetic biocontrol of vertebrates refers to multiple facets of science and its implementation. Ethical considerations in this context can be grouped into three categories. The first, relates to societal expectations for a fuller range of values and interests to be included and represented in science decision-making. Issues relating to public participation in science, the diversity of knowledge, its production and use fall into this category of ethics. More commonly, ethical considerations relate specifically to the conduct of scientific projects, in how a range of risks are managed and the extent to which the broader principles of responsible research are applied. Questions relating to animal welfare are included in this category. Finally, there are broader epistemic and moral considerations which attempt to address higher order questions. These include, for example: managing the consequences of inaction; decision-making under conditions of uncertainty, and the genetic modification of sentient animals.

Technology readiness

While genetic tools hold great promise for a long-term, scalable solution to invasive pest species, there is a long lead-time for the science to meet management expectations. This uncertainty, and the current lack of a suitable 'proof of concept', means that decision-makers are effectively being asked to consider a hypothetical tool that may or may not live up to expectations. Furthermore, funding the science designed to provide the foundational proof of concept may be difficult to attract because of the slow pace of science discovery to date. However, there seems to be a shared understanding that it is acceptable to invest early funding into genetic biocontrol research and development, even if the focus in not on the investor's 'preferred' target species.[1]

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1 Recent national survey results challenge the common view that the public generally opposes all genetic modification technologies. For more information, see https://research.csiro.au/synthetic-biology-fsp/public-attitudes/

Environmental management or environmental conservation

There appears to be a clear division in decision-making perspectives, typically centring around whether stakeholders frame the use of genetic biocontrol technologies as a tool for environmental 'conservation' or for environmental 'management'. While conservation and management are fundamentally linked concepts in that they both rely on the management of harmful invasive pest species, the two perspectives do tend to elicit different motivational profiles. Workshop participants hailing from management were inherently cautious of potential risks and the possible social fallout if something were to 'escape' (based on GM mistakes of the past), or uncertainties around the control of 'genetic manipulation'. A common thread amongst management stakeholders was the importance of building 'community confidence' and making decisions that considered the broader acceptability of gene drives. There was also a sense that decisions around the support of different genetic biocontrol technology initiatives would likely be driven by a prioritisation process that considered where losses might be greatest and whether other non-genetic interventions (e.g. border controls) might need additional support in the short-term.

Stakeholders from the perspective of conservation are unapologetic in their goal to conserve. Given the rapid rate of species decline at the hands of invasive pests, there is little heed paid to 'social license' considerations beyond acknowledgement that social considerations are important. Assessment of social approval may derive from a like-minded base without the necessary representativeness of the population as a whole. However, this is not problematic for those decision-makers with conservation in mind because their position is clear – the end goal of technology development ought to be a substantive gain for conservation. Decision-making with conservation in mind clearly articulates the urgency and need for immediate action and resourcing of genetic tools that can address conservation at scale. Interestingly, decision-making for investment into technological development relies heavily on science and science advisory networks. That is, relationships with communities of practice.

While larger investment decisions are made by executives and comprise inputs from many sources, the process also relies on the many informal relationships that individuals have with key information brokers. Stakeholders from a conservation perspective are often not-for-profit organisations, whose activities in this space may best be directed towards lobbying for the advancement of genetic biocontrol science.

Overseeing the management and conservation perspectives are the higher-level goals of Commonwealth government departments, who must weigh up current and future funding of research and existing investments in invasive species management. There is no impetus for genetic tools to target any one species, but rather, the Commonwealth government considers themselves to be investors in new and exploratory ways of looking at invasive species management. In a manner of speaking, this stakeholder should be seen as a 'seed' funder with a diverse portfolio of investments advancing genetic biocontrol of invasive species. There is a strong reliance on research and a desire to remain neutral, shying away from endorsing any particular pest control tool. Decision-making at the Department level is formalised and often involves a tendering process and meeting other formalised obligations such as policy considerations, legislative requirements and regulatory limits, and ultimately generating political will.

Regional decision-making

State and territory-based government stakeholders balance pursuit of both management and conservation goals. Decision-making at this level is highly pragmatic, typically based on limited funding and resourcing, with long-term programs the exception rather than the norm. These stakeholders are often tasked with overseeing large areas of land with multiple pest issues causing significant, simultaneous, problems.

There is tension between funding invasive species management for public versus private benefit; in many cases the biosecurity activity is predominantly for private benefit (e.g. wild dog fencing). Decision makers at this level are open to considering any genetic options across both plants and animals, as long as they don't have significant negative impacts. Decisions at this level are made in complement with other environmental departments, state and regional committees; with branch management strategies to guide where efforts are focused. It is clear that this level of decision-making, while being a joint approach involving much consultation, is also a very complex and constrained process, based on regional priority plans which are quite specific and limited in scope (Figure 5). Despite the differing priorities at this level of decision-making, risk associated with genetic biocontrol technologies was consistently identified by these stakeholders. This includes political risk, which stakeholders felt would come into play if there was a real or perceived risk to environment, industry or the community. Ultimately, it was considered that it is not possible to have a generalisable decision making framework at this level as priorities and levers for action differ.

While there is a need to invest in efficacious technology, early funding of platform research for genetic biocontrol technologies may not fall within the remit of regional government. At the regional level, there is greater appetite for funding relatively less risky advanced research and field trials that benefit traditional control programs, but additionally will fill knowledge gaps required to progress genetic biocontrol related science. For example, sequencing specific genomes and furthering knowledge of landscape scale population genetics and ecology of target species. However, there is low trust in genetic biocontrol technology research and development among stakeholders and some publics, and a fear of the potential for vocal opponents to influence the political base, whether these concerns are supported by science or not (Carter et al. 2021), because of past (biocontrol) 'failures'. However, despite the clear constraints to state-level decision-making, there is an urgency among some stakeholders to control significant species such as feral cats, and the potential of genetic tools to alleviate traditional community concerns around animal welfare of invasive pests, is a strong lever for investment.

Genetic biocontrol technology solutions are complex to understand and communicate and require substantial and constructive discourse with and within the community. As such, this Report strongly supports investment in an engagement process across rural and urban citizenry, that includes indigenous populations, and that builds clarity around and confidence in the purpose, outcomes and benefits in such solutions.

Summary Point 1: Development of innovative, effective and acceptable methods for vertebrate pest management will require multi-stakeholder support, consideration of social risks and acceptability, and include cultural and ethical factors relevant to genetic biocontrol technology.

- Establish a comprehensive and inclusive stakeholder research and engagement strategy.
- Plan for early and ongoing engagement with communities, Traditional Owners and publics to raise awareness and build trust.

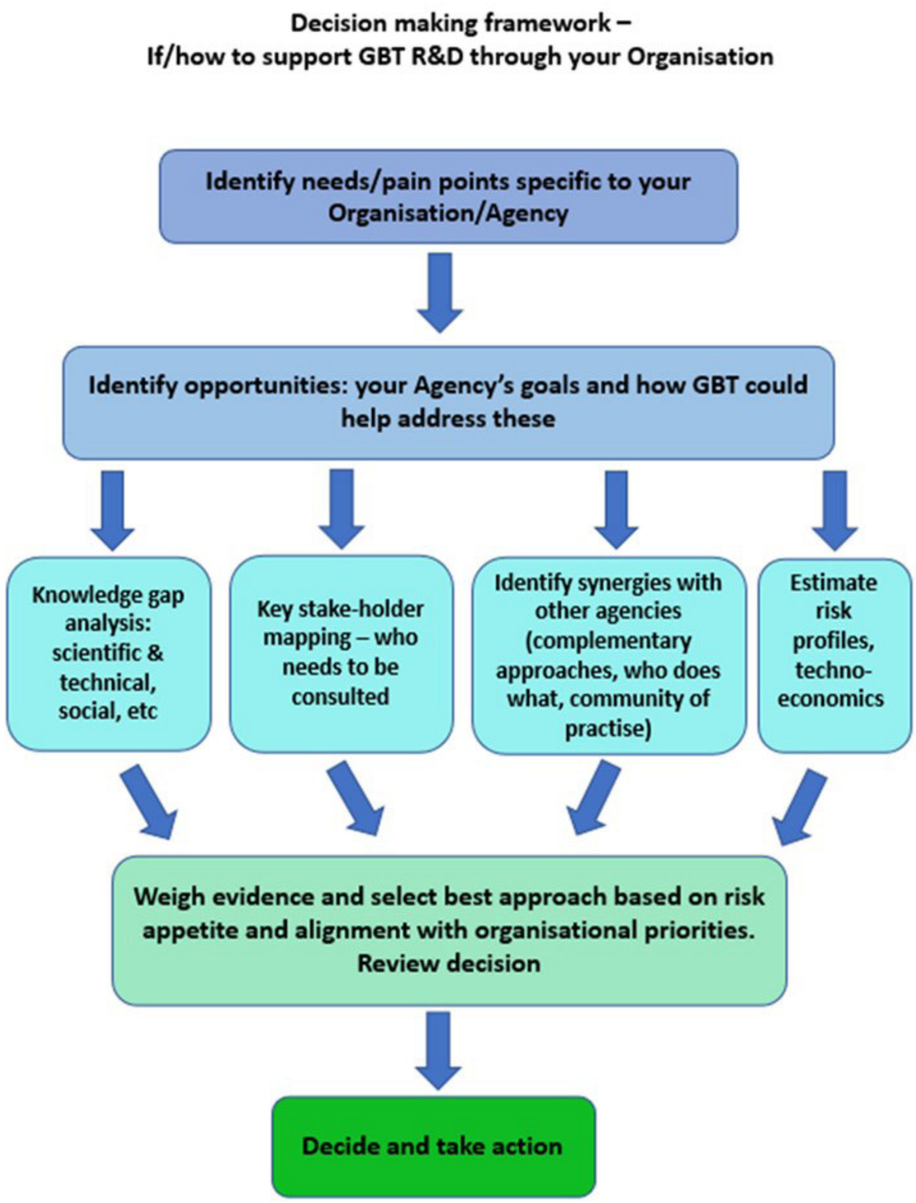

Figure 5: Organisation process for Genetic Biocontrol Technology Investment planning and development.

5.2.3 Trade implications

Potential Impact of genetic biocontrol technologies on international trade

Animals that are involved in the deployment of genetic biocontrol technology will inevitably be categorised as genetically modified organisms (GMOs — also defined by certain organisations under the term living modified organisms, LMOs). The requirements for appropriate regulation and licence of their release will encompass thorough assessment of risk, containment, and monitoring.

It can be assumed that in the country of deployment, the LMO will have undergone a rigorous process of evaluation to deliver the datasets required by the relevant regulatory authorities. In Australia, this will begin with the Office of the Gene Technology Regulator under the Department of Health and the Department of Agriculture, Water and the Environment, and extend to the relevant State and Territory authorities and Departments. Developing an official national framework agreement governing proposed deployments would be a desirable outcome.

Although Australia has no international land borders, internal state borders are an important consideration. In the international context the possibility exists that cross-border movement could occur via human mediated shipments to and from locations associated directly or indirectly with a deployment.

Key issues for genetic biocontrol technology in relation to international trade of agricultural products

Greater than 98% of world trade involves countries that are signatories to the General Agreement on Tariffs and Trade (GATT; established in 1948), with an additional 36 countries accepted into the agreement since 2016. Provisions of the GATT include phytosanitary requirements to ensure that bulk materials exported and imported between international jurisdictions meet standards to ensure that invasive plant and animal pests are not transferred with those traded materials. The relevance of GATT to genetic biocontrol technology is provisions that could be invoked to create trade barriers to products from countries that have deployed a Genetic Biocontrol Technology (GBT) and whose export products might be subject to claims of contamination by an LMO.

There are 164 countries that operate under the rules, agreements, and negotiations of the World Trade Organisation (WTO). Amongst these is the Agreement on Technical Barriers to Trade (TBT; 1995). The TBT Agreement obliges State members to notify each other of any proposed technical barriers to trade. The notification period must provide sufficient time for comments and discussion with three conditions being necessary for consideration:

- The measure must be a technical regulation or an evaluation of a conformity assessment procedure.
- There must either be no relevant international standard or, if there is, the measure must not conform to it.
- The technical regulation must have a considerable effect on international trade.

The relevant international protocols that could be brought to bear on potential contamination of goods with a genetic biocontrol technologies LMO are the Food and Agriculture Organisation (FAO) Guidelines for The Revision of National Phytosanitary Legislation (2007). These are enacted internationally as the International Standards for Phytosanitary Measures (ISPM). Countries apply these through requirements for Sanitary and Phytosanitary Standards (SPS), which are controlled by Phytosanitary Certification of export (import) agricultural products. Australian agricultural products for export are already subject to these measures.

A WTO member country is within its rights to express concern about the potential presence of a genetic biocontrol technologies LMO in goods to be imported. The inherent nature of a genetic biocontrol technologies LMO is likely to mean that it will be categorised as an Invasive Alien Species (IAS), which would be subject to the standards for pest risk analysis (namely, ISPM No. 2: Guidelines for pest risk analysis and ISPM No. 11: Pest Risk Analysis for quarantine pests including analysis of environmental risks and living modified organisms). These cover the environmental risks of LMOs including risks to biodiversity. This could include requirement to develop risk analysis control measures and regulations under the framework of the phytosanitary law.

Appropriate ISPM regulations, measures and controls are already in place in relation to IAS. The LMO aspect introduces an additional consideration, that of the of the Cartagena Protocol on Biosafety, but it is subordinate to the ISPM. ISPM No. 11 (4002) on pest risk analysis includes an annex on phytosanitary risks that may be associated with LMOs. All currently traded LMOs are plants or plant products, and they are covered under the basic definitions in the phytosanitary law and no special terminology is defined. The regulation of LMOs that are plants or plant products is part of the regular mandate of the importing country's National Plant Protection Organisation, which has the power to approve or deny approval for the import of plants or seeds which are the products of biotechnology.

While currently there are no LMO animals, or food products from LMO animals that are traded internationally, the key issue regarding genetic biocontrol technologies is that it is only a subsection within pest animal risk management considerations. It remains to be seen whether WTO member countries will seek to use the Cartagena Protocol in addition to the ISPMs and the WTO under the TBT Agreement.

Monitoring of traded goods to assure freedom from material originating from genetic biocontrol technologies

An important component of a GBT deployment will be the development of methods for the detection and monitoring of LMOs and of residues from LMOs containing genetically modified material. DNA is the key material of concern with respect to the LMO and it is widely considered as both highly stable and a reliable signature of identification (as per its use in forensic science in a legal context), even in samples from an open environment (i.e. eDNA). The use of PCR technology is both sensitive and highly specific, particularly in the context of genetic biocontrol technologies which will incorporate very distinct DNA signatures. It should be possible to establish accepted 'methodologies' that can be used to certify agriculture goods prior export and for assessment of materials prior to import should it be required. This could be incorporated into existing Phytosanitary protocols to provide additional levels of confidence with respect to the ISPMs and the Cartagena Protocol.

Assurances of containment and monitoring of genetic biocontrol technologies

Should an effective genetic biocontrol technology be generated it will have to undergo rigorous contained and, eventually, open field trials. This will be a requirement to pass through the various stages of regulation and to gain the appropriate approvals and licences before making a transition to a viable control system for any given pest animal. The licencing and approval would most certainly require post deployment monitoring. This data would also have relevance to the key question in relation to the potential for LMOs or biological residues emanating from them, to become contaminants in agricultural goods destined for international trade, and potentially also for domestic cross-border trade. Thus, establishing effective methods to monitor the pest animal in the wild and in the production environment and the identification of the LMO will be a valuable component of post deployment monitoring. This will be essential to establishing the data sets for registration and regulation, to follow the effectiveness of the genetic biocontrol measure and to provide methods to complement or enhance current ISPM protocols.

Summary Point 2: Develop a risk analysis of potential impacts and appropriate methodologies and accreditation for post-deployment monitoring of Living Modified Organisms (LMOs) with the appropriate authorities. Although mediated by generating LMOs, subject to the Cartagena Protocol, current ISPM protocols are overarching and can fulfill trade obligations.

5.2.4 Clear advantages of genetic biocontrol technologies

For most established vertebrate pests, broadscale control options are currently lacking and use of some techniques is increasingly challenged on animal welfare grounds (see Section 4). Smaller scale management for vertebrate pests, including exclusion fencing is expensive and requires ongoing maintenance. Nonetheless, any new technology, including genetic biocontrol, needs to have clear advantages over existing technologies and minimal negative environmental and/ or economic consequences. While acknowledging that any technology needs to be safe, generally acceptable to the wider community, and not inhibit trade, stakeholders identified that any investment in new technologies for vertebrate pest control was also required to show increased efficacy and humaneness over current techniques (Push Factors, Table 3). These participants also unanimously identified having 'proof of concept' in a vertebrate as being a clear driver for further investment in genetic biocontrol technologies.

Table 3: Themes emerging from structured workshops describing the environments in which decision-makers work (this table first appeared in Carter et al. 2021, in prep).

INVESTMENT DECISION-MAKING ENVIRONMENT	
Push Factors (towards investment in genetic biocontrol)	Proof of concept; species specificity
	Established social license
	Better than current methods; affordable
	Realistic time frame
	Demonstrable effectiveness, safety, conformity
Pull Factors (away from investment in genetic biocontrol)	Effects on market access; international trade implications
	Negative community perceptions
	Loss of confidence in reliability and transparency of data
	Flow-on ecosystem effects
	International mistakes (herein)
	Organised opposition
	Uncertainty: who is investing; is it a national priority
	Fragmented policy and regulatory framework
Current Reality	Opportunities for co-investment and partnership
	Dynamic funding schemes
	Animal welfare priority
	Balancing alternative control options
	Well-defined pathway to impact
	Program and strategy alignment
	Alignment with sustainability goals and industry profiles
Deal breakers/Game changers (factors that would be considered unacceptable and likely to derail investment efforts)	Trade insecurity or market blocks
	Evidence that undermines stakeholder confidence
	Impacts on charismatic non-target species
	Radical failure – environmental escape; ecosystem decline

5.3 Proof of Concept

There was a shared understanding by stakeholders that it is was necessary to invest early funding into research and development of genetic biocontrol, even if the focus was not on the participants preferred species. Importantly though, stakeholders wanted to see a clear pipeline from model animal laboratory studies to real world implementation in other pest species, e.g. a 5–10-year strategy. This was commonly expressed by Australian terrestrial conservation organisations who consider feral cats the greatest pest threat but not the ideal animal model for proof of concept. Industry and NGOs indicated willingness to invest in promising technology provided a clear pathway to real world application was evident. A pipeline needs to include explicit stage gates for investment/research decisions along the length of the development process. With this in mind selection of the appropriate model organism is a critical aspect of this overarching strategy.

Workshopping the applicability of Genetic Biocontrol Technologies to vertebrate pest species in Australia:

A total of seven individual pest species scenarios were developed prior to Workshop 1 as a result of an online survey (November 2019). These scenarios served to focus discussion on individual species' contexts, harnessing specific expertise and interests in the room. Short descriptive narratives outlining the 'invasive species problem' in relation to key biological, ecological, and economic cost considerations to environment and industry were created. The species for which scenarios were developed included: carp, feral pigs, cane toads, foxes, rodents, feral cats, rabbit, and invasive pest birds. (Appendix 3 contains the scenario narratives developed for each species).

Rodents and rabbits were overwhelmingly selected as the best candidates for genetic biocontrol technology development with the commonly cited reasons being: species impact, fecundity, existing knowledge about species' biology, and laboratory/controlled trialability. Various social, technical, business and ecological imperatives were weighted differently for different species depending on their impacts. Rodents received the most selections (sum=73) particularly for technological development (n=26) and business case (n=22). Second ranked were rabbits (n=55) with most selections for business case (n=24) and ecological imperative (n=18). Third was carp (n=51) with most selections for social acceptance (n=16) and technological development (n=16). Fourth was cane toads (n=41) with most selections for social acceptance (n=21) and technological development (n=10). The fifth ranked species was feral cats (n=21) with most selections for ecological imperative (n=12). The remaining species of foxes (n=4), pigs (n=3), birds (n=0) and none (n=0) had very few selections (Figure 6).

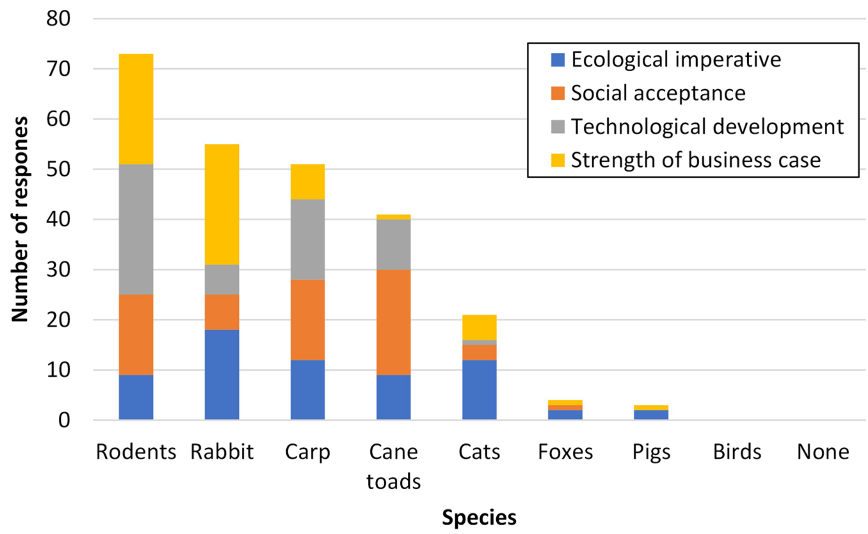

Figure 6: Prioritisation of pest species for focus of genetic biocontrol research across four dimensions of issues (ecological imperative, social acceptance, technological development and business case). Workshop participants (n = 36) selected two priority species for each issue. Each bar represents the sum of selections by workshop participants for each issue.

While feral cats were regarded as Australia's most intractable environmental vertebrate pest, the association of domestic cats with humans is likely to be perceived as a relatively more difficult barrier in terms of social acceptability (cf. Mankad et al. 2019). Conversely, stakeholders considered carp and cane toads as good model candidates for genetic biocontrol technologies research, thus providing a steppingstone in the process for gaining social acceptability for the technology. Carp and cane toads are also small, easily housed, and have had recent investment in genetic research and development. Above all though, rodents (and rabbits to a lesser extent) ranked highest as the preferred model species for developing 'proof of genetic biocontrol technologies concept'. These species are also small, easily housed, have fast generation times, with existing knowledge of their genome/genetics, biology, ecology, and have environment and economic impacts throughout their invasive range (e.g. Campbell et al. 2019, Goodwin et al. 2019, Long et al. 2020).

Development of GBT will be facilitated through coordinated implementation of a Science Roadmap that takes into account current national and international investments in this area, differences in appetite and funding sources by various private and public stakeholders, and the science knowledge gaps that need to be filled in the journey from technology proof-of-concept to realistic implementation.

An R&D pipeline towards genetic biocontrol of key vertebrate pest species in Australia can be broadly divided into four phases for each target species of interest:

- Proof of concept in a model animal species;
- Acquisition of essential background data and closing of knowledge gaps for the target species;
- Transfer of the technology to the target species; and
- Implementation and rollout, with all elements accompanied by ongoing engagement with regulators and relevant key stakeholders including the public.

Effective genetic biocontrol approaches have not yet been demonstrated for vertebrate species. Work is currently underway in Australia aimed at demonstrating proof of concept of genetic population control in zebrafish (as a fish model species) and laboratory mice (mammalian model system). There is broad agreement that the successful demonstration of this technology in vertebrate model species is a prerequisite for potential future development and application of this technology to control other high-profile mammalian pest animals such as rabbits, feral cats or foxes, or pest fish like carp or tilapia. The immediate (next 5 year) R&D strategy into genetic biocontrol therefore needs to focus on facilitating the delivery of proof-of-concept in the respective model species (Figures 9a & b, phase 1a), while at the same time providing essential underpinning background data for other target species (Figures 9a & b, phase 1b).

5.3.1 Model species

Selection of the most appropriate model system hinges on two critical features (i) the availability of techniques for building and introducing a genetic biocontrol tool into the germline of the species, and (ii) the generation interval of the species (i.e. the time it takes to reach sexual maturity and thus pass on and/or show the functional control trait; Figure 7). For these reasons the mouse is an ideal model system in which to develop and assess genetic biocontrol systems since it has been a leading model organism in the field of animal biotechnology (Roenthal and Brown 2007). Their age to sexual maturity is 6-8 weeks (Silver 2001), so it is possible to incorporate several specific genetic constructs in mice to create lines of mice for cross breeding and assessment within the space of a year. This short generation interval enables the development of experimental protocols for population studies that follow the transmission and effect of introducing a single or small number of mice carrying the genetic biocontrol tool. Similar studies in insects have been able to demonstrate successful spread and the biological effect of genetic biocontrol tools (Kryou et al. 2018).

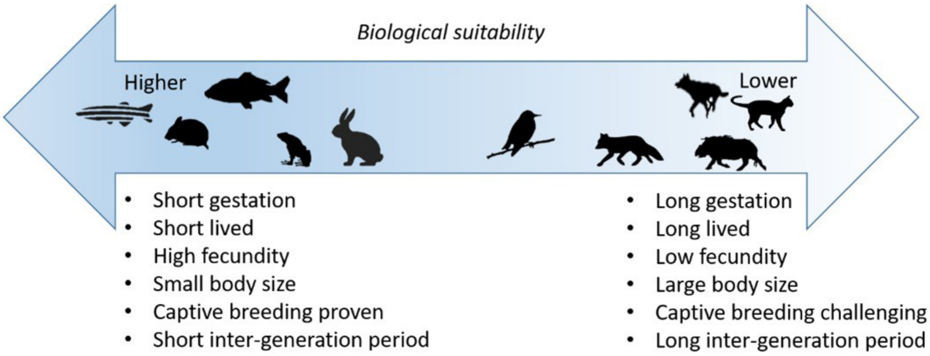

Figure 7: Species that rank highly as proof-of-concept 'model animals' for the initial demonstration of genetic biological control technology in a vertebrate, are not necessarily those with the highest ecological and / or social imperative for the application of new technologies to aid management. Rather, appropriate model species will be those whose reproductive biology and captive keeping requirements are conducive to successful demonstration of genetic biological control technologies in a laboratory setting.

Zebrafish also represent an excellent model system for genetics in vertebrates (Holtzman et al. 2016). Generation interval is similar to mice (10–12 weeks), enabling assessment of biological outcomes and efficacy of any genetic biocontrol tool(s). Translation to a target species is close in relation to invasive carp in the Murray–Darling Basin catchment (and some other regions) as both are cyprinid fish. However, the generation interval for carp, though it can be as a little as 1 year, is generally reported to on average 3–5 years in the wild. Genetic systems for manipulation of carp are not well developed, but a genome sequence is available and technical feasibility is high.

Research and development into development of genetic biocontrol technologies has commenced in Australia under various funding initiatives. Table 4 outlines known funding into Genetic Biocontrol Technology development.

Table 4: Current Funding into Genetic Biocontrol Technologies for vertebrate pests (this table is based on available information at the time the report is published and may not cover all relevant work currently underway in Australia).

Species target/ model	Description	Lead Institution/ Researcher	Funding	Investment	Date
Mouse (model)	Homing gene drive development (fertility)	University of Adelaide / P Thomas	ARC	$427,000	2019-21
Mouse (model)	X-shredder development	University of Adelaide/ P Thomas	CSIRO CERC Fellowship	$360,000	Current
Mouse (model)	Development and modelling of gene drive strategies, including further X-shredder development.	University of Adelaide/ P Thomas	NSW Gov/CISS	$1,797,190	2021–2024
Mouse (model)	Development and modelling of gene drive strategies.	University of Adelaide/ P Thomas, P Cassey	ARC and CAGT Ltd	$1,092,000	2019–21
Mouse (target)	Mouse populations genetics	CSIRO / P Brown	GRDC	$515,081	2020–2023
Mouse (model/target)	Small animal CRISPR genome editing facility for research in health, biosecurity and agriculture	CSIRO/ F Delerue	CSIRO appropriation	$272,727	Current
Mouse (model/target)	Base-editor control method development	Macquarie University/ M Maselko	CSIRO appropriation	$50,000	2020–2022
Zebrafish (model)	Self-stocking incompatible male system	Macquarie University / M Maselko	CISS	$341,803	2020–2022
Zebrafish (model) European Carp (target) Cane toad (target)	Development of strategies for gene drive	University of Melbourne/ S Frankenberg	DAWE	$1,390,545	2021–2023
Rabbit (target)	Wild rabbit population genomics, Gene Drive Utility and Risk Determination Pipeline	CSIRO/T Strive	MLA/ CSIRO	~$160,000 (embedded in larger rabbit biocontrol pipeline project)	2020–current
Rabbit (target)	Assessing Sperm Transfection Assisted Genome Editing for rabbits - pilot	CSIRO/C. Cooper, R. Hall	CSIRO appropriation	$15,000	2020–21
Rabbit (target)	Development of strategies for gene editing	University of Melbourne/ S Frankenberg	Foundation for Rabbit Free Australia	$20,000	2021–2023
Cane toad (target)	Deletion of toxin activation and fecundity	CSIRO/ M Tizard	CSIRO R+ Fellowship	$450,000	2016–2019
Cane toad (target)	Development of gene inactivation technology	CSIRO/ C Cooper	CSIRO appropriation	$35,000	Current
All Species	Social science: acceptability of technology solutions	CSIRO / A Mankad, L Carter / E Hobman	CSIRO appropriation	$415,000	2018–2019
Cane toad, possibly more	Development of genome assets for gene drive evaluations	CSIRO/T Walsh, R Rane	ARDC /CSIRO/various	$50,000	2021–2023
Ship rat	Development of genomic resources for ship rat research	CSIRO/O Edwards	PFNZ	$200,000	2018–2020
			Funding Total to Date:	**$7,341,346**	

5.3.2 Target species

While initial advances in development of genetic control systems will focus on model systems, further work to increase biological and ecological knowledge in other target species with high impacts should continue. The list of Established Pests of National Significance includes rabbits, foxes, cats, cane toads, pigs and rodents on islands, all of which have current Threat Abatement Plans in force. Implementation of genetic biocontrol in target species requires key knowledge gaps to be closed. These include understanding of gene flow, density dependant reproduction, mate selection, age and sex-specific fecundity and the impact of geographic and climate factors. There is also a requirement for a reference genome, population genomics data and artificial reproductive techniques to be established in order to enable integration of the genetic tool (Figure 8). Research supporting the development of virally vectored immunocontraceptive strategies have generated foundational knowledge in the ecology and reproductive biology for a few key species that are still relevant within current management strategies. Stakeholder investment will be needed to support research that will fill key knowledge gaps in the development of genetic biocontrol strategies. Such data will also provide valuable insights to enable better use of current control measures and may reveal new opportunities and strategies.

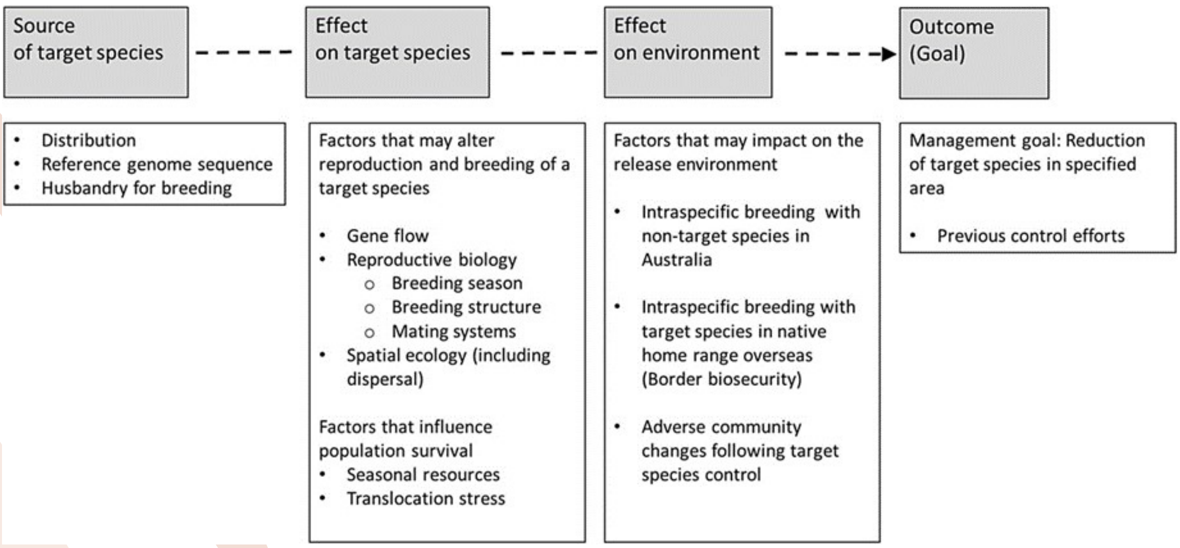

Figure 8: Conceptual model to illustrate the types of biological information required to reduce gaps and uncertainty about the spread and persistence of a gene drive construct focusing on invasive species management. From: Moro et al. (2018) Global Ecology and Conservation 13.

It is clear from the priority analysis that the key species on which to focus fall into two categories. For mammalian pests, the mouse is an obvious model species for pest rodents (and potentially other mammals). Research pathways are already established, and rodents are a target species with both economic and ecological drivers and there is the added benefit of international collaborative networks already in place (GBIRd https://www.geneticbiocontrol.org/). An early target mammalian species could also be rabbits as they have similar life-history strategies to rodents (short-lived, high fecundity), are easily kept in captivity, have had previous investment in field and genetic research and have a high economic and environmental imperative for their control (Figure 9a). For aquatic pests, the zebrafish is a closely related model for the carp target species, with advanced knowledge of the species' genetic system (Figure 9b). In addition, recent advances have made the cane toad a model system and a target species, with notably high public acceptability for this technology for use with this pest.

In addition, such data will increase our understanding of the pest species, their demographics, reproductive strategies, migration patterns and possible source and sink populations. Such research therefore constitutes a relatively risk-free investment that will provide valuable additional resource to improve the current conventional management strategies, even if a decision was made to not proceed with genetic biocontrol strategies for a particular species.

However, if proof of concept was achieved in the model species, work could immediately proceed to the next research phase (Figures 9a & b, phase 2, 5-10 years) transferring successful genetic biocontrol designs into the target species, prior to entering the final implementation and impact assessment phase (Figures 9a & b, phase 3, 10-20 years). Any pathway to deployment will likely include 'contained' population-level trials that will be subject to OGTR regulation. Such trials will require highly secure containment facilities that may not currently exist. There is merit in considering offshore islands as 'final trial' or 'first deployment' locations that minimise the any potential spread of GMOs but this will require considerable stakeholder engagement.

Monitoring of genetic biocontrol technologies post deployment

Should an effective genetic biocontrol technology be generated it will have to undergo rigorous contained field trials. This will be a requirement to pass through the various stages of regulation and to gain the appropriate approvals and licences before making a transition to a viable control system for any given pest animal. The characteristics of genetic biocontrol systems and both the scientific and community expectations related to the balance of effectiveness and containment, make it highly likely that the LMO concerned would have to be released in significant numbers and on repeated occasions. This would serve two purposes: (1) to determine the impact of the release on the local level of the specific pest animal; (2) to monitor the location, prevalence and density of the LMO in the environment.

In addition to the monitoring of goods originating from agricultural businesses that choose to use genetic biocontrol technologies, and/or adjacent properties or districts, it will be important to demonstrate the containment of LMOs to the area in which a genetic biocontrol technology is deployed. This will be tightly linked both to post deployment monitoring and to the overlay of geospatial modelling that is used to predict the movement of the LMOs and genetic biocontrol technology post deployment. The overarching objective of the technology is to suppress population expansion of the target species to the point at which the technology self-limits (i.e. the point of local extinction). However, current mouse population modelling has been conducted over time periods that demonstrate that the target species (and therefore LMOs) may be present at harvest and potentially during storage, hence the need for residue analysis. But those models can predict with confidence, how and where the organism is likely to spread. Well-designed post deployment monitoring would include boundary assessments to give clear parameters to defining assurance of geographic containment of LMOs.

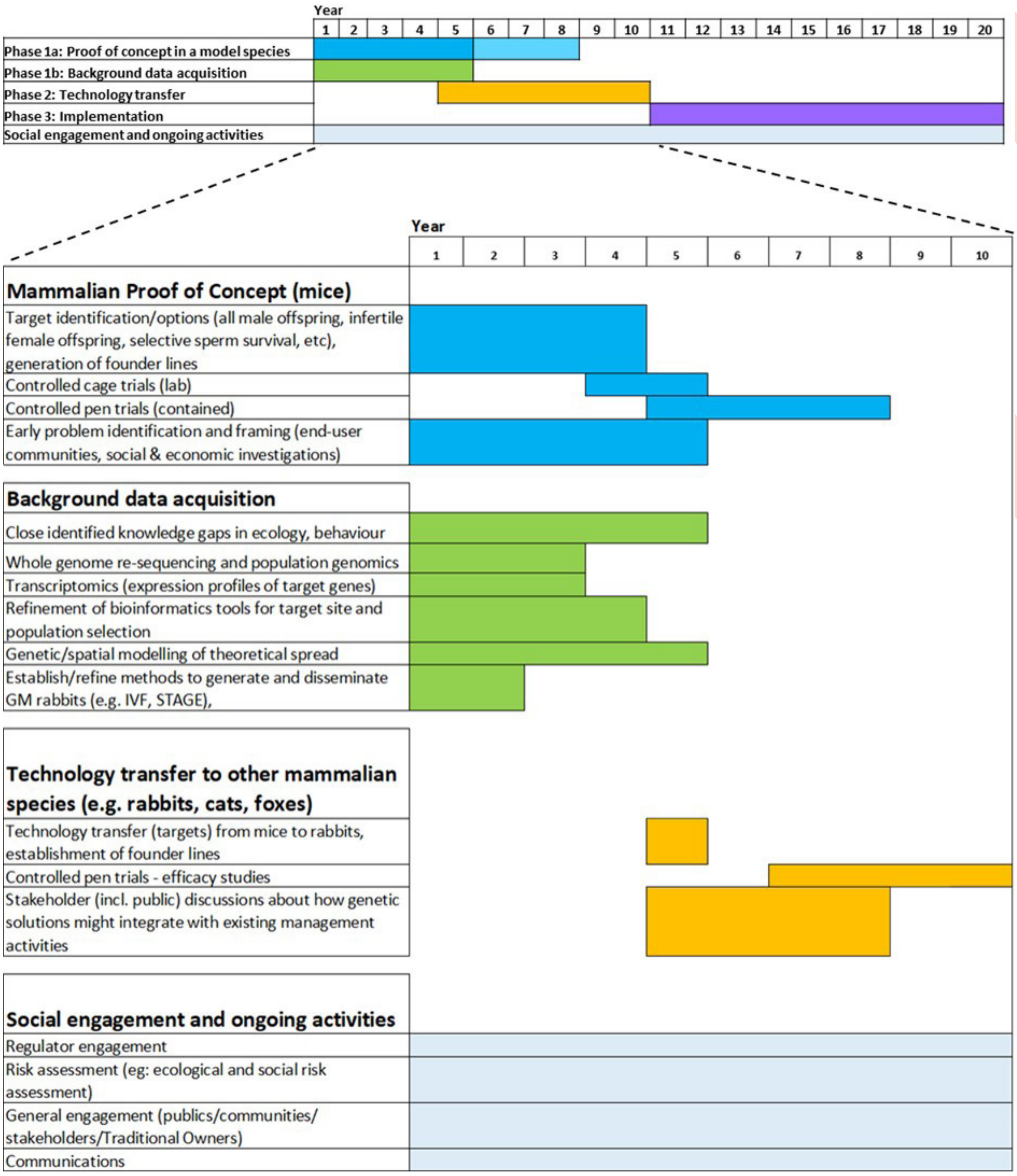

Figure 9a: Broad outline of a potential Roadmap for a mammalian genetic biocontrol.

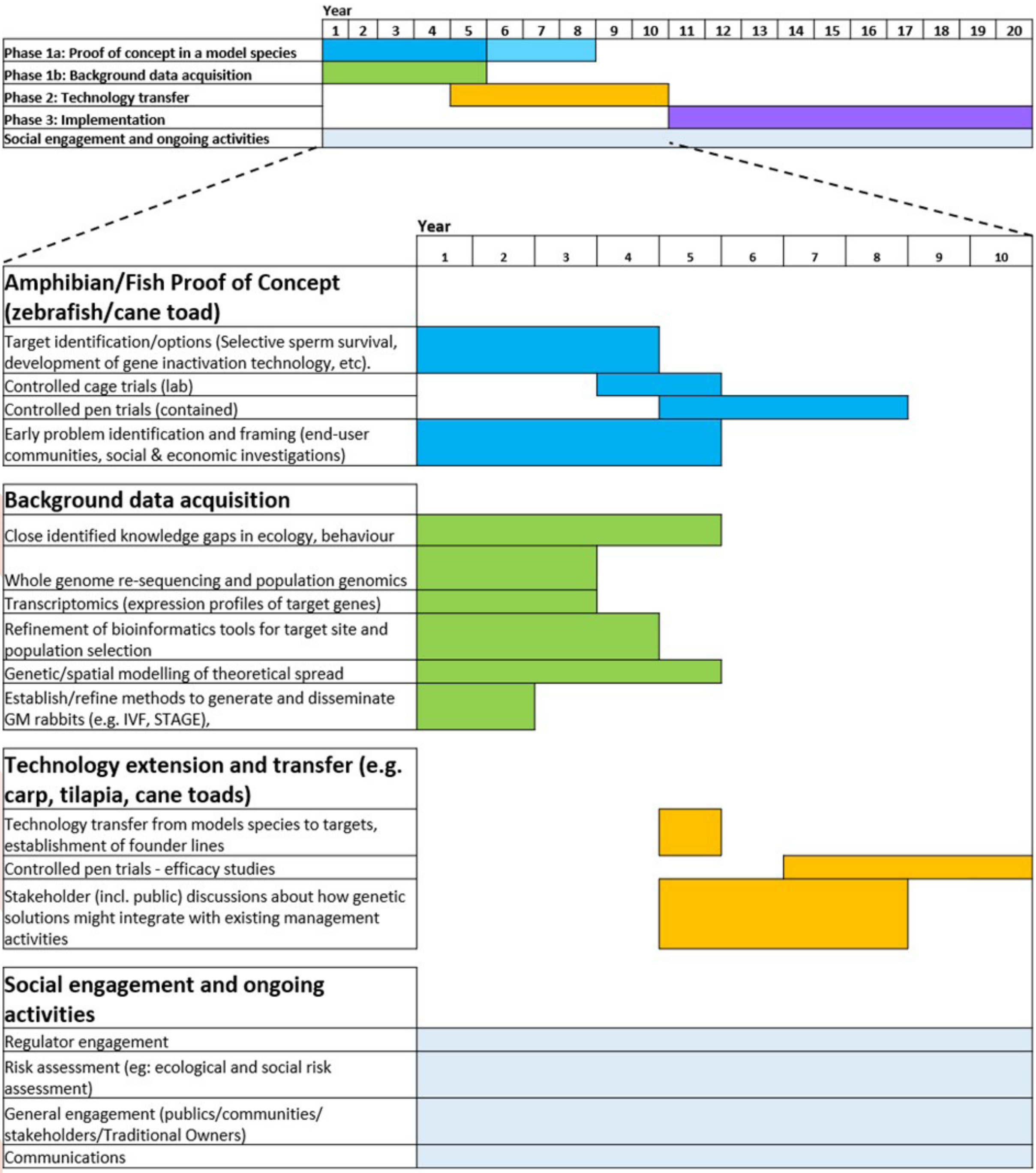

Figure 9b: Broad outline of a potential Roadmap for amphibian/fish genetic biocontrol.

Summary Point 3:

Establish a clear pipeline from animal laboratory studies to real world implementation of genetic biocontrol technologies that will guide and focus the efficient development and implementation of technologies and prioritisation of target species.

5.4 Governance

Clear and transparent governance of any genetic biocontrol technologies development was a recurring theme with stakeholders. Perceptions of fragmented policy and regulatory frameworks stem from the multiple departments/states/NGOs involved in managing pest animals with seemingly minimal integration in some instances. There are also several policy documents and council bodies (discussed in Section 1) relating to pest animal management, but none explicitly include policy on genetic biocontrol technologies.

Current work in the genetic biocontrol technologies space in Australia includes a wide range of researchers from numerous institutions, including academics developing proof of concept technology and modelling to landscape managers, and community organisations (e.g. RSPCA). Similarly, direct investment in genetic biocontrol technologies in Australia also originates from various sources, including the Department of Agriculture, Water and Environment, the Australian Research Council, CSIRO, CISS, and some universities (Table 4). However, additional research into the supporting information (population genetics, ecology, social acceptability, etc) is undertaken by a much larger group of stakeholders sometimes unknown to each other. In addition, there is a sizable international effort in the 'genetic biocontrol technologies' space particularly targeting rodents (GBIRd, Campbell et al. 2019; Godwin et al. 2019) and social acceptability of genetic technologies more generally (https://research.csiro.au/synthetic-biology-fsp/public-attitudes/), demonstrating the global interest in this area. Some organisations may not have the financial resources available for investment in research, but would be invaluable in developing social/community acceptability (e.g. RSPCA).

With such a wide breadth of stakeholders with various interests in the development of genetic biocontrol technologies and a range of governing bodies (See Section 1) it would be beneficial to have a centralised system for oversight, coordination and communication among the parties and the wider community. Such a system, a 'Community of Practice', would be most effective if it was independent, included representatives from a wide range of stakeholder groups, and provided an accessible, respected repository of knowledge and clarity around regulatory processes and requirements. Ideally, such a community of practice would not duplicate existing authorities, but could be imbedded within a National government committee (e.g. Environment and Invasives Committee). This community of practice could build on the National coordination and strategic planning delivered through the Centre for Invasive Species Solutions Vertebrate Pests Genetic Biocontrol Steering Committee.

Summary Point 4:

Establish a governance structure to ensure clear oversight and national coordination of genetic biocontrol technologies investment, research, and development in vertebrate pests in Australia.

5.5 Other Considerations

There are other factors that need to be considered and acknowledged within this discussion. The workshop participants noted that there will always be competing resource demands placed on organisations undertaking pest animal management (e.g. bush fires, climate change impact mitigation, exotic disease or other biosecurity outbreak(s) and changing priorities when managing multiple pest species. Various organisations also have differing priorities, timelines for investment and risk appetites that need to be considered (Figure 8). There is also an immediate ongoing obligation to control pests until new technology is available. The operational use of any genetic biocontrol technologies for vertebrate pest animals is a long way away (>10 years, perhaps many more) and some pest species may not be amenable to genetic biocontrol technologies because of their life history strategies or community aversion to use in some species. Therefore, it is imperative that research and development of other alternative, innovative control measures continue (e.g. fertility control, virus-based methods, etc). In addition, Australian genetic biocontrol technology researchers should heed lessons learned from international colleagues. Any major failures could dull or stop stakeholder interest/investment in this technology, affect social acceptability and consequently sway governments willingness to invest in the technology. Public rejection of this technology would affect government investment.

Several non-government organisations (NGOs) have raised concerns about research into an application of gene drive technology in the open environment. These concerns have been taken to both the Conference of the Parties to the Convention on Biological Diversity (CBD COP) and the International Union for the Conservation of Nature (IUCN). There have been efforts at these meeting to instigate a moratorium on all gene drive research. To date this has not been successful. For example, the CBD COP rejected a request for a moratorium in Egypt in 2018 (Callaway 2018). The IUCN recently adopted Motion 075—"IUCN Principles on Synthetic Biology and Biodiversity Conservation" (2020) the key take home message of which are: Case-by-case [analysis] decision making; Staged assessment of risks and benefits; Governance; Knowledge gaps and research needs; and knowledge transfer and capacity building. Conversely, the international NGO, People for the Ethical Treatment of Animals (PETA), have come out publicly to support genetic biocontrol technology for mouse control (https://www.peta.org.au/news/mice-bio-control/).

Much of this is considered in two key publications from National Scientific Academies, demonstrating a broadly consultative considerations weighing up the major opportunities and concerns arising from this emerging technology. The first was Gene Drives on the Horizon (Collins et al. 2016, National Academy of Science Engineering and Medicine) a substantial document that provided comprehensive coverage of the state of the reported literature and unpublished data and planning predominantly in the US. The second was a more focused document commissioned by the Australian Council of Learned Academies with the objective of understanding the implications of the emerging gene drive technology for pest and environmental issues of concern to Australia (Synthetic Gene Drives in Australia; implications of emerging technologies; Hoffman et al. 2017, Australian Academy of Science).

5.6 Summary

In addition to addressing safety and trade concerns, stakeholders articulated a need for demonstrable efficacy as a condition for investment in genetic biocontrol technologies. Particularly critical was evidence that proposed genetic biocontrol technologies will provide improvements over existing conventional control methodologies with respect to costs and management outcomes. Other aspects of efficiency that were deemed as favourable for a potential genetic biocontrol technology included relatively long-lasting controls of pest populations, and techniques that did not require large-scale release of modified organisms. Participants sought a clearly defined pathway with a defined timeframe to a mature product in addition to rigorous pilot studies that could demonstrate proof-of-concept. However, only a limited number of stakeholders expressed willingness to invest in early research and development required for such proof-of-concept studies in genetic biocontrol technologies. We emphasise that the framework presented in this document, is built around opinions / advice that represent a snapshot in time (December 2020) of a subset of potential stakeholders and that the issues identified here-in may change (in type, magnitude, priority etc.) over time.

6 CONCLUSION

Current conventional pest control methods have failed to prevent the substantial economic, environmental and social impacts from vertebrate pests across multiple jurisdictions. Therefore, there is a clear need to support new research and development programs that aim to deliver innovative, transformational, effective, and acceptable methods for established vertebrate pest management. Genetic biological control technologies strive to achieve this by altering the genes of an organism to enable effective pest control over potentially large, landscape scales.

However, whilst the potential exists for genetic biocontrol technologies to deliver a game changing advantage to vertebrate pest managers, successful development and implementation of the technology hinges on a number of critical factors. Targeted engagement with key stakeholders highlighted important factors that influenced their level of support for genetic biocontrol technologies. These include, demonstrating the safety and efficacy of genetic biocontrol technologies (e.g. ability to contain a release, species-specificity), and extrapolation and modelling of data from laboratory studies of model vertebrate species. Learning from and incorporating international research findings, will further help to build both stakeholder and public confidence in the safety and efficacy of the technologies within Australia.

Public engagement and the communication of genetic biocontrol technology science should commence immediately and continue throughout the duration of all phases of genetic biocontrol research, development and implementation. Such programs should recognise that public 'acceptance' itself may not be the ultimate end goal and that pursuing outcomes that more broadly reflect public tolerability towards innovative solutions, or seeking to genuinely engage affected groups in dialogue, are more likely to build trusted relationships with segments of society.

Successful development of genetic biocontrol technology will inevitably lead to the animals being classified as living modified organisms (LMO or genetically modified organisms, GMO). As such, appropriate regulation, licencing and risk assessment will be brought to bear and must be addressed before any release of modified animals. Importantly, post-deployment monitoring of the modified animals and any associated genetic biocontrol technology contaminants, will be necessary to assure Australia's trade security.

Whilst the case for vastly improving vertebrate pest management in Australia is strong, new advances, including genetic biocontrol technology, must have clear advantages over existing technologies. Currently, the level of interest and support for genetic biocontrol research and development favours the pursuit of ongoing collaborations across a variety of disciplines (e.g. genetics, ecology, social science, communication, policy and regulation). Co-ordination of this multi-disciplinary work would benefit from the formation of a centralised system. Such a system could provide an independent source of governance and knowledge.

Australia has an enviable environment for development of genetic biocontrol technologies that provides a clear advantage for significant progress in coordinated and integrated advancement in the major factors applicable to development of this technology. This is due to our excellent scientific technical capability, an established risk assessment community, a society that is able to be engaged, and a strong demand for applications given the scale of vertebrate pest impacts. Establishment of a decision and implementation framework with agreed approaches to further development and strong investment in a science roadmap, will realise these current advantages and unlock the significant potential for major advances in genetic biocontrol technologies for vertebrate pest management. This will ultimately deliver substantial economic, environmental and social benefits to Australia.

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8 GLOSSARY

APAS — Australian Pest Animal Strategy

APVMA — Australian Pesticides and Veterinary Medicine Authority

CISS — Centre for Invasive Species Solutions

CRISPR — Clustered Regularly Interspaced Short Palindromic Repeats

CRISPR-Cas9 — CRISPR associated protein 9 - gene editing tool

CSIRO — Commonwealth Science and Industrial Research Organisation

DAWE — Department of Agriculture, Water and Environment.

DJPR — Department of Jobs, Precincts and Regions

DNA — Deoxyribonucleic acid

DPI — Department of Primary Industries. New South Wales

DPIRD — Department of Primary Industries and Regional Development, Western Australia

EIC — Environment and Invasives Committee

EPBC — Environment Protection and Biodiversity Conservation Act 1999

FAO — Food and Agriculture Organisation

GATT — General Agreement on Tariffs and Trade

GBT — Genetic Biocontrol Technologies

GMO — Genetically Modified Organism (equivalent to LMO)

GRDC — Grains Research and Development Corporation

IAS — Invasive Animal Species

IGAB — Intergovernmental Agreement on Biosecurity (Australia)

IPAPF — Invasive Plants and Animals Policy Framework, Victorian Government

ISPM — International Standards for Phytosanitary Measures

IUCN — International Union for Conservation of Nature

LMO — Living Modified Organism (equivalent to GMO)

MLA — Meat and Livestock Australia

NBC — National Biosecurity Committee

NGO — Non-government Organisation

OGTR — Office of the Gene Technology Regulator.

PCR — polymerase chain reaction: test to detect genetic material

RHD — Rabbit Haemorrhagic Disease

RNA — Ribonucleic acid

RSPCA — Royal Society for the Prevention of Cruelty to Animals

SPS — Sanitary and Phytosanitary Standards

TBT — Technical Barries to Trade

VVIC — Virally-vectored immunocontraceptive

WTO — World Trade Organisation

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10 APPENDICES

Appendix 1: Genetic Technologies for Vertebrate Pest Management Workshop Program (Workshop 1)

Monday 10 February 2020

(Waterhouse Theatre, Building 101, CSIRO Black Mountain, Canberra)

TIME	TOPIC
8:30-9am	Coffee and Registration - QR code/weblink for Zeetings link will be available
9.00-9:30am	**The Workshop Frame** • Welcome and Introductions – Project team *Purpose: Set up the context for the day and outline the purpose and nature of this workshop including Research Ethics Consent for Participation.* • Connecting individuals *Purpose: Inviting participants to connect around what has piqued their interest in being at the workshop.*
9.30 – 10.30am	**Scene Setting Talks** *Key topics surrounding pest animal management, genetic technologies and social attitudes, then explore the issues/opportunities at the intersection of the topics* 1. Vertebrate Pests in Australia – challenges and opportunities 2. Genetic technologies and Regulation considerations 3. Social Attitudes to genetic technologies 4. Vertebrate Pests in Australia: preliminary survey findings
10:30	**Morning Tea and Panel Discussion** *Q&A conversation with the speakers that responds to questions raised via Zeetings from Scene Setting Talks.*
11-12:30pm	**The Risks and Benefits of genetic biocontrol** *rotating small group planning/discussion*
12.30-1:30pm	**Lunch Break**
1:30-3.00pm	**Scenario planning for the future** *Explore real investment opportunity where Genetic Technologies could be deployed. Small group planning/discussion.*

Time	Topic
3.00-3.15pm	**Afternoon Tea**
3.15-4.00pm	**Gallery tour of Scenarios** *Purpose: Connect with varying scenarios and offer diverse input*
4.00-4.30pm	**Wrap up and next steps** - how will data/insights be shared - next steps/actions - further workshops/research methods

Appendix 2: Decision Making processes for investment in genetic biocontrol - Program (Workshop 2)

Date 8/12/2021

(Online — 2 Zoom workshops, am and pm)

TOPIC	DETAIL	METHOD	TIMING
Arrival and Zoom support	Online support for people coming in –explain break out/use of chat/screen/ capture of data share etc	Plenary	5 mins
Introduction and welcome	• Acknowledgement of country • Welcome and purpose of the workshop • The value of the workshop for the project team and for invitees. – The workshop flow and how we will work in the virtual platform method – Outline research ethics considerations as it applies to the workshop	Plenary Plenary Plenary	3 mins 2 mins 2 mins
Scene Setting **–** what's the problem GT is looking to solve	• Insights and learning from the first workshop: – what we heard, what we learnt, what surprised us – what we better understand now about the potential role Genetic Biocontrol technologies might play in management/eradication of invasive species including target potential species. • Our assumptions on how decisions are made in addressing the current invasive species problem. • The idea: Genetic Biocontrol Technologies– an understanding of the tech and potential application to resolve the various problems with current methods (using `examples of various species).	Conversational presentation	**15 mins** <7 mins + 8 mins Q&A
Resolving current pain points Current decision making practices	BREAKOUT: Separate into smaller groups. (Breakout rooms) Work through the Decision Making Canvass PLENARY: Invite one participant to share their observations and insights	2 X Break out groups (inc 3-6 invitees)	**50 mins** 40 mins 10 mins
Genetic Biocontrol Technologies as an investment consideration Decision making factors	Separate into smaller groups (breakout rooms). Work through the GBT Canvass PLENARY: Invite one participant to share their observations and insights		**70 mins** 60 mins 10 mins
Close out	Wrap up and thank you.	Plenary	**5 mins**

APPENDIX 3: (PRE-DEFINED) PEST SCENARIO NARRATIVES USED IN WORKSHOP 1

Feral Pig Scenario

Scenario: Feral pig (*Sus scrofa*)

- Females and juveniles usually live in small family groups.
- Adult males are typically solitary.
- Sows begin breeding from 6–8 months, gestation 112–114 days.
- Produce two litters of 4–10 piglets (average of five) a year, in good conditions.
- Weaned after 2–3 months.
- High (10-100%) juvenile mortality, adults living up to five years.

Image by Steve Maxwell

Feral pigs are habitat generalists and are yet to reach their full range potential in Australia. In 2004, feral pigs were estimated to cause over $100 million damage annually to both agriculture and biodiversity across Australia. Feral pigs facilitate the spread of weeds and plant pathogens, damage crops, and cause habitat degradation due to their rooting behaviour and trampling of native vegetation. They also impact and degrade culturally significant sites, particularly those associated with riparian or wetland areas. Feral pigs also predate upon and compete with both livestock and native fauna. Feral pigs are capable of harbouring a range of exotic and zoonotic diseases, as well as transmitting numerous endemic diseases of agricultural and public health significance due to their unrestricted movement.

Current strategies for managing feral pigs are not adequate to address burgeoning populations of feral pigs throughout Australia. Genetic technologies to aid in the management of feral pigs have not yet been proven.

Feral Cat Scenario

Scenario: Feral cats (*Felis catus*)

- Predominantly solitary and nocturnal.
- Male cats tend to roam over larger range sizes compared to female cats.
- Feral cats can breed from approximately one year of age
- They have a short gestation period (65 days) resulting in up to three (average two) litters of 2–7 kittens each year.
- High kitten mortality, however, survivors can live up to seven years (average five years).

Image by Darren Marshall

Domestic and feral cats are the same species, differing only in terms of their level of domesticity. The species is considered one of the most threatening invasive species worldwide. Feral cats occupy over 90% of the Australian continent and are recognised by the Environment and Invasives Committee as an extreme threat category for Australia (the highest threat).

Predation by feral cats is a key threatening process listed under the Environmental Protection and Biodiversity Conservation Act 1999. Predation by feral cats has contributed to the extinction of at least 20 Australian mammal species and continues to threaten 75 critically endangered and near threatened mammal species, as well as 40 threatened birds, 21 reptiles and four amphibians.

Current strategies available for feral cat management are failing to negate the catastrophic impact this pest causes on native wildlife. Genetic technologies to aid in the management of feral cats have not yet been proven.

Fox Scenario

Scenario: European red fox (*Vulpes vulpes*)

Image by Sean Passarin

- Solitary by nature, exhibiting both monogamy and polygamy.
- High mortality (50–60%) within first year, average longevity approximately two years.
- Breed once a year, within family groups usually only dominant female produces a litter of cubs.
- Pregnancy lasts 51–53 days and cubs are born early Aug to late Sept.
- Litter size varies from 3 to 5 cubs per vixen with 85–97% of vixens pregnant each season in simple pair-mating systems.
- Young foxes typically disperse and are sexually mature by 9–10 months.

The European red fox (Vulpes vulpes) followed the rapid spread of foxes across the Australian continent in the later 1800s and is now a firmly established pest across the majority of mainland Australia and Tasmania. Foxes have long been recognised as a serious threat to native wildlife and as a damaging predator to small livestock industries. In 2004, foxes were estimated to cause in excess of $227 million / year damage to agriculture and the environment.

Current strategies available for fox management are failing to negate the catastrophic impact this pest causes on environmental and economic assets. Research into immunocontraception of foxes has previously been undertaken; with one of the major challenges being management of the pest at landscape scales. Modern genetic technologies to aid in the management of foxes have not yet been proven.

Feral Rabbit Scenario

Scenario: Rabbits (*Oryctolagus cuniculus*)

- Can start breeding at ~four months of age.
- Gestation period of 28–30 days.
- Litter sizes of up to six kittens.
- Can mate the same day as giving birth, which can lead to several subsequent litters in a good season.
- High kitten mortality, survivors live to an average of ~five years.

As one of Australia's most damaging pests, rabbits cost agricultural industries >$200 million/year. They cause massive ecological damage by competing for resources and causing land degradation. Rabbits also help sustain large populations of feral cats and foxes, key drivers of mammalian species extinctions in Australia. Biological control of rabbits using viruses has been extremely successful over the past 70 years, however, viruses have not been a silver bullet and it is widely recognised that a pipeline approach of novel tools and strategies are needed for sustained continental-scale rabbit control.

Genetic biocontrol approaches aimed at biasing the sex ratio of rabbit populations have been suggested as part of this control pipeline for ongoing suppression or possible eradication of feral rabbits from Australia. However, genetic technologies to aid in the management of feral rabbits have not yet been proven.

Rodent Scenario

Scenario: Rodents (invasive rats and mice)

- Small mammals, omnivorous with high rates of population increase and turnover.
- Can start breeding at ~three months of age.
- Gestation period of 21 days and litter sizes of up to 12 pups.
- Can mate the same day as giving birth, which can lead to multiple litters in a good season.
- Average field lifespan <1year.

Image by Julianne Farrell

Plagues of house mice (>1,000 mice/ha) cause enormous economic and social stress to rural communities in Australia. The mouse plague in 1993/94 caused about US$60 million in damage to crops, intensive livestock industries, and rural communities. In 1999, over 500,000ha of cropping land was baited with zinc phosphide for mouse control.

The house mouse and the black rat are identified as key threatening processes under New South Wales and Australian environmental legislation, for their role in the extinction of at least 20 species of birds, invertebrates and plants on Lord Howe Island. Introductions of rats on islands have caused ecosystems to breakdown, especially on Islands where species have evolved in the absence of mammalian predators. Rats disrupt ecosystem function through predation of animals and plants, which in turn can cause interruption of pollination, nutrient pathways, and seed predation, in some cases leading to forest collapse.

Genetic biocontrol approaches aimed at biasing the sex ratio of rodent populations have been suggested as part of possible eradication of feral rodents from islands. House mice, being the model laboratory animal, are currently being used to test genetic editing techniques though it has not yet been successful in the mammalian model.

Carp Scenario

Scenario: Feral carp (*Cyprinus carpio*)

- Carp cause major degradation to valuable river systems through their feeding habit of stirring up of mud.
- Ecosystem changes have catastrophic impacts particularly on native fish and waterbirds.
- Males mature at 2–4 years of age and females at 3–5 years depending on water temperature.
- A female of 4–5 kg, can produce 1 million eggs or more depending on fish condition, water temperatures and habitat quality.
- Mortality rates are high (>90%) in their first year.

Image by Peter West

Carp were first introduced to Australia more than 100 years ago and are now widely established throughout the Murray-Darling Basin. There are no native cyprinids in Australia. Their disturbance and re-engineering of waterway ecosystems causes silt and nutrient suspensions that blocks sunlight, impacting zooplankton and aquatic invertebrates that are critical food sources for native fish. The siltation also causes problems for essential irrigation systems and at times promoting dangerous algal blooms.

Current strategies of netting/trapping and commercial inland fishing for carp management are failing to negate the catastrophic impact this pest causes on native wildlife. A significant flow on effect of ecosystem changes is the impact on recreational amenities particularly for the recreational fishing industry that is worth billions of dollars.

Genetic technologies to aid in the management of carp are being investigated in the US as a potential strategy to mitigate environmental impacts but would need to be tailored to the particular conditions in the Murray-Darling Basin.

Cane Toad Scenario

Scenario: Cane toads (*Rhinella marina*)

Cane toads continue to spread across northern tropical Australia.

- Predators die due to unavoidable consumption of toxin in the toad's neck.
- Cane toads can breed from approximately one year of age.
- A single female can lay up to 30,000 eggs, and can breed twice a year, tadpole to adult survivorship is only 0.1-0.5% — but can still yield 30 new adults per cycle.

Image by Cathy Zwick

Cane toads were released around the east coast of Queensland in the late 1930s and radiated quickly through much of Queensland and New South Wales. They crossed into the Northern Territory and are now invading northern regions of Western Australia. The invasion zone continues to spread towards the west and south but is predicted to slow due to unsuitable habitat (temperature and water availability). However, this natural boundary may be affected by climate change and by genetic adaption of the toads (now being observed in toads from new vs. established invasion zones). Lost populations of predators (which can drop by up to 90% following a toad invasion) do not appear to properly recover over time, and local extinction events have been reported. Small native vertebrates (marsupial, reptile and amphibians) are impacted by loss of forage and territory, and through toad predation as they can also become prey to large adult toads.

Current approaches to cane toad control (e.g. fencing off water bodies, tadpole traps, toad-busting catches) are ineffective at scale. Genetic technologies to aid in the management of cane toads are in the early stages of being investigated and have not yet been proven.

Pest Bird Scenario

Scenario: Introduced invasive pest birds

Biology will vary, example below is for starlings:

- Typically, 2 but up to 3 clutches laid per year
- Average clutch size: 4–5, 60-70% fledgling success, ~50:50sex ratio [slight male bias].
- High juvenile (~60%) and adult (~50%) natural mortality
- Capable of very large (>100km) dispersal behaviour

Image by Peter Tremain

Pest birds, particularly European starlings, blackbirds and sparrows conservatively cause losses in excess of $313 million / year to agriculture (including horticulture) industries. This estimate does not include the substantial environmental and social impacts caused by introduced pest birds. European starlings alone, have the potential to cause $176 million / year losses to the Western Australian economy should the species establish to its full potential in this state. There have been notable advancements in the field of avian genetic technologies, primarily through research into the precision breeding of poultry for safe food production. The same, or similar, technology has potential to assist invasive pest bird management.

Group activity around pest species:

Q: How might we move forward with a genetic control approach for this pest? Below are some suggested discussion points

What do you think are the **key challenges** when considering a potential genetic biocontrol approach for introduced pest birds in Australia?	How might we overcome some of the **key challenges**? (listed at left).
How might we **deploy** genetic technologies to assist introduced pest bird management?	How might we **fund** the RD&E required to advance genetic technologies for introduced pest bird management?
(Counterfactual): If genetic biocontrol or other ground-breaking strategies were not implemented to control introduced pest birds, what would happen if we continued to rely on **current control methods**?	Other?
What are the biggest questions or gaps that need addressing?	

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