Framing Challenges and Opportunities for Canada

Expert Panel on Regulating Gene-Edited Organisms for Pest Control

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THE COUNCIL OF CANADIAN ACADEMIES
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This project was undertaken with the approval of the Board of Directors of the Council of Canadian Academies (CCA). The members of the expert panel responsible for this report were selected by CCA for their special competencies and with regard for appropriate balance.

This report responds to a request from the Sponsor, Health Canada's Pest Management Regulatory Agency, for an independent assessment. The Sponsor had no involvement in either panel selection or report development; any opinions, findings, or conclusions expressed in this publication are those of the authors, the Expert Panel on Regulating Gene-Edited Organisms for Pest Control, and do not necessarily represent the views of their organizations of affiliation or employment.

Library and Archives Canada

ISBN: 978-1-990592-30-0 (book)
978-1-990592-31-7 (electronic book)

This report should be cited as:

CCA (Council of Canadian Academies). (2023). *Framing Challenges and Opportunities for Canada*. Ottawa (ON): Expert Panel on Regulating Gene-Edited Organisms for Pest Control, CCA.

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This assessment was made possible with the support of the Government of Canada

The Expert Panel on Regulating Gene-Edited Organisms for Pest Control would like to acknowledge the First Nations, Inuit, and Métis peoples who have stewarded the lands now known as Canada since time immemorial.

The Council of Canadian Academies (CCA) acknowledges that its Ottawa office is located on the unceded, unsurrendered ancestral home of the Anishinaabe Algonquin Nation, who have cared for the environment of this territory for millennia. Though our offices are in a single location, our work to support evidence-informed decision-making has potentially broad impacts across Canada. We at the CCA recognize the importance of drawing on a wide range of knowledge and experiences to inform policies that will build a stronger, more equitable, and more just society.

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Expert Panel on Regulating Gene-Edited Organisms for Pest Control

Under the guidance of its Scientific Advisory Committee and Board of Directors, the CCA assembled the **Expert Panel on Regulating Gene-Edited Organisms for Pest Control** to undertake this project. Each expert was selected for their expertise, experience, and demonstrated leadership in fields relevant to this project.

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Message from the President and CEO

Environmental pests are ubiquitous and defined by human priorities related to agricultural and ecological sustainability, public health, and environmental stewardship, among others. Gene-editing technologies are being added to the pest management toolkit and may prove to be transformative. These technologies, which enable the alteration of pest-organism genomes, are promising but rapidly evolving, and face critical questions about their efficacy, safety, and appropriateness.

Genetic pest-control tools could dramatically shift our relationship with the environment, not only because of their potential impact on the ecosystem of which we are a part, but also because of their challenge to the social and cultural values that shape decisions surrounding their use. These issues call for urgent consideration: Climate change, expanded international trade, and resistance to conventional control agents have intensified existing pest problems and contributed to new ones, with wide-ranging implications for food security, public health, and conservation. Understanding how these tools might be used to mitigate threats—and under which circumstances they should not be deployed—should be part of any policy discussion.

Framing Challenges and Opportunities for Canada reviews the potential applications and impacts of genetic pest-control technologies, and the implications for research and development. It examines the roles that adaptive risk assessment and public engagement might play in anticipating and mitigating concerns raised by genetic pest-control approaches. The report maps the limits of Canada's current regulatory framework and envisions opportunities for a more holistic approach to regulating pest management—one that better prepares Canada for a range of eventualities and sets new standards.

I want to extend my appreciation to the Expert Panel, chaired by Dr. Bob Slater, for its thoughtful consideration of the issues and for the contribution to the public discussion this assessment will thoughtfully inform.

Eric M. Meslin, PhD, FRSC, FCAHS, ICD.D
President and CEO, Council of Canadian Academies

Message from the Chair

Gene-editing technologies present new opportunities for pest management at a time when globalization and climate change have intensified many pest-related challenges, and current pest-control methods have become less effective. In Canada, research activities dedicated to genetic pest management have been modest—limiting risk-assessment capabilities, inhibiting technological development, and fostering regulatory uncertainty.

The risks posed by genetic pest-control tools are environmental, social, cultural, ethical, and economic; assessing and managing them will require sustained public engagement with stakeholdersand Rights-holders. New pest threats occur with regularity; the rate at which they do is poised to increase as climate change shifts the major ecological zones in North America. The United States shares pest problems with Canada and is already investigating genetic pest control in earnest—a reality that underscores the need for comprehensive and regional approaches toward governance. A lack of experience risks a lack of preparedness.

Addressing deficits in research funding in Canada and gaps in the domestic regulatory landscape are critical steps needed to confront current and future pest threats. Careful consideration of each step of the regulatory lifecycle will be important, particularly given the need for flexibility and improved horizontal coordination. This novel technology will require adaptive regulatory practices and managed expectations, for when expected outcomes don't work according to plan—adaptation is critical. Success will hinge on greater collaboration across disciplines, departments, agencies, and governments; after all, ecological zones do not map neatly onto geopolitical authority structures. The weakest link in the chain will define the integrity of the system.

It has been a pleasure to serve as Chair of this Panel. I would like to thank my fellow Panel members for their contributions and thoughtful deliberations throughout the process, and the CCA team for their steadfast support. Finally, I would like to thank the sponsors for submitting this question and making our work possible.

Robert Slater, PhD, C.M.
Chair, Expert Panel on Regulating Gene-Edited Organisms for Pest Control

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Peer Review

This report was reviewed in draft form by reviewers selected by the CCA for their diverse perspectives and areas of expertise. The reviewers assessed the objectivity and quality of the report. Their confidential submissions were considered in full by the Panel, and many of their suggestions were incorporated into the report. They were not asked to endorse the conclusions, nor did they see the final draft of the report before its release. Responsibility for the final content of this report rests entirely with the authoring Panel and the CCA.

The CCA wishes to thank the following individuals for their review of this report:

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The peer review process was monitored on behalf of the CCA's Board of Directors and Scientific Advisory Committee by **Malcolm King, FCAHS,** Professor of Community Health and Epidemiology, University of Saskatchewan. The role of the peer review monitor is to ensure that the Panel gives full and fair consideration to the submissions of the peer reviewers. The Board of the CCA authorizes public release of an expert panel report only after the peer review monitor confirms that the CCA's report review requirements have been satisfied. The CCA thanks Dr. King for his diligent contribution as peer review monitor.

Acknowledgments

The Panel and CCA staff would like to express their sincere appreciation to the following people, who provided valuable input and support for this assessment: **Tanya Brigden,** PHG Foundation, University of Cambridge, and **Henry Lickers,** a Haudenosaunee citizen of the Seneca Nation, Turtle Clan. Dr. Lickers is a Canadian commissioner of the International Joint Commission and was the director and environmental science officer of the Mohawk Council of Akwesasne for 45 years.

Executive Summary

Gene-editing technologies are changing approaches to pest management. Rapidly evolving but unproven gene-editing tools could potentially mitigate the impacts of pests in public health, conservation, and agricultural contexts. The use of these tools, however, is accompanied by uncertainties about possible impacts on species and ecosystems, along with broader socioeconomic and cultural risks. Increased globalization and climate change are intensifying pest problems. These factors, combined with the waning effectiveness of many common pest-control tools, will contribute to growing pressure from both native and invasive pests if left unchecked. Opportunities to manage pests with greater effectiveness, lower costs, and increased safety therefore require consideration.

Gene-editing technologies introduce novel ways to alter the genomes of pest organisms. Current genetic pest-control approaches include precision-guided sterile insect technique and gene-drive technologies, but other approaches will soon follow with technological advances. Gene editing can be applied to a wide variety of species to impart a diverse set of traits. Before implementation can occur in pest-control settings, however, decision-makers will be tasked with addressing multiple unknowns. Questions remain about the efficacy of these tools, their safety, and their appropriateness: Will it be suitable to deploy gene editing in the natural environment and how will gene editing fit into the wider pest control toolbox?

To answer these and other salient questions, Canada will need to leverage expertise in research and development (R&D), and in society more broadly. Doing so will require investments to bolster capacity. Current regulatory frameworks and their risk assessment processes will require adaptations to meet the scientific and social challenges posed by gene-editing tools. Canada will also need to determine how its regulatory approach will align with international jurisdictions, particularly given the R&D leadership in this area by its closest neighbour and partner, the United States.

The Panel contends that Canada needs to be better prepared to tackle these questions. The lack of international clarity and the presence of uncertainty present an opportunity to establish a governance regime tailored to Canada and its national interests. The following report identifies what is currently known, what remains unknown, and what steps might be taken to guide the development and deployment of genetic pest-control tools in Canada. Using this report to inform next steps, Canada can establish regulatory structures that advance solutions to global challenges and serve as a model for other jurisdictions.

Answering the Charge

What are the scientific, bioethical, and regulatory challenges regarding the use of gene-edited organisms and technologies (e.g., CRISPR/Cas9) for pest control?

The design and use of genetic pest-control tools require multiple forms of expertise, including ecology, ethics, molecular biology, as well as knowledge from other scientific and non-scientific fields. A main challenge is identifying and coordinating this expertise and channeling it toward the development of new tools that rely on gene editing. It also remains unclear whether off-target effects or other long-term consequences resulting from gene editing will significantly affect the safety and efficacy of these products. In this respect, the evidence base is currently limited and will need to be expanded to identify the relevant strengths, limitations, and risks. However, given the characteristics of some of these tools (e.g., self-sustaining gene drives), the line between testing and open release becomes blurred, which puts emphasis on ensuring comprehensive risk management and biosafety practices.

A key ethical challenge in the use of genetic pest control is to determine when and whether these technologies should be used. Ethical issues also arise concerning how the technology is developed. How should humans intervene in nature? How might the use of genetic tools in one region negatively impact populations and ecosystems elsewhere? Is it being developed to give rise to public good? Some ongoing projects aim to address a public health crisis — malaria in sub-Saharan Africa, for instance — where existing tools are waning in effectiveness and lives are at stake. This work follows principles of responsible research and innovation by involving potentially impacted stakeholders in R&D, program design, and implementation. However, significant human and financial resources are required to develop genetic pest-control tools, and it remains to be seen whether these can be made viable. Lessons from earlier pest-control programs involving live organisms suggest that the non-profit and public sectors may play significant roles in translating this technology. Current initiatives in genetic pest control are being spearheaded by these sectors in order to tackle public health challenges and establish leading practices in public engagement in the process.

The regulatory challenges in genetic pest control are multifaceted. Gene-edited organisms may need oversight from multiple departments and agencies, and they could cross international borders while challenging paradigms in risk assessment. Examples of older technologies with a higher technological readiness level are already exposing the looming difficulties facing regulators. In the United States, for instance — as in Canada — products of biotechnology are generally regulated

as *products*, rather than according to the *processes* used to create them. This approach has been challenged in the case of genetically modified mosquitoes, due to a lack of jurisdictional clarity and uncertainty about how to conduct appropriate risk assessments. Risk assessment is essential in regulation, but lack of evidence and experience with these products has resulted in nonlinear paths through the regulatory apparatus. These challenges could be duplicated in Canada and it remains to be seen whether ongoing reforms might address them.

A larger domestic issue relates to the lack of relevant R&D in Canadian laboratories. Consequently, there is a dearth of experienced scientists who can participate in regulating these technologies. This may be addressed through investments in regulatory science, but it will also demand close collaboration with U.S. counterparts to ensure that lack of experience does not translate to lack of preparedness.

What is the current state of R&D and bioethics of gene-edited organisms for pest control?

Currently, there is a limited number of genetic pest-control technologies that are advanced enough to be involved in field trials. Nevertheless, proof-of-concept results have been demonstrated in a growing number of organisms, for both self-limiting (and therefore transient) as well as self-sustaining (potentially persistent) implementations. The persistence of a genetic pest-control tool, as well as other aspects of its design and application area, will greatly influence its potential for commercialization. Overall, technology translation faces several barriers to coordinate expertise, funding, and stakeholders in what remains a high-risk and costly investment. This is particularly true in Canada, where funding may be difficult to obtain — and relevant public funding sources difficult to coordinate — with implications for the training of highly qualified personnel vital to enabling progress. The science is rapidly evolving, and the diversity of target species and mechanisms of action is expanding through our increased understanding of gene editing and pest biology. Canada, however, is not currently among the countries where R&D is taking place intensively, which could limit internal capacity to explore potential solutions to pest problems relevant to Canada's national interests.

From an ethical perspective, efforts are being dedicated to the social and ecosystem impacts of the development and implementation of genetic pest-control tools. Given how these tools can dramatically shift human relationships with environments, critical examination is required when it comes to the practices that facilitate and restrict their use. Centrally, engagement with broader publics, including those typically excluded from such processes, has been raised as valuable in all stages of development and use. These complex conversations

pose numerous challenges and are guided by social and cultural values in different regions and contexts.

What are the novel hazards and risks to human health and the environment posed by the use of gene-edited organisms for pest control, including gene drives?

Gene-edited organisms, and those carrying gene drives in particular, present several risks. For one, it is possible that the resulting interventions are impossible or impractical to recall or reverse. Many risks associated with these technologies are common to earlier pest-control programs involving the release of live organisms. These include several environmental risks relating to efficacy and biosafety, but also novel social, cultural, and economic risks that may have been comparatively under-explored in earlier settings. Gene drives do, however, present certain unique risks relating to gene transfer and the possibility of gene drives becoming integrated into closely related or distant species following release. Unanticipated impacts could also arise because of limited experiences with the long-term consequences of gene editing; the associated risks can only be identified through empirical evidence, which is currently lacking. Other issues relate to long-term effects that might be impossible to isolate in controlled trials and, relatedly, effects linked to interactions within ecosystems that are impossible to replicate in controlled experimental environments.

Currently, implementations of gene drives have demonstrated that developers retain a level of control over the drive properties. As such, some risk mitigation approaches can be engineered directly into the design of the drive or the context of its deployment, for instance by ensuring that the drive is self-limiting. However, scenarios may arise where the most appropriate tool may be self-sustaining, such that exposure to novel risks is high. In this respect, it is important to be mindful of the context and objective about the intervention. In early stages, it will be crucial to adopt a case-by-case and adaptive approach to risk assessment. This approach could be tailored to account for an evolving evidence base, in order to provide a robust but proportionate level of risk management to avoid hazards.

What are the biodiversity and bioethical considerations of altering the genetics of, or eliminating, a wild pest/disease vector population? Are there potential implications for invasive species management and broader ecosystem benefits provided by pests?

The design of a pest-control program, as dictated by its objective and the nature of how gene editing is implemented, will heavily influence the implications for biodiversity and bioethics. Some genetic pest-control tools introduce a novel means for humans to intervene in the natural world, while others may resemble

(from a practical standpoint) existing pest-control approaches. The use of gene editing does, however, raise overarching questions. Established pest-control approaches such as the sterile insect technique already rely on the release of live modified organisms, but gene editing represents a more deliberate, controllable, and specific alteration of a wild animal. This distinction is more prominent in the context of gene drives, where inheritance is biased toward the desired gene edit.

Opinions on whether nature should be edited in this manner will be diverse and potentially polarized, and they may be impossible to resolve. Implementing these tools necessitates social consideration and negotiation specific to regions and contexts. In this respect, it will be crucial to bolster the evidence base to better ascertain the risks, benefits, efficacy, and cost-effectiveness of these tools. Staged testing will not address all these issues but is, at the minimum, a mandatory requirement to collect context-specific data that could support the use of gene-edited organisms; it will also allow for a comparison to alternative pest-control tools.

The undetermined effectiveness of many genetic pest-control tools in real-world applications complicates many of these discussions. Pest problems can be sudden and require immediate action. Particularly in the context of invasive species, the need to act swiftly may outweigh concerns surrounding risks. Although the discourse is, at times, directed toward specific extreme scenarios, such as self-sustaining thresholdless gene drives for suppressing pest populations, it remains to be seen whether such genetic constructs fulfill their designs in practice. Risks to biodiversity and ecosystems (e.g., food webs) are real but not *a priori* greater than they are for other biological control interventions. Lessons from integrated pest management stress that knowledge of ecosystems and pest biology greatly enhances success and can guide the effective combination of pest control tools. As such, high-risk gene-editing tools, in particular gene drives, require extensive comparative analysis against other control options before finalizing their use. Nevertheless, the risk of unanticipated effects resulting from the eradication of a pest using gene-edited organisms is a legitimate concern and underscores the importance of meaningful engagement and transparent decision-making.

What is the current regulatory landscape in Canada and internationally with respect to products of gene editing, including regulatory control of laboratory research on gene-drive organisms?

The state of preparedness of the current regulatory landscape for gene-edited organisms in Canada is currently low and may require proactive efforts to disentangle jurisdictional issues at multiple levels and bolster capabilities in risk governance. The statutory responsibilities of individual federal agencies dictate which among them will be responsible for regulating a given product. Although

the division of responsibilities in Canada is not as explicitly defined as it is in the *U.S. Coordinated Framework for the Regulation of Biotechnology*, a similar spirit exists to guide applications toward the appropriate regulatory body on a case-by-case basis. Experiences in the United States have highlighted several gaps in the standard assessment approaches used by regulatory agencies to deal with genetically modified organisms (GMOs) for pest control. Similar risks exist in Canada. The assessment processes for chemical pest-control agents, as well as those for biological control, possess vulnerabilities with respect to regulating the full range of prospective genetic pest-control products. In the United States, the Environmental Protection Agency has played a growing role in this area, and similar developments could occur at Environment and Climate Change Canada, notably depending on reforms to its New Substances program.

There is more to regulatory oversight than approval, however. In most pest-control contexts, the governance of these technologies will require the federal government to work closely with provincial and territorial counterparts, regional and municipal actors, and Indigenous Rights-holders. Several ongoing regulatory activities, such as monitoring and risk management more broadly, will demand shared resources and a need for proactive engagement and partnerships to proceed in areas of uncertainty and risk. Failure to do so could exacerbate the potential for political misalignments or create the perception of illegitimacy in oversight processes and jurisdictional responsibilities. Substantial attention has been paid to finding regional governance solutions in the context of malaria control in Africa in order to avoid these eventualities prior to the release of gene-edited mosquitoes.

Several relevant soft-law approaches for governance are also being proposed or operationalized at national and international levels. Individual tools, such as registries, standards, and testing guidelines, will assist in establishing a common language while enabling inclusive and transparent technology development. These could be very relevant to the Canadian context due to the lack of domestic R&D activities. International commitments, such as the *United Nations Declaration on the Rights of Indigenous Peoples* and the *Convention on Biodiversity*, are also salient to Canadian activities in this area. They define hard and soft requirements with respect to diverse issues, including transnational movement of modified organisms, access and benefits-sharing, consent, and intellectual property. These policy instruments and agreements could provide crucial guidance on gene-edited organisms and help define guardrails and promising practices on deployment and use, while the Canadian regulatory environment builds oversight capacity.

What are the lessons from previous approaches to risk communication, transparency, public consultations, and public confidence/engagement relating to regulation of similar products of novel technology (e.g., genetically modified crops), including experiences from other jurisdictions?

Public skepticism and concern around scientific technologies broadly, and GMOs specifically, may influence community perception of genetic pest-management programs, including political perceptions and regulatory burden. As gene-editing tools can have significant and unknown impacts on ecosystems — impacts that spread across jurisdictional borders — public engagement serves as an important tool to not only address public concern but also enable public participation in program design and implementation. Communication and consultation activities can offer value by carefully examining and engaging the unique and diverse publics that exist in each implementation context. Communication practices can be most effective when they accurately outline benefits as well as limitations of the technology, and when they are tailored to specific contexts. Consultation activities are meaningful when they include feedback loops that can influence policy directions.

There are additional opportunities, however, to imagine how broader public input can be used to strengthen programs and management processes. Throughout program design and implementation, commitments to increase public participation can bolster collaborative capacity. Such actions enable relationship-building, knowledge-sharing, and meaningful engagement according to ethical approaches. Public input may also offer value in increasing a program's effectiveness, as drawing from diverse expertise can help achieve a broader range of goals. Conducting public engagement begins by mapping out the various roles members of the public may play in relation to a pest-control program, and understanding how different forms of engagement, at different stages of a program, can be designed and used. In Canada, program stakeholders, community members and leaders, and — importantly — Indigenous peoples as Rights-holders require consideration through engagement activities. This can be assisted through the creation and use of advisory committees. Transparency, trust, reflexivity, and adaptability have been stressed as factors influencing program success and are highlighted as best practices. There is an opportunity for Canada to be a leader in advancing inclusive and sustained public engagement practices, which can be replicated by jurisdictions around the world.

Glossary

Adaptive regulatory practices and **adaptive management** are flexible approaches whereby emergent data and input are assessed on an ongoing basis, the result of which can modify previously established policies and strategic directions. One central component to adaptive regulatory practices and management includes enabling input from stakeholders with diverse expertise and perspectives (Kuzma, 2019; Kokotovich *et al.*, 2022).

Biosafety is the design and use of equipment, practices, and infrastructure that ensure protection from the unintended release of, or exposure to, biological hazards, toxins, or infectious agents (US HHS, 2017). Biosafety risks can be measured with levels, applied in correspondence to standards, and enacted with policies and protocols to ensure harm does not come to species or ecosystems (Emerson *et al.*, 2017; O'Brochta *et al.*, 2020; Millett *et al.*, 2022).

CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) is a group of identical repeats of DNA sequences interspaced by highly variable sequences found naturally in the genome of organisms such as bacteria and archaea as a defense system in their immune response (Al-Attar *et al.*, 2011). The combination of CRISPR with associated Cas proteins constitutes the CRISPR/Cas system, which is applied to gene-editing applications. For example, **CRISPR/Cas9** has been the subject of considerable interest and innovation for applications across several domains (Mali *et al.*, 2013). In this report, the usage of CRISPR denotes CRISPR/Cas systems generally, whereas the usage of CRISPR/Cas9 is specific to that gene-editing system.

Ethics are processes used to determine which actions might be right or wrong (e.g., acceptable or unacceptable, or just or unjust) for whom or for what, in which contexts, and under which conditions (WHO, 2021a). Broadly, ethical inquiries examine and evaluate the impacts of actions that have been taken or might be taken in the future (Preston & Wickson, 2019). Ethics can be informed by regulations, policies, and laws, but these do not limit the parameters of ethical inquiries (Preston & Wickson, 2019; WHO, 2021a). **Bioethics** is the branch of ethics concerned with biology and biological systems (PennState, 2023).

Gene editing is the technological process of changing DNA sequences at one or multiple points in the DNA strand through inserting, removing, or modifying a single base or multiple genes. CRISPR/Cas9 has emerged as a popular tool for gene editing (Bowen-Metcalf, 2023). **Gene drive** is the process involving gene editing whereby gene-edited traits in a species are spread more quickly to subsequent generations than would occur through traditional inheritance (Roberts, 2022).

Pest is a subjective human concept to describe a living thing that has a negative impact on human activities or human life. Pests, for example, can destroy infrastructure, threaten food sources, spread diseases, or cause annoyance and discomfort (Gov. of Maine, 2022).

Public engagement is an umbrella term for numerous activities and methods used to gather populations together in order to address important topics and issues (Nabatchi & Amsler Blomgren, 2014; Scheufele *et al.*, 2021).

Publics is a term used as an alternative to "the public" or "the general public," one that emphasizes the plurality and diversity of individuals constituting social life (Scheufele *et al.*, 2021).

Risk is the product of hazard and exposure (HC, 2009). The characterization of hazard and exposure pathways is a central component of assessing the risks of pest-control products (HC, 2000).

Contents

1

Introduction

The past 150 years have seen the development of many approaches to managing pests: toxic pesticides based on arsenic or mercury, effective but persistent chemicals such as DDT, and the deployment of other organisms. Effective pest control has reduced disease-transmitting insect populations and increased crop yields and food safety. Some early chemicals resulted in harm to human, animal, and ecological health; since the early 1930s, however, chemical regulation has improved and products are now more thoroughly evaluated for their risks to human and animal health, and the environment. In Canada, major changes resulted from the *Canadian Environmental Protection Act* of 1988, which, among other things, requires that decisions be made in the interest of human health and the biosphere upon which life depends. Concurrently, pests have begun adapting to the methods used to control them. This has required the development of new generations of chemicals and, for some crop pests, the widespread adoption of hybrid varieties of genetically modified crops that express proteins toxic to insects. Managing pests with increased safety and greater effectiveness involves designing and using new strategies and tools, with each new approach carrying benefits and risks.

Recent advances in genetics have created next-generation techniques to address pest challenges — namely the use of genetic tools to modify pest organisms. Gene editing — the altering of individual genes in a species — offers a new means for targeting pest organisms, with uncertain consequences. It has gained prominence in recent years with the introduction of CRISPR/Cas9 technology, a gene-editing technique that provides a relatively inexpensive and versatile platform for editing the genomes of organisms. Several examples of genetic pest control depend on exploiting the potential heritability of changes imparted through gene editing. For instance, an organism can be modified through gene editing to contain a *gene drive*, which allows a particular trait to be passed along through a population at a rate greater than what could be achieved by conventional inheritance. In this way, gene-editing tools can be used to alter populations of pest organisms in order to control population size or dictate which traits they possess. Doing so raises several important scientific and ethical questions, however, as well as a host of regulatory, social, and ecological challenges.

As a novel technology for pest control, it is not clear what the effectiveness and impacts might be of using gene-edited organisms. The uncertainties of releasing organisms carrying a gene drive have not yet been characterized for most applications. Risks to ecosystems and the environment need to be well characterized, and adaptive management is required to address any unforeseen problems. Questions also remain about how best to obtain social consent and approval for their use, and for what kinds of problems. Various species of organisms (native and invasive) can interfere with the balance of an ecosystem or the well-being of other species, but the term *pest* remains a human construct. Whether an organism is seen as a pest or not

depends on underlying values and cultural factors, and these same social considerations will influence how or whether to control an organism. Similar considerations factor into debates on appropriateness: which situations would justify the use of gene-editing technologies that could cause potential harm to a species or its surrounding environment? The answers to these questions, as well as other crucial issues, are unresolved even as several applications are on the cusp of field testing.

Pest management challenges are taking place in an increasingly globalized and uncertain world, and they are aggravated by climate change. Concurrently, technological advancements are providing the capacity for new tools and techniques for pest management programs. Technologies are pushing the boundaries of scientific understanding, necessitating changes to regulatory and administrative methods and processes.

1.1 The Charge

Recognizing the opportunities, challenges, and implications of using gene-edited organisms and genetic technologies for pest control, Health Canada's Pest Management Regulatory Agency ("the Sponsor") asked the Council of Canadian Academies (CCA) to provide an evidence-based and authoritative assessment answering the following question and sub-questions:

What are the scientific, bioethical, and regulatory challenges regarding the use of gene-edited organisms and technologies (e.g., CRISPR/Cas9) for pest control?

- What is the current state of research and development, and bioethics of gene-edited organisms for pest control?
- What are the novel hazards and risks to human health and the environment posed by the use of gene-edited organisms for pest control, including gene drives?
- What are the biodiversity and bioethical considerations of altering the genetics of, or eliminating, a wild pest/disease vector population? Are there potential implications for invasive species management and broader ecosystem benefits provided by pests?

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- What is the current regulatory landscape in Canada and internationally with respect to products of gene editing, including regulatory control of laboratory research on gene-drive organisms?
- What are the lessons from previous approaches to risk communication, transparency, public consultations, and public confidence/engagement relating to regulation of similar products of novel technology (e.g., genetically modified crops), including experiences from other jurisdictions?

1.2 The Panel's Approach

In response to this request, the CCA convened a multidisciplinary and multisectoral expert panel to address this charge, with representatives from Canada and abroad. Panel members' expertise included practical experience related to the biological and environmental sciences, and knowledge of governmental regulatory processes, including risk assessment practices and bioethics.

The work of the Expert Panel on Regulating Gene-Edited Organisms for Pest Control ("the Panel") began at a time when COVID-19 pandemic measures were being lifted, and its process was carried out in a mix of virtual and in-person meetings. The Panel met five times over the course of a year to review evidence, discuss implications, and deliberate on its charge. Work focused on the scientific, regulatory, and bioethical challenges regarding the use of gene-edited organisms and technologies for pest control. Although Canada is the geographic focus of this report, the Panel also reviewed international efforts and approaches for meeting the identified challenges. The dialogue on gene editing in this context is intrinsically international, considering the ability of pests to cross borders and the global nature of trade and research and development (R&D).

1.2.1 The Assessment Scope

Early discussions with the Sponsor clarified the assessment's scope and goals. Although the Sponsor emphasized ethical and regulatory issues in its charge, the socioeconomic impacts of genetic pest-control technologies were also deemed to be within scope, given the potential ramifications resulting from their use. Similarly, the scope of this report also includes biodiversity and agroecological concerns. The breadth of potential target organisms for gene editing is such that the Sponsor asked the Panel to consider a broad range of organisms, provided these could be regulated as pesticides (e.g., fungicides, herbicides, insecticides).[1]

1 Gene-edited microbes are an exception, given that the Sponsor possesses existing regulatory approaches for microbials (including genetically modified examples).

A focus on insects

The assessment is focused primarily on insect examples at the Sponsor's request and due to the advanced state of those applications. The lessons learned from other applications of biotechnology and previous biological pest-control strategies were deemed in scope. Human health considerations were limited to those relating to the impacts of gene-edited organisms on disease vectors. Human-focused genetic technologies (e.g., the use of gene therapies or gene editing in humans) or the potential human health implications of consuming genetically modified foods were considered out of scope. Furthermore, the scope does not include gene-editing applications in plants, including crops for food or other uses. The Panel acknowledges, however, that these applications can be adjacent or closely related to pest control in several contexts and might therefore share common challenges, notably surrounding governance.

A focus on regulation and governance

The central goal of the Panel's assessment is to support the establishment of an appropriate regulatory framework for genetic pest control in Canada. At the time of this report, the Canadian federal regulatory system has not approved pest-control products based on gene editing. The government has, however, clarified its approach for regulating certain products of gene editing in agriculture (i.e., seeds), which reflects how this technological platform is soon to become a fixture in the food system, among other areas. How these novel pest-control technologies fit into existing frameworks and might interact with oversight at other levels of government also presents ambiguity. Beyond regulations, the legitimacy and potential effectiveness of decision-making regarding the use of these tools requires an understanding of several relevant societal contexts. The underlying technology is novel, and societal perceptions of it are evolving. The range of potential applications is broad, with an equally broad set of stakeholders.

A focus on meaningful engagement

The Panel recognizes that the decision to use gene-edited organisms gives rise to several themes pertinent to groups such as small- and large-scale farmers, fishers, and conservationists. As with earlier uses of biotechnology products for agriculture, there are concerns about the impact on the Rights and autonomy of Indigenous peoples and other equity-deserving groups in Canada. Specifically, gene-edited organisms could spread into Indigenous communities' local environments without their knowledge or consent, violating inherent rights or Treaty Rights.

There are also equity concerns in the distribution of benefits and risks arising from the deployment of gene-edited organisms for pest control. Indigenous communities should not be excluded from benefiting from these technologies, nor should they

disproportionately bear the burden of risk. Importantly, it has been highlighted that Indigenous communities and expertise can play a lead role in developing and implementing these technologies (Box 1.1). This raises the importance of representation and participation in governance, since cultural values are reflected in notions of risks and benefits. There are unique socioeconomic risks shared by Indigenous communities given the relationships they hold with their land and its ecosystems. These risks are potentially exacerbated by a lack of representation in the development and implementation of gene-edited organisms for pest control, from R&D to decision-making. Where applicable, the Panel, some of whom work with Indigenous scholars and leaders, draws attention to these unique implications to highlight opportunities for responsible governance and innovation.

Box 1.1 Indigenous Participation and Collaboration

Pest challenges are rooted in specific contexts. They may occur due to multiple interacting drivers relating to physical, ecological, and social conditions — the abundance of food, the absence or seasonal variation of predators and the suitability of the climate are all examples of such drivers. Indigenous knowledge can inform an understanding of these drivers, especially given the relationship many Indigenous peoples have with the natural environments in which they are situated. As of 2021, there are more than 1.8 million First Nations, Métis, and Inuit people in Canada and more than 600 First Nations communities (CIRNAC, 2021b; StatCan, 2023). Differing communities and Nations possess a wide diversity of cultures and languages, governing practices, and relationships with natural ecosystems.

There are numerous important considerations when engaging Indigenous peoples in pest-management contexts. In encountering the use of gene-editing technologies, Indigenous peoples' interest and concerns may primarily be focused on how well the technology works, what it can achieve, and what repercussions or risks accompany its use. Indigenous perspectives will be concerned with how knowledge is shared through regulatory processes, and with the influential roles Indigenous leaders and communities might play in programs that, for example, preserve biodiversity and encourage an equal distribution of benefits (H. Lickers, personal communication, 2023).

Challenges arise in the regulatory context when incorporating the *United Nations Declaration on the Rights of Indigenous Peoples* (UNDRIP) and Duty to Consult, as outlined in Section 35 of the *Constitution of Canada*.

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Yet regulatory and governing challenges need not be the sole defining characteristic of Indigenous participation and collaboration on the potential use of genetic pest-control tools. Collaboration between what is typically called "Western" (or mainstream) science and the science used and practised in Indigenous communities can generate mutually beneficial outcomes for all parties. While benefits relating to a specific program can be identified, additional benefits can include ongoing relationship-building and cross-cultural exchanges (H. Lickers, personal communication, 2023).

Numerous theories and specific case examples detail how this collaboration may occur. *Two-Eyed Seeing* was introduced and developed by Mi'kmaq Elders Albert and Murdena Marshall as a means of drawing on Indigenous and mainstream science in parallel, allowing for the co-production of knowledge in a manner that is mutually beneficial (Bartlett *et al.*, 2012; Reid *et al.*, 2021). Others have described the need for similar processes and relationships, expanding upon Two-Eyed Seeing and offering new expressions, such as *Three-Eyed Seeing*; *weaving, bridging, and braiding*; and *walking on two legs* (Hopkins *et al.*, 2019; ECCC, 2022h; Dickson-Hoyle *et al.*, 2022; Johnson *et al.*, 2023). Though offering unique perspectives rooted in distinct cultures, these terms collectively refer to applying the most suitable tools and learnings in collaborative processes that generate shared outcomes.

There have been many examples of Indigenous science collaborating with mainstream science in, for example, salmon genomics (Genome BC, 2021b), aquatic resource management (Deur *et al.*, 2015), forest management to combat climate change (Onishi & Stuart-Ulin, 2022), water-quality monitoring (Wilson *et al.*, 2018), and wildlife research and management (Goldfarb, 2016). Specific research projects incorporating *Two-Eyed Seeing* and *walking on two legs* are evident in the contexts of research conducted on the Saskatchewan River Delta (Abu *et al.*, 2020) and in forest restoration in British Columbia (Dickson-Hoyle *et al.*, 2022). Importantly, one philosophy or approach cannot be easily and readily applied to any context, especially given the diversity of Indigenous peoples. As noted by Henry Lickers (personal communication, 2023), "when you talk about co-management it resonates in different ways with different people." Gene-edited organisms are the products of modern technology based on western-based science, but the consequences of their deployment into complex ecological networks may lend themselves to deeper understanding and increased benefits through other ways of knowing and interacting with the natural world.

1.2.2 Sources of Evidence

The Panel's report was based on a review of several types of evidence. This review used the *Web of Science* library database, and an open-source bibliographic software was used to iteratively determine keywords relevant to the charge. Following screening, a limited number of articles were found to be specific to Canada. This was supplemented by grey literature comprising policy documents, government publications, webinars, and reports by national and international organizations.

There is an important caveat to highlight, however: the lack of Indigenous knowledge on the Panel. Consistent with the CCA's assessment process, the Panel relied on the published work of Indigenous organizations and scholars who are prominent in this area in order to support discussions. Additionally, Henry Lickers, a Haudenosaunee citizen of the Seneca Nation, Turtle Clan, and Canadian commissioner of the International Joint Commission, met with the Panel to share stories and his experiences.

1.2.3 The Panel's Interpretation of Key Concepts and Terms

For the purposes of this report, the Panel agreed to use the term *gene-edited* to encompass forms of genetic modification that are site-specific changes in the genome using site-directed nucleases or other targeting methods to change genes. The Panel considers gene editing in the pest-control context, with special emphasis on techniques that can persist in the wild. Similar pest-control programs relying on older genetic technologies also exist; although these are not the focus of the Panel's charge, their use is relevant in certain contexts, as highlighted throughout this report.

Due to the abundance of technologies described in the published literature, including those relying on gene editing, the Panel distinguishes between newer and older techniques. Pest-control programs based on gene-edited organisms offer novel considerations, but some implementations derive from earlier efforts involving the use of live organisms for pest control. Acknowledging issues or promising practices encountered in earlier pest-control contexts allowed the Panel to highlight regulatory and policy challenges that newer (and future) technologies pose. Lastly, the Panel deemed it most appropriate to address ethical concerns broadly while also incorporating specific bioethical implications as appropriate.

1.3 Report Structure

Chapter 2 discusses the context of — and motivation for — gene-editing technologies for pest control. It provides an overview of several applications and introduces the social context in which gene editing is developing, including potential impacts. **Chapter 3** describes the state of R&D on gene-edited organisms for pest control, discusses opportunities to support the responsible development and deployment of these technologies in the Canadian context, and presents some potential translation and commercialization challenges. **Chapter 4** sheds light on complications posed by gene-edited organisms in standard approaches for assessing risk in pest control. It discusses several risks to public health, the environment, and society that accompany the release of gene-edited organisms and how these risks might be heightened by uncertainty surrounding the implementation of these technologies. The chapter explores how these risks can be assessed and the evolving set of tools being developed for risk governance, given the central role of this process in decision-making and oversight. **Chapter 5** identifies the social and policy challenges that accompany efforts in public engagement. When established as a core component of pest management initiatives, effective public engagement aligns with ethical practices. This chapter details why public engagement is needed and outlines best practices for effectively doing so in the pest-management context. **Chapter 6** discusses the emerging governance landscape, focusing on national and international friction points that decision-makers will have to confront. This chapter takes the issues and lessons highlighted in previous chapters and describes emerging choices for the Canadian context, which could guide the establishment of strong foundations for the governance and use of gene editing for pest control. Finally, **Chapter 7** offers the Panel's perspectives on the charge, along with future considerations.

2

Context and Motivation for Developing Genetic Pest Management

Chapter Findings

- Pest management consists of a diverse set of tools and practices, which need to be coordinated according to the context and severity of a pest problem.
- Interest in the use of novel pest-control approaches occurs in numerous sectors and stems from the multiplication of pest problems and the waning effectiveness of conventional tools.
- Climate change is inextricable from the context of pests due to its potential impacts on ecosystems and pest biology, leading to a complex interplay among key pests, their control, and climate change in Canada.
- The science underpinning gene editing is rapidly evolving and contributes to an increasing variety of prospective mechanisms of action in genetic pest control, across numerous species.
- Emerging applications in genetic pest control can be categorized according to their persistence, threshold, objective, mechanism of action, and range.
- The potentially broad range of applications for genetic pest control may affect numerous relevant stakeholders and Rights-holder groups; these vast social and cultural landscapes will shape technology development and perception.
- Some approaches share similarity to earlier pest-control programs, while others represent novel interventions in the natural environment, raising several ethical questions surrounding their appropriateness and use.

Pest as a term refers to species that diminish productivity in agriculture, apiculture, aquaculture, forestry, and horticulture. Pests also threaten the health and biodiversity of ecosystems and are responsible for significant public health challenges. Pest status, however, is not intrinsic to any species but is instead defined in relation to specific interests (e.g., economic) and therefore reflects social values. Pests operate in diverse settings and, as such, a wide range of tools (based on various technologies) is used to manage them. New tools are nevertheless always in demand due to changing pest pressures and their potential resistance to control agents. Recent developments in genetic technologies applied to pest organisms offer potential new approaches to meet this demand. This chapter introduces the context in which genetic pest control is beginning to emerge.

The chapter begins with a brief overview of common pest-control tools and approaches used in recent history. The discussion then considers how decision-making surrounding their safe and effective use typically proceeds, with an emphasis on the lack of clarity on how genetic pest-control tools fit into existing practices. The section concludes on the implications of climate change, given its growing role as a driver for pest problems through physical effects and ecological disruption.

The chapter focus then moves to a description of gene editing and the science underpinning genetic pest control. Different implementations of gene editing and other related technologies have given rise to numerous prospective pest-control tools, including extensions of existing approaches as well as more controversial examples. Although the science is rapidly evolving, the Panel uses this setting to provide a conceptual summary of how these tools compare with each other and previous pest-control programs involving live organisms. Finally, gene-editing technologies generate interest and concern in society, and their potential use in pest management programs will resonate in social, political, and commercial contexts, for experts as well as the public. Through a discussion of the social, ethical, and economic opportunities and risks accompanying the use of genetic pest control, the Panel highlights the social backdrop in which these technologies are used.

2.1 Pest Management: Principles and Trends

In any ecosystem, pests are naturally being controlled. However, the level of control is at times incompatible with human priorities, leading to interventions (Kogan, 1998). The challenges caused by pests are multiplying in number, spreading into new environments, and causing a range of issues for agricultural practices, biodiversity, and public health, all against the backdrop of a shifting climate (Ng *et al.*, 2019; IPPC Secretariat, 2021; Skendžić *et al.*, 2021). As a consequence, pest control is evolving continuously, driven by the limitations of available control methods, tools, and systematic practices (USDA, 2014; Deguine *et al.*, 2021; Tabashnik *et al.*, 2023). Recent developments in genetic technologies have paved the way for theoretically promising applications in pest control, but it is uncertain whether these new tools fit into the current toolbox.

Pest management spans a broad spectrum of techniques and methods, and strategies have changed in response to technological developments and pest resistance

From the 1920s to the 1950s, the introduction of species that target insect pests was a common strategy in North America (McClay *et al.*, 2021). These species acted as biological control agents, consisting of enemies or predators to the pest, with

numerous successes in pest control (McClay *et al.*, 2021). Starting in the 1950s, however, the rate at which new biological control agents were released in North America began to diminish in contrast to the rate of introduction of new fungicides, herbicides, and insecticides — chemical pest-control agents (Phillips McDougall, 2018; McClay *et al.*, 2021).[2] In Canada, for example, insecticides such as DDT were used from the 1940s to the 1960s to eliminate pests in apple orchards (Dixon *et al.*, 2014). Several of these chemical agents employ distinct modes of action, but many are broad-spectrum; such products can have a negative influence on non-target species (including natural enemies of the targeted pest that provide biological control) (Hill *et al.*, 2017).

The use of chemical agents over several decades has caused some of the species exposed to them to develop resistance, resulting in lower effectiveness of these products and the supplementary use of different classes of chemical agents to maintain satisfactory control (Hawkins *et al.*, 2019; Baute, 2020). Chemical agents remain a cornerstone of pest management programs, but are costly, indiscriminate, and increasingly diminishing in effectiveness (Baute, 2020). In the context of vector-borne diseases, a pest control agent becoming gradually ineffective directly leads to increased disease burdens (Lopes *et al.*, 2019). Decreasing effectiveness can also result in environmental pollution due to the need to apply greater amounts of product, undesirable side effects among non-target organisms, or the re-occurrence of pest populations. The implementation of new tools for durable and species-specific biological control could be desirable.

Frameworks grounded in ecology exist to guide decision-making about the coordinated use of diverse tools to establish effective pest-control programs

There are several contemporary methods for managing and controlling pests using a variety of tools in addition to those described above. Approaches exist to prevent pests from entering (and spreading) through an environment, and to react to their established presence with suppression and eradication tactics. Integrated control, or what has since become known as integrated pest management (IPM), was in part spurred by evidence that the over-reliance on chemical control methods presented several unwanted consequences (Kogan, 1998). IPM as currently practised refers to the decision-making processes and management structure used for effectively managing pests by incorporating economic, environmental, and social factors (Kogan, 1998; Gov. of BC, 2023). IPM principles are used for staple crops in many countries and applied to numerous other settings besides agriculture (e.g., forests and urban ecosystems) (Vreysen *et al.*, 2007).

2 Notably, concerns surrounding biological control agents attacking non-target species dovetailed with the output of the chemical pest-control industry to spur more widespread use of the latter (Vreysen *et al.*, 2007).

The Government of British Columbia (2023) describes six core elements of IPM including:

- preventing the infestation of ecosystems (notably, agricultural production sites) by pests;
- identifying pests (as well as their natural enemies), and assessing their potential for damage;
- monitoring the impact of pests in an environment;
- decision-making on pest interventions, which typically focus on economic and environmental considerations;
- intervening in environments with "behavioural, biological, chemical, cultural and mechanical methods to reduce pest populations to acceptable levels;" and
- evaluating the overall success of a pest management program.

The tools used to implement IPM include agricultural practices such as crop rotation to disrupt the establishment of pest populations, mechanical methods, biological practices, and the use of chemical agents (Barzman *et al.*, 2015; PennState Extension, 2016). Pest control tools are often combined, since each method employs a different mode of operation — offering varying levels of selectivity and impact on pest pressures (Vreysen *et al.*, 2007). For example, in order to be effective, a program to eradicate New World screwworm (*Cochliomyia hominivorax*) required the coordination of a sterile insect control program (Box 2.1) combined with quarantines, monitoring livestock affected by the pest, cultural practices in the management of the livestock, and public outreach activities to promote collaboration among stakeholders (Vreysen *et al.*, 2007). Consistent coordination of these multiple activities, where effectiveness may be limited in isolation, was instrumental in program success and enabled its benefits to be extended from the United States into Central America (Wyss, 2000).

Box 2.1 Sterile Insect Technique in Pest Control

Some concerns about biological control have revolved around unwanted ecological impacts (Collatz *et al.*, 2021) arising from the release of (potentially) exotic species into ecosystems. Sterile insect technique (SIT) represents a specific type of biological control, one that relies on disrupting reproduction to reduce pest populations. SIT programs involve a mass release of sterilized versions of organisms from the target pest population. These organisms (typically insects) are mass-reared and sterilized in a facility (Section 3.2) before being released into the environment occupied by a population of pests (Klassen & Vreysen, 2005).

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The objective of the approach is that wild-type insects mate with the released sterile insects, such that no viable offspring are produced. By the end of the insects' lifespan, the large number of non-productive mating events between wild-type and sterile insects results in a smaller subsequent generation of pests. The appropriateness of SIT depends on pest biology and cannot be applied to all pest problems, but it has been used effectively in several settings and has inspired applications in genetic pest control (Thistlewood & Judd, 2019; Dyck *et al.*, 2021) (Section 2.2).

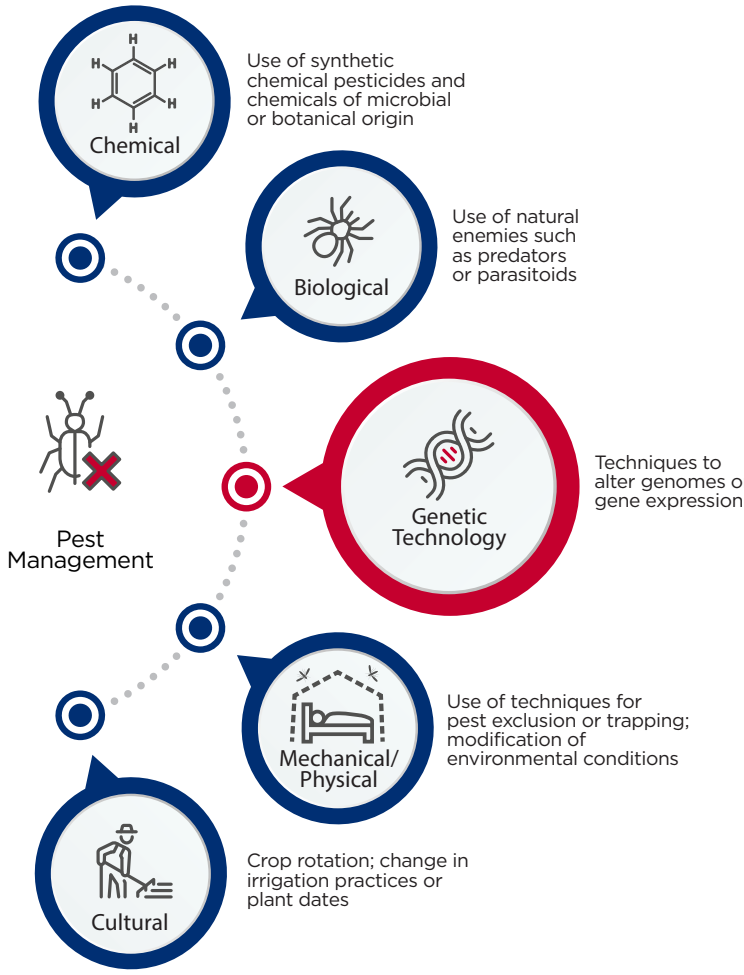
This pest-control strategy involves the modification of live organisms by humans, but in an untargeted way, since the insects are commonly sterilized through irradiation (resulting in several mutations) (IAEA, 2008). The sterility of the insects is a crucial property: it ensures that the final release marks the end of the pest-control program, since the insects have a limited lifespan and do not produce offspring. For this reason, organisms in an SIT program are deemed beneficial insects and are, in some jurisdictions, subject to more lenient regulatory requirements than those for other programs involving the release of live organisms (Kapranas *et al.*, 2022) (Section 6.1).

The prospect of new genetic pest-control tools demands an understanding of how these tools might fit into existing practices

Frameworks such as IPM consider the fact that pest control tools span a wide range of practices, and that these might need to be combined to affect satisfactory control. The IPM paradigm can act as a system for supporting decision-making for this purpose by taking into account costs, benefits, and impacts from the standpoint of growers, society, and the environment (Kogan, 1998). The implementation of IPM nevertheless remains challenging due to complexity, as it relies on the understanding of ecology (namely, the interactions between species) and pest biology (Vreysen *et al.*, 2007). There also exist difficulties in operationalizing general IPM principles to specific contexts due to social (e.g., education, training) and logistical (e.g., coordination, governance) factors, among others (Kogan, 1998; Deguine *et al.*, 2021).

Recent advances are laying the groundwork for applying genetic technologies to control pests by modifying the properties of pest organisms, which creates a new category within the existing set of IPM practices (Figure 2.1). The prospect of these technologies being applied to pest control has been anticipated for some decades (Smith, 1980). However, even during that time, it was cautioned that the success of integrated control methods has typically resulted from improved understanding of ecological considerations, and not from "a silver bullet" new technology

(Kogan, 1998). Questions remain as to where genetic pest-control tools will lie within decision-making systems such as IPM, particularly given the uncertainty surrounding efficacy, safety, and risk (Chapter 4).



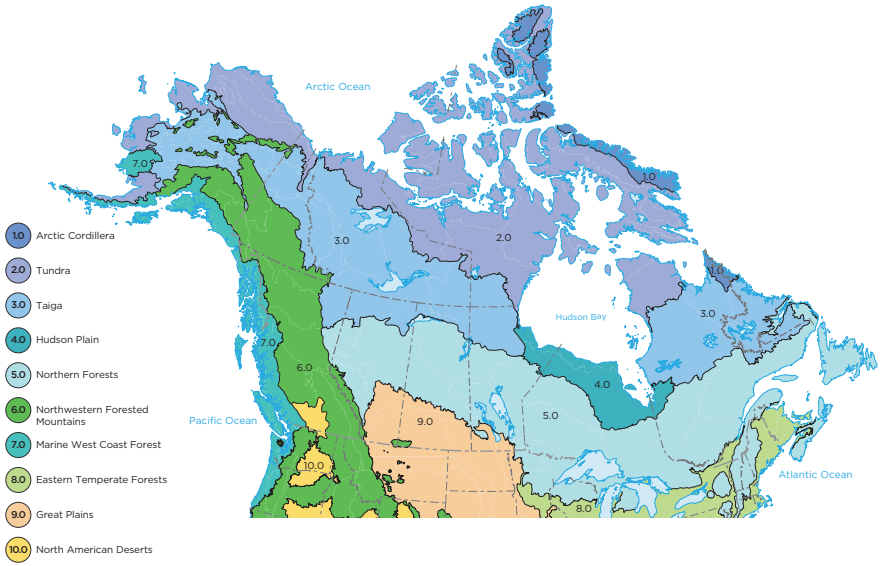
Adapted from Dara (2019)

Figure 2.1 Categories of Pest Management Tools Used in IPM, Soon to Include Genetic Pest Control

The different tools used in pest control can be divided into distinct categories within an integrated pest management (IPM) framework. Guidelines assist in decision-making surrounding their use. Genetic pest-control tools are poised to add a new category to this framework, but it is uncertain how these might be deployed according to IPM guidelines, and therefore whether they should be used and how.

Climate change and pests impact one another, contributing to increased pressures and risks

Rising temperatures and accompanying variations in precipitation will establish conditions where pests, such as invasive weeds, can flourish where they previously could not (Wang *et al.*, 2022). Indeed, climate change is shifting the overlap areas of the major ecological zones in North America (Figure 2.2). Several of these zones straddle the Canada–United States border (Batllori *et al.*, 2017), and may include key agricultural areas; for instance, the corn belt in Ontario has been warming for decades (Eyzaguirre *et al.*, 2017). This has significant implications: insects and plants presenting a threat to Canada could find new areas where they can thrive.



Adapted from US EPA (2022a)

Figure 2.2 Map of Level 1 Ecological Regions of North America

Although the border defines the laws and practices in pest management in Canada and the United States, ecozones do not. Large areas of the U.S. Midwest are in the same ecozone as much of the prairie provinces. Most of British Columbia is contiguous with the U.S. Pacific Northwest as well as part of Idaho. Similarly, most of the growing area of Ontario overlaps with the adjacent U.S. ecozone.

One example is the destructive western bean cutworm (*Striacosta albicosta*), which causes direct damage in corn and, in some cases, makes entire crops worthless by causing increased toxin levels (Michel *et al.*, 2010). Prior to 2000, this pest was confined to the U.S. Midwest. However, by 2017, populations had expanded into Ontario, and from Ontario to Nova Scotia (Smith *et al.*, 2019). Milder winters are

adding to a number of interacting drivers, ranging from changing insecticide use to migration, which together have allowed the cutworm to reach eastern Canada (Hutchison *et al.*, 2011; Hobson *et al.*, 2022). Tools currently used to manage insects in corn crops include insecticides and the use of insecticidal proteins isolated from *Bacillus thuringiensis* (commonly referred to as Bt, after the namesake bacterium) and incorporated into corn hybrids through genetic modification (Gewin, 2003). Bt has been an effective tool for many years. However, tolerance has emerged in populations of the major corn insect pests in eastern Canada (Smith *et al.*, 2019; Meinke *et al.*, 2021) and beyond (Tabashnik *et al.*, 2023). Although this can be mitigated by proper management, tolerance to Bt and other insecticides is inevitable and demands the development of alternative chemical agents and the modification of agricultural practices (Meinke *et al.*, 2021; Farhan *et al.*, 2022). By contributing to pest migration and over-wintering potential, climate change may add to the risk of resistant populations establishing themselves outside of their historical range (Ma *et al.*, 2021). Efforts to monitor resistance susceptibility will thus need to account for the influence of climate change.

Pests can also contribute directly to climate change through the indirect consequences of the damage they create. Major epidemics of native forest pests, such as the mountain pine beetle (*Dendroctonus ponderosae*) in British Columbia and parts of Alberta, and the eastern spruce budworm (*Choristoneura fumiferana*) in eastern Canada, destroy large (and increasing) areas of forest ecosystem (NRCan, 2013, 2022a). In doing so, they directly cause economic harm and indirectly impact employment in small communities where forestry is a major industry (Chang *et al.*, 2012; NRCan, 2022b). In the absence of pest pressures, an intensively managed forest (and most harvested wood) represents a net carbon sink (Hennigar & MacLean, 2010; ECCC, 2022a). The mountain pine beetle epidemic leads to decomposing wood, changing the forest from carbon sink to carbon source and producing CO_2 on a scale comparable to transport emissions (Kurz *et al.*, 2008; ECCC, 2022b).[3]

2.2 Genetic Population Control Methods for Insect Pests

Several tools relying on the use of genetics have recently appeared to meet the pest management challenges above. Some consist of new ways of pursuing historically effective control approaches (such as SIT), while others have been spurred by advances in gene editing, specifically. The consistent focus on developing more efficient and precise gene-editing tools has led to the current

3 Transport accounts for roughly 10 times the pine beetle-related emissions reported by Kurz *et al.* (2008). However, that study reports on the impacts of only a single insect species. Other pests, including spruce budworm, likewise also result in a significant release of CO_2 (Dymond *et al.*, 2010).

technology landscape, largely based on CRISPR (Sander & Joung, 2014) (Box 2.2). A range of approaches for genetic pest management are being developed at a rapid pace, relying on either the suppression of pests or the alteration of pest populations to reduce their negative impacts. Technology advances quickly, however, and challenges exist to extrapolate observations from controlled environments onto outcomes in real ecosystems. The following paragraphs explore these challenges, and compare and contrast new and old approaches while also presenting ways to categorize emerging genetic pest-control tools.

Box 2.2 CRISPR Leading the Pack

CRISPR was born out of the basic biological characterization of a bacterial and archaeal immune system that could directly target the DNA of invading phages. In 2010, researchers realized that the system could be easily and flexibly repurposed for targeting the genome of any organism, which established CRISPR as a popular tool for making site-directed edits in eukaryotic genomes. Among CRISPR systems, CRISPR/Cas9 has distinguished itself from other gene-editing tools by providing lower costs and faster, easier, and more precise gene editing compared with conceptually similar but more cumbersome approaches, such as zinc finger nucleases (ZFNs) and transcription activator-like effector nucleases (TALENs) (Friedrichs *et al.*, 2019b).

The primary advantage of CRISPR/Cas9 over previous gene-editing tools is the ease of target recognition, enabling more flexibility in designing and affecting changes (Lino *et al.*, 2018). In addition, several delivery mechanisms exist for CRISPR/Cas9, such that developers possess several options for bringing the system to various eukaryotic cells where the target DNA might be located within an organism (Lino *et al.*, 2018). Taken together, these properties have enabled the demonstration of genome editing using CRISPR in a broad range of organisms (as reviewed in Sander & Joung, 2014) and paved the way for applications in pest control.

Basic principles for applying gene editing to pest control can be identified, and approaches based on SIT are among the earliest examples

There are currently two main approaches proposed for implementing genetic pest management: suppressing a wild population (temporarily or durably) and modifying the traits of a population such that its members may no longer act as

pests (as reviewed in Hay *et al.* (2010) and Alphey & Bonsall (2018)). For example, gene editing could be used to introduce heritable traits that can reduce the fitness of target pest populations over time, in the hopes of suppressing pest populations (Siddall *et al.*, 2022). Precision-guided sterile insect technique (pgSIT) builds on decades of work using sterile insects for pest control but promises a more efficient process for a broader range of organisms. Conventional SIT (Box 2.1) relies on radiation or other means to sterilize insects prior to release, which can result in imprecise alterations to insects that can impact their fitness, requiring additional screening, calibration, and quality control to characterize the insects and select those that meet the criteria for release (IAEA, 2008).[4] By contrast, pgSIT uses CRISPR technology to specifically disrupt genes that control female viability or male fertility. This leaves the properties of the organism otherwise unaffected, thereby increasing the precision of the SIT (Kandul *et al.*, 2019; Li *et al.*, 2021). Laboratory proof-of-concept pgSIT studies have been successful in fruit flies (*Drosophila spp.)* (Kandul *et al.*, 2019) and mosquitoes (*Aedes aegypti*) (Li *et al.*, 2021), with both research groups using modelling to show the promise of the technique in the field.

Although there is a substantial technological readiness gap between bench demonstrations and deployment in a real-world setting, pgSIT acts as the extension on what are occasionally referred to as first-generation genetic pest-management approaches (Siddall *et al.*, 2022). These approaches are currently being tested in several experiments involving mosquitoes and certain insect pests in agriculture (Waltz, 2015, 2017b; NEA, 2021). First-generation programs rely on older technology than gene editing, such as genetic modification via plasmid vector (Phuc *et al.*, 2007) or the deliberate infection of mosquitoes with *Wolbachia* parasites (Crawford *et al.*, 2020; Ross *et al.*, 2022).[5] The work on those technologies is not the core focus of the Panel's report, but is occasionally highlighted in the context of emerging challenges for gene-edited organisms since it remains the subject of ongoing debate at the social and regulatory levels.

4 In the case of radiation, for example, the process of sterilization can also impact the visual sensitivity of the insects, their ability to disperse upon release, and other aspects of their behavior that can inhibit the likelihood of mating with their wild counterparts (IAEA, 2008).

5 Male mosquitoes infected with *Wolbachia* can mate with uninfected counterparts but will not produce offspring due to cytoplasmic incompatibility (Ross *et al.*, 2022). In addition, *Wolbachia* infection has been known to prevent certain species of mosquito from carrying human pathogens (i.e., pathogen interference) for reasons that are not yet fully understood (Moreira *et al.*, 2009).

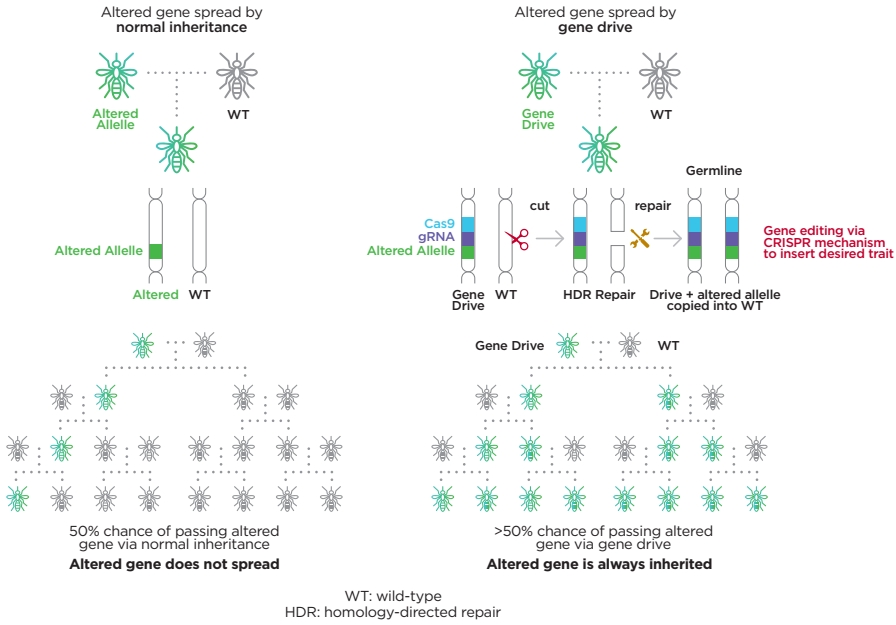
Gene drives are designed to override laws of inheritance to ensure that specific genes are always passed along to offspring, and can be used to spread traits through populations

Traditionally, Mendel's law of segregation implies that, in sexual reproduction, an offspring inherits genetic material from each of its parents (Zanders, 2022). In simple cases, this means that if one parent possesses a trait but the other does not, an offspring will have a 50% chance of inheriting that trait. Gene drives, however, are "selfish" genetic constructs that bypass Mendel's law (Siddall *et al.*, 2022). In doing so, the drive can make a genetic trait spread through a population at a rate faster than it would via Mendel's law (Oberhofer *et al.*, 2020; Siddall *et al.*, 2022) (Figure 2.3). By virtue of their ability to bias inheritance, gene drives can also interfere with natural selection: if the drive affects an edit to the genome that impairs fitness, that trait may not be bred out of the population, since the gene drive might ensure propagation to subsequent generations (Siddall *et al.*, 2022).

Some selfish genetic elements are naturally occurring (Burt & Trivers, 2006). For example, in many parts of the world, the red flour beetle (*Tribolium castaneum*) carries a selfish genetic element in the form of a gene with the property of conferring lethality to embryos born to females bearing that gene, unless a copy is also inherited from the male (Beeman *et al.*, 1992; Beeman & Friesen, 1999). This results in progeny whose genetic makeup is therefore biased toward carrying the selfish genetic element.

This mechanism has been studied and harnessed to develop gene drives based on so-called *Medea*[6] selfish genetic elements (Akbari *et al.*, 2014; Buchman *et al.*, 2018). At the population level, biased inheritance is achieved by eliminating genotypes that do not carry the target gene. Similar results can be achieved through homing mechanisms that replicate the target gene (e.g., using CRISPR/Cas9), such that an embryo will carry two copies of the gene when it would have otherwise carried one (Windbichler *et al.*, 2011) (Figure 2.3). In this example, importantly — in addition to the target gene — the genetic information that encodes CRISPR/Cas9 will also, in theory, self-replicate at all suitable sites. This ensures that the drive continues to propagate across subsequent generations (Steinbrecher & Wells, 2019). A third mechanism is under-dominance, where the selfish genetic element confers a fitness cost to the organism, in the event that it only possesses a single copy of the gene (Reeves *et al.*, 2014).

6 *Medea* stands for maternal effect dominant embryonic arrest.



Adapted from Synthego's The Bench Blog, CRISPR Applications; Roberts (2022) and Shah (2022)

Figure 2.3 Inheritance Biased by CRISPR Gene Drive

Mendel's law dictates that 50% of genetic material is inherited from either parent during reproduction. The pathway on the left demonstrates how a genetic element of interest might propagate through a group of insects following this law. The pathway on the right shows the result of the inheritance process for an insect that has been gene-edited to carry a heritable selfish genetic element. When the modified insect reproduces with a wild-type mate, 100% of its offspring carry the selfish genetic element. This element then continues to propagate through the population as those offspring mate with other members of the population.

Genetic tools are continually diversifying from a scientific standpoint, and their salient features and mechanisms of action can help categorize function in pest control

The technical implementation of gene drives and other engineered selfish genetic elements can proceed through various designs and will depend on considerations related to genetics, as well as a thorough understanding of the basic biology of the target organism. Naturally occurring elements can be adapted through modern tools to operate in different organisms. For example, elements that operate in a similar way as the *Medea* construct described above have also been demonstrated using CRISPR/Cas9, in the form of so-called antidote-toxin drives that rely on

influencing embryonic viability (Champer *et al.*, 2020).[7] Despite variability in the molecular biology underpinning genetic pest-control tools, some of their properties allow for categorization and better understanding of their potential uses and risks (Section 4.3). For example, Overcash and Golnar (2022) propose five functional characteristics to define the architecture of a gene drive, but these are potentially applicable to other genetic pest-control tools:

- The **objective** of the drive describes its purpose from a pest control standpoint (e.g., population suppression, population replacement).
- The **mechanism** describes the process by which a drive operates. Three mechanisms have currently been implemented: interference drives, where the presence of the genetic construct interferes with reproduction changing the distribution of genes in a population (e.g., *Medea*, antidote-toxin drives); replicator drives, that involve the copying of genes (e.g., homing drive; Figure 2.3); and, under-dominance drives, as described earlier.
- The geographic **range** can be qualitatively understood as either localized or unrestricted. This property is not intrinsic but will depend on an interplay of genetic (e.g., design of the gene drive) and biological (e.g., dispersal of the target organism) factors.
- The **persistence** describes the duration for which a genetic pest-control intervention will persevere in the environment. *Self-limiting* interventions eventually disappear. SIT and its genetic analogues, such as pgSIT, are self-limiting. In contrast, an intervention can also be *self-sustaining* and therefore persistent. A replacement gene drive might be self-sustaining to ensure a durable alteration of a pest population.
- The **threshold** relates to the density of released organisms needed for a gene drive to achieve its purpose. Through their design and mechanism of action, gene drives can have low or high thresholds. Homing drives might possess a low threshold, since their mechanism relies on replicating genetic material. Under-dominance approaches, in contrast, are high-threshold, and may require the release of high-densities of gene-edited organisms outcompeting wild-type counterparts. Environmental factors will also influence the threshold.

This categorization provides guidance on how programs might compare with one another and with earlier pest-control approaches. This potentially helps link the biological properties of a genetic pest-control tool to regulatory frameworks (Overcash & Golnar, 2022). It also presents complex genetic processes in plain

7 This process relies on gene editing to introduce a gene drive (antidote) and disrupt an essential gene (toxin). If the correct genotype (combinations of toxin and antidote) is not found in a developing embryo, it will not survive. This is similar to but more general than *Medea*, which is constrained to specific species (e.g., red flour beetles, fruit flies) as the result of reproductive biology (Champer *et al.*, 2020).

language for the purpose of clear communication with non-experts (e.g., decision-makers) (Overcash & Golnar, 2022). Table 2.1 provides an overview of some of the examples discussed thus far in the context of such a classification scheme.

Table 2.1 Characterizing Pest Control Tools Involving Live Modified Organisms

	Potential range and persistence in target population			
	Self-Limiting		Self-Sustaining	
	High Threshold (Localized)	Low Threshold (Non-Localized)	High Threshold (Localized)	Low Threshold (Non-Localized)
Population Suppression	SIT, pgSIT, and gene drives (e.g., under-dominance)	Gene drives (e.g., *Medea*)	Gene drives (e.g., under-dominance)	Gene drives (e.g., homing)
Population Replacement	Gene drives (various)	Gene drives (various)	Gene drives (various)	*Wolbachia*, and gene drives (various)

Adapted from Devos *et al.* (2022a)

The release of a gene drive could represent a new form of environmental intervention, raising concerns about unanticipated consequences in light of persistent unknowns

The functional description of genetic pest-control tools as shown in Table 2.1 underscores how these tools share certain commonalities. Some approaches are, on the surface, not so different from biological control or SIT programs. Others approaches, however, represent a potentially novel means for humans to intervene in the environment through pest control (Figure 2.4). Among these, gene drives in particular are viewed with anticipation and skepticism. The release of a certain type of drive (e.g., self-sustaining, low threshold) could potentially alter entire populations of organisms according to human priorities; this example is, however, one of several implementations, each offering a range of potential risks and impacts (Section 4.2).

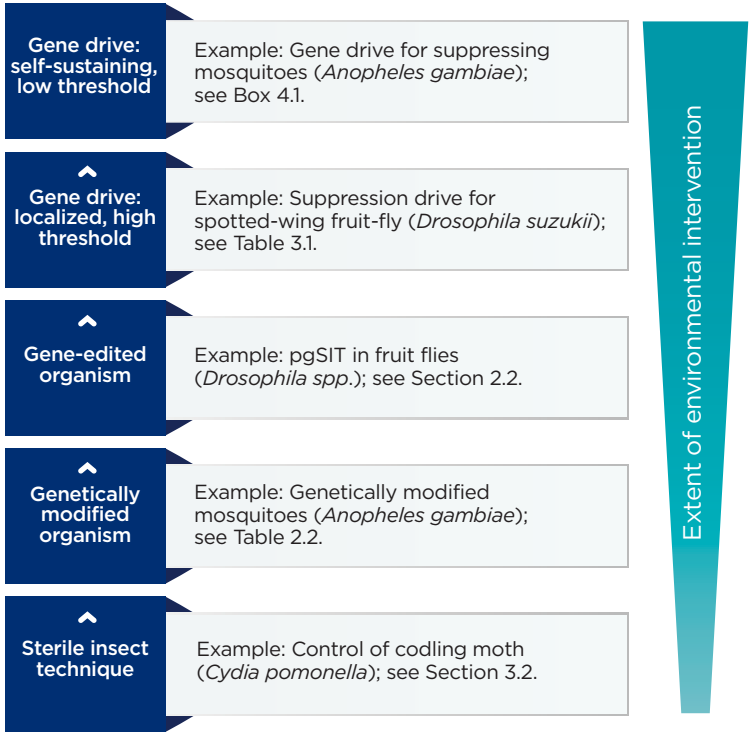


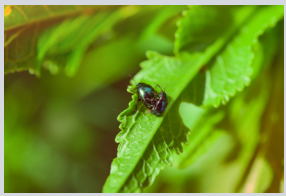
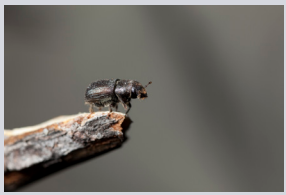
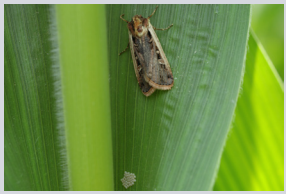
Figure 2.4 Increasing Levels of Environmental Intervention for Pest-Control Programs

The examples described in this report can be ranked in terms of the extent of environmental intervention they represent. The diagram is for descriptive purposes only and emphasizes that gene editing may establish new boundaries in pest control.

There are also many ways gene drives may not work exactly as intended. From the standpoint of efficacy, it remains unclear whether these approaches will translate from laboratory proof-of-concept stage to effective use in practice. The genes that are being edited dictate the characteristics of the drive, and detailed understanding is essential to predict the effectiveness of the gene drive in the wild (Lester *et al.*, 2020). Several factors will also come into play including geography, ecosystem characteristics, and population dynamics, among others (Dhole *et al.*, 2020; Frieß *et al.*, 2023); these complexities challenge efforts to

predict real-world ecological impacts. Similar issues arise in forecasting the long-term fate of the drive from a genetic standpoint. Gene editing using CRISPR is a precise method, but unintentional off-target effects (such as unintended point mutations, deletions, insertions, inversions, and translocations) could occur in real-world scenarios . These effects can render gene drives useless or introduce unintended traits in the host organism over the course of time (Zhang *et al.*, 2015; Modrzejewski *et al.*, 2020). Effectiveness and risk will therefore be influenced both by microscopic processes and the macroscopic context of deployment (Devos *et al.*, 2022b). The promise of specificity and durability accompanying the use of gene-edited organisms for pest control therefore belies areas of lingering uncertainty that extends to the potential ramifications. As gene-editing science evolves, greater clarity will emerge about which pests might be edited with sufficient accuracy to warrant consideration for a pest-control program. Table 2.2 presents a non-exhaustive list of some pests with Canadian relevance.

Table 2.2 Pest Examples Relevant to the Canadian Context

Pest	Pest Context	Region(s)
Flea Beetle 	• Destroys **canola** one of Canada's most prevalent and valuable crops (Knodel & Olson, 2002; CCC, n.d.). • Currently used insecticides remain effective, but repeated usage has economic and environmental repercussions (Cárcamo *et al.*, 2017).	**Prairies and Western Canada**
Sea Lice 	• Damages health of wild and farmed **salmon**, a species with high economic and cultural value (DFO, 2022; Braun, 2022). • Current pest-management activities are extensive but lacking; genetic research on salmon and sea lice is advancing (Guragain *et al.*, 2021; Genome BC, 2021b; Skern-Mauritzen *et al.*, 2021).	**Western and Atlantic Canada**
Mountain Pine Beetle 	• Destroys **forests**, with consequences for climate change, biodiversity, and the forestry industry (Kurz *et al.*, 2008; Safranyik *et al.*, 2010; NRCan, 2022a). • Beetle range is expanding rapidly and the means for controlling its impact are waning (NRCan, 2022a).	**Western Canada**
Western Bean Cutworm  Image courtesy of Dr. Art Schaafsma	• Destroys **corn** crops (Smith *et al.*, 2019; Farhan *et al.*, 2022). • Cutworm spread is rapid and significant (from the U.S. Midwest into central and eastern Canada) (Michel *et al.*, 2010).	**Central and Atlantic Canada**
Mosquitoes (various species) 	• The spread of **malaria** is primarily in sub-Saharan Africa and a significant health burden (WHO, 2022); previously used interventions are losing effectiveness (Tizifa *et al.*, 2018). • Gene-edited mosquitoes are close to deployment for public health applications (Target Malaria, 2020a). • These examples could establish precedents in frameworks for governance and testing, and are therefore relevant to Canada, despite the low domestic prevalence of the targeted diseases.	

2.3 Social, Ethical, and Economic Considerations

Technologies using gene-edited organisms for pest control are emerging in multiple social contexts and being developed for a broad range of applications, in some cases in areas where differing values and priorities may come into tension. In certain implementations (Table 2.1), these technologies can represent environmental interventions beyond what has historically been employed for pest control (Figure 2.4); as such, each application context presents distinct social, ethical, economic, and cultural concerns. Table 2.2 provides a window into these concerns by highlighting a handful of species (among countless others) corresponding to Canadian pest problems. Each species — through impacts on agriculture, conservation, and forestry — implicates different stakeholders, communities, and socioeconomic interests across geographic and ecological areas.

To fully grasp the relevant context for these technologies, it is also necessary to go beyond conventional socioeconomic factors to explore the public perceptions and ethical implications of these technologies, given the wide range of social environments in which they may be deployed.

This section provides a brief and non-exhaustive overview of the range of potential socioeconomic impacts of genetic pest control, recognizing that much remains unknown about the performance of these technologies outside of laboratory settings. To fully grasp the relevant context for these technologies, it is also necessary to go beyond conventional socioeconomic factors to explore the public perceptions and ethical implications of these technologies, given the wide range of social environments in which they may be deployed.

The deployment of gene-edited organisms for pest control will have socioeconomic impacts but their estimation is complicated by lingering unknowns

The genetic pest-control tools described above are being developed across a growing range of target species (Section 3.1) and across several domains where socioeconomic impacts might be felt should the technologies achieve their promise. Firstly, R&D activity is underway to establish genetic pest-control programs that curb the spread of vector diseases such as malaria, Zika, and dengue (Target Malaria, 2017; NEA, 2021; Oxitec, 2022).[8] If successful, these programs might greatly reduce the extensive human suffering caused by these

8 Some of the most advanced initiatives draw on earlier technologies, but applications using gene editing are also foreseen (Target Malaria, 2020a).

diseases (see, for example, WHO, 2021b). In addition to public health impacts, major vector diseases also impose economic burdens, particularly in countries where these diseases are endemic (Shepard *et al.*, 2016; Sarma *et al.*, 2019). As such, effective mosquito control could realize economic benefits (Halasa-Rappel & Shepard, 2019). These could also be extended to agriculture and forestry, where the direct and indirect costs of pest activity (and of waning control methods) can be substantial (Aukema *et al.*, 2011; Chang *et al.*, 2012; Gardner Pinfold, 2013; Varah *et al.*, 2020; Crystal-Ornelas *et al.*, 2021). Genetic pest control could contribute to the conservation of ecosystems or endangered species, and help native species adapt to climate change (Sandler, 2017).

These potential benefits hinge on the effectiveness of the interventions but must be weighed against several socioeconomic concerns. In addition to the possibility that they are simply not effective (or not deployed effectively), gene-edited organisms might present risks to non-target populations (Section 4.2). This has potentially negative economic implications due to the risk of damage to food webs or other crops in agricultural settings (Courtier-Orgogozo *et al.*, 2017). The use of genetic pest-control tools also has trade implications between jurisdictions where these technologies may be regulated or perceived differently (Marchant & Allenby, 2017).

Application areas will influence the socioeconomic benefits of genetic pest control, as will the choice of implementation: the specific case of self-sustaining gene drives might be very complex (Mitchell *et al.*, 2017). In addition to differences in benefits, questions exist surrounding the distribution of these and associated costs, both for development and use (Baltzegar *et al.*, 2018). For example, the use of these technologies could have impacts on the agroecological movement — that is, practices to intentionally preserve biodiversity in order to benefit from the ecosystem services it provides (Kremen *et al.*, 2012). The off-target risks posed by genetic pest control could disproportionately impact these growers, who participate in alternative agricultural models rather than those using decision frameworks such as IPM (Section 2.1). Governance decisions for gene-edited seeds have taken specialized growers (in this case, organic growers) into account in regulatory guidance, specifically due to the disproportionate risk burden placed upon their operations by the use of gene editing (CFIA, 2023b). The decisions underpinning how gene-edited organisms are developed and released, including how and for whom the risks and benefits will manifest, therefore requires broad social reflection (Long *et al.*, 2020).

The public consists of diverse actors whose perceptions of genetic pest-control initiatives will be at least partially influenced by experiences with genetically modified organisms

Social considerations span ethical concerns, spiritual practices, and diverse cultural values and practices in rural and urban communities, and across diverse populations, including among Indigenous peoples (Macnaghten & Habets, 2020; Taitingfong & Ullah, 2021; Davies *et al.*, 2022). To account for this, in the context of biological control, Catton (2021) provides a non-exhaustive outline for groups of publics in terms of client communities, conservationists, Indigenous peoples, activists, and other concerned groups (Table 2.3). Clearly demarcating these public groups — and distinguishing stakeholders from other publics — can be complex because individuals hold various social positions and act in different capacities in different contexts (Shackleton *et al.*, 2019). Importantly, Indigenous peoples in Canada hold specific positions as public members; they cannot be considered "stakeholders" given their status as inherent Rights-holders, as outlined in the *Constitution of Canada* (GC, 2021a) and international law and policy. The passing of Bill C-15, *An Act Respecting the United Nations Declaration on the Rights of Indigenous Peoples*,[9] affirms these Rights and outlines a corresponding implementation framework in Canada (GC, 2021b). There are concerns, for example, about how these technologies may impact the Rights and autonomy of Indigenous peoples and other equity-deserving groups in Canada, as these gene-edited species could spread into and affect their communities (Meghani, 2019). Therefore, there is need for adequate community engagement from the onset of research, in agreement with UNDRIP and with consideration for human rights standards and fundamental freedoms in relation to all citizens (UN, 2007; AAS, 2017; Emerson *et al.*, 2017). Canada's *UNDRIP Action Plan* does not specifically address pest management but details processes to enhance Indigenous peoples' influence on and participation in federal decision-making, which include, for example, strengthening collaboration in resource management (GC, 2023).

9 The *United Nations Declaration on the Rights of Indigenous Peoples* (UNDRIP) is a universal and internationally recognized framework of the "minimum standards for the survival, dignity, and well-being of the Indigenous peoples of the world and it elaborates on existing human rights standards and fundamental freedoms as they apply to the specific situation of Indigenous peoples" (UN, 2007).

Table 2.3 Examples of Public Groups Concerned with, Interested in, and Invested in Biological Control Practices

Public Group	Defining Features
Client Communities	• Those who use biological control in a production setting (e.g., conventional, and organic farmers, ranchers, private and government foresters), and who derive their living from land • Those interested in sustainable production practices • Funders (e.g., commodity groups) • Public health advocates and practitioners
Conservationists	• Those who manage ecosystems (e.g., government, non-profit, or private) • Conservation researchers and practitioners • Those invested in conserving and restoring biodiversity
Indigenous Peoples	• First Nation, Métis, and Inuit Elders, governments, organizations, and communities responsible for managing ancestral, treaty, or designated lands, as well as broader ecosystem health • Those who often derive physical, mental, and spiritual sustenance directly from the land (e.g., through hunting and other cultural practices)
Ecological Activists	• People with strong, often value-based opinions on environmental management, food production, or pesticides • Those willing to spend considerable time and effort influencing others' perspectives
Other Concerned Groups	• Those professionally unconnected with agriculture or ecology but concerned about food safety and sustainability, and environmental health • Those who support, promote, and are invested in Canadian economic activity and in, for example, agricultural, aquacultural, or forestry industries • Experts and non-experts concerned with the use of science and technology in society

Adapted from Catton, H. (2021) with permission from CSIRO Publishing

This table illustrates how biological control achieved through the release of live organisms potentially implicates a broad range of public groups. Although genetic pest control and biological control are not strictly analogous, both approaches share common public groups given their common objectives and application areas. The public groups depicted in the table do not represent an exhaustive list and should not be interpreted as categorically siloed; features listed may apply to multiple groups. Differing relationships with science, scientific evidence, and governments may be present across all groups.

While people in Canada typically demonstrate low levels of science skepticism and comparatively high levels of "faith" in science (Rutjens *et al.*, 2022), concerns and debates around genetically modified organisms (GMOs) in food and agricultural

contexts have been taking place in Canada and abroad for over 20 years (Wunderlich & Gatto, 2015; Rutjens *et al.*, 2022). Surveys of the Canadian public suggest a lack of extensive knowledge of the processes used to create GMOs but show that concerns nevertheless exist around GMO safety (The Strategic Counsel, 2016; Holliday & Korzinski, 2017). The Strategic Counsel's 2016 report noted that 61% of people surveyed in Canada attributed "mostly negative" associations to the term "genetic modification," and 26% expressed "extremely negative" impressions (The Strategic Counsel, 2016). Survey research from 2018 showed that slightly more than 50% of people in Canada would not want to eat food that was genetically modified using CRISPR/Cas9 (Shew *et al.*, 2018). Macnaghten and Habets (2020) highlighted how, in the context of GMO foods, the hyping of benefits, a lack of public and stakeholder engagement, and a lack of regulatory consistency among international jurisdictions all contributed to the rise of GMO controversies, specifically public mistrust and skepticism. Antecedent GMO skepticism may have some influence on public perceptions of using gene-editing technologies for pest-control programs, in Canada and abroad (Baltzegar *et al.*, 2018; Nawaz & Satterfield, 2022; Jones 2019).

There is value in understanding the public's perspective on using gene-editing technology in pest management contexts

Catton (2021) highlights factors that can shape public perception of biological control.[10] There is a lack of specific research examining public perspectives in Canada on genetic pest-control in broad as well as specific contexts. Moreover, the issue of public perception can be complicated by the portrayal (or promotion) of these technologies in public discourse. Gene-editing technologies such as CRISPR/Cas9 demonstrate accuracy in controlled laboratory settings but face uncertainty when advancing toward real-world applications (Bier, 2022). Like numerous other technologies, concerns have been raised around the potential "hyping" or promotion of gene-editing tools (Lebrecht *et al.*, 2019; Shah *et al.*, 2021). Hype distorts the likelihood of an application's success, downplays uncertainty, and shifts focus away from solutions void of commercial benefits (Lebrecht *et al.*, 2019). The hyping of gene drives could also align with concerns of the "technological fix" whereby a technology such as CRISPR is presented as an over-simplified solution to a complex social, ethical, and environmental problem, such as that caused by a pest (NASEM, 2016; Preston & Wickson, 2019). Hyping can exacerbate already-present trust issues and tensions that exist among the

10 Influential factors include diverse "values, cultures, and location," which influence how and whether pests come to be defined or perceived as such (see also Courtier-Orgogozo *et al.* (2017)); ecosystem management (e.g., protecting biodiversity); food production practices; systems for managing risk (e.g., "analytic" versus "experiential" systems); communication and knowledge transfer issues (e.g., media representations); and — as observed in GMO food contexts — levels of trust in individuals and institutions working in science or with governments (see also Wohlers (2015) and Macnaghten & Habets (2020)).

developers of technologies, government, and broader members of the public in Canada (e.g., Macnaghten & Habets, 2020; Edelman, 2023).

Discerning the level of trust in specific regulatory agencies and comfort levels around gene-editing technologies may also offer benefits to regulatory bodies and participating commercial entities as a means of clarifying the starting points for relationship-building.

National and regional public perception research in New Zealand, the United Kingdom, and the United States illustrates overall concerns about using gene-editing technologies, but it also reveals the contexts in which using these tools might be deemed acceptable, such as where food security and biodiversity could be protected, or where the spread of disease could be reduced (Funk & Hefferon, 2018; Hudson *et al.*, 2019; Brossard *et al.*, 2019; Kohl *et al.*, 2019; MacDonald *et al.*, 2022). Research broadly shows that the public lacks the knowledge to understand and evaluate the use of such technologies, and that trust in program administrators stands as a central factor (Brossard *et al.*, 2019; MacDonald *et al.*, 2022; Goldsmith *et al.*, 2022). Understanding public perspectives and integrating that knowledge into programs can form a central component of public engagement activities (Chapter 5). Discerning the level of trust in specific regulatory agencies and comfort levels around gene-editing technologies may also offer benefits to regulatory bodies and participating commercial entities as a means of clarifying the starting points for relationship-building.

Debates exist around whether humans have the right to modify and exert power over the natural world, but there is no straightforward resolution to these issues

Practising ethics refers to determining the "correctness or justifiability" of activities. It is an iterative process, incorporating various participants, perspectives, and values, that encompasses but is not limited to the parameters established in laws and policies (WHO, 2021a). Like the emergence of all novel technologies, the broad ethical concerns around using gene-editing technologies for managing pests are not new or unique. Ethical inquiry focuses on how and by whom a technology is used, and what its impacts might be. It examines power dynamics among actors and evaluates trade-offs between risks and benefits (Sandler, 2020; de Graeff, 2022). Issues such as these pertain to the emergence of all technologies with widespread social use and impacts, but some ethical aspects are specific to the pest management context, notably the theme of human interventions in the natural world.

Using gene-editing tools for pest management purposes highlights the diverse, complex, and — in some cases — contradictory relationships humans have with the environment.

Using gene-editing tools for pest management purposes highlights the diverse, complex, and — in some cases — contradictory relationships humans have with the environment. Humans instrumentalize the environment for their needs but also strive to protect and respect it for its inherent or "intrinsic" values (WHO, 2021a; de Graeff, 2022). Debates around exerting power over the natural world exist among the general public as well as in academic contexts (Kohl *et al.*, 2019; Carter *et al.*, 2021; de Graeff *et al.*, 2023). The general public typically frames these debates as humans "playing God," where an authoritative order or "naturalness" in the world is conceptualized as distinct from human activity, and where infringing upon it constitutes an immoral or unjustifiable breach of power (Carter *et al.*, 2021; de Graeff *et al.*, 2023). Academic debates commonly hinge on the intrinsic value of natural life as opposed to its instrumental value (i.e., human uses of nature); this is described, for example, through the concept of *biocentrism*, which serves as a basis for the ethical parameters of engagement (NASEM, 2016; de Graeff *et al.*, 2023). Debates seek to determine whether, and in which contexts, it is justifiable for humans to intervene or exert authority over the natural world. De Graeff *et al.* (2023), for example, argue that genetically editing mosquitoes to reduce the spread of malaria can be morally justifiable on the grounds of self-defence without dismissing the tenets underpinning a biocentric position.

Importantly, these broad debates are value-centric and may not be (or perceived to be) aligned with scientific realities or processes (Carter *et al.*, 2021). Public perceptions, opinions, and beliefs are value-laden and cannot be responded to solely with scientific information (Chapter 5). Further, what might be viewed as morally reprehensible by one community might be perceived as uncontroversial by another. As such, there is no simple way to resolve high-level debates rooted in cultural beliefs. Public engagement practices, explored in detail in Chapter 5, can be more constructive by avoiding broad themes of what constitutes "naturalness" and by triaging community engagement based on those most impacted by a specific intervention (WHO, 2021a).

Actionable, ethical debates encompass multiple topics that relate to different stages of program design and implementation

Branching off from broad debates are those pertaining to a technology's application — more specifically, how and when different actions should be taken (Sandler, 2020; WHO, 2021a). Broadly, themes can be situated under the umbrella term "efficiency and necessity" (Sandler, 2020). This entails evaluating the risks versus the benefits of a particular intervention, examining the degree to which risks are manageable, and asking whether an intervention is cost-effective (especially compared with a competing intervention) and how the public and regional or adjacent legislative bodies are engaged in these processes (Sandler, 2020; WHO, 2021a). Ethical considerations include questions about when public engagement is required and what constitutes adequate engagement (Chapter 5). Considerations of impact and justice centre on determining fairness around all relevant decision-making.

Ethical evaluations address each tool and stage in a program's process to determine who might be impacted. It has been stressed, for example, that the information used for decision-making (e.g., risk assessments, risk-benefit analyses) needs to be accessible to and easily interpretable by the public — even adapting dense, technical, quantitative reports where possible (Hayes *et al.*, 2014). Access considerations apply to who could benefit most from the technology and whether granting access for some might negatively impact others (NASEM, 2016). The notion of intergenerational justice assesses similar impacts around risks and benefits, but from an expansive timeline that incorporates future generations and has significance in the context of climate change (de Graeff, 2022).

In the Panel's view, ethical considerations can help governing bodies design and implement frameworks that incorporate diverse public knowledge and perspectives. This report highlights core ethical considerations respective to each chapter's main topic: R&D (Chapter 3), risk assessment (Chapter 4), public engagement (Chapter 5), and governance (Chapter 6). Many ethical debates around gene-editing applications typically focus on assessing impacts on stakeholders and other publics, and the incorporation of their perspectives into decision-making (WHO, 2021a). Therefore, Chapter 5 draws the most explicit links to ethical practices in genetic pest control.

3

Research and Development Environment

Chapter Findings

- Canada is not currently undertaking intensive R&D activity in gene-edited organisms for pest control, despite having research capacity in related fields.
- Better alignment among Canada's main public research funders is needed to develop the necessary personnel, and channel the correct expertise, toward responsible technology development.
- Canadian research institutions might look to international R&D efforts to inform biosafety protocol updates for regulating research on genetic pest control at public institutions.
- Investments in regulatory science will facilitate the translation of these technologies into a Canadian context, such that their safe and effective use can protect Canadian interests. The implications are not only economic in nature but also reflect social and cultural issues.
- Uncertain profitability hinders the incentives for private enterprise to develop new genetic pest-control products despite having the intellectual property to do so.
- Private-public partnerships might provide an avenue for technology translation, but any potential value would be weighed against efficacy and costs; these are areas of continued uncertainty.

The application of gene editing for pest control emerged from decades of fundamental and applied research across various fields. Current gene-editing techniques can target a wide range of potential organisms, including several species that act as pests in Canada. This chapter provides an overview of current R&D activities in genetic pest control, and potential barriers encountered in the Canadian context. The discussion begins by introducing challenges in supporting related R&D activities in the Canadian ecosystem. In addition to funding challenges, the Panel highlights necessary reforms to biosafety policies for laboratory research and discusses promising approaches for fostering responsible research and innovation, and for building capacity to develop and regulate genetic pest-control products tailored to Canadian contexts. The chapter then describes potential difficulties in translating research into genetic pest-control products for real-world applications. Difficulties include those relating to intellectual property (IP) protection for technologies and their associated data, as well as financial barriers. The latter issue may factor into

which technologies are developed or prioritized, and influence which stakeholders are involved, since genetic pest control will necessarily call on different business models than conventional pest-control agents.

3.1 Research Environment

Providing a comprehensive overview of the number of gene-editing research projects on species considered to be pests is outside the scope of the Panel's work — and is, for that matter, a fast-moving target. Among these projects, however, gene drives represent an application area of significant interest. In the Panel's view, the rapid pace of progress in this area provides a reasonable indication of technological progress in gene editing for pest control more broadly. The first demonstrations of gene drives in insects were reported in 2015 (Gantz & Bier, 2015; Gantz *et al.*, 2015). By 2019, there were upwards of 50 ongoing gene-drive projects at various stages of technological readiness (Steinbrecher *et al.*, 2019). In the three intervening years, the range of target insect species doubled to 32 (Steinbrecher *et al.*, 2019; Wells & Steinbrecher, 2022). These initiatives tend to be geared toward population suppression in order to solve pest problems in agriculture and, to a lesser degree, public health (Wells & Steinbrecher, 2022).[11] Efforts also exist with conservation applications in mind (Steinbrecher *et al.*, 2019). The scope of R&D in gene drives, and genetic pest control broadly speaking, is poised to continue growing as gene-editing technology continues to progress and additional compatible target pests are identified.

Table 3.1 presents a non-exhaustive selection of examples of current gene-drive target species that have either an established or a potential presence in Canada (e.g., due to a changing climate). At least two examples possess a relatively high technological readiness level — meaning they could be eligible for trials outside a laboratory in the near future. This table also highlights the prominence of U.S. researchers in this domain. These examples tend to be funded through R&D funding agencies and private philanthropies (Steinbrecher *et al.*, 2019).

11 Applications in public health are, however, among those possessing the highest technological readiness (Steinbrecher *et al.*, 2019; Wells & Steinbrecher, 2022).

Table 3.1 Gene Drives Under Development for Species Found in Canada

Species	Application Area	Technological Readiness	Location of R&D Activities
Common fruit fly (*Drosophila melanogaster*)	Agriculture	High. Proof of concept demonstrated in laboratory (Oberhofer *et al.*, 2021)	United States
Spotted-wing drosophila (*Drosophila suzukii*)	Agriculture	High. Proof of concept demonstrated in laboratory (Buchman *et al.*, 2018)	United States
Red flour beetle (*Tribolium castaneum*)	Agriculture	Low. Organism identified as promising candidate for gene drive, but research into biology is ongoing (Rylee *et al.*, 2022)	United States
Southern house mosquito (*Culex quinquefasciatus*)	Public health	Medium. Initial steps toward creating drive demonstrated in laboratory (Feng *et al.*, 2021)	United Kingdom, United States
German wasp (*Vespula germanica*)	Conservation	Low. Gene drive proposed, wasp genome sequenced (Lester *et al.*, 2020)	New Zealand
House mouse (*Mus musculus*)	Conservation	High. Proof of concept demonstrated in laboratory (Gierus *et al.*, 2022)	Australia, United Kingdom, United States

Adapted from Steinbrecher *et al.* (2019)

Canadian research capacity in genetic pest control is low, and the structure of the funding landscape challenges support for R&D

To make any significant headway in the use of gene-editing technologies for pest control, specialized researchers and regulators are needed. In Canada, the training of such highly qualified personnel (HQP) generally takes place in academic or other research institutions (OECD, 2022). Graduates and post-doctoral fellows leaving their university can, in theory, respond to the changing needs of innovation in science as they advance through their careers. However, the level of federal investment in R&D has stagnated in Canada over recent years (OECD, 2022), particularly in agriculture and the agri-food sector (AIC, 2017). In the public sector alone, research expenditures in these areas are approximately one order of magnitude higher in the United States than they are in Canada (AAFC, 2017; USDA, 2022a).

Most federal funding of university-based research is awarded through competitive processes and geared toward the generation of HQP or trainees (NSERC, 2022a). Canadian public funders are the main source of support for these researchers; however, these funders currently allocate scant direct investments to the applications of gene-edited organisms for pest control. For example, a search of funding awarded by the Natural Sciences and Engineering Research Council (NSERC) or the Social Sciences and Humanities Research Council (SSHRC) revealed only four grants containing "gene drive" in the title or research summary for the 2020-2021 fiscal year, with only one project pertaining to pest control (NSERC, 2022b; SSHRC, 2022). Genome Canada, meanwhile, funds activities in pest monitoring through genomics but does not currently fund research on gene-edited pests or gene drives (Genome Canada, 2022). Similarly, the relatively recent New Frontiers in Research Fund (NFRF) programs are also not funding research in this area (CRCC, 2022). Although NFRF programs are designed to support potentially high-impact interdisciplinary work, they might be unsuitable for genetic pest control given that the technology is arguably already past proof-of-concept stages.

The absence of direct support for programs on gene-edited pests (or gene drive) does not necessarily imply that Canada is unable to participate in R&D in genetic pest control. In the Panel's view, however, it does reflect the absence of a comprehensive approach for building capacity in this emerging area.

The absence of direct support for programs on gene-edited pests (or gene drive) does not necessarily imply that Canada is unable to participate in R&D in genetic pest control. In the Panel's view, however, it does reflect the absence of a comprehensive approach for building capacity in this emerging area. Researchers at Canadian institutions are active in several areas that contribute to the development of gene-edited organisms for pest control, such as genetics, molecular biology, ethics, ecological population dynamics, and economics, among other fields (Gould, 2008). Conventional funding programs (e.g., NSERC's Discovery Grant program) offer the flexibility and a relatively long funding period to pursue collaborative or interdisciplinary research. However, the funding levels of conventional programs would be insufficient to support major R&D activities in genetic pest control in a standalone way, when benchmarked against the investments dedicated to major international R&D initiatives (Box 3.1).[12] Support for R&D in novel pest-control tools will necessarily require combining

12 Grant sizes for this program generally lie in the range of $30,000 to $40,000 annually for a duration of five years (NSERC, 2020).

several types of expertise and knowledge, and therefore may struggle to come about through typical funding streams in Canada.

Box 3.1 Major R&D Investments Outside of Canada

Several non-traditional sponsors are supporting gene-drive research within the genetic pest-control field, internationally. The U.S. Defense Advanced Research Projects Agency (DARPA) is a major funder in this area with investments reported at between US$65 million and US$100 million (Haridy, 2017; Neslen, 2017). These funds are officially dedicated to the development of tools that address potential threats from the malicious uses of gene drives.

Philanthropic organizations are also visible and active in the gene-drive research space. The Bill and Melinda Gates Foundation and the Open Philanthropy project provide core funding of over US$10 million per year for Target Malaria, though other agencies also contribute (Target Malaria, 2017, 2021). The United Kingdom's Wellcome Trust highlights gene drives within its funding activities in emerging technologies (Wellcome, n.d.), while the Tata Foundation has also supported such research for several years by establishing the Tata Institute for Active Genetics and Society, hosted by University of California San Diego, with US$70 million of funding (Robbins & Fikes, 2016).

In addition to the need to coordinate multiple funding streams, other structural aspects of the fragmented R&D funding system in Canada create barriers to the development of capacity in genetic pest control. Funding and infrastructure may be distributed across a variety of actors and stakeholders in genetic pest control. In agriculture, for instance, since 1886, federal and provincial departments have provided the majority of funding and infrastructure for research (AIC, 2017). Agriculture and Agri-Food Canada (AAFC) has, for example, historically been the main repository for taxonomic and genetic research on insects, including those that affect forestry, while the Ottawa Research and Development Centre also has large collections. Resources of this type provide support to scientific research in numerous areas, including pest control and monitoring (AAFC, 2010; GC, 2018b; NRCan, 2020). Field research on forest insects to maintain expertise in the event of novel pest infestations has involved research scientists at Natural Resources Canada, often in conjunction with university-based researchers (AAFC, 2010).

Provincial research priorities are designed to be responsive to industry needs and are often leveraged with federal funds (AAFC, 2022) or funds from growers' associations linked to the major crops in a region, such as canola in the prairie provinces (CCC, 2022). The major agricultural universities in Canada conduct research and training in this area supported by provincial funds (Gov. of ON, 2022) and, to a lesser extent, grower funds leveraged by Mitacs or NSERC (Mitacs, 2023; NSERC, 2023a). Research on issues such as genetic pest control requires a sustained commitment that, in the Panel's view, provincial or grower funds have not tended to provide in Canada. In consequence, of the above is that Canadian universities can face challenges for participating in both basic and translational research in pest-control technology.

Updated policies on biosafety and containment can provide clarity for researchers and ensure safe laboratory research using novel biotechnologies at public institutions

There are indications that Canadian institutions have not yet crafted policies and infrastructure to meet the emerging biosafety and biosecurity risks (Section 4.2) that may arise over the course of R&D activities in gene editing. Novel biotechnology applications may call for ecological risk mitigation approaches that exceed traditional biosafety protocols (Wyss Institute, 2015a). In a recent study, researchers interviewed at several Canadian agricultural institutions stated they were unaware whether specific requirements exist concerning safety or disclosure for work involving CRISPR/Cas9 (Phillips & Macall, 2021). A survey of biosafety professionals (the majority working in the United States) similarly indicated that experts were not currently confident that guidelines and facilities were sufficiently prepared for safe handling of organisms modified through gene editing or carrying gene drives (O'Brochta *et al.*, 2020). Moreover, consideration of the accidental release of modified organisms during manufacturing, R&D activities, and transport is currently a regulatory gap in Canada (ECCC, 2022c).

Gene drives, specifically, provide a motivation for establishing such guidelines and policies, since they are generally designed to deliberately spread genetic constructs, with accompanying risks (Section 4.2). Research centres active in this field are adapting internal policies to avoid unwanted outcomes, but many laboratory policies are not sufficient for overseeing gene-drive research, due to their emphasis on biosafety risks caused by pathogens (van der Vlugt *et al.*, 2018; Millett *et al.*, 2022). Several research institutions in the United States have proactively established internal policies, given the anticipation of government oversight if such policies are not put in place (Wyss Institute, 2015b). The associated laboratory safety and containment requirements include additional environmental or physical controls (Wyss Institute, 2015b), to ensure various levels of molecular, ecological,

reproductive, and physical containment (Stanford University, 2022). These levels might be defined generally, or specifically to applications. In Australia, a set of criteria for confinement is used for the safe handling of insect vectors (ASTMH, 2019), while other guidelines exist to define physical containment levels for research involving genetically modified live organisms more generally (OGTR, 2013).[13]

The codification of safety standards and the enforcement of compliance at institutional levels can be challenging. Academic laboratories operate at the cutting edge of R&D and are frequently left to be self-governed according to internal policies, in part to foster an environment conducive to new discoveries; challenges exist in designing and extending regulatory activities to these institutions. For example, real and perceived tensions exist between regulatory oversight and academic freedom, and misunderstandings can occur surrounding roles and responsibilities in the context of environmental, health, and safety management (Huising & Silbey, 2013). Bottom-up approaches to operationalize laboratory safety policies involving all implicated stakeholders have been shown to be effective, by taking into account institutional culture and how stakeholders relate to one another (Huising & Silbey, 2011); these approaches have already been used to define a laboratory risk management plan specific to gene drives at research centres in the United States, for example the Wyss Institute (2015a). These initiatives can be bolstered by third-party accreditation bodies that play a role in assessing institutional readiness and compliance for work with modified organisms (O'Brochta *et al.*, 2020). Before gene-editing — and particularly gene-drive — research becomes more prevalent in Canadian laboratories, there may be a need to ensure that policies, standards, and institutional infrastructure are updated to manage the heightened laboratory safety requirements.

Support for integrative collaboration across sectors and disciplines may translate to an increased capacity for responsible gene-editing innovation in Canada

Some research sponsors have increasingly recognized their role in facilitating the ethical development of technologies and responsible research conduct, usually in the context of funding R&D to address societal challenges (CCA, 2021). As such, funding R&D need not be restricted only to basic or translational science; Canadian sponsors and institutional actors can participate in advancing the state of knowledge in additional crucial areas pertaining to the ethical development, deployment, and governance of gene-edited organisms. Such initiatives could be instrumental in defining guidelines surrounding genetic pest control while regulations adapt (Section 6.2) or facilitating engagement with actors outside of the R&D sector.

13 The Australian government has already provided clarification on its existing standards in the context of gene drives and established an accompanying licensing process (OGTR, 2021).

For example, GeneConvene is a U.S. initiative supported by the Foundation for the National Institutes of Health (FNIH) that acts as an education and outreach hub for public health applications of genetic pest control, including gene drives (FNIH, 2022). Research funded through the Bill and Melinda Gates Foundation and Open Philanthropy has also led to the establishment of soft governance tools in the form of a set of guiding principles based on advancing science for public good; promoting good governance and stewardship; encouraging transparency in data-sharing; facilitating meaningful engagement (including funding to conduct it); and building capacity through education in areas relevant to research, such as science, ethics, biosafety, and regulation (Emerson *et al.*, 2017). So far, several of the major public and non-profit sponsors of genetic pest-control R&D have co-signed these principles, demonstrating the role research funders can play when it comes to defining parameters for responsible R&D (Emerson *et al.*, 2017).

If guidelines and principles outlined in good governance are to be sufficiently developed and respected, then ethics, engagement, and social dimensions will need to be integrated into their development early on. Indeed, lessons could be learned from the years of R&D involving GMOs for food where social concerns around ethics, economics, ecological impacts, and social benefits were given scant attention in regulatory frameworks and implementation practices (Macnaghten & Habets, 2020). While not bound by legal parameters, a code of ethics for gene-drive research offers value for self-regulating scientific communities by ensuring critical analysis of risks versus benefits across society broadly (Annas *et al.*, 2021). All researchers, especially early-career researchers, will need to be aware of and engaged with these codes of ethics; this, in turn, requires resources and incentives that funders and research institutions can provide.

The approach used in the GeneConvene initiative follows Responsible Research and Innovation (RRI) core principles and emphasizes an orientation for innovation that goes in "ethical, inclusive, democratic and equitable" directions (Owen *et al.*, 2012). A core RRI component is reflexivity on the part of institutions — that is, reflecting on and being critical of their assumptions and activities (Wynne, 2006; Thizy *et al.*, 2019). This approach can contrast with conventional ways of framing innovation and research, either as curiosity-driven or to meet a market need. Funding agencies can play a role in this area by working alongside scientists and influential social actors to co-define expectations as well as support and educate researchers in developing governance and oversight models (Owen *et al.*, 2012). Through such deliberative approaches, the types of impacts desired by society might be determined, allowing science and innovation to better align outputs to societal needs.

In Canada, initiatives of this type can fall within the scope of GE³LS research (the study of genomics and its ethical, environmental, economic, legal, and social

aspects) as defined by Genome Canada (Genome BC, 2021a). GE^{3}LS research projects are interdisciplinary and connect scientists with stakeholders from the social sciences and humanities (or policy-makers), in order to produce a clearer understanding of the implications of new genomic technologies in parallel with scientific development. Such programs pursue these aims by facilitating the co-development of research areas (Box 3.2), rather than having non-scientific components included as an afterthought — a weakness for which this program has been previously criticized (Kosseim & Chapman, 2011). Gene editing offers a broad field of applications, such that the operationalization of RRI principles might be challenging and context-dependent (Bruce & Bruce, 2019). Within a narrow scope, gene-drive research features many characteristics of responsible innovation thus far (Russell *et al.*, 2022), particularly in some high-profile cases such as Target Malaria. However, sponsors will need to provide the necessary incentives to maintain current trends.

Box 3.2 Bridging Disciplines, Stakeholders, and Cultures

The Summer Internship for INdigenous Peoples in Genomics (SING) program operates in multiple countries worldwide, facilitating the advancement of Indigenous researchers in genomics (SING Consortium, n.d.). SING aims to eliminate disciplinary and cultural barriers to build capacity. The Canadian chapter of the initiative provides training opportunities and workshops, most notably to facilitate and promote Indigenous participation in GE^{3}LS (Indigenous STS, 2022). In doing so, participants can "gain an awareness of the uses, misuses, opportunities, and limitations of genomics as a tool for Indigenous peoples' governance" (SING Canada, 2022).

NSERC's Discovery Horizons and Collaborative Research and Training Experience programs have also emerged as mechanisms for capacity-building in interdisciplinary research and promoting inclusive research collaborations (NSERC, 2021, 2023b). Funding is awarded through a competitive process, however, and standalone requests for proposals on topics such as gene-edited organisms for pest control do not occur. Partnering with local and interested First Nations' communities to encourage Indigenous students to work in basic research offers potential exploration. Within this context, Elder Marshall's *Two-Eyed Seeing* (Box 1.1) would be a useful framework, as it has been used successfully in other scientific contexts (Bartlett *et al.*, 2012).

Efforts may be needed to bolster regulatory science, since the challenges posed by novel, first-in-class technologies are heightened in areas where domestic R&D capacity is low

There is a lack of clarity as to how research in genetic pest control might be effectively supported in the Canadian system. The absence of a comprehensive approach to fund this work, combined with the lack of participation by Canadian researchers in major gene-drive projects, limits domestic R&D capacity. This in turn limits Canada's prospects for leading in both technology development and regulatory capacity, since the HQP involved in regulatory science tend to be trained in Canadian public institutions. R&D activities underway elsewhere (Table 3.1) could impact Canada, however, since the resulting technologies may be proposed for use in Canada or deployed in the United States, potentially affecting shared Canada-U.S. ecozones (Figure 2.2). In either case, stakeholders in regulatory science will have to respond to these developments but may lack practical experience with cutting-edge tools.

Capacity-building in this area may be accomplished through multiple avenues. Sponsors could establish pathways that allow Canada's researchers to contribute to ongoing initiatives in genetic pest control through collaboration, or by supporting research in risk assessment or the social dimensions accompanying the use of gene-edited organisms (Section 4.1). In other jurisdictions, the connections between R&D activities and regulatory activities can be explicit. The U.S. Department of Agriculture's Animal and Plant Health Inspection Service (USDA APHIS) has, in response to R&D activities, invested in scientific resources that support research on several aspects of genetic pest control, in order to improve understanding of these tools from a regulatory perspective (USDA APHIS, 2022). A recent agreement between the University of California and the Tata Foundation is designed to support the training and development of HQP and encourage partnerships between researchers and policy-makers; it features a transnational exchange component between social science and humanities researchers in the United States and India. The objective of the latter component is to support domestic capacity-building for technology adoption in India (Tata Trusts, 2016).

Fellowships also exist through the American Association for the Advancement of Science (AAAS) and the National Academies of Sciences, Engineering, and Medicine (NASEM), that connect individuals to government departments for work in science policy or federal R&D (AAAS, 2022a; NASEM, 2022). Policy issues could relate to internal processes but also transnational initiatives in pest-control policy grounded in science diplomacy (AAAS, 2022b). Several additional programs also exist through individual regulatory agencies to establish connections between basic research and regulatory science, specifically (NIH, 2020; USDA, 2022b; US FDA, 2022). An analogous program for bridging science and policy

Over the medium to long term, however, failure to produce enough HQP will limit Canada's ability to play a major role when it comes to guiding the technological and regulatory development of genetic pest control.

exists in Canada but is not focused on regulatory science and occurs at a smaller scale than the previous U.S. examples (Mitacs, 2022). Over the medium to long term, however, failure to produce enough HQP will limit Canada's ability to play a major role when it comes to guiding the technological and regulatory development of genetic pest control. A clearer path from the HQP-producing institutions toward public sector regulatory science could better prepare Canada to anticipate and manage new products based on gene editing.

3.2 Translation of Research to Applications

Pest control is a major business. In the U.S. agricultural system alone, crop protection is a US$50 billion industry (Phillips McDougall, 2018). Industry R&D investments in this sector are high (e.g., 7–10% of their sales over the last 50 years (Phillips McDougall, 2018)), reflecting both the size of the stakes and the demand for new products with increased efficacy or better safety profiles. However, Canada represents a comparatively small market, which guides R&D and market approvals accordingly. Several additional challenges exist in this area, requiring careful consideration by decision-makers in terms of guiding policy and investments in Canada. Genetic pest-control products differ from conventional agents in how they are manufactured and operate, leading to uncertainty for commercial development and corresponding business models. This section describes the numerous barriers for establishing genetic pest-control products and programs, and how these will influence decisions about which applications will be pursued or prioritized, and by whom.

The IP landscape for gene editing presents barriers to new entrants due to the dominance of large players and unpredictability related to ongoing patent disputes

Inventions can be assigned patents, granting developers a temporary monopoly on the use of the associated technology in exchange for the disclosure of the invention and how it functions. This arrangement incentivizes technology development in the private sector, since patents grant firms exclusive rights to market a product or license an invention. Different jurisdictions will follow different rules to determine what constitutes an invention and whether it is patentable. In the context of gene editing, for example, entire organisms cannot

be patented in Canada, but the novel traits they exhibit, or the processes used to modify them, are potentially eligible for patent protection (CBAN, 2022).
The CRISPR/Cas9 gene-editing system lies at the centre of a longstanding and global IP ownership dispute that some experts predict could take several more years to resolve (Ledford, 2022).[14] The IP assets involved in the dispute grant the owners the exclusive right to develop large swaths of gene-editing applications using CRISPR/Cas9, in any number of organisms, or to issue licences to extend these rights.

Despite the controversy surrounding patent ownership, large multinational firms have entered into several licensing agreements with the patent-holders (and companies acting as their surrogates). This gives these firms the freedom to operate for potentially developing pest-control applications using CRISPR/Cas9 (CBAN, 2022).[15] These firms and their subsidiaries are also active in pest control (accounting for over 65% of the market share in agrochemical sales (ETC Group, 2019)) and have become major patent-holders themselves when it comes to applications of CRISPR/Cas9 (CBAN, 2022). The dominance of large agricultural firms in this area presents certain unique risks. For example, in an analysis of gene-drive patents in the United States, Montenegro de Wit (2019) identified applications of gene drives to increase the susceptibility of weeds to agrochemicals produced by the patent-holders. In this way, the resulting gene drives would conceivably *increase* the use of chemical pest-control agents under the pretext of addressing weed problems.

The current IP landscape is leading to concerns over risks, such as the previous example, and the potential exacerbation of power imbalances between technology developers and communities (Montenegro de Wit, 2020), with implications for regulatory oversight (Ching & Lin, 2019) and the distribution of risks and benefits (Brown, 2017). Although CRISPR/Cas9 is hailed as a technology that both small- and large-scale inventors can use due to its low technical barrier of adoption, the question of IP could be challenging to address without access to legal expertise and resources. Alternative CRISPR platforms based on different proteins than Cas9 are being developed, in part to avoid restrictions on freedom to operate encountered in the present IP landscape (e.g., Hera Biolabs, n.d.), but these are not as established as CRISPR/Cas9. From a development standpoint, the extent to which large multinational companies control IP could challenge small players seeking to commercialize products, as they will need to obtain licences or else face the risk of litigation (Rodriguez Fernandez, 2020).

14 The IP ownership status of CRISPR/Cas9 in Canada is similarly unclear. However, in the event it is resolved, the broad rights afforded to IP holders in other jurisdictions would also apply in Canada (Phillips & Macall, 2021).

15 Certain licensing terms do, however, explicitly prohibit gene-drive applications (Broad Institute, 2016).

Tensions may arise between a desire to protect IP and principles that promote responsible development, such as transparency and inclusivity

The protection afforded to innovators by patents and other forms of IP contributes to lowering risks in the commercial environment. Patent-holders can pursue legal action if their inventions are used by others, even unknowingly or inadvertently, without prior permission (e.g., through licensing). For example, gene-drive organisms that disperse outside of their intended deployment area could make individuals or groups inadvertently benefiting from this dispersal liable for damages (Meghani, 2019). This concern is reminiscent of earlier events involving the appearance of genetically modified crops on the properties of growers who did not purchase them, due to pollen drifting in the air; patent-holders successfully sued some of these growers for damages (Glascoe, 2018). Similar situations — particularly for applications using CRISPR/Cas9 (CBAN, 2022) — could arise with gene-edited organisms, given the variety of traits that could be made available through genome editing. In this respect, the robustness of IP rights — themselves bolstered through trade agreements (see, for example, GAC, 2020a) — can be incongruous with the spirit or letter of several international agreements concerning the protection of biodiversity or the Rights of Indigenous peoples (Meghani, 2019)[16] — agreements salient to the global governance of gene-edited organisms (Brown, 2017).

Furthermore, data relating to trials or studies conducted to obtain regulatory approval for gene-edited pest control are also subject to IP protection. In many situations, confidentiality around methods or data can help impart or maintain competitive advantages, particularly for smaller entities. In the context of gene-edited plants, some inventors may avoid disclosing information until field trials have begun (Phillips & Macall, 2021). Field-trial data for registered products, meanwhile, enjoy the protection of confidentiality; through Canadian regulators, confidential test data and other business information are protected for 10 years (GC, 2022a). The confidentiality between regulator and producer can be valuable to both parties as it protects commercial interests and incentivizes transparency beyond that which is legally required.[17] It could also, however, contribute to a real or perceived lack of transparency in the technology development process, from a public standpoint.

In RRI, the participation of societal actors in the process of innovation during R&D activities requires transparency (Von Schomberg, 2011). If innovators are to be responsive to outside stakeholders, this could require providing access to valuable

16 Tensions may also arise with respect to access and benefits-sharing (ABS) commitments on traditional knowledge and genetic resources, such as those prescribed through the *Convention on Biodiversity* and associated protocols (UN CBD, 2011; WIPO, 2018).

17 The failure to disclose any data of relevance while registering a new pest-control product carries significant financial penalties (GC, 2002).

IP early during the development lifecycle. This highlights one of several conflicts between RRI frameworks and conventional IP practices (König *et al.*, 2015), since, in typical commercial settings, it can be counterproductive to disclose IP unless it can be protected through patents. (Unpatentable IP might instead be kept confidential as a trade secret.) The disclosure of valuable data — which could advance the scientific state of knowledge, particularly for gene drives (Taitingfong *et al.*, 2022) — potentially hinges on the perceived commercial value of maintaining such data as proprietary.

In some cases, such as Target Malaria's non-profit model, technological progress is accompanied by open-access publications and creative approaches to IP, in order to facilitate knowledge-sharing with governments of countries impacted by malaria (Target Malaria, 2020b).[18] For technologies developed for profit, however, it is currently unclear how the need for transparency will be reconciled with commercial incentives for confidentiality, and to what extent the mechanisms used to protect test data for crops and chemicals also apply to gene-edited organisms. The time and investments required to bring new pest-control products to market is substantial (Phillips McDougall, 2018) and could create tension between the need to provide an environment that supports innovation — by protecting valuable business information for product developers — and the need to establish a robust and shared evidence base to support risk assessment for novel pest-control products based on gene-edited organisms (Section 4.1).

Pest-control programs based on gene-edited organisms challenge conventional business models

The deployment of gene-edited organisms for pest control could come at considerable expense. Such programs will require the mass rearing of organisms for this purpose. In the case of insects, examples from 20th-century SIT programs (Section 2.1 and Box 2.1) suggest that establishing facilities to do so requires investments of up to US$10 million (Alphey *et al.*, 2011). More recently, similarly large funding commitments have been made for facilities to produce *Wolbachia*-infected mosquitoes (Goh, 2022; WMP, 2023). These facilities also require ongoing investments for staff and consumables (i.e., feed), or for expenses associated with release (Alphey *et al.*, 2011), resulting in substantial recurring costs.[19]

These costs scale with the facility's production capacity, but the capacity required for a genetic pest-control program depends on the application context. For example, the effectiveness of a SIT program is sensitive to the ratio of sterile to wild-type insects (Brown *et al.*, 2019). Similar considerations — the ratio of modified to unmodified

18 Target Malaria participants have also licensed IP to the private sector for agricultural applications (Biocentis, n.d.).

19 Biological control programs have diverse logistical requirements. Program costs vary accordingly but have typically fallen within an order of magnitude of US$1 million (Naranjo *et al.*, 2019).

organisms — play a role in genetic pest control, particularly for control achieved through reproductive means (e.g., pgSIT; Section 2.1). In the case of gene drives, the design of the drive and its intended objective (i.e., suppression or replacement) will factor into capacity requirements for the facility due to the interplay between drive properties and population dynamics (Dhole *et al.*, 2020; Frieß *et al.*, 2023).[20] The direct and indirect costs associated with regulation and monitoring must also be considered and can be challenging to estimate (Brown *et al.*, 2019).

The economics for self-sustaining interventions could differ from other pest-control approaches that rely on mass rearing. With SIT, or self-limiting pest management approaches (Section 2.2), every reared organism will contribute to a fraction of the total benefit resulting from the release. An optimal number of organisms may exist to suppress a pest in a given context from a cost-benefit standpoint, but, even if the facility produces additional insects, these will contribute some marginal benefit (Brown *et al.*, 2019). Moreover, the facility will also be required to produce a consistent number of insects on repeated occasions, given the transient nature of sterile insects (IAEA, 2008). Gene drives, however, can be engineered to sustain themselves. This fact could lower the need and market for the rearing facility to continue producing output at full capacity (Brown *et al.*, 2019), which might limit the potential for that facility to recuperate initial investments.

In sum, facility size could weigh more heavily on the economics of a pest-control program for gene drives than for earlier approaches; facilities of these types are not always easily repurposed for other uses (IAEA, 2008). This poses commercial risks for potential developers unless the market is large. Although gene-edited insects could conceivably be less expensive to rear than their counterparts from a SIT program,[21] a substantial initial investment might nevertheless be required for infrastructure in an environment where the efficacy and value of genetic pest-control products remain unknown.

The application area for gene-edited organisms for pest control will influence commercial models, dictating resourcing levels, stakeholders, and values

In addition to the challenge of securing investments to finance the facilities for rearing gene-edited organisms, there exist additional costs, including for field trials, logistics, regulatory compliance, and monitoring. These costs, combined with persistent uncertainties surrounding effectiveness, increase the commercial

20 Coordination with other pest-control approaches is one means by which SIT programs have been made more economical; reducing pest populations prior to the release of sterile insects can reduce the necessary production capacity (and therefore cost) (Brown *et al.*, 2019).

21 SIT facilities might require specialized equipment (e.g., radiation sources) to sterilize the insects and sort them according to sex, in the case of mosquitoes (IAEA, 2008).

risk for potential developers (Mitchell *et al.*, 2017). Moreover, since a genetic pest-control program is an area-wide pest-control technique, the resulting benefits and harms could extend beyond the initial deployment site (Vreysen *et al.*, 2007). These factors may require different commercial models in comparison to conventional pest-control products. For example, although agrichemical pest-control products also require large R&D investments and substantial efforts to obtain regulatory approval (Sparks & Lorsbach, 2017; Phillips McDougall, 2018), users will likely need to purchase the product with regularity, while non-users will typically not experience a direct benefit from its use. Such products may therefore generally demonstrate larger potential user bases and longer timescales for cost recovery and profit.

This contrast is further complicated by potential delays in the manifestation of economic benefits resulting from area-wide pest-control programs involving live organisms. In some biological control programs, the time horizon for the appearance of benefits can be years (Naranjo *et al.*, 2019). Recent models for *Wolbachia*-infected mosquitoes similarly predict that economic benefits could take up to a decade to surpass cumulative program costs (Brady *et al.*, 2020). These timelines may be politically, socially, and economically daunting, even given evidence on the high cost-benefit and cost-effectiveness for pest-control programs of this type when they have proven successful (O'Neill *et al.*, 2018; Collatz *et al.*, 2021; Naranjo *et al.*, 2019).

Despite the fact that resources to develop and deploy genetic pest-control products exist in the private sector, the incentive to develop such products may be low, particularly in application areas where the benefits may not be linked to profit, such as public health (Brown, 2017).[22] To address challenges outlined above, particularly those relating to large upfront and recurring costs, development might instead occur in the public or non-profit sectors (Brown *et al.*, 2019). This is consistent with earlier control programs involving SIT and biological control, which faced similar commercial or economic barriers, and were developed either in the public sector or through consortia such as private-public partnerships or groups of non-governmental organizations (Brown, 2017; Naranjo *et al.*, 2019). For instance, a North American pink bollworm (*Pectinophora gossypiella)* eradication program is led by growers in the United States and Mexico but also co-funded by public sponsors, such as the U.S. Department of Agriculture (Brown, 2017).

Such partnerships could be established in response to various incentives. Public investments in development or infrastructure could, for example, offset some financial risk and entice private sector participation in aspects of program

22 A recent review of target insects for gene drives, for example, reveals that R&D skews toward programs for agriculture pests, as opposed to conservation applications (Wells & Steinbrecher, 2022).

delivery (IAEA, 2008).[23] The establishment of partnerships over broad geographic areas could be incentivized by economies of scale in insect-rearing facilities (IAEA, 2008; Brown *et al.*, 2019), albeit with increased logistical costs related to coordinating across stakeholders (Klassen & Vreysen, 2005). Trade-related considerations could also draw potential stakeholders together toward an area-wide pest-control program and provide motivation for leveraging public funds (Jones *et al.*, 2019). This might be particularly relevant in the context of neighbouring jurisdictions wishing to avoid the importation of a pest, or to account for a pest's natural movement across borders (Jang *et al.*, 2014).

Partnerships, additionally, can unlock different potential streams of funds and expertise depending on the application context. Public health and conservation pest-control activities potentially have access to various options of external co-funding from sponsors through grants (IAEA, 2008). Target Malaria follows a non-profit model, and the program (and its affiliated researchers) is supported through funds ranging from research sponsors — public and philanthropic — to national government agencies, as well as the World Bank (Target Malaria, 2021). The Okanagan-Kootenay Sterile Insect Release (OKSIR) program is a longstanding SIT program in British Columbia that aims to control the codling moth (*Cydia pomonella*), a major orchard pest. Although SIT was a mature technology by 1992 when OKSIR was launched, the program required a $7.4 million investment on behalf of the federal and British Columbia governments to build a facility for rearing sterile moths (OKSIR, 2011). The operating costs have since been primarily covered through parcel taxes on growers, grants from other agricultural associations, and property taxes from landowners in the control area (OKSIR, 2011).

These challenges, taken together, reflect a need to identify areas where Canada might possibly benefit from joining activities taking place internationally to meet common threats. R&D in this area is resource-intensive, and it also demands significant time, owing to the need for research, testing, and regulatory compliance. Therefore, given the relative lack of basic research activity occurring in this field in Canada, a forecasting exercise to identify areas where Canadian national interests are at particular risk and where leadership may be required could be valuable. In the Panel's view, efforts in horizon-scanning of technology and pest risks are needed to guide investments and establish the necessary partnerships for genetic pest control. In this way, stakeholders and applications might be identified proactively, facilitating early engagement in technology development for pest management using gene-edited organisms.

23 Private actors in SIT programs have participated in maintenance, release, software, and equipment, for example (IAEA, 2008).

4

Determining and Managing Risks

Chapter Findings

- The risk assessment process is central to decision-making in pest control, but its legitimacy hinges on a body of evidence that does not currently exist for genetic pest-control programs.
- Gene drives designed to be self-limiting and localized might be assessed using conventional means and staged testing, in order to promote safety and collect evidence.
- Self-sustaining gene drives may require the development of other assessment methods and modelling tools.
- Novel risks arising in a given implementation of genetic pest control must be isolated through assessment against other pest-control techniques.
- Adaptive risk assessment is a necessary tool to account for the evolving body of evidence, and can also be used to obtain valuable stakeholder and Rights-holder input for risk identification and prioritization.
- In genetic pest control, risk management and risk assessment are strongly linked, iterative, and inform one another; this may represent a departure from typical decision-making which proceeds in a one-way, linear fashion.

Pest management is central to addressing the wide range of harms that agricultural pests and vectors of disease can cause. Evidence-based practices to formally assess these approaches are necessary to inform decision-making surrounding their use. These practices typically involve the assessment and management of the risks and benefits presented by an intervention to control pests. The objectives and mechanisms of action for prospective genetic pest-control products may require the consideration of new risks, which may require approaches to risk governance with a broader scope than is conventional (Figure 4.1).

The novelty of the technology, combined with the diversity of potential target species and environmental and social deployment contexts, multiplies these potential risks. Environmental risks might include impacts to biodiversity or to the environment and native ecosystems, as well as risks to the health of humans and animals. However, additional risks will arise owing to a collective lack of experience with these technologies. The unknown efficacy of genetic pest control, along with lack of harmonization in international regulations and trade, could lead to significant economic risks from the use

of these technologies in agriculture. Additional social and cultural risks may also present themselves in pest contexts where different value systems intersect. Various stakeholders and the general public may distrust the use (or motives behind the use) of these technologies.

Figure 4.1 A More Holistic Approach to Risk Assessment

A schematic representation of a more holistic approach to risk assessment that includes the conventional environmental risk frameworks, together with consideration of social, cultural, and economic risks accompanying the development and implementation of new pest-control technologies.

The risk assessment process is a key component of governance (Section 6.1), and the legitimacy of its design and findings can be important for fostering public trust. This chapter introduces conventional practices for risk assessment and management and discusses some of the unique issues raised by genetic pest control. It then explores examples of risks across the categories shown in Figure 4.1 in greater detail. Finally, the chapter concludes with an overview of potential frameworks for broadening responsible risk governance, including practices that are underway in genetic pest-control trials.

4.1 Assessing Potential Pest-Control Interventions

Decisions to initiate any pest-control program or compare alternatives are based on analytical methods and standard processes. The introduction of new pest-control tools can be limited by gaps in data and real-world experience. This can challenge decision-makers and developers in defining what evidence is necessary for the implementation of new tools in new contexts. Risk assessment frameworks provide an approach to supporting decision-making. The use of systematic procedures for risk assessment can nevertheless help our understanding of how these tools contrast with others, where evidence surrounding risks is already known and has been identified (Section 2.1).

Risk assessment based on problem formulation is a standard approach to support decision-making in pest-control applications

Legislation defines how a new product should be registered for pest control. In Canada and elsewhere, this normally implies an assessment of the hazards posed by a product (Turner *et al.*, 2018; PMRA, 2021a). *Hazard* denotes adverse effects, such as harm to health or to the environment. Risk assessment investigates these hazards — how they may come to pass and through which endpoints they might be recognized — to establish whether the permitted uses[24] of the product meet the standard of reasonable certainty of no harm (GC, 2002). Risk assessment scrutinizes the various hazards and their associated levels of exposure to determine the main risks associated with the use of a pest-control product for a particular purpose (HC, 2000). In doing so, the assessment process also reveals uncertainties and evidence gaps (HC, 2000; Devos *et al.*, 2021).

Canadian legislation requires that applications for registering new products are accompanied by analyses of risks to human health and the environment, but the law does not prescribe a specific analytical methodology for doing so (PMRA, 2021a). This allows for flexibility in risk assessment, such that new applications may not necessarily require additional legislation but instead a different operationalization of existing legislation. Risk assessments can thus proceed differently depending on the focus (e.g., human health or environment); however, despite this variability, it is common practice for risk assessments to begin with problem formulation (PMRA, 2021a). This step defines protection goals for a pest-control intervention, stating what the intervention aims to achieve and how (PMRA, 2021a; WHO, 2021a). The objective is to compel risk assessors to take broad protection goals expressed in policy, and operationalize them into context-specific goals (Garcia-Alonso & Raybould, 2014). Figure 4.2 depicts how a typical risk assessment process based on problem formulation might proceed. Protection goals, once defined, guide risk assessors

24 *Permitted uses* dictate the level of risk exposure; in the case of a conventional pest-control agent, this might combine the frequency, duration, and quantity of an agent to which an individual might be exposed (HC & Ipsos, 2020).

toward the definition of assessment endpoints.[25] These represent what will need to be assessed in order to estimate the likelihood of an adverse impact on protection goals (Garcia-Alonso & Raybould, 2014). Assessment endpoints can subsequently be used to establish risk hypotheses for testing, which lead to measurement endpoints that define the relevant experimental data or evidence required by the assessment (Sanvido *et al.*, 2012; Devos *et al.*, 2015).

Protection Goals

Specified through policy and reflected in legislation

Examples: biodiversity, ecosystem services (including provisioning, regulating, and cultural services)

Operational Goals

Defined by or with regulators

Example: release should not result in displacement of key species

Assessment Endpoints

Collection of possible indicators of negative impacts on protection goal

Example: establishment of populations of gene-edited organisms outside of target area

Testable Risk Hypotheses

Used to define and prioritize studies that can inform effects on assessment endpoint

Example: gene-edited organisms do not have characteristics that increase their persistence in the environment as a result of the gene-editing process

Measurement Endpoints

Delineates the evidence required by assessors, to be collected experimentally or otherwise

Example: test gene-edited organisms for increased fitness relative to wild-type in environmental conditions corresponding to the geographic extent of the release site

Adapted from Turner *et al.* (2018)

Figure 4.2 Process for Operationalizing Environmental Risk Assessment Based on Protection Goals

Problem formulation can be operationalized through a five-step process, allowing the connection of protection goals to endpoints. The above example is for environmental assessments, but it also applies to the assessment of risks to human health.

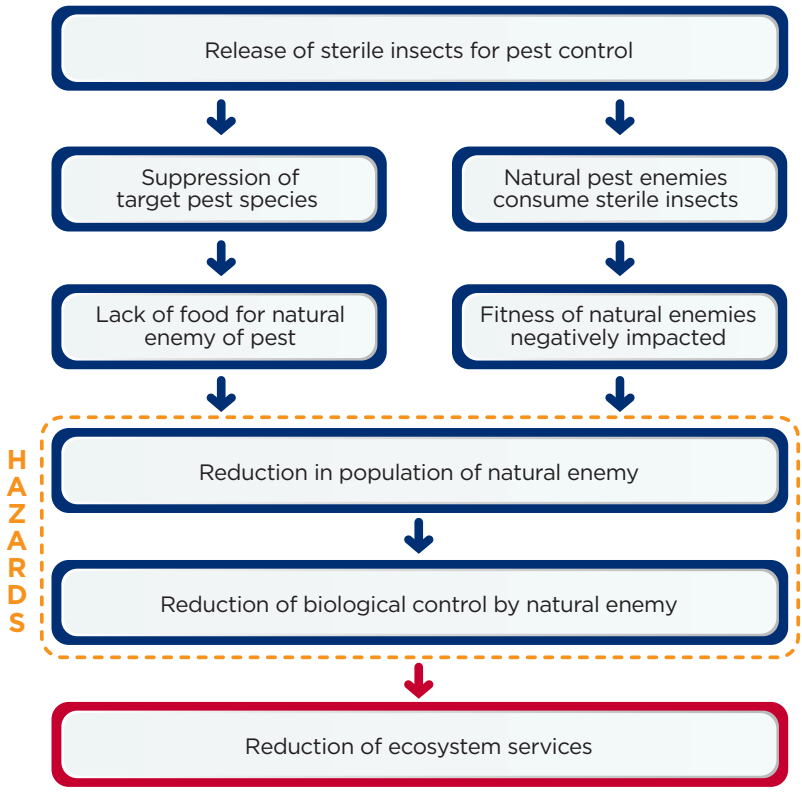
25 *Assessment endpoints* might include the entity to be protected, the attributes of that entity, the unit of measurement, and the spatial and temporal scales of protection (Garcia-Alonso & Raybould, 2014).

The analysis and ranking of risks can reveal which evidence is needed and where uncertainty is highest, while also facilitating comparisons among pest control tools

Within the process described in Figure 4.2, assessment endpoints can be used to delineate what constitutes an adverse effect, according to a threshold determined by assessors. Assessors can use this information to build scenarios or pathways to harm, outlining the causal and sequential steps resulting from a pest-control intervention that might result in an unwanted outcome (Sanvido *et al*., 2012; Romeis *et al*., 2020). In a guidance document for assessing the risks of deploying genetically modified mosquitoes, the World Health Organization (WHO) stresses that establishing causal pathways for specific harms is key to providing a means for risk-based hypothesis-testing, identifying knowledge gaps, and prioritizing relevant experiments (WHO, 2021a). In some cases, evidence may exist to address a risk hypothesis, while in others it will not. These evidence gaps help to define experimental work needed to collect the relevant data, for instance, through field trials.

Two example pathways to harm are shown in Figure 4.3 and describe possible ways in which the release of sterile insects in an SIT program can result in the loss of ecosystem services. In these examples, ecosystem services are represented by the loss of the ecosystem's capacity to control the pest population with the pest's natural enemies (i.e., biological control).[26] In the first pathway (Figure 4.3, left), the release of insects results in the desired effect of population suppression of the pest species (the objective of the program). However, in this hypothetical ecosystem, a natural enemy (such as a predator native to the ecosystem) might be accustomed to feeding on the pest, and the reduction of the pest population indirectly leads to a knock-down effect, where the natural enemy population also decreases. Consequently, the ability of the natural enemy to provide biological control of the pest species will be diminished should the pest rebound after the SIT insects are no longer present (Box 2.1). The second pathway (Figure 4.3, right) presents a different scenario with a similar outcome: the pest's natural enemy might consume the sterile insects instead of its typical prey which, given the transient presence of these insects or their differing nutritional value, could negatively impact the ecological fitness of the natural enemy. This would also result in a diminished population and a concomitant reduction of the ecosystem's capacity for biological control of the pest by its natural enemy.

26 *Ecosystem services* is a broad concept that includes provisioning (e.g., food production), regulating (e.g., biological control), and cultural (e.g., cultural heritage) services. An environmental assessment will typically include several of these examples as protection goals, in addition to biodiversity and other environmental issues salient to the context (Garcia-Alonso & Raybould, 2014).



Adapted from Romeis *et al.*, (2020); Romeis & Widmer (2020)

Figure 4.3 Possible Pathways to Harm to Ecosystem Services Following the Release of Sterile Insects for Pest Control

These examples provide information on causal pathways, hypotheses, and designs for experiments that can inform the decision to release live organisms for pest control. They do not, however, include several additional characteristics of a real ecosystem, such as population dynamics, or nuances in the interactions among various species. It is not possible to assert *a priori* whether either of these pathways is more likely, or how they compare.

Several jurisdictions follow a risk assessment process similar to that described above, with variations to account for whether the assessment focuses on environment, ecology, or health (Nienstedt *et al.*, 2012; US EPA, 2014; PMRA, 2021a). The process is also applicable and widely employed across a range of pest-control approaches, from conventional chemical agents to biological control (Romeis *et al.*, 2020; PMRA, 2021a). The proposed method of pest control will largely dictate which evidence will be needed or prioritized in decision-making, since it will influence which of the causal pathways to harm are most relevant to prioritize and translate into risk hypotheses

The proposed method of pest control will largely dictate which evidence will be needed or prioritized in decision-making, since it will influence which of the causal pathways to harm are most relevant to prioritize and translate into risk hypotheses and endpoints.

and endpoints (EFSA GMO Panel, 2020). For this reason, some argue that conventional risk assessment tools can be repurposed for the governance of gene-edited organisms for pest control, including gene drives (Turner *et al.*, 2018; Romeis *et al.*, 2020). The use of adapted versions of conventional practices builds on previous experience in risk assessment and, importantly, allows for better comparison with other interventions, once the necessary evidence has been collected (Romeis *et al.*, 2020; Devos *et al.*, 2022a). Ongoing research and guidance documents published by the WHO and Target Malaria (Box 4.1) follow this approach, and could be bolstered through additional scientific research. There is a long history of public sector funding for risk-related research at international and national levels, through work by the WHO, the Organisation for Economic Co-Operation and Development (OECD), and national agencies such as the U.S. Environmental Protection Agency (U.S. EPA) (Whittaker, 2015; US EPA, 2013). Opportunities for Canadian contributions to emerging assessment practices will, however, depend on capacity (Section 3.1).

Box 4.1 Adapting Risk Assessment to New Technology

Genetic pest-control programs under development for controlling mosquito populations in order to curb malaria transmission are being tested in increasingly realistic conditions (Target Malaria, 2020a). These tests are proceeding gradually to manage risks while addressing the current paucity of evidence that stymies risk analysis capabilities. The work follows methodologies similar to those described previously, with certain adaptations. In addition to studying potential hazards arising from the release of genetically modified (and eventually gene-edited) mosquitoes, the WHO recommends considering hazards associated with the process of producing the organisms. This, for example, includes conducting studies to observe whether there are any changes in the behaviour of the organisms as a result of the modification, which could alter their effectiveness as control agents or impact the health of humans, non-humans, or the environment (Shelton *et al.*, 2020; WHO, 2021a).

(Continues)

(Continued)

The risk assessment process should explicitly explore hazards relating to the novel genotype or phenotype of the organism in a given environment, as compared to hazards posed by an alternative pest-control approach (e.g., insecticides). The choice of suitable comparators depends on the endpoint being evaluated (WHO, 2021a), and comparators should, if possible, be selected to mirror the intended outcome of the genetic pest-control program (EFSA GMO Panel, 2020). Prior to field tests, for example, comparators could be unmodified organisms from the parent line[27] but, as tests progress, emerging findings might dictate a range of new endpoints and comparators (EFSA GMO Panel, 2020; WHO, 2021a).

Following this guidance, an environmental risk assessment for *Anopheles gambiae* mosquitoes, altered to carry a gene drive for population control, was carried out and identified 46 distinct pathways to harm (Connolly *et al.*, 2021). These identified pathways to harm indicate, for example, a potential for increased disease transmission among humans and animals. The exposure levels for any of these potential harms will be influenced by the extent of population suppression, such that the risk assessment may need to be periodically reviewed (Section 4.3) and informed by models of population dynamics (Connolly *et al.*, 2021).

Real-world data and monitoring allow risk assessment to be bolstered by cost-benefit and cost-effectiveness analyses, to compare pest control tools and aid in decision-making

Risk assessment is ubiquitous in the regulation of pest-control products, but it has limitations. Although it can estimate the likelihood of a product creating a hazard given specific levels of exposure, Whittaker (2015) argues that decision-makers might be tempted to focus on risk minimization through the management of exposure, rather than on the elimination of risk. Minimization, however, is accomplished differently in the context of a chemical pest-control agent (e.g., by controlling where/when it is distributed) versus a live organism. For programs resulting in the establishment of a self-sustaining and mobile population of gene-edited organisms, exposure could be an evolving factor and challenging to quantify. Moreover, even in cases where data are available, it can be challenging to quantify risks, forcing assessors to base the conclusions they communicate to

27 Unmodified organisms reared in a laboratory setting may have different fitness than true wild-type ones. In some cases, this might limit the applicability of this comparator (EFSA GMO Panel, 2020; WHO, 2021a).

decision-makers on relative magnitudes (Hayes *et al.*, 2014). Despite its systematic nature, the linear approach of cataloguing pathways to harm also fails to account for competing and/or nonlinear pathways (Connolly *et al.*, 2021).

As more evidence surrounding use emerges, value and potential outcomes might be used to assess gene-edited organisms for pest control and complement risk assessment. Careful monitoring of outcomes will therefore be a necessary component of novel pest-control programs based on genetic technologies (Box 4.2). Doing so provides an opportunity to assess a potential intervention based on its expected value, such that alternative approaches can undergo a cost-benefit comparison. For example, value assessments are carried out for potential pest-control agents in Canada, provided their use does not present unacceptable risk for health or the environment (PMRA, 2021a). This process considers the efficacy of the product alongside any potential benefits for human health, the environment, and social and economic impacts (including trade implications and competitiveness).

Similarly, for biological control, petitioners in Canada must carry out a cost-benefit analysis comparing their proposed approach against other pest-control options (or against inaction) (Mason *et al.*, 2017). The list of benefits might be considered across a broad spectrum: agriculture, forestry, politics, consumer concerns, economic interests, conservation, and biodiversity (Collatz *et al.*, 2021). The specific context (e.g., public health versus agricultural settings) of a pest-control intervention will influence which benefits are most relevant to measure, and whether this analysis is feasible. In an economic analysis, the perspectives of farmers may differ from those of other stakeholders, for example, and it is more straightforward to assess costs and benefits for private businesses than externalities for society (Onstad & Crain, 2019).

In cases where it is not feasible to measure benefits, cost-effectiveness can also be employed for assessing the suitability of a control program (Brown *et al.*, 2019). From the standpoint of Canadian regulation, even in the absence of scientific certainty, pest-control measures for preventing adverse impacts to the environment of human health can be used, provided they are demonstrably cost-effective (GC, 2002). However, several gaps remain in researching cost-effectiveness of pest-control products (Brown *et al.*, 2019).

Box 4.2 Measuring the Benefits of Genetic Pest-Control Programs

Often, pest-control programs are initiated to reduce harm caused by pests or realize benefits precluded by their actions. In some cases, suppressing pest populations below a certain density is enough, but the link between pest populations and their impacts is not always linear. This issue has been raised in the context of controlling vector-borne diseases using new tools. At present, only the studies led by Project *Wolbachia* in Singapore have directly demonstrated the public health impact of the pest-control program based on modified insects (NEA, 2022). Releases carried out thus far have resulted in both suppression of pest populations and, importantly, a correlated reduction in observed dengue cases (NEA, 2021).

Similar public health benefits have not yet been measured in other genetic pest-control trials. Trials on the effectiveness of genetic approaches to suppressing mosquito populations in lab and field settings have thus far focused on measuring insect populations and not any subsequent epidemiological impacts (Carvalho *et al.*, 2015; Hammond *et al.*, 2021). Large trials are underway at various locations across the Florida Keys, where seven million transgenic mosquitoes were released in 2022 (Oxitec, 2022). Despite being geared toward obtaining regulatory approval by measuring pest-control efficacy, these trials may in fact be unsuitable for substantiating the public health benefit due to low-level prevalence of the associated diseases in the Florida Keys (Waltz, 2022).

In the Panel's view, it is implausible to think that gene-edited organisms will be the first line of defence against pests, in either the near or distant future. The overhead associated with the production of gene-edited organisms alone would prevent this (Section 3.2). However, developing the necessary expertise to map benefits and risks to the design of genetic pest-control programs offers options to meet potential catastrophes that result from existing pests or new invasive species.

4.2 Confronting Risks

In some settings, gene-edited organisms, and gene drives specifically, will present novel risks. However, similarities exist with previous approaches for managing pest populations, highlighting the importance of considering lessons learned from past interventions involving live organisms. Within gene editing for pest control, gene drives are emphasized more in this section, given the high technological readiness of certain applications and the correspondingly high availability of associated scholarship on the topics of risk assessment and management. Table 4.1 provides an overview of some of the hypothetical risk assessment challenges posed by gene drives. The Panel stresses that many of these risks will be common to other genetic pest-control implementations, however; this section demonstrates that, even within the specific area of gene drives, there will be case-by-case differences in risks based on program objectives, design, and context.

Gene editing is a technologically novel field, and wrestling with uncertainties and evidence gaps is a key challenge

The use of gene-edited organisms (and gene drives specifically; Table 4.1) to control pests will entail identifying risk factors, some of which will be uncertain. Hayes *et al.* (2014) argue that, in the context of risk assessment, there are three relevant forms of uncertainty: epistemic uncertainty due to a lack of knowledge about the system being assessed; statistical uncertainty relating to the inherent variability of quantities being measured, or to limits in accuracy set by precision or sampling; and linguistic uncertainty where qualitative statements are subject to interpretation. These different forms of uncertainty can arise in parallel; although it may be tempting to focus on statistical uncertainty, since those quantities are tractable, epistemic uncertainty can be very relevant in the context of novel technology.

Table 4.1 Potential Environmental Risk Assessment Issues Resulting from the Release of an Organism Carrying a Gene Drive

Risk Category	Potential Environmental Risk
Persistence and spread	• Change in resistance to pest-control agents • Change in fitness • Spread beyond intended geographic range • Effects from introgression of transgene in sexually compatible species • Effects following horizontal transfer of transgene to another organism
Stability of drive over time	• Population dynamics over evolutionary timescales • Stability of genetic construct • Long-term effects, such as interaction among multiple transgenic modifications
Human and non-human animal health	• Toxicity and allergenicity • Epidemiological efficiency • Impacts on pets or livestock • Change in pathogenicity (e.g., disease vector) to target/non-target organisms
Target populations	• Failure to achieve intended outcomes • New species fills ecological niche vacated by target • Changes in agricultural or land management practices • Long-term adverse effects arising from reduced genetic diversity
Non-target populations	• Impacts on endangered species • Changes to food webs • Impacts on ecosystem services

Adapted from Legros *et al.* (2021)

The environmental risks listed here provide a general overview and are arranged in an arbitrary order; they cannot be ranked or prioritized *a priori*. The Panel stresses that each particular pest-control program, and the associated ecological context, will strongly influence the relative importance of these risks, and that, in some cases, many of these risks may be found to be remote. Examples that have no direct analogue in non-genetic pest-control interventions are noted in teal.

Problem formulation helps reduce uncertainty by challenging assessors to consider many possible outcomes and demanding that they establish causal relationships. Even so, uncertainty surrounding the most likely or relevant pathways to harm cannot be fully resolved in the absence of real-world data. In the case of novel interventions, risk prioritization might instead be shaped through workshops or consultations (Roberts *et al.*, 2017; Teem *et al.*, 2019), or identified computationally using bioinformatics (Romeis & Widmer, 2020). Connolly *et al.* (2021) highlight this issue as one that limits their risk assessment, since the plausibility of a pathway to harm has to be based on expert opinion, which is subject to bias (de Graeff *et al.*, 2022). For this reason, the pathways will need to be revised and updated frequently to reflect the evolving state of knowledge (Connolly *et al.*, 2021). In this respect, the risk landscape and value of gene-drive organisms for pest control can only be clarified through experimentation and monitoring (Box 4.2).

The ability of gene drives to spread geographically exacerbates uncertainties, and may challenge researchers' ability to bound risks using controlled experiments

Controlled laboratory studies in contained environments can provide valuable empirical data to test hypotheses made during risk assessment, identifying the most relevant potential risks within those analyzed following problem formulation. In a natural environment, however, the rate at which introduced organisms will (or will not) interact with other organisms is uncontrolled and impossible to assess fully. For complex ecosystems, or pest-control programs occurring over long timescales, the number of variables to account for increases significantly, which translates to uncertainty. This is particularly true for persistent genetic pest-control programs, such as ones where the introduced organisms carry a self-sustaining gene drive (Devos *et al.*, 2022a) (Section 2.2). Dispersal following establishment will potentially lead to encounters with species that were not assessed in risk analysis or trials — an issue encountered previously in biological control (Collatz *et al.*, 2021).

Previous experiences suggest that broad dispersal is not a given. A review of biological control programs for weeds analyzed dispersal data from 66 arthropod and 11 fungal biocontrol agents and concluded that dispersal was typically on the order of a kilometre per year for many agents (Paynter & Bellgard, 2011). Dispersal was, however, highly variable depending on the organism and context. Biological control agents tend to be non-native to where they are deployed because they target non-native invasive pests; agents may therefore encounter several natural barriers. Moreover, the selection of these agents is guided by a strict testing regime to determine which strains are most suitable to a given geographic context

(De Clercq *et al.*, 2011; Kenis *et al.*, 2019). In a gene-drive program, however, a modified version of an established pest will be released. Given that this pest is already ecologically embedded within its environment, it will potentially encounter fewer barriers for dispersal. In fact, high dispersal would even be desirable for some gene-drive applications, as the fitness costs associated with the drive might otherwise make it ineffective at achieving a desired outcome (Legros *et al.*, 2021).

For self-sustaining drives, no field trial can fully satisfy risk assessment requirements, as it will never encompass the full range of possibilities for physical or ecological environments (Kuzma *et al.*, 2017).[28] As a result, a comprehensive assessment of possible risks, prior to release into the wild, might not be experimentally feasible, leading to an increased reliance on mathematical modelling (EFSA GMO Panel, 2020). Although modelling is a powerful and well-developed tool, the precise implementation of various ecological factors can strongly affect predictions (Dhole *et al.*, 2020). Modelling is, moreover, not a direct substitute for empirical evidence. Model limitations and failures to acknowledge and manage uncertainties are additional issues that can arise from the lack of evidence (Verma *et al.*, 2023; Frieß *et al.*, 2023).

If the dispersal of the drive is large, the likelihood of the drive establishing itself outside the target area and in unintended ecosystems increases. So too does the likelihood of the target species interacting with other potentially compatible species where gene flow could occur (Legros *et al.*, 2021) (Box 4.3). There is a balance to be struck between a drive that disperses too little (achieving nothing), and one that over-disperses (generating unforeseen ecosystem impacts) (Romeis *et al.*, 2020). A tension thus exists between the intended outcome of the program and the resulting risks (Table 2.1). This tension can be exacerbated by the drive design, which might limit the ability of field trials to reliably simulate the real-world dynamics of the drive in the wild (EFSA GMO Panel, 2020).

28 Transportation and trade represent important vectors for pest migration and could also further broaden the necessary scope of risk assessment in ways that cannot realistically be accomplished through empirical tests (Kuzma *et al.*, 2017).

Box 4.3 Vertical and Horizontal Gene Transfer

The efficient transfer of genetic material at faster-than-Mendelian rates (Figure 2.3) is a key characteristic of a gene drive. The ensuing bias in inheritance leads to concerns about the fate of a gene drive if it manages to be integrated into the genome of an organism from a different, non-target species. Gene transfer, as this process is known, can proceed vertically or horizontally.

Vertical transfer would occur through sexual reproduction, for instance, if an organism carrying a drive were to reproduce with a compatible organism from a different species (Hayes, 2018). The resulting hybrid offspring could inherit the gene drive, leading to unknown consequences (Legros *et al.*, 2021). This builds on concerns already occurring in biological control settings, where very efficient hybridization can act to displace existing species (Collatz *et al.*, 2021). Gene transfer might hamper the definition of target and non-target species, with implications for risk assessment. For example, the *Anopheles gambiae* species complex consists of multiple mosquito species, some of which do not act as disease vectors but are sexually compatible with those that do (Connolly *et al.*, 2023). A gene drive released in target species might easily transfer to a species that is not considered a pest, with ecological, biodiversity, and ethical implications. This concern will demand clearer definitions of target organisms and efforts to monitor for the likelihood of hybridization pathways and potential outcomes (Wolf *et al.*, 2023; Connolly *et al.*, 2023).

In horizontal transfer, genetic material moves from one organism to another through different means than reproduction. This process can proceed through intermediate organisms, such as viruses or parasites, which might act to transfer genetic material from one species to another via several distinct mechanisms (Courtier-Orgogozo *et al.*, 2020). Although the likelihood of such an event occurring is generally low, there is evidence that horizontal gene transfer has taken place across distantly related species throughout history (see, for example, Keese, 2008). The fate of the transferred gene can be uncertain, and it is also uncertain where a drive would integrate in a new genome, and whether it would remain functional. Nevertheless, for a stable population of gene-edited organisms carrying a self-sustaining gene drive, the probability of horizontal transfer of the drive to non-target species is small but non-zero and could factor into risk assessment (Courtier-Orgogozo *et al.*, 2020).

Risks to biodiversity are influenced by the mechanism of action and design of genetic pest-control programs

The decline of biodiversity is an accelerating global challenge (Nature Editorials, 2022). Biodiversity-related risks presented by gene drives arise from their mechanism of action, the impacts on populations of target species, and the resulting influence on non-target species. Within a given target species, the potential for durable establishment of a self-sustaining gene drive could contribute to the loss of genetic diversity, with associated risks (Snow, 2019). Beyond those concerns, the release of gene-edited organisms could disrupt complex ecosystems through interactions between target and non-target organisms. For instance, in conservation settings, a gene-edited organism carrying a gene drive could be designed to suppress a pest species that is exerting pressure on a threatened species. Its introduction, however, could disrupt a precarious equilibrium; the likelihood of the drive achieving the desired objective depends on the interplay of ecology and genetics (Alphey & Bonsall, 2014; Dhole *et al.*, 2020). The propagation of a drive might be more efficient for a higher density of released organisms, but this might translate to higher pest pressure. If the sudden increase in pest pressure occurs before the gene drive becomes established, ecological cascades and irreversible damage could result (Serr *et al.*, 2020).

Organisms carrying a gene drive can be functionally equivalent to an invasive species, particularly in the event of the broad dispersal of a self-sustaining gene drive. Risk assessment might therefore be used to target unlikely events with potentially outsized negative consequences. For this reason, Connolly *et al.* (2022) suggest considering possible worst-case scenarios (such as total population suppression by a drive) in selecting risk hypotheses for testing under these circumstances. Approaches borrowed from the study of invasive species might also help identify risks of these types more clearly. In this vein, fault-tree analysis can identify chains of multiple events that, if combined appropriately and in the appropriate sequence, will give rise to a hazard (Hayes *et al.*, 2014). This approach can be particularly helpful in determining how worst-case scenarios might occur in complex systems, allowing risk assessors to work backwards from unwanted outcomes.

Human health risks require consideration alongside potential benefits, which will need to be weighed against environmental risks

A key potential benefit to human health using gene-edited organisms for pest control is the reduction of the spread of disease (Box 4.4), as exemplified by efforts to control malaria-transmitting mosquitoes (Alphey, 2016). In this context, a number of direct risks to human health have already been identified, such as allergenicity and toxicity associated with the gene-edited mosquitoes. Other risks relate to unforeseen epidemiological effects, such as disease transmission increasing as a result of the gene drive, or gene-edited organisms becoming effective vectors for other diseases despite no longer transmitting malaria (Connolly *et al.*, 2021).

Alternative approaches to managing malaria involve various other pest control tools, including conventional chemical agents, which pose their own risks to human health (Tizifa *et al.*, 2018). Predicting the likelihood of a gene drive's success involves weighing the risks against the benefits. However, this issue is complicated by defining relevant ecological risks (Table 4.1). Cost-effectiveness analysis can disentangle potential trade-offs between environmental and health risks (Brown *et al.*, 2019), but tensions can exist due to the time needed to collect evidence and pressure to act (given the disease burden). Further, the risks and uncertainties tied to an intervention must also be weighed against non-intervention and maintaining the status quo.

Box 4.4 A Hypothetical Gene Drive to Combat West Nile Virus in Canada

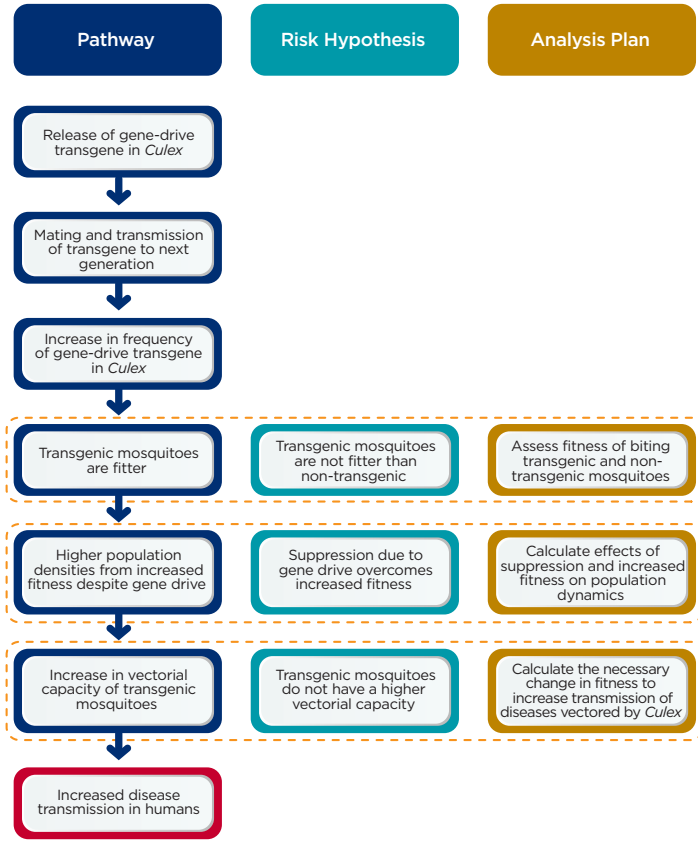
Climate change is expected to increase the risks of mosquito-borne illnesses in Canada (Ng *et al.*, 2019). The Panel therefore explored a hypothetical assessment scenario in which a gene drive is proposed to combat this risk. The *Culex pipiens* species complex is a family of mosquito species, several of which act as vectors for diseases, including West Nile virus (Feng *et al.*, 2021); several species from this complex are already established in parts of Canada (Gorris *et al.*, 2021). Predictions from climate change models suggest that the extent to which these mosquitoes are found in Canada is likely to expand, resulting in higher risk of the diseases they carry (Ng *et al.*, 2019; Gorris *et al.*, 2021).

(Continues)

(Continued)

The feasibility of introducing a gene drive into this mosquito is currently being studied (Feng *et al.*, 2021) and could be a promising avenue for addressing potentially worsening disease burdens due to this species, in light of its resistance to insecticides (Lopes *et al.*, 2019). West Nile case clusters have historically been observed in urban settings in North America owing, in part, to the high densities of hosts and the suitability of particular urban environments as habitats (Ruiz *et al.*, 2007; Little *et al.*, 2017). This suggests that large population centres would be the most likely areas for deploying a control program based on need, which would influence problem formulation in the risk assessment.

Connolly *et al.* (2021) found that the main protection goals for potential genetic pest-control programs against malaria were biodiversity, water quality, human health, and animal health. In the case of a gene drive deployed in an urban Canadian setting, similar protection goals might be defined but interpreted differently based on the difference in settings. From there, it would be possible to begin defining plausible pathways to harm that might inform risk hypotheses and the definition of relevant endpoints.



Adapted from analysis in Connolly *et al.* (2021)

Figure 4.4 Potential Pathway to Harm: Hypothetical Use of Gene Drive Mosquitoes to Curb Transmission of West Nile Virus

This figure describes one of several potential pathways to harm, and the accompanying risk hypotheses and analysis plans for the assessment. This pathway — where the deployment of a gene-drive mosquito worsens the disease burden through increased transmission — supports three possible hypotheses, which can be explored through research and experimentation. The analysis plan explains how each of these hypotheses might be addressed and which type of expertise is needed.

Gene drives give rise to social, economic, and cultural risks that can be impractical to include in risk assessment and may be better addressed through governance.

The issues foreseen in environmental or ecological contexts could be exacerbated by the diversity of the sociopolitical environments in which decisions will be made. The corresponding stakeholders (and their respective priorities) vary at a societal level. Diversity of values and priorities among stakeholders has implications for how uncertainty can be addressed, since — even when risk-benefit analysis is available — social parameters such as risk perception and risk tolerance will vary according to societal context (Collatz *et al.*, 2021). The decision-making process for using unproven technology to tackle the burden of malaria, for instance, involves different considerations and values than the process for managing crop pests.

Certain implementations of genetic pest management have been shown to achieve near-total replacement or suppression of populations in trials (Carvalho *et al.*, 2015; NEA, 2021), which could raise cultural risks due to misalignments in value systems. Specifically, an organism could hold cultural value for some community members or stakeholder groups despite acting as a pest from an ecological or economic standpoint (Kuzma, 2020). In this way, the objective (e.g., population suppression) or mechanism (e.g., gene editing) of pest control might bring cultural values in conflict with others (Maguire, 2004; Hudson *et al.*, 2019). Reflections on what a pest is and how it should be dealt with manifest differently across society (Lebrecht *et al.*, 2019) — which could be particularly heightened in the context of Indigenous communities. Some communities might favour interventions that encourage renewal and biodiversity within an ecosystem (Berkes & Davidson-Hunt, 2006), in contrast to either the potential extirpation of a species or the restoration of extinct species — even if that species previously held cultural value (Barnhill-Dilling & Delborne, 2019). The integration of Indigenous science into risk assessment can begin to address the latter challenges (Box 4.5), but only if the resulting findings are permitted to influence decision-making.

Unintended outcomes from gene drives might also lead to negative economic consequences. These could offset any benefits resulting from the pest-control program, and uncertainty surrounding the efficacy of gene drives will exacerbate efforts to predict such economic impacts (Mitchell *et al.*, 2017). In light of certain disincentives for private enterprise to spearhead the deployment of these technologies (Section 3.2), the risk of economic failure could largely be borne by the public, with the potential for backlash given the large investments needed to develop the control program (Mitchell *et al.*, 2017). Numerous indirect economic risks are also posed by gene-edited organisms for pest control, such as trade issues resulting from lack of regulatory alignment, and the potential loss of

certification for specialized growers due to the ingress of gene-edited organisms onto their lands (Baltzegar *et al.*, 2018).[29] Finally, work on gene drives could, under some circumstances, be considered dual-use research and is therefore scrutinized for its potential to be weaponized or used maliciously, rather than for pest control (Ching & Lin, 2019).

Integrating these disparate forms of risk into a conventional assessment framework may prove difficult. Many reflect conflicts or tensions in societal values expressed through regulations and policy, with implications for the establishment of governance and decision-making frameworks for gene-edited organisms (Table 4.2). In fact, taken together, these risks could also manifest as geopolitical harms in the event that gene-edited organisms traverse borders (Kofler, 2018) or are inadvertently transported to other jurisdictions through trade (Hulme, 2021). Such transnational issues are being explored with the goal of establishing regional governance structures (AUDA-NEPAD, n.d.) (Box 6.5). Developing the expertise to assess and manage economic and sociocultural risks is an area where Canada could provide value to partners involved in the regional governance of gene-edited organisms (Section 6.2).

Table 4.2 Potential Social, Economic, and Cultural Risks Resulting from the Release of an Organism Carrying a Gene Drive

Area	Potential Risk
Social	• Loss of public trust • Backlash against technology • Malicious use of dual-use technology
Economic	• Trade complications • Loss of certification for specialty growers • Ineffective pest suppression in real-world setting
Cultural	• Modification or harm to culturally valued species by direct action of drive • Harm to culturally valued species (or habitat) by indirect action of drive • Marginalization of values that are under-represented in decision-making

Adapted from Legros *et al.* (2021)

29 This issue also raises legal risks due to intellectual property rights (Section 3.2).

4.3 Risk Management and Mitigation

Current limitations in understanding the underlying technologies and ecological systems in which they will be deployed might undermine conventional risk assessment. Risk assessment is typically understood as relating to pre-implementation, whereas risk management commonly refers to post-implementation. Although conventional decision-making frameworks for some pest-control interventions follow a linear path (Figure 4.5), that linearity might be disrupted when it comes to gene-edited organisms.

Adapted from PMRA (2021a)

Figure 4.5 Sequential Decision-Making Process for Conventional Pest-Control Programs

Regulatory agencies might follow a linear risk assessment process. In this example, based on a PMRA model, the first step of the process is problem formulation, including the definition of protection goals as outlined in Section 4.1. From there, the risk assessment process involves risk analysis and the definition of pathways and endpoints. Risk management includes the identification of risk mitigation tools and the creation of a risk management strategy. The final steps of the process are monitoring and evaluation, which includes activities such as incident reporting, enforcement and compliance of regulations, surveys, and the dissemination of data or findings (PMRA, 2021a).

On this basis, some stakeholders have therefore concluded that the safest course to manage the risks of gene drives is the adoption of precautionary measures, including but not limited to moratoria on their release (Ching & Lin, 2019). Although civil society organizations encouraged a ban prior to the 2018 *United Nations Convention on Biological Diversity* (CBD), a moratorium on releasing drives in the wild has so far been rejected at the United Nations level (SynBioWatch, 2016; Callaway, 2018).[30]

30 Efforts continue in support of bans, particularly in the European Union (WeMoveEurope, 2022; Save our Seeds, n.d.).

Instead of bans, various precautionary measures have been set out in the form of principles following the 2018 CBD. These measures focus on international coordination in the development and implementation of novel or adapted risk assessment and management methodologies as described here (Ching & Lin, 2019), as well as on inclusivity — namely regarding the consent of local communities and Indigenous peoples (UN CBD, 2018) (Box 5.1). In considering the potential departures from standard practices discussed here, the Panel stresses that opportunities exist beyond the present context; these practices ought not be viewed as additional requirements specific to gene-edited organisms but might also be considered across pest management more broadly.

Opportunities for risk mitigation occur at numerous points in the design of genetic pest-control programs

Assessors can link the hazards identified during risk assessment to potential risk mitigation tools, which can be employed in response to observed developments during a pest-control program. However, an important distinction between gene-drive approaches and conventional biological control or SIT is that, in the former, program developers can exert control over the intrinsic properties of the released organism through gene editing. Some risk mitigation approaches are built directly into the design of a gene drive, such as Daisy-chain[31] drives or split drives (e.g., antidote-toxin drives, see Section 2.2) (Verkuijl *et al.*, 2022). In this way, the type of employed gene drive influences its persistence in time and propensity to spread, with implications for risk exposure (Devos *et al.*, 2021; Overcash & Golnar, 2022).

Given that genetic pest-control programs rely on the release of live organisms, many approaches to mitigation would have much in common with earlier SIT or biological control programs. These approaches focus on the need to contain organisms and prevent them from inadvertently spilling over outside of the target area. For example, very isolated environments, such as islands, might be targeted for trials or pilot programs, given that they can virtually eliminate the likelihood of spillover (Lanzaro *et al.*, 2021).[32] Similarly, SIT program developers have built production (and test) facilities in environments or climates where an escaped organism could never survive (IAEA, 2008). Containment facilities with targeted measures for transgenic mosquitoes have been established in Burkina Faso through Target Malaria, with dedicated protocols to prevent the escape of organisms and the spread of genetic material through unintended breeding with wild-type organisms (Guissou *et al.*, 2022).

31 Daisy-chain drives are designed in such a way that a functioning gene-drive element can only be passed down a finite number of times, after which point the drive no longer biases inheritance (Verkuijl *et al.*, 2022).

32 The isolated nature of these environments can also contribute to an enhanced vulnerability to invasive species. This has, in some cases, created an impetus for proposals to deploy gene drives (GBIRd, 2022).

Step-wise testing facilitates risk management by providing a slow transition from the controlled environment found in a containment facility to (potential) open field trials, and is a core component of WHO guidance on testing genetically modified mosquitoes (WHO, 2021a). It allows researchers to progressively fill in evidence gaps identified during risk assessment, and can include built-in protocols for demonstrating safety requirements at each stage before proceeding to the next (Devos *et al.*, 2022b). Proceeding in a step-wise fashion may not be applicable for all programs, however, particularly for gene drives designed to spread far beyond the intended release site (Romeis *et al.*, 2020).

In areas of high uncertainty, adaptive and inclusive approaches to risk assessment can mitigate risks, provided these approaches are periodically reviewed and revised

Risk assessment frameworks based on scientific evidence and statistical analysis can lose accuracy and reliability in the absence of data (Kuzma, 2019). Uncertainty might therefore lead assessors toward false assumptions (based on the data available) or endpoints that only reflect broad political or socioeconomic values, leaving aside those held by impacted communities. In these cases, risk assessment tools that emphasize procedural validity may be helpful. Instead of focusing strictly on the evidence, assessors could examine the risk assessment process itself to determine its reliability and identify its limitations. Anticipation would also play a role in this framework, given the possibility of unanticipated runaway effects and the need to establish contingency plans that are revisited as more information or tools become available to understand and manage risks. A procedurally robust framework would increase the number of relevant stakeholders involved in the risk assessment process. In this framework, the emphasis would not only rest on safety or pathways to harm, as in traditional approaches, but also on relationships of accountability among stakeholders (Kuzma, 2019).

Jasanoff (2003) highlights these relationships of accountability as an important contribution to risk assessment and management in areas where scientific ventures present high uncertainty, uncontrollable outcomes, or strong context dependence. In this way, an assessment might not only define hypotheses and protocols for their testing and evaluation (Devos *et al.*, 2022b) but also the corresponding roles or responsibilities of various relevant actors, including technology developers, regulators, and the public (Kuzma *et al.*, 2017). Involving the public in the risk assessment process is seen as a potentially useful contribution to governance[33] — it is a means for involving potentially impacted

33 Similarly, members of the public could participate in *benefits assessment* following a similar problem formulation approach (Kokotovich *et al.*, 2022). This, together with input on risk assessment, can shed light on decision-making surrounding the use of gene drives instead of other interventions.

communities in technology development early on, such that they might guide, inform, or interpret risk assessment through the expression of values or the contribution of knowledge (Jasanoff, 2003; Owen *et al.*, 2012) (Box 4.5).

Box 4.5 Traditional Knowledge in Environmental Risk Assessment

The use of traditional knowledge can strengthen environmental risk assessment. It is a form of knowledge steeped in local context and one that adopts a more holistic and long-term view of the environment than western-based scientific approaches (Abu *et al.*, 2020). Several challenges exist in bridging the gap between these ways of knowing (Reid *et al.*, 2021), but doing so can be vital for assessing long-term change in complex ecosystems or the impacts of major infrastructure projects (Keeyask, 2011). There are various established frameworks to harness multiple ways of knowing for mutual benefit, beyond filling gaps in western-based scientific knowledge (Box 1.1).

New Zealand's Ecological State Assessment Tool (ESAT) is a cross-cultural digital platform developed on this basis, in order to assist with the monitoring and evaluating of conservation and natural resource management (Belcher *et al.*, 2021). ESAT has been applied to pest control for tracking quantitative as well as cultural and social indicators. Importantly, the cooperative approach between Indigenous and non-Indigenous actors might help mitigate the possibility of Indigenous values being marginalized, especially in areas where tension arises between western-based science and traditional knowledge.

The Government of Canada has begun to include these forms of knowledge in regulatory processes that underpin decision-making (e.g., in the context of endangered species (COSEWIC, 2017)), but the associated legislative changes do not include amendments relevant to pest control (GC, 2019a) (Section 6.1). The risk assessment processes described in Chapter 4 represent important opportunities to include other voices and ways of knowing, in light of the continued uncertainty surrounding risks and benefits.

Stakeholder engagement can contribute to problem formulation by, for example, defining protection goals (Connolly *et al.*, 2022) (Figure 4.6). Since the public involved in this engagement process will influence the identification and weighting of priorities (Section 2.3), possible biases will need to be taken into consideration. The results of two applications of problem formulation with

stakeholder input revealed differences and nuances in the expressed priorities in the context of gene-drive mosquitoes to combat malaria (Roberts *et al.*, 2017; Teem *et al.*, 2019). Other programs may elicit broad divergence of opinions and an inability to reach consensus; procedurally robust frameworks could assist in resolving these situations by strengthening the legitimacy of decision-making in the eyes of stakeholders.

Figure 4.6 Adaptive Risk Assessment Process Based on Problem Formulation

A paucity of evidence exists surrounding the use of gene-edited organisms for pest control, such that standard risk assessment and management processes may benefit from modifications. For instance, the linear assessment process based on problem formulation may instead become iterative, where each step of the process is revisited as evidence becomes available and risks can be revised. This process might also involve deeper engagement with stakeholders and impacted communities at each step, to draw upon knowledge and inform prioritization.

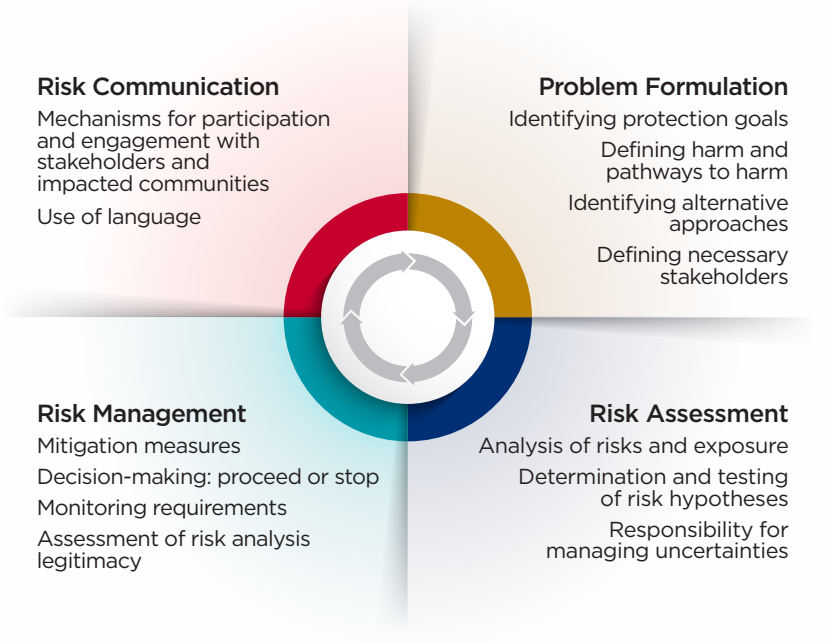
Monitoring and periodic evaluations of ongoing projects are resource-intensive but necessary for effective risk management and mitigation

A central challenge for risk management includes monitoring (over numerous timescales). Monitoring of social and ecological environments — especially the latter — requires diligent and carefully planned practices around data aggregation, analysis and sharing (Kuzma, 2018; Devos *et al.*, 2022b). Responsibilities for monitoring may also be either explicitly or implicitly shared across numerous stakeholders due to jurisdiction (Section 6.1) or as a result of conditions placed on the regulatory approval for deployment. As such, monitoring requirements, associated roles and responsibilities, and resourcing should all be considered as early as possible in program design. In this way, resulting data can be as useful as possible for testing predictions against observations and can inform ongoing assessment in an iterative manner (Hayes *et al.*, 2014).

Ongoing monitoring and evaluation across several areas provides key evidence to feed into adaptive risk governance.

Committing to monitoring plans will be particularly important for genetic pest-control programs, given the challenge this has historically posed for biological control programs where post-release studies are carried out, at times inconsistently, due to lack of resourcing or logistical support (Hajek *et al.*, 2016; Messing & Brodeur, 2018). In addition to monitoring gaps from ecological and entomological perspectives, Onstad and Crain (2019) note that economic evaluations of pest-control programs are not consistently carried out. Ongoing monitoring and evaluation across several areas provides key evidence to feed into adaptive risk governance.

The resulting risk governance process scrutinizes both evidence and processes and may be more suitable than a linear one for the oversight of novel pest control tools (Figure 4.7). When new knowledge and evidence allow stakeholders to change practices and standards, the boundaries between risk assessment and risk management may become blurred; this is what Devos *et al.* (2022b) term "dynamic interplay" between assessment and management processes. In this approach, a periodic re-evaluation of procedures is needed, which could subsequently underpin a phased approval process (Devos *et al.*, 2022b). Such an approach could combine naturally with tiered testing through field trials, where experiments, post-release monitoring, and the measurement of outcomes could inform revisions to risk assessment while also providing the necessary time to consult with stakeholders and Rights-holders.



Adapted from Kuzma *et al.* (2017) with permission from Taylor & Francis Ltd, and Devos *et al.* (2022b)

Figure 4.7 Adaptive Approach for Governing Risks Throughout the Development of a Genetic Pest-Control Program

Risk communication is consequently an important component of this approach. The framing of potential genetic pest-control programs might allude to uncertainty or potential catastrophes, which can influence how various stakeholders might interpret or perceive the associated risks (Catton, 2021). Both risks and benefits evolve in the context of an adaptive risk management framework as new findings become known. This may necessitate channels to effectively communicate the changing landscape through robust engagement.

5

Approaches to Public Engagement

Chapter Findings

- Public engagement activities may facilitate public input, participation, and collaboration, depending on how they are designed and implemented.
- Public engagement activities more closely align with ethical approaches when they involve collaboration with diverse populations and have the potential to influence policy.
- Empowering public engagement can be a complex, challenging endeavour, which requires resources and reflection to implement effectively.
- Conducting engagement with publics in Canada requires extensive consideration for those most impacted by a program, including Indigenous peoples.
- Increased collaboration among invested actors, including Indigenous experts, can be mutually beneficial for communities, industry, and governments.

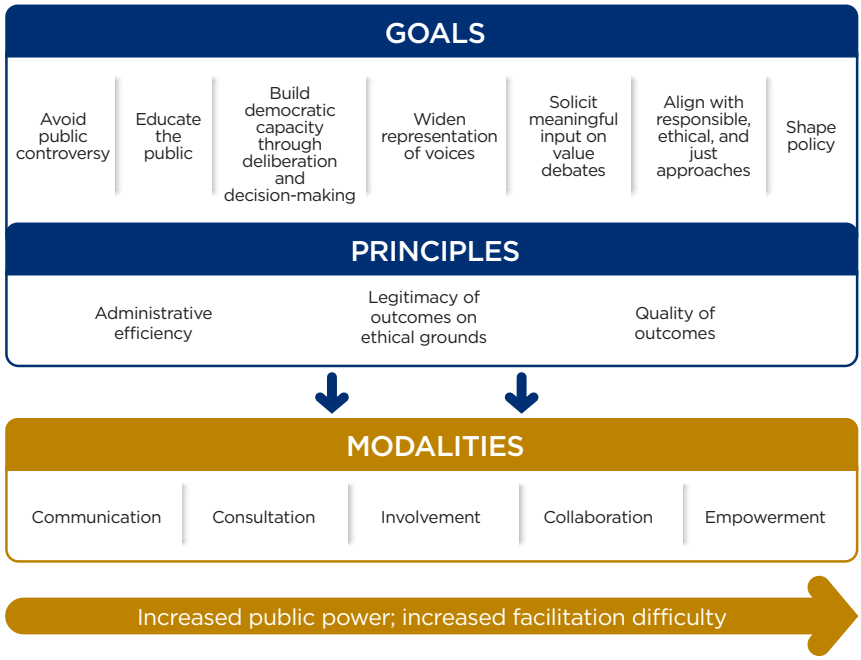
Conducting public engagement is a core component of pest management activities, especially with regard to impacted communities and at-risk ecosystems. Consideration for public engagement is heightened in the context of genetic pest-control tools, given their ability to cross jurisdictional borders and their potential to significantly alter environments. Increased participation from publics can align with ethical practices and bolster a program's effectiveness. In turn, benefits may be generated for various invested and impacted parties, including Indigenous peoples, who are inherent Rights-holders in locations where the technology might be used. This chapter outlines the goals and logistics of public engagement approaches, highlighting relevant examples from Canada and abroad. It also discusses challenges and benefits that accompany these approaches.

5.1 Overview of Public Engagement Approaches and Purposes

The public can be broadly defined as those involved in, concerned with, and impacted by pest management tools and strategies (NASEM, 2016) (Section 2.3). Canada's cultural diversity is expressed through its rural and urban populations and its growing immigrant communities, in addition to regional diversity for both Indigenous and non-Indigenous populations. Individuals and communities can have different and potentially contrasting views on the role of human activity in the natural world (Onstad & Crain, 2019; Bunten *et al.*, 2021) (Section 2.3). As defined in the 2016 National Academies of Sciences, Engineering, and Medicine (NASEM) report, effectively engaging these publics means "seeking and facilitating the sharing and exchange of knowledge, perspectives and preferences between or among groups who often have differences in expertise, power, and values" (NASEM, 2016). The social sciences, including studies of public engagement approaches, are often not detailed in pest-management literature and guidance documents (Catton, 2021; Hartley *et al.*, 2022). This gap in addressing the social context, combined with earlier public controversies over genetically modified organisms (GMOs), has led to calls for reconceptualizing public engagement practices (Macnaghten & Habets, 2020).

Public engagement activities serve different functions and can either limit or enhance public involvement

Public engagement goals can include mitigating backlash, educating and informing, enabling input for policy design and implementation, and aligning with ethical considerations (Figure 5.1). Forms of public engagement can consist of traditional or social media discourse, surveys, focus groups, citizen assemblies, government arrangements, multi-stakeholder partnerships, or public inclusion on scientific advisory committees (Scheufele *et al.*, 2021). Schairer (2019) details a typology of engagement activities that include inquiring, influencing, and involving. *Inquiring* concerns building actionable information; *influencing* highlights activities that impact decisions, actions, or behaviors; and *involving* pertains to spreading power to groups invested in program outcomes, including those with limited authority and influence (Schairer *et al.*, 2019). In the context of CRISPR, Scheufele (2021) maps out the goals, principles, and modalities that constitute public engagement approaches, with modalities acting as a category header for different activities (Figure 5.1).



Adapted from Scheufele *et al.* (2021)

Figure 5.1 Public Engagement Goals, Principles, and Modalities

Public engagement goals are outlined by principles and enacted through modalities. Modalities refer to the design and implementation of engagement activities that work toward achieving goals. When moving from *communication* to *empowerment*, the facilitation difficulty increases along with the power granted to the public.

Scheufele (2021) outlines how *communication* is typically unidirectional and top-down, consisting of, for example, public service announcements, information videos, newsletters, or social media posts. *Consultation* is still typically one-directional (from management to the public) but can include more interactive engagement, such as town hall sessions, surveys, citizen panels, focus groups, or even referenda. *Involvement* broadens the engagement scope to include public perceptions, values, and beliefs, and occurs throughout program development and implementation, including at earlier and later stages. Public *collaboration* consists of a collective approach to identifying problems, drafting solutions, and implementing actions. Consensus conferences are an example where knowledge, ideas, and program pathways can be co-created and actualized among participants. *Empowerment* provides the most power to the public, enabling members to hold positions that influence policy directions.

Collaborative and empowering activities elevate diverse actors, groups, and communities into influential participatory and partnership roles at various — or all — stages of program design and implementation (Long *et al.*, 2020). The Responsible Research and Innovation (RRI) framework outlines robust democratic practices that move beyond standardized notions of technology development to generate increased coordination and cooperation among actors with diverse perspectives (Owen *et al.*, 2012). Programs that include diverse voices and values are framed as aligning with ethical practices (Long *et al.*, 2020; EC, 2021).

All public engagement activities need to identify which diverse publics require engagement while also acknowledging that some, and potentially large, sectors of the public may be skeptical or have significant knowledge gaps around how gene-editing technologies work and what risks they carry (Kolopack *et al.*, 2015; Thizy *et al.*, 2019) (Section 2.3). In biological control contexts, perceptions and acceptance of risk can have considerable variability among diverse publics (Catton, 2021). Where some see uncertainty as a risk or threat, others might interpret that risk as an opportunity (Wohlers, 2015). As described in Chapter 4, assessing risk requires scientific discernment alongside social deliberation (Hartley *et al.*, 2022).

5.2 The Value and Limitation of Common Public Engagement Approaches

Communication and consultation are two common public engagement activities. Both can achieve public engagement goals but do not typically enable high levels of collaboration and power-sharing.

Communication activities can inform and educate, but they are typically limited in increasing public participation in policy design and implementation

A *communication* approach typically consists of disseminating information to the public. This information could include the details of a pest management program, data presented in regulatory approval processes, or technical information on how gene editing works. Communication activities as commonly practised have been referred to as the *(information or knowledge) deficit model*, which argues that non-experts' skepticism about and concern with technologies stem from a lack of knowledge and expertise. In response, the model argues that providing the public with accurate information addresses this skepticism (see, for example, Gross, 1994; Brunk, 2006; Wynne, 2006). This model has been critiqued for its ineffectiveness and its inability to adequately understand the basis for public concern. Indeed, the public, in some cases, perceives science itself to be problematic (Brunk, 2006; Wynne, 2006; Seethaler *et al.*, 2019; Williams & Kuzma, 2022). As such, when enacting the information deficit model, institutions may fail to reflect on their

scientific and policy-related practices, which can inhibit a clear understanding of public criticism (Wynne, 2006). In the GMO context, for example, responses to public concerns narrowly focused on safety and risk without incorporating a range of other social, regulatory, and consumer concerns (Macnaghten & Habets, 2020).

Public engagement that consists solely of communicating science and government activities does little to advance public participation. Oxitec's initiative to suppress the *Aedes aegypti* mosquito population in parts of Brazil, for example, was framed as having "full transparency" and incorporating "vigorous and proactive community engagement" (Carvalho *et al.*, 2015). It was stated that the project had support and consent from numerous stakeholders, including the regional health secretary and local community leaders (Carvalho *et al.*, 2015). Kofler *et al.* (2019), however, raised concerns around the focus of the project's consultation on education, observing how residents remained excluded from actual decision-making, thus limiting their roles for impactful influence.

Communication activities have value, despite fulfilling only a principally knowledge-dissemination role. Given the lack of public knowledge about gene-editing technologies (Section 2.3), communication efforts can help bolster the accuracy of public perspectives, some of which may be influenced by misinformation (see, for example, CCA, 2023). Case studies have proven the value of communication efforts that provide the public with opportunities to learn (O'Doherty *et al.*, 2010; Pare Toe *et al.*, 2022a). Communication is most valuable when it is accurate, engaging, tailored to specific audiences and contexts, and conducted in a self-reflexive, evaluative manner (Cooke *et al.*, 2017; Riedlinger *et al.*, 2019). It is also most effective and relevant when co-created with communities, incorporating local language and culture (CIHR, 2020; Pare Toe *et al.*, 2022a) (Section 5.4). For example, to disseminate COVID-19 health information through Indigenous communities in Canada, a collaborative project among researchers, artists, Cree Elders, and educators created widely watched videos using a Cree-speaking raven called Kahkakiw (CIHR, 2020).

Public consultation boosts interactivity compared with communication activities and becomes increasingly meaningful when its outcomes influence policy

Compared with communication, consultation increases public participation by soliciting the expression of local perspectives in reaction to programs (Scheufele *et al.*, 2021). In Canada, consultation practices are commonly used in managing natural resources (CCA, 2019). Here, decision-making lies with the government, as do the corresponding responsibility and accountability for program implementation, whereby public consultation is typically used to gain perspectives and feedback. Experts have viewed this consultation as most

appropriate when broad consensus on program objectives and trade-offs are evident and where relevant knowledge underpinning program directions is high (CCA, 2019). Genetic pest-control approaches face considerable uncertainty, however (Section 4.2); current consultation practices may therefore benefit from critical analysis and modification.

Numerous problematic issues have been raised around commonly used consultation practices, inclusive of obtaining consent. When it comes to conducting impact assessments or managing natural resources in Canada, unbalanced power dynamics can limit Indigenous participation, and assessment procedures may be insufficient at incorporating expressions of Indigenous knowledge (CCA, 2019; Blue *et al.*, 2021). Howlett and Migone (2010) have argued that the consultation approach for biotechnology in Canada is "educational:" rather than using engagement with the public to inform policy-making, engagement typically strives to achieve social acceptance of products. Indeed, many of the salient regulatory processes engage outside stakeholders either late in the process or not at all — with the tacit assumption that stakeholders will be receptive to the proposed intervention (Kuzma & Williams, 2022). This results in exclusion from early decision-making on how to address pest problems, and this lack of transparency can contribute to missed opportunities to build trust and effective collaboration. Even among stakeholder groups that generally view genetic pest-control approaches favourably, trust is a key variable (Goldsmith *et al.*, 2022).

Issues of trust and inadequate consultation have considerable relevance in the context of communities often marginalized in policy proceedings, such as Indigenous peoples (Kung, 2018). In the proposed Trans Mountain pipeline extension, for example, Canada's Federal Court of Appeal declared government consultations with Indigenous communities not sufficiently meaningful (FCA, 2018). Similarly, in regulatory practices around approving genetically modified salmon, cultural perspectives and broad public concerns about the technology heard during the consultation process were claimed to be not sufficiently "legitimate" (Kuzma & Williams, 2022). In this case, public outreach only took place after major project decisions had been made (Kuzma & Williams, 2022). One key component of effective consultation includes determining consent requirements for impacted communities — on legal or ethical bases — and establishing a plan for obtaining such consent given the specific program and context (WHO, 2021a). Obtaining informed consent necessitates sufficiently communicating the reasoning for an intervention, while detailing all potential impacts and risks. The participation of ethical and legal experts can greatly assist this process (WHO, 2021a). Public input is an essential component of obtaining consent, a process that has heightened relevance for Indigenous peoples in Canada (Box 5.1).

Box 5.1 Indigenous Peoples and Issues of Consent

There are cases where genomic research and project implementation have led to harms for Indigenous communities (Garrison *et al.*, 2019; CRISPRcon, 2020). The processes for requiring and obtaining consent are relevant for Indigenous peoples and communities, since the deployment of gene-edited organisms may spread across borders, potentially impacting cultures, livelihoods, and self-determination (Meghani, 2019). Sovereignty and autonomy in land uses are at play where the traditional knowledge and biomaterials of Indigenous peoples may be illegally or unjustly appropriated without providing benefit to those communities (Efferth *et al.*, 2016).

The Cartagena *Protocol on Biosafety to the Convention on Biological Diversity* addresses this, specifically outlining the requirements of free, prior and informed consent from Indigenous communities (George *et al.*, 2019; BCH, 2021). While Canada has not signed the Cartagena Protocol, it supports its objectives and actively participates in related discussions (ECCC, 2020). Clarifying what Canada perceives as a "lack of clarity and predictability in terms of [the Cartagena Protocol's] implementation and enforcement" would strengthen engagement on related issues (ECCC, 2020).

Also relevant to the Canadian context is an obligatory duty to consult Indigenous peoples based on Section 35 of the *Constitution Act, 1982*, which recognizes and affirms "existing aboriginal and treaty rights," which have been interpreted to encompass cultural, social, political, and economic rights, including the right to practise one's own culture (Slattery, 2007; GC, 2022b). In accordance with the Constitution and affirmed by five cases in the Supreme Court of Canada, the duty to consult places a responsibility on Canadian governments and agencies to understand "how and when their activities could have an adverse impact on Aboriginal and treaty rights" (CIRNAC, 2021a). In determining potential impacts, governments are required to engage in meaningful consultation with communities, as outlined in the *Impact Assessment Act* (GC, 2019b); however, specific consultation protocols can vary significantly and be inadequate (Library of Parliament, 2019; Bankes, 2020).

Although consultation practices are generally designed and implemented by governing bodies without public direction, they are not necessarily ineffective at enabling publics to impact policy. For example, in early 2023, after an "extensive" consultation process with industry and First Nations communities, a decision was made to not permit licence renewals for 15 salmon aquaculture sites in Atlantic Canada (DFO, 2023). While debate surrounds the impact of salmon farming on ecosystems (Labbé, 2023), this example demonstrates how current consultation practices can influence policy directions. Meaningful consultation therefore includes asking whether activities enable spaces for diverse and marginalized groups to provide input (Section 5.4), and whether that input has the potential to influence policy.

5.3 The Benefits and Challenges of Collaborative and Empowering Public Engagement

Empowering public engagement is contingent on increased collaboration and power-sharing among stakeholders and impacted communities. This vision of public engagement moves beyond informing, educating, and seeking approval, and creates increased opportunities for publics to influence policy at design and implementation stages (O'Doherty *et al.*, 2010; Blue *et al.*, 2019; Scheufele *et al.*, 2021). Greater stakeholder and public participation in processes can align more closely with notions of ethical practices, but various challenges accompany its enactment.

Increased collaboration and power-sharing aligns with notions of an ethical approach

The use of gene-editing technologies involves normative and value-laden decision-making, which can be strengthened through the input of multiple social actors' knowledge, perspectives, and values (WHO, 2021a). The concept of *epistemic justice*, for example, works toward outlining problems and drafting solutions whereby a diversity of views are reflected (EC, 2021). This entails considering the different relationships humans have to nature, socioeconomic progress, and pests. Considerations of *multispecies justice* may address potentially exploitative human activities in the natural world and position humans as inherently connected to nature, whereby each co-exists in non-hierarchical positions of uniqueness and value (Celermajer *et al.*, 2021).

Blue *et al.* (2019) articulate how ensuring a "parity of participation" along lines of "redistribution (who gets what), recognition (who is included and heard), and representation." Ideally, all engagement occurs where relationships have been built and maintained among all invested publics — including but not limited to Indigenous

peoples, especially in contexts where trust might be fragile (Montenegro de Wit, 2019; CRISPRcon, 2020; Catton, 2021; Taitingfong & Ullah, 2021). Although establishing and maintaining trust can be challenging, building good-faith relationships that enable parties to assess and shape a project's foundational principles, values, and practices offers the advantage of generating mutually shared benefits across diverse populations (Taitingfong & Ullah, 2021). Governing entities can aid these processes by acting with *institutional reflexivity*, which is important to critically evaluating and, in turn, modifying established practices (Wynne, 2006; Blue *et al.*, 2021). Overarching goals for these engagement practices include enabling diverse public input on identifying and reducing risks (Section 4.3), and sharing potential benefits among populations, including those with insufficient financial capacity to access the technology (Annas *et al.*, 2021; Blue *et al.*, 2021; EC, 2021). For significantly impacted publics — especially those with sovereignty over lands where gene-editing technologies might be used — community power might consist of the ability to significantly modify projects if the terms and conditions are deemed to be in conflict with community interests (Long *et al.*, 2020).

Increasing public empowerment involves diversifying power structures and governance networks that promote collaboration and transparency

Increased diversification and an expansion of powers among actors have been called for in genetic pest-control contexts (Kofler & Taitingfong, 2020; Long *et al.*, 2020). Establishing divisions or committees in government departments might prove beneficial in building trustworthy relationships; co-developing problems, solutions, and practices; and identifying risks based on diverse value systems. Environment and Climate Change Canada (ECCC), for example, is the first federal department to form an Indigenous Science Division (ISD), appointing its first director in 2022. Broadly, ISD's objective is to "advance reconciliation in ECCC's science and research activities" (GC, 2022c). More specifically, the division is tasked with "bridging, braiding, and weaving" Indigenous science into western-based science practices, in order to "carry out the department's mandate to protect and conserve healthy wildlife populations across Canada and minimize threats to Canadians and their environment" (GC, 2022c) (Box 1.1).

Further initiatives include preliminary discussions around changes to the *New Substances Notification Regulations (Organisms)* administered by ECCC and Health Canada (HC). This program is re-examining how public engagement can be undertaken, including through the Voluntary Public Engagement Initiative (VPEI) (ECCC, 2022c, 2022d). As stated in the pre-consultation document, the VPEI's objective is to facilitate the sharing of "scientific information, test data, and traditional knowledge" among stakeholders and members of the public so that public participation can inform discussions and assessment processes relating to

risk at early stages of a program (ECCC, 2022c). In this regard, ECCC is examining what constitutes effective and meaningful public participation at all different stages of decision-making and risk assessment, and how greater transparency might be achieved (ECCC, 2022c).

Given pests' ability to cross borders, numerous governing initiatives have been proposed internationally. Some have proposed a "global observatory" — an assembly of experts, stakeholders, and invested individuals from diverse regions, political cultures, and disciplines, whose meetings would consist of deep reflections about the use technologies through interdisciplinary exchanges (Jasanoff & Hurlbut, 2018). Proposals have also included a global data registry that would work toward ensuring data-sharing and transparency across projects worldwide (Taitingfong *et al.*, 2022). Others have outlined the need for a neutral, third-party coordinating body that could liaise among developers, local communities, and government-associated entities, ensuring the enactment of a deliberation framework that would combine differing perspectives, expertise, and worldviews into standardized reporting, recommendations, and transparent information-sharing protocols (Kofler, 2018).

Numerous challenges are present when public engagement becomes increasingly collaborative and empowering

Conducting engagement that is reflexive and highly collaborative requires considerable institutional capacity and resources (Kuzma *et al.*, 2017; Thizy *et al.*, 2019). This might be especially evident with first-in-class technologies where public engagement approaches are implemented for the first time. Program timelines could be strained when adapting broad engagement strategies to local environments and being flexible in response to public input (e.g., unexpected responses to programs, language complications, shifting local governance). Policy-makers act within restrictive timeframes and budgets, however, and extending assessment timelines can generate conflicts with national or international timelines (ECCC, 2022c).

For regulators, pest control tools are scrutinized primarily on the exclusive basis of scientific evidence. A science-based regulatory system is the linchpin of government oversight of potentially hazardous technologies and presents numerous advantages from the standpoints of predictability and international harmonization. Science, however, has at times been used to undermine legitimate social or cultural issues raised in a decision-making process (Williams & Kuzma, 2022). The emphasis on "science-based" processes is neither value-neutral nor apolitical (Meghani & Kuzma, 2017), and it can perpetuate power imbalances in

Broad impacts beyond science are often cited to promote the deployment of biotechnology products, yet proponents have also been shown to simultaneously argue against regulatory processes that could scrutinize these products on non-scientific grounds.

decision-making by overlooking viewpoints on the basis of their substance or the lack of scientific legitimacy of the actors making them.[34] Broad impacts beyond science are often cited to promote the deployment of biotechnology products, yet proponents have also been shown to simultaneously argue against regulatory processes that could scrutinize these products on non-scientific grounds (Williams & Kuzma, 2022).

A central challenge is thus attempting to integrate engagement into regulatory processes, since doing so will invariably disrupt conventional science-based processes. Other existing challenges speak to the overarching priorities and culture of the underlying institutions. Consultation processes are seen by some to introduce delays to the perceived detriment of a country's regulatory system — given the fast-paced and highly competitive environment of biotechnology (Kuzma & Williams, 2022). A guidance document speaking to potential reforms to the ECCC New Substances program echoes this sentiment, stating that consultation is seen to create delays or misalignment with other regulatory regimes (ECCC, 2022c).

Further, while the general public might argue for the necessity of its participation in assessment processes, challenges can be evident in ensuring participation occurs (Kuzma *et al.*, 2017; Scheufele *et al.*, 2021). Attendance at conferences, town hall events, or public meetings, for example, may be difficult for those with limited time or financial resources (Kuzma *et al.*, 2017; Scheufele *et al.*, 2021). In cases where public events are well attended, questions might be asked around legitimate community representation and whether participation was balanced and equal among attendees (Scheufele *et al.*, 2021). On one hand, an unmoderated event might disproportionately enable dominating voices. On the other hand, a heavily moderated event might generate more diverse participation but could be over-managed, distorting the genuine expression of sentiments and perspectives (Scheufele *et al.*, 2021). Complications may also be evident around conflicting power dynamics. In the context of bridging Indigenous and western-based

34 Along a similar line, in discussing approaches to regulating agricultural biotechnology in Canada, the Canadian Food Inspection Agency states that they work with Health Canada to "regulate for safety and efficacy of these products but are not responsible for evaluating need. The issue of whether or not these products are 'necessary' is left to the market place to determine" (CFIA, 2016).

sciences, unequal power dynamics may result in the unethical use of Indigenous knowledge or disenfranchise volunteers working with limited time and resources in comparison to, for example, government officials conducting well-financed professional tasks (CCA, 2019). Though challenging to implement, increasingly participatory public engagement can provide valuable learning experiences — an element of reflexive practices (Wynne, 2006; Blue *et al.*, 2021). Indeed, much can be learned from various international and national initiatives (Box 5.2).

Box 5.2 Public Engagement Initiatives in International Contexts

New Zealand's Environmental Protection Authority (EPA NZ) has a mandate to incorporate Māori perspectives into decision-making. The Ngā Kaihautū Tikanga Taiao, for example, is a Māori committee tasked with providing Māori-based advice to the EPA NZ and its various functions, including but not limited to the development and implementation of monitoring activities, and the policies and processes that make up Māori engagement (EPA NZ, 2019).

Norway and Denmark have both employed extensive public engagement as central components of genetic modification regulation. The Danish example of "Consensus Conferences" — which initiate dialogue between policy-makers and the public on technology-related challenges and solutions — began in the 1980s and has been replicated in numerous other contexts (Scheufele *et al.*, 2021). Norway's *Gene Technology Act* includes "ethical justification, social acceptance and the principle of sustainable development," thus creating a more restrictive legal process for GMO permissibility (as cited in Feldman *et al.*, 2022). The *Aarhus Convention* of the United Nations Economic Commission for Europe established public participation requirements in GMO decision-making practices (UNECE, 2023). It has been argued that Norway's process, in particular, has succeeded in expanding public engagement from a simple risk assessment context into broader governance (Macnaghten & Habets, 2020).

(Continues)

(Continued)

In the United Kingdom, the Sciencewise initiative generates discussions among public representatives, experts, and policy-makers, resulting in summative reports that are fed back into the policy-making process (Sciencewise, n.d.). Some research has suggested, however, that years of ongoing dialogue between the public and policy-makers in the United Kingdom has had "little impact" on public policy (Smallman, 2018). Indeed, in each of these international cases, critical reflection would be required to discern effectiveness and limitations. With the Danish Consensus Conferences, for example, report summaries of these events did not necessarily have considerable influence on policy-making processes (Scheufele *et al.*, 2021). Regardless, granting opportunities for people to express concern and vocalize feedback may be appreciated by publics and offer intangible value.

5.4 Best Practices in Public Engagement

Concrete details about what constitutes effective public engagement can be lacking in genetic pest-control guidance documents and academic literature (Hartley *et al.*, 2022). The outlining of best practices often relates to specific genetic pest-control contexts (e.g., conservation, malaria control) or to a particular stage of a program's implementation (e.g., risk assessment). This section highlights aspects of public engagement that could be applied to a range of potential implementations and their different stages. Complementing the definition of different publics (e.g., stakeholders, communities, Rights-holders) is the need to envision different levels of engagement that exist internally and externally among these publics, project members, and additional institutional bodies (Figure 5.2).

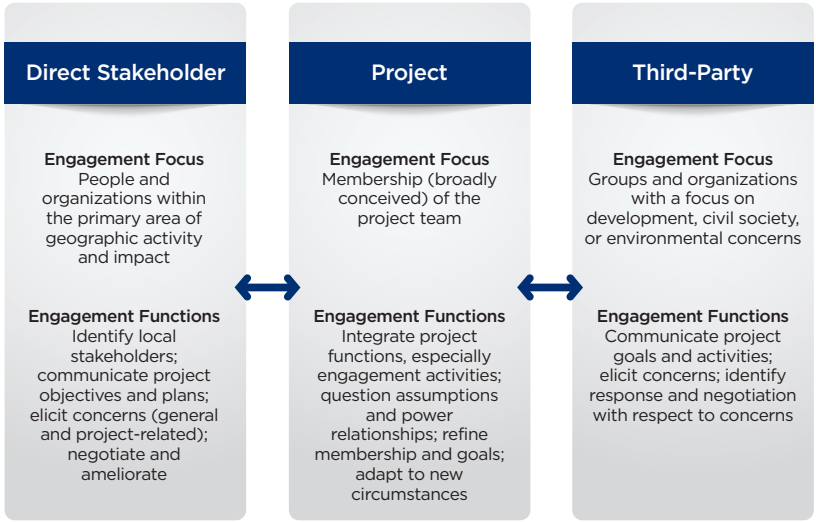


Figure 5.2 A Description of Engagement Focus and Function Across Three Different Levels

Engagement activities exist on the levels of stakeholders, project team members, and broader organizations and groups. As shown by the horizontal arrows, different levels of engagement are not siloed but impact the activities at other levels. Engagement functions consist of activities and responsibilities for and among actors in different roles related to the project. These functions can be performed iteratively or cyclically in response to project developments, and are expanded upon in Table 5.1.

Core components of effective and meaningful public engagement are accountability, adaptability, and transparency

Given that pest-control initiatives encounter degrees of public acceptability and trust (Sections 2.3 and 5.2) and that each specific context consists of unique populations and sociopolitical circumstances, public engagement approaches can be most impactful if designed and conducted with contextual sensitivity and specificity. Forest conservationists would, for example, have at least some differing values and motivations than large-scale farmers seeking to reduce pest management costs (Catton, 2021). Program managers may wish to consult with ethicists to design and implement engagement strategies that can identify which local leaders, institutions, and influencers might need to be engaged, and how

(e.g., through which formal or informal processes) (Thizy *et al.*, 2019; WHO, 2021a). This might have added pertinence, for example, in assessing requirements for obtaining consent or authorization (WHO, 2021a).

A collaborative approach applied to each context — one that involves publics — would allow a range of stakeholders to define and elaborate on a pest-related problem and how genetic tools might offer solutions. The tenets of "anticipatory public engagement" describe the creation of interactive spaces where publics reflect on their environments and corresponding challenges broadly, and not solely in response to a specific program's design or objective (Macnaghten, 2021). Focus group sessions could provide valuable insight into how a community perceives a particular pest and its surrounding ecosystem prior to learning of a potentially new tool or initiative (Macnaghten, 2021). These sessions could reveal, for example, that decreasing the presence of an invasive species is highly desired by residents (e.g., carp in Minnesota rivers and lakes (Erickson *et al.*, 2022)). Perceptions could also be gleaned through "uninvited" public engagement, where publics engage topics on their own terms, free from government agenda-setting (Wynne, 2007). Examples might include analyses of public discourse in the form of social media posts, blogs, media stories, or public demonstrations. Here, the public might exhibit different and potentially more critical perspectives than those heard at government outreach events (Wynne, 2007).

As projects develop, public engagement activities can respond to new evidence and changing environments while striving to maintain transparency, accessible data, and meaningful deliberations around risks, benefits, and strategies (NASEM, 2016; WHO, 2021a). In outlining "core commitments for field trials of gene drive organisms," scholars have outlined how — for increased fairness and transparency, and to ensure accountability and soundness of trial design — partnerships are needed among all stakeholders, including relevant communities and local experts (Long *et al.*, 2020). Having publics engaged in these processes helps diversify risk assessment and management practices (Annas *et al.*, 2021).

Public engagement efforts that meaningfully activate public participation have the potential to "promote accountability, enhance social learning, and stimulate socially acceptable and potentially innovative answers to environmental problems" (Blue *et al.*, 2021). As such, these efforts — specifically in regard to Indigenous peoples, but also applying to other invested communities — can enable inclusive environments where expressions of diverse knowledge and values are shared through co-created outputs and practices (e.g., narratives and storytelling, theatre performances, visual materials) (Chen & Burgess, 2021; Taitingfong & Ullah, 2021).

For instance, a public engagement initiative in British Columbia concerning genomic research activities on salmon showed how group perspectives can

emerge from meaningful social interaction (O'Doherty *et al.*, 2010). Participants had ample time to discuss the topic in different dynamic environments where they could learn from experts and express views broadly, all with the knowledge that findings from the engagement would be used to inform policy-makers (O'Doherty *et al.*, 2010). Regarding Target Malaria activities, Pare Toe *et al.* (2022a) highlighted how local theatre proved instrumental in educating and generating community participation. These activities, additionally, found solutions to the linguistic challenges of translating technological genetic concepts into local languages. Similarly, Hudson *et al.* (2019) demonstrated the processes necessary to evaluating how the use of genetic technologies in ecosystems aligns or conflicts with various Māori concepts and values (e.g., whakapapa, mauri, kaitiakitanga, mana). This collaborative process allowed Māori to meaningfully evaluate gene-editing technologies' impacts while simultaneously allowing non-Māori to gain greater insight into Māori principles and worldviews; in this cross-cultural exchange, *meaningfully* signifies Māori being able to interpret and evaluate the technologies through frameworks unique to their culture. Similar cooperative cross-cultural exchanges could also take place in Canada. Indeed, there have been many instances of constructive, mutually beneficial collaboration between Indigenous and non-Indigenous scientists (Box 1.1).

Transparency can be reflected in numerous practices. When informing and educating publics around the potential benefits and risks of gene-editing technologies, communication efforts ensure accuracy by not hyping potential benefits or downplaying potential risks (Shah *et al.*, 2021). Clearly outlining established as well as unknown risks, and transparently disclosing program options and alternatives (including repercussions from inaction), offer the potential for an accurate evaluation of an intervention (Essl *et al.*, 2017; Stirling *et al.*, 2018). Further, the processes used for defining risks and benefits can ideally be collectively constructed among invested parties (NASEM, 2016; Stirling *et al.*, 2018). Ensuring knowledge-translation of scientific information can extend beyond providing access to potentially dense and indecipherable data, creating interactive sessions focused on community participation (Hayes *et al.*, 2014; Taitingfong *et al.*, 2022). Sharing data through open-access journal publications and, if possible, global registries can help genetic pest-control projects align with the relevant codes of ethics to which all scientists in the field are bound (Taitingfong *et al.*, 2022).

Transparency is not necessarily viewed favourably when it comes to protecting intellectual property (IP), but registries could be designed in such a way that requirements for disclosure evolve in parallel with the progress of a trial (Warmbrod *et al.*, 2022). Similarly, other incentives could be used to offset concerns that transparency would act to the detriment of competitiveness. In the context of

gene-edited crops, a post-market certification system has been proposed to incentivize technology developers to share information and data about their products in exchange for certification demonstrating their commitment to transparency (Kuzma & Grieger, 2020). Regarding engagement with Indigenous communities, the Collective Benefit, Authority to Control, Responsibility, and Ethics (CARE) Principles can help ensure that Indigenous values and interests are incorporated in decision-making around data pertaining to their communities (Carroll *et al.*, 2022).

Well-designed public engagement includes activities tailored to program stages

Engaging the public early and often is seen as a core constructive element of public engagement (WHO, 2021a). Engagement at a relatively early stage can help address and mitigate potentially emotionally charged, reactive, and polarized discourse (O'Doherty *et al.*, 2010). This upstream approach enables developers to obtain key insights early, with ample time to incorporate feedback (Feldman *et al.*, 2022). Further, clearly defining objectives early can avoid overly simplistic tokenism or overly impractical inclusivity (de Graeff *et al.*, 2022).

Public engagement activities can be considered across the four core phases of program implementation (Table 5.1). Broadly, in any genetic pest-management context, best practices include identifying all relevant publics, discerning the most impacted and influential of those parties, and integrating those individuals, communities, and organizations into program plans (WHO, 2021a). It is advantageous to assess ethical and legal requirements throughout all stages (WHO, 2021a; Millett *et al.*, 2022). Further considerations include the potential creation of advisory bodies for specific applications, which could involve multiple stakeholders as well as regulators and technology developers (Allan *et al.*, 2020; Kuzma & Williams, 2022). These bodies can bring stakeholders and publics together, establishing decision-making deliberation that gives voice to minority views that might otherwise be suppressed in a plebiscite (Kofler, 2018; de Graeff *et al.*, 2022). The legitimacy of these bodies may depend on, for example, sufficient local representation, an absence of conflicts of interest, and activities codified through certification frameworks that satisfy an inclusive development model (Kofler, 2018). Existing multilateral organizations could support the formation and actualizing of these bodies, creating broader connections between local developments and global policy evolution (Kofler, 2018). This can result in mechanisms that continuously review and revise policy, monitor technology development, and establish methods for evaluating governance approaches (Millett *et al.*, 2022). In a novel but fast-moving technological environment, small-scale initiatives that draw on principles of adaptive, multi-stakeholder governance may provide valuable insights that can be generalized to other settings (Millett *et al.*, 2022).

Table 5.1 Potential Public Engagement Activities Across the Four Phases of a Project

Phase	Activities
1. Proof-of-concept/ laboratory stage	• Identifying relevant geographic locations and corresponding publics (e.g., stakeholders, leaders, member groups, key influencers) • Relationship-building with the most influential actors • Learning public perspectives and local relationships to environments and pests • Developing initial engagement plans and budgets • Planning communication strategies that incorporate local knowledge and culture • Equipping expert team members with knowledge-transfer tools and training • Providing the public interactive opportunities with scientists, officials, and laboratories • Initiating field-study plans (e.g., data collection and reporting) with regional participants • Consulting with government authorities and community leaders on the need for consent, authorization, and financial support • Evaluating the need for an external ethics advisory committee
2. Moving into confined field studies	• Increased learning about, and relationship-building with, local populations • Allowing space for diverse opinions and participation from most-impacted publics • Assessing regional sociocultural dynamics and forecasting potential social change (e.g., elections, emerging local issues) • Developing engagement plans with the most influential actors • Co-developing program objectives and plans, including plans for ongoing access to program developments • Establishing roles, terms, and expectations with all program participants • Solidifying authorization and consent requirements, and obtaining approvals to satisfy government officials, partner institutions, community authorities, and regulatory bodies • Seeking input from ethics committees and regulatory bodies (if deemed valuable) • Establishing adherence to accountability mechanisms, relevant legal frameworks, human rights principles, and research ethics protocols
3. Large- and small-scale releases	• Ensuring information and perspective exchanges among all program participants, identified partners, and publics • Ongoing monitoring and assessment of regulatory and contractual requirements (especially if human subjects are involved) • Monitoring program developments to perform ongoing risk and benefit assessments • Ongoing public engagement activities to generate feedback and enable access to program developments • Assessing plans to monitor the program and address adverse events • Conducting broad public engagement activities (e.g., social/mass media campaigns, surveys) • Distributing program data and logistical information to relevant parties • Gauging public reception to programs
4. Implementation and post-implementation	• Evaluating and determining the need for follow-on monitoring programs and assessing roles to be played by local communities and regional actors • Ensuring ongoing access to information and findings for regional, provincial/territorial, national, and international bodies (where valuable or needed) • Assessing the delivery of ethical obligations

Reproduced from WHO (2021a)

6

Governance of Gene-Edited Organisms for Pest Control

Chapter Findings

- Canada's current regulatory framework for pest control uses a case-by-case approach; the diversity of potential gene-edited organisms could test the limits of this framework's versatility.
- The type of pest-control product can dictate which departments or agencies are responsible for its regulation, potentially creating jurisdictional gaps or redundancies in oversight for genetic pest control.
- Despite ongoing reforms, regulatory uncertainty and the absence of explicit coordination among federal agencies and other jurisdictions might translate to challenges in risk governance.
- The regulatory lifecycle presents several opportunities for relationship-building and consultation. Meaningful engagement will be important for governing genetic pest control, in order to manage risks and promote trust.
- Risk assessment is a central component of regulation. Bolstering engagement allows regulators to build valuable implementation experience in understanding sociocultural risks.
- Monitoring could link federal regulators to key actors at sub-national and local levels, and catalyze the creation of partnerships to build capacity and trust while mitigating risks that accompany environmental regulation in a federated setting.
- Soft-law approaches, including guidelines, standards, and other policy tools, are instrumental in governing gene-edited organisms while regulatory systems find ways to adapt.
- Close partnerships with the United States will be crucial to build Canadian capacity for the responsible development, governance, and use of gene-edited organisms for pest control.

Earlier chapters provided an overview of the broad potential of gene editing and the associated promise and risk in its application to pest control. Additionally, the report detailed the relevant social and ethical dimensions, and approaches to engagement with stakeholders and publics. Each of these distinct issues plays a role in the governance of gene editing for pest control and represents an area where policy-makers may exert influence. This chapter focuses on governance in Canada and provides an overview of the broad challenges and looming decisions facing regulators.

It is first necessary to outline the processes and actors typically involved in the regulation of pest control. From there, the existing federal regulatory framework is analyzed in the context of how the challenges posed by genetic pest control might be met. In this respect, the Panel reviews past experiences in similar jurisdictions to inform decision-makers in Canada, as well as hypothetical scenarios that could result in regulatory uncertainty. The chapter then discusses several key choices emerging in this uncertain landscape. Decision-makers at every level can consider novel and collaborative solutions in response to these choices, in order to ensure the responsible development and use of these technologies and determine their appropriateness for solving pest problems.

6.1 Current Governance Environment

Legislation governing pest control and the release of live organisms predates gene editing; as such, no single piece of existing legislation can adequately govern these technologies. This is not necessarily a weakness, since legislation designed to fit specific technologies can have limited longevity in the face of technological innovation (Kuzma, 2013). Instead of developing new legislation, regulatory agencies in Canada are required to consider how existing legislation might ensure the safe use of gene editing for pest control, prompting them to identify where additional policies or guidelines might be needed. A number of federal and provincial/territorial agencies and departments are likely to be involved in the oversight of gene-edited organisms for pest control (Friedrichs *et al.*, 2019a).

Live organisms and chemical agents are regulated differently for pest control in Canada; existing frameworks could struggle with gene-edited organisms

Federal guidelines for agricultural biotechnology products provide a potentially useful starting point to understand how the oversight of new technologies might proceed. Table 6.1 offers an overview of the division of responsibilities across federal agencies in Canada for regulating products of biotechnology. A central feature of the Canadian regulatory environment is its focus on the characteristics of a product and not the process used to create it (Ellens *et al.*, 2019). For example, gene editing has been the focus of recent updated guidance for seed regulations, given the potential for new products based on gene editing to rapidly begin appearing on the marketplace (AAFC, 2023a). Rather than amend the *Seeds Act* or revise the corresponding *Seeds Regulations*, the federal government has opted to provide policy guidance for the interpretation and operationalization of these instruments (CFIA, 2023a).

Table 6.1 Division of Regulatory Responsibilities for Agricultural Biotechnology Products in Canada

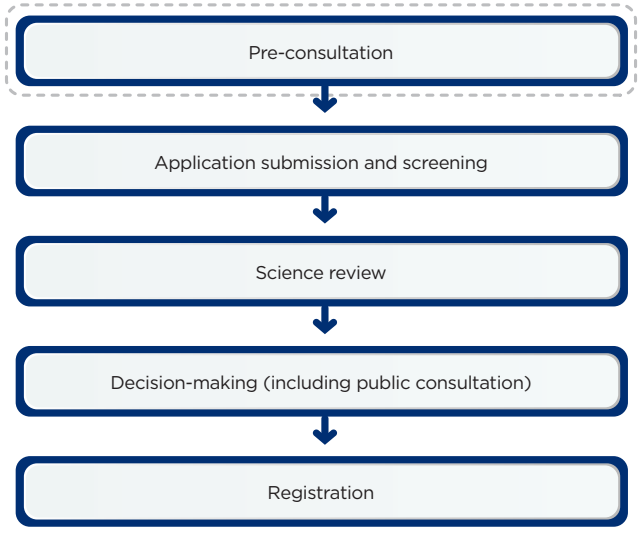
Agency/Department	Product Type	Legislation	Regulations
Pest Management Regulatory Agency; Health Canada	Pest-control products	*Pest Control Products Act*	*Pest Control Products Regulations*
Environment and Climate Change Canada; Health Canada (with regulations administered by Fisheries and Oceans Canada)	Fish products	*Canadian Environmental Protection Act, 1999*	*New Substances Notification Regulations (Organisms)*
Canadian Food Inspection Agency	Plants with novel traits	*Seeds Act*	*Seeds Regulations*
	Novel fertilizers and supplements	*Fertilizers Act*	*Fertilizers Regulations*
	Novel livestock feeds	*Feeds Act*	*Feeds Regulations*
	Veterinary biologics	*Health of Animals Act*	*Health of Animals Regulations*
Health Canada	Novel foods	*Food and Drugs Act*	*Food and Drug Regulations; Medical Devices Regulations; Cosmetic Regulations*
Environment and Climate Change Canada; Health Canada	All animate products of biotechnology for uses not covered under other federal legislation	*Canadian Environmental Protection Act, 1999*	*New Substances Notification Regulations (Organisms)*

Adapted from CFIA (2016)

Within the federal government, the Pest Management Regulatory Agency (PMRA) is responsible for regulating the use of pest-control products in Canada. It does so through the *Pest Control Products Regulations*, which operationalize the *Pest Control Products Act* (PCPA). The main focus of PMRA is on chemical pesticides (PMRA, 2022a).[35] The regulatory process that PMRA follows when it registers a new

35 "A pesticide is any product, device, organism, substance or thing that is manufactured, represented, sold or used as a means for directly or indirectly controlling, preventing, destroying, mitigating, attracting or repelling any pest" (PMRA, 2019).

pest-control agent is illustrated in Figure 6.1. The registration of a new chemical pest-control agent in Canada requires several data sources describing its chemical and physical properties as well as its potential safety risks.[36] Applications deemed complete will undergo a science review. The first component of this process is an assessment of risks to human health and the environment; it follows a similar approach to the one described in Section 4.1 (PMRA, 2021a).



Adapted from PMRA (2020)

Figure 6.1 Registration Process for New Pest-Control Agents in Canada

The decision-making process for new pest-control products varies according to the type of registration and product involved. The pre-consultation phase is optional and displayed in dashed lines. The decision-making process is driven by the results of the science review, but comments received during the public consultation step are considered in the final decision to proceed with registration.

36 The data requirements vary to some extent according to the broad sector in which the agent is intended to be used (e.g., forestry and agriculture, industry, society) as well as the specific application area (e.g., food-crop greenhouse) (PMRA, 2006).

If an agent is found to present an acceptable level of risk and provide value, it can be recommended for registration, at which point PMRA opens an online public consultation period. Comments collected during this period are considered by PMRA prior to reaching a final decision to register the pest-control agent and approve it for use in Canada (PMRA, 2020, 2022b).

PMRA occasionally coordinates the assessment of pest control products with regulators from other jurisdictions through joint reviews (HC, 2010), as well as with other federal agencies (PMRA, 2022c). One example of this is in the context of biological control. The lead agency for regulating the import and first release of a live organism for biological control purposes is not PMRA but rather the Canadian Food Inspection Agency (CFIA) under the *Plant Protection Act*.[37] This regulatory path proceeds through the formation of a review committee composed of members from multiple agencies, including PMRA, with defined roles and responsibilities (CFIA, 2022a). The committee also includes representatives from provincial/territorial government departments, academia, and industry. The role of PMRA within this committee is to ensure that provisions of the PCPA are considered, with respect to human health, the environment, and the potential value of the biological control program. The review committee coordinates the assessment of the potential biological-control intervention, where risk-benefit analysis is carried out based on available experimental data and estimates of impacts (Barratt *et al.*, 2021).

Both frameworks described above demonstrate strengths with respect to potentially regulating gene-edited organisms for pest control but also several weaknesses. For example, despite its flexibility, the focus of the PMRA-led process is on chemical pest-control agents. This is reflected in the language used in its guidelines and resources — from risk assessment to monitoring and enforcement (PMRA, 2021a, 2021b). Procedurally, nothing precludes PMRA from conducting a robust risk assessment on a proposed genetic pest-control program, but this assessment would proceed differently than it would for a chemical agent and could require coordination with other agencies, given some of the unique considerations involved.

The biological control regulatory framework, meanwhile, is designed with live organisms in mind. It calls on a multi-agency review body whose personnel are identified and assembled on a case-by-case basis; this could be well suited for assessing genetic pest-control programs. This advantage is offset by several key issues, however. Firstly, given the current evidence gaps for gene-edited organisms, a risk-based regulation is more cautious than a risk-benefit one as used for biological control; secondly, the standard decision-making process in

37 Some biological control agents are commercial products, such as microbials, in which case PMRA will generally regulate (Mason *et al.*, 2017).

biological control is not transparent. For pest-control products, the registration of a new agent through PMRA is preceded by a consultation step and followed by the online publication of the rationale that led to a decision. The decision-making surrounding biological control programs does not involve any public engagement and, in contrast to the PMRA process, the assessment is not required to be made publicly available (CFIA, 2022b); this lack of transparency and opportunity for public input could result in a lack of public trust and potential criticism of the technology (Section 5.2). Finally, with the exception of Newfoundland and Labrador, there are no provincial/territorial restrictions on the movement of arthropod biological control agents in Canada following CFIA authorization for introduction and use (Mason *et al.*, 2017).[38] Provincial/territorial laws can, however, restrict the use of pest-control agents registered by PMRA through additional regulations or licensing requirements (PMRA, 2019; Gov. of SK, n.d.).[39] A regulatory framework that would decouple a gene-edited organism — one carrying a self-sustaining gene drive, for instance — from its application context presents risk, given the interplay among the properties of the organism and how, where, and when it is released.

Genetic pest-control products will encroach on several federal regulatory jurisdictions, which could lead to ambiguity surrounding responsibilities

The federal regulatory systems in Canada and the United States are not identical but do share structural similarities. Both jurisdictions focus on the properties of a product, not on the processes used to manufacture it (Ellens *et al.*, 2019; Entine *et al.*, 2021). One important difference is that, in the United States, the handling of biotechnology products follows the *Coordinated Framework for the Regulation of Biotechnology.* The spirit of this framework reflects an intent similar to the Canadian approach, namely that existing rather than new legislation be used to govern these technologies (OSTP, 1986; Schairer *et al.*, 2021). The U.S. framework is often revisited and adjusted to account for new developments, however, and explicitly provides clarity surrounding roles and responsibilities for agencies as well as guidelines for coordination among agencies (US EPA, 2017).[40] Technologies such as the Oxitec *Aedes aegypti* mosquitoes nevertheless expose areas where regulatory uncertainty exists in the United States, despite the *Coordinated Framework* (Figure 6.2 and Box 6.1). For example, the Oxitec mosquitoes and a

38 It is recommended that regulators are informed about the intent to redistribute a biological control agent (Mason *et al.*, 2017).

39 Restrictions could, however, expose provinces, territories, or municipalities to lawsuits (Vis-Dunbar, 2008).

40 The framework also outlines pathways, timelines, and expectations for potential developers (with case studies for illustrative purposes) and is further bolstered by supplementary documents published by individual agencies to help maneuver the framework (see, for example, US FDA, 2009).

similar product (based on the *Wolbachia*-infected *Aedes* mosquitoes) experienced vastly different regulatory journeys, with the latter being regulated entirely by the U.S. Environmental Protection Agency (U.S. EPA) "treating the *Wolbachia* bacterium itself as a pesticide" (Schairer *et al.*, 2021).

USDA 2010–2011

Oxitec submits application to conduct field trials with OX513A mosquitoes in Florida, United States

USDA is determined to not have regulatory jurisdiction

U.S. FDA 2011–2017

Oxitec submits new application for a trial, and submits environmental assessment

U.S. FDA approves the trial, but it is delayed due to mixed reactions from local communities

U.S. EPA 2017–Present

U.S FDA transfers regulatory jurisdiction to U.S. EPA

Oxitec requests permit to conduct trials for more advanced mosquito technology

Experimental permit granted following evaluation of risks to environment and human health

Experimental permit extended by U.S. EPA to allow for more trials in Florida and California

Sources: Oxitec (2017); US EPA (2020); Waltz (2021)

Figure 6.2 Regulatory Pathway and Timeline for Genetically Modified Mosquitoes in the United States

The road to regulatory approval for Oxitec's genetically modified *Aedes aegypti* mosquito technology has taken over a decade and involved multiple regulators (as listed above, the U.S. Department of Agriculture (USDA), Food and Drug Administration (U.S. FDA), and Environmental Protection Agency (U.S. EPA)); this highlights some of the challenges for technology developers and regulators alike in governing these technologies. See also Box 6.1.

In Canada it is plausible that similar jurisdictional ambiguity could occur for these technologies. It is unlikely that OX513A would have been regulated by CFIA through Canada's *Health of Animals Act*, since — unlike in the United States — there has been no federal guidance to consider inserted DNA constructs as "animal drugs," a step that originally directed Oxitec's application to the U.S. FDA

(US FDA, 2009).[41] However, as a pest-control technology consisting of a live modified organism, OX513A could conceivably have fallen under the jurisdiction of both PMRA and Environment and Climate Change Canada (ECCC) through the PCPA or the *Canadian Environmental Protection Act* (CEPA) (GC, 1999, 2002). In this context, regulation under the PCPA allows for CEPA exemption, while regulation under the *Plant Protection Act* (e.g., in biological control) does not (GC, 1999).

Box 6.1 Multi-Agency Decision-Making in the United States Highlights Challenges

Oxitec's OX513A genetically modified mosquitoes were designed to suppress wild *Aedes aegypti* populations through a modified type of SIT (Box 2.1), in order to curb vector-borne disease transmission. The technology was assessed for more than ten years by regulators in a process marked by confusion about which agency had regulatory jurisdiction and how the underlying legislation should be applied (Figure 6.2). The mosquitoes were first regulated as a new animal drug by the U.S. FDA, with a focus on the safety of the inserted DNA construct to the animal and its efficacy at suppressing target populations but not on potential environmental or ecological impacts (Meghani & Kuzma, 2017).

The U.S. FDA decision to allow trials to proceed (pending local approval) was undermined by community opposition, as expressed in a referendum (Roen, 2016). Shortly thereafter, following the release of a new guidance document for industry by the U.S. FDA, the application — which by then involved a new strain of mosquito[42] — was transferred to the U.S. EPA and regulated under the U.S. *Federal Insecticide, Fungicide, and Rodenticide Act*. The new guidance provisioned that genetically modified mosquitoes for control of mosquito populations would be regulated by the U.S. EPA, whereas those for combating disease would be regulated by the U.S. FDA — making the regulatory agency dependent on the claim of the product developer.

(Continues)

41 For a hypothetical gene-edited mosquito, one modified to lose the capacity to carry dengue or another vector-borne disease, the *Health of Animals Act* could plausibly be triggered, since the accompanying regulations govern veterinary biologics (CFIA, 2011).

42 Oxitec had, by that time, improved its technology and substituted the OX513A with a new strain named OX5034, one with similar properties, in its regulatory application (Schairer *et al.*, 2021).

(Continued)

The U.S. EPA process involved a broader environmental and human-health risk assessment, supported by empirical data and modelling, which took into account many of the issues that were not considered in the environmental assessment carried out for the U.S. FDA application (US EPA, 2020). However, at the time, there were no peer-reviewed studies on the new strain from Oxitec. In contrast to leading practices in engagement (Section 5.4), the public and outside experts were unable to scrutinize or comment on the assessment document until after the U.S. EPA's approval of the permits (Allan *et al.*, 2020; Kofler & Kuzma, 2020).

Pre-submission consultations (Figure 6.1) could assist technology developers (and PMRA) in ascertaining which additional agencies need to become involved, but this process is done on a case-by-case basis. Moreover, although PMRA is party to several memoranda of understanding (MOU) relating to interagency collaboration and cooperation, these vary in scope (PMRA, 2017).[43] Although an MOU may signal the need for planning and delegation across agencies, it does not necessarily provide guidance on assigning responsibilities (i.e., lead agencies) in areas of jurisdictional ambiguity (see, for example, HC, 2008). Interagency collaborations in Canada will face challenges in avoiding risk assessment pitfalls experienced under similar circumstances in the United States, particularly if clarity surrounding coordination is lacking.

Pest-control products approved by federal regulators are subject to multi-jurisdictional oversight with respect to their use and impacts; cooperation will be crucial to avert risks

Multiple federal government agencies may be called upon to provide input for assessing pest-control products. However, as described earlier, stakeholders from other levels of government or other sectors may also play a role in this process, particularly in biological control (CFIA, 2022a). This role becomes greater once a pest control tool goes into use due to the division of powers in Canada. Many pest-control interventions are environmental ones, particularly those involving gene-edited organisms, given the risk factors outlined in Section 4.2.

The division of powers as described in the *Constitution Act, 1867* does not define "the environment," precluding a clear allocation of responsibilities among federal and provincial jurisdictions (Becklumb, 2013; GC, 2022b). The Act does specify, for example, that provinces are responsible for the management of its Crown lands,

43 PMRA has, however, alluded to plans to "strengthen linkages" with ECCC as part of its ongoing reforms (PMRA, 2022c).

municipalities, and "local or private" matters.[44] Meanwhile, federal jurisdiction is explicit for boundary waters, fisheries (including fish habitat and water quality), and migratory birds but not for other wildlife. As such, issues relating to conservation (i.e., species at risk) and environmental assessment do not fall under any specific jurisdiction but might be regulated provincially, territorially, federally, or cooperatively (Becklumb, 2013).

Due to this shared jurisdiction, the ways in which environmental regulations are operationalized in Canada can vary and evolve, which Scott (2018) cautions has serious implications for ecology, environmental health, and climate change mitigation. This may present a risk surrounding unintended ecological or environmental outcomes of genetic pest control: when instances of such harms arise, the issue of jurisdiction can be unclear or subject to fierce debate, particularly if it implies political costs, loss of revenue, or the need for public spending (Scott, 2018). Political factors may influence how (and how quickly) jurisdictional tensions are addressed in conducting effective environmental oversight, and these tensions can therefore influence the distribution of environmental burdens and benefits (Scott, 2018). Recent examples illustrate this risk, such as the politicization of environmental monitoring (see, for example, Djuric, 2022; Snowdon & Weber, 2023) and cases where effective environmental oversight has been inhibited by adversarial relationships among governments or agencies (Benzie, 2023; CP, 2023).

Moreover, despite the Constitution recognizing "existing Aboriginal and treaty rights" (GC, 2022b), in practice there is significant complexity in applying the division of powers as it pertains to environmental regulation on Indigenous lands. Jurisdictional responsibility is allocated partly as a function of whether the land falls under "self-government agreements, treaty or land claim" (Scott, 2018). For example, reserve lands, which are defined by the Government of Canada as lands set aside for exclusive use by First Nations peoples, have historically fallen under federal jurisdiction through the *Indian Act* (GC, 1985). However, the 1996 *Framework Agreement on First Nation Land Management* established mechanisms by which First Nations can re-establish authority over environmental management on their lands, beyond the provisions of the *Indian Act* (GC, 1985, 2022d; LABRC, n.d.-a).[45] Although this agreement focuses primarily on land-use planning and resource management, it also includes provisions for environmental assessment and protection based on First Nations laws (which, as of 2022, take precedence over federal laws in situations of conflict) (GC, 2022d; Hayden *et al.*, 2023).[46]

44 The situation becomes more complex in the territories which, despite being under federal jurisdiction per the Constitution, possess some of the powers of the provinces for certain environmental issues (e.g., water management) (Becklumb, 2013).

45 There are 204 First Nations across Canada participating in the agreement in some capacity as of May 2023 (LABRC, 2023).

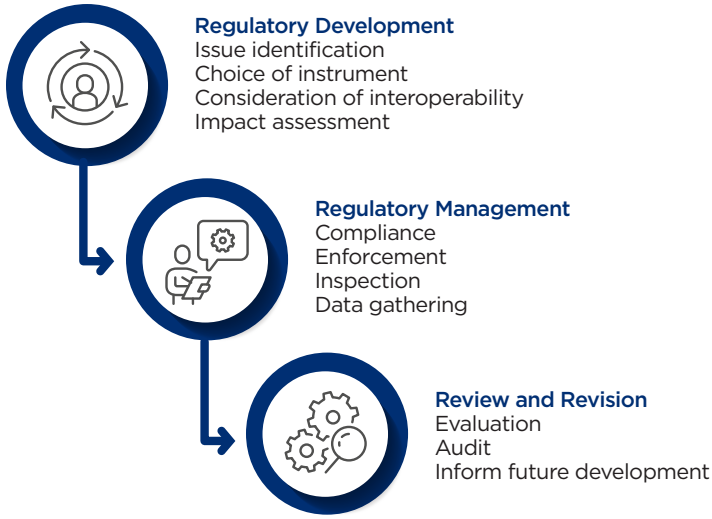
46 Federal environmental assessment legislation are applied on an interim basis until First Nations laws come into force (LABRC, n.d.-b).

The realization of environmental management authority may require bolstering regulatory capacity in communities (ECCC, 2018b), with programs underway to do so (GC, 2014). Furthermore, the agreement is limited to First Nations peoples, specifically, and does not apply to other Indigenous peoples (Powell, 2023). Traditional lands typically extend beyond reserve lands, however, further complicating jurisdictional consideration; in many parts of the country, Treaty Rights extend beyond the borders of reserves and into Crown lands, which fall under provincial jurisdiction (Becklumb, 2013; Powell, 2023).

Taken together, this provides a snapshot of the challenges that could arise in the governance of genetic pest-control programs, should they be carried out on, or have implications for, Indigenous lands. Powell (2023) identifies four broad areas where environmental law and Indigenous Rights become intertwined, two of which — wildlife conservation and water — could be salient to pest-control applications for conservation purposes. Moreover, in the context of agriculture, where many technologies are currently being developed (Section 3.1), Indigenous peoples may be important stakeholders and Rights-holders. They participate in the agricultural sector, both as growers and lessors of First Nations reserve lands for use by non-Indigenous farmers (Arcand *et al.*, 2020). This jurisdictional complexity continues to evolve alongside multiple parallel developments in Canadian legislation and jurisprudence concerning environmental protection, the implementation of the *United Nations Declaration on the Rights of Indigenous Peoples* (UNDRIP) (Section 2.3), and ongoing assertions of inherent jurisdiction (Scott, 2018; Powell, 2023).

The regulatory process is not a discrete event but a lifecycle, one that offers several avenues to establish partnerships and pursue engagement

Given the implications and potential broad reach of genetic pest control, the proactive establishment of partnerships could be critical to mitigate the influence of overarching political misalignments and the lack of clarity regarding division of powers. The specific process of regulatory approval discussed earlier sits within a wider regulatory lifecycle, which accompanies any regulatory instrument used to operationalize public policy. This lifecycle (Figure 6.3) begins with the development of a regulation and is followed by regulatory management, a process involving numerous activities, ranging from compliance and enforcement to communication with the public about laws and regulations.



Adapted from GC (2018a)

Figure 6.3 Three Regulatory Lifecycle Stages and Examples

This figure illustrates the lifecycle of a regulation. Policy-makers are tasked with determining the appropriate form of a regulatory process. Afterwards, regulatory management becomes the key issue. Careful consideration of each step of the regulatory lifecycle will be important for governing genetic pest control. This may be particularly true given the involvement of numerous departments and agencies. Issues occurring at any point along the lifecycle risk propagating up- or downstream, to the detriment of the overall regulatory program.

In considering the development of federal regulatory instruments, the Treasury Board Secretariat emphasizes the importance of engagement with stakeholders throughout the process, and the need to coordinate with other levels of government (GC, 2018a). The regulatory lifecycle (Figure 6.3) comprises numerous discrete tasks, each of which lends itself to opportunities for engagement or collaboration. In some cases, these activities are prescribed within a process; for example, during regulatory development, stakeholders are consulted through discussions of "possible policy approaches," and again following approved draft regulations (ECCC, 2018a).[47] For genetic pest control, given the breadth of considerations and uncertainty, it may prove valuable to proactively consider how other elements of the lifecycle can be used to build partnerships in governance. As echoed throughout this report — in various contexts — partnerships leveraging skills, knowledge, and

47 It is up to departments and agencies to identify stakeholders and participants for engagement during these early stages (GC, 2018a).

resources may be needed for genetic pest control. In governance across jurisdictions and sectors, these might allow for better use of scarce resources by reducing duplication, establishing relationships and dialogue, and leveraging institutional expertise (GC, 2018a; Macnaghten & Habets, 2020; Reid *et al.*, 2021). Although increasing the number of stakeholders in decision-making carries upfront logistical costs, many area-wide pest-control interventions have historically relied on partnerships, since these can help augment the cost-effectiveness of a program through economies of scale (Vreysen *et al.*, 2007).

Monitoring is one area where these activities naturally occur. Pest monitoring in particular is an area where stakeholders bring human and financial resources together to address a shared priority (see, for example, PPMN, n.d.; AAFC, 2022, 2023b). In addition, regulators and academic scientists collaborate with Indigenous communities for environmental monitoring (Wilson *et al.*, 2018; Peacock *et al.*, 2020; Bowles *et al.*, 2022). In the Panel's view, monitoring could provide opportunities for bolstering engagement and collaboration in governance for genetic pest control (Box 6.2). Efforts can be made to broaden the scope of those partnerships following leading practices in engagement (Section 5.4), such that, on a case-by-case basis, the appropriate stakeholders are involved and empowered to participate in overseeing the deployment of novel pest-control technology in diverse contexts.

Box 6.2 Beyond Monitoring: Indigenous Land Management Principles

Earlier sections of this report introduced the risk that gene-edited organisms used for pest-control purposes could exacerbate existing threats of biodiversity decline (Section 4.2). Programs exist for applying alternative ecological practices to mitigate these risks and could enable effective community-led governance of pest control. Indigenous land management practices have been linked to higher levels of biodiversity than those used in other protected or even non-protected areas (Schuster *et al.*, 2019). Guardianship involves Indigenous-led governance and management approaches for protected areas. This includes testing and monitoring, but also control over land-use and marine-use policies (ILI, n.d.).

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Several such programs exist (see, for example, Land of the Ancestors, n.d.; Seal River Watershed, n.d.) and are linked through national networks and pan-Canadian initiatives (Land Needs Guardians, n.d.). The federal government has provided growing investments toward these initiatives to aid in establishing Guardianships across the country (ECCC, 2018c). Some of these resources have been drawn from climate change funding envelopes. The federal government is enabling flexibility in terms of decision-making and funding in these initiatives through governance structures that reflect the distinct First Nations, Inuit, and Métis communities involved. It is unlikely that genetic pest control would be eligible or fall within the purview of such a program but, if so, it could be carried out through a process where communities are central to decision-making (ECCC, 2018c).

6.2 Emerging Choices in Shaping the Governance Landscape

The discussion above reflects the general uncertainty about how existing regulatory structures at both national and sub-national levels will be applied to gene-edited organisms for pest control. This uncertainty is exacerbated by the fact that several of the implicated federal agencies are currently undergoing reforms, ranging from the review of legislation to changes in processes and policies. When projected across this changing regulatory landscape, the Panel's findings in terms of R&D barriers (Chapter 3), risk assessment (Chapter 4), and the social dimensions of these technologies (Chapter 5) raise several key questions for decision-makers moving forward.

The role of CEPA as the "safety net" for biotechnology products may apply to some genetic pest-control programs, such as gene drives

The main legislative components for regulating biotechnology in Canada (Table 6.1) tend to be applied based on the specific end-use of the product, but CEPA stands out. It has a unique role within this framework as a "safety net," one applied to "all animate products of biotechnology for uses not covered under federal legislation" (CFIA, 2016). The relevant regulations in this case are the *New Substances Notification Regulations (Organisms)* (NSNR (O)), which govern new organisms introduced to Canada or previously introduced organisms applied to new purposes (ECCC, 2010). Products regulated through this process are added to the Domestic Substances List and include disparate organisms ranging from genetically modified salmon (Box 6.3) to gene-edited human immune cells for use in clinical trials (ECCC, 2021).

The information requirements for a new substance notification are relevant to gene-edited organisms for pest control. For instance, new registrants must describe the modifications to a proposed organism, the genetic stability of these modifications, and the potential for the dispersal of traits by gene transfer (ECCC, 2010) (Box 4.3). The organism's biological and ecological characteristics must be provided, including related field studies. The scope of the risk assessment, as defined by CEPA, is broadened by the interpretation of "toxic" in that legislation (Box 6.3); as such, the assessments are carried out by both Health Canada and ECCC (ECCC, 2021). Moreover, in contrast to the biological control approach described earlier, the NSNR (O) has provisions for Significant New Activity (SNAc): an organism listed on the Domestic Substances List must be re-assessed before being used in a different manner or setting (HC, 2022a). Living organisms regulated under the PCPA are not subject to SNAc provisions, however, which has potential implications for genetic pest control (HC, 2022a).

Box 6.3 Interagency Coordination for Genetically Modified Salmon in Canada

Canada was one of the first countries to provide regulatory approval for a genetically modified food animal: the AquAdvantage genetically modified salmon. It was also the first country where products derived from this animal reached the market (Waltz, 2017a; Bodnar, 2019). This salmon is engineered to exhibit significantly faster growth in early life compared with wild-type Atlantic salmon (HC, 2016). Its pathway to market approval began in 2012 and took four years, involving three distinct assessments led by different agencies. Health Canada assessed the salmon for safety and nutrition as food, while CFIA did so for safety and nutrition as livestock feed (HC, 2016). ECCC subsequently became involved through Section 64 of CEPA, which defines environmental impacts that could lead a substance to be considered "toxic" (combining risks to human health, the environment, or biological diversity) (ECCC, 2010). For example, potential harmful effects on biodiversity include the capacity for the engineered salmon to outcompete wild salmon (e.g., for food and resources).

Under an MOU with ECCC and Health Canada, Fisheries and Oceans Canada (DFO) coordinated an assessment of the environmental risks posed by the manufacture of AquAdvantage salmon in Canada (DFO, 2019). The assessment concluded that the potential risk to wild populations was high, but that exposure to this risk was low; the project moved forward (DFO, 2019). The facility has since stopped rearing salmon, however, since it was deemed too small for production at commercial scales (Yarr, 2023).

Following recent CEPA reforms, the federal government is also updating the NSNR (O) with an emphasis on transparency and modernization, as a way to keep pace with technology and reduce ambiguity (ECCC, 2022e, 2022f). A related 2022 discussion paper, published by ECCC — which does not currently reflect official government policy — suggests using CEPA to regulate gene drives specifically, and gene-edited organisms released into the environment (ECCC, 2022c). It also alludes to the potential new requirement that applicants demonstrate the "need for a new living organism," which would expand regulatory scope beyond risk or safety (ECCC, 2022c).

Many procedural components of the NSNR (O) raise questions about how PMRA and ECCC might appropriately and efficiently allocate responsibilities in areas where both agencies may claim jurisdiction, given that CEPA could be triggered by many potential implementations of genetic pest-control programs, and gene drives in particular. As Table 6.2 shows, the case studies discussed in a 2016 report on gene drives by the National Academies of Sciences, Engineering, and Medicine (NASEM) could all conceivably fall under ECCC jurisdiction due to environmental risks (NASEM, 2016). Resolving this ambiguity will be important to avoid inefficiencies or duplication. For some substances, such as microbial biocontrol agents, the PMRA-led environmental assessments have been deemed sufficient to exempt these substances from the NSNR (O) (Cuddeford, 2005), but it is too early to tell whether similar policies will be followed for gene-edited organisms. Given the contrast between the two agencies' respective mandates, the appropriateness of ECCC regulating all genetic pest-control programs is debatable and will present a dilemma for technology developers and policy-makers alike.

Table 6.2 Hypothetical Canadian Regulatory Approaches for Cases Discussed in the 2016 NASEM Report, *Gene Drives on the Horizon*

	Mosquito	Mosquito	Mouse	Plant
Objective	Use a gene-drive mosquito to suppress transmission of dengue to humans	Use a gene-drive mosquito to suppress transmission of avian flu among birds	Use a gene-drive mouse to eradicate invasive mice from islands	Use a gene-drive plant to eliminate a weed species
Potential Regulatory Authority	PMRA: Use of pest-control agent to control pests ECCC: Import of animate product of biotechnology	PMRA: Use of pest-control agent to control pests CFIA: *Animal Health Act* ECCC: Import of animate product of biotechnology	ECCC: Import of animate product of biotechnology	CFIA: *Plant Protection Act* ECCC: Import of animate product of biotechnology
Agency/ Department: Assessment(s)	PMRA and ECCC: Risk assessment for the environment and human health	PMRA and ECCC: Risk assessment for the environment and human health CFIA: Environmental assessment and assessment of risk to animal health	ECCC: Risk assessment for the environment and human health	CFIA: Plant pest risk analysis ECCC: Risk assessment for the environment and human health
Areas of Regulatory Uncertainty	In all cases, CEPA could conceivably be triggered due to the presence of a novel organism. Past experiences suggest that agencies might separate aspects of risk assessment to suit specializations, but on a case-by-case basis. The PCPA conceivably gives PMRA priority due to its focus on controlling pests for the mosquito examples. However, PMRA's direct regulation of live organisms is limited to micro-organisms and would necessarily involve the participation of other agencies. CFIA would not possess direct jurisdiction over three of the four examples, despite being the main agency responsible for biological control involving live organisms, since those examples pose no threat to plant health.			

Data source: NASEM (2016)

Risk assessment is a springboard toward multi-stakeholder governance. Regulatory reforms appear to acknowledge this but will need to resolve ensuing tensions

In the Oxitec mosquito example (Box 6.1), the approval process for conducting experimental trials proceeded from the top down, as is typical practice. Multiple U.S. federal regulatory agencies considered the application dossier prior to granting permits, pending the approval of state and local governments. Despite federal approval, these permits were denied, in some cases, following plebiscites (Waltz, 2021). Under the pathway initially followed by the original application, however, no formal public consultation would have taken place. In the end, the public had been provided the opportunity to participate in information sessions and meetings throughout the regulatory process, but the consultation that followed the U.S. EPA assessment of the technology was not perceived to address longstanding public concerns and opposition to the project (Maxmen, 2012; Allan *et al.*, 2020). Although the motivations underlying opposition to these technologies are varied, the real or perceived sense of being excluded from decision-making (e.g., surrounding risk) contributes to frustration on the part of the public and fuels mistrust (Maxmen, 2012).

The main categories of risk for gene-edited organisms (gene drives in particular) are revisited in Figure 6.4. Depending on the application, regulators could consider risks across each of these categories following processes described in Section 4.1. However, as noted earlier, a lack of evidence and standards challenges the operationalization of risk assessment and the definition of relevant endpoints. This has led to calls for adaptive risk governance processes, which might focus, at first, on procedural robustness (Kuzma, 2019). These processes could subsequently converge toward more conventional assessment methodologies as more evidence becomes available. The departure from standard practices is complicated by several factors; although legislation does not typically dictate how risk assessment should be carried out, standard practices do exist and are crucial for projecting regulatory predictability and facilitating comparisons (Nienstedt *et al.*, 2012; Garcia-Alonso & Raybould, 2014; PMRA, 2022d). Introducing adaptive measures within established practices across the lifecycle is therefore not without costs.

An important component of adaptive risk governance involves participation by stakeholders other than regulators or technology developers in the risk assessment process (Teem *et al.*, 2019; Kokotovich *et al.*, 2022). Endpoint definition in risk assessment strongly reflects values, which in turn demands the input of impacted communities (Kuzma, 2019), particularly given the intergenerational and transboundary risks presented by gene-edited organisms (Millett *et al.*, 2022). Moreover, these interventions will be tied to very specific contexts — genetic pest-control programs will be directed toward local problems, with correspondingly local risks and benefits (Box 6.4), which underscores the need for public participation in

Genetic pest-control programs will be directed toward local problems, with correspondingly local risks and benefits.

risk governance, given the numerous scientific uncertainties (Kofler, 2018). In adjacent areas, pilot programs have already been carried out in agriculture for gene-edited crops where governance responsibilities are shared by stakeholders, experts, and technology developers to obtain a comprehensive overview of risks and benefits (Jordan *et al.*, 2022). In Canada, some initial steps have been taken in this direction, in the context of the recent ECCC Voluntary Public Engagement Initiative (ECCC, 2022g) (Section 5.3). This policy aims to enable increased public participation in risk assessment for new living organisms subject to NSNR (O) regulations, and allows the public to contribute information, data, and traditional knowledge for incorporation into the assessment of risks related to the environment and human health, as required by CEPA (ECCC, 2022c).

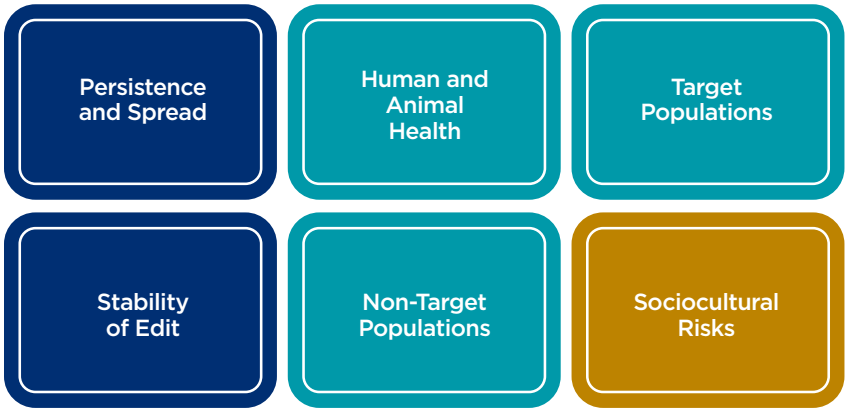

Figure 6.4 Main Risk Categories Presented by Genetic Pest Control

As described in Section 4.2, areas concerning efficacy are shown in blue, biosafety in teal, and broader impacts in gold. The main challenge, at present, revolves around the lack of evidence pertaining to these categories. However, endpoints reflect values, and there are opportunities to guide the assessment process through tighter engagement with communities, both within and across these broad categories.

Upcoming revisions to the New Substances program could expand on this initiative. The discussion paper accompanying consultations about these revisions acknowledges that, in its current design (an online comment portal), the new engagement process has not yet resulted in the intended uptake or input (ECCC,

2022c).[48] Namely, public input thus far has focused on concerns or questions about impact and process, rather than contributing data, scientific input, or traditional knowledge (ECCC, 2022c). However, the document signals that other forms of adaptive risk governance could be options for regulators in the context of CEPA — for example, a periodic reassessment of risks to account for the consequences of climate change. It also mentions that gene drives (as first-in-class technologies) could specifically be allotted greater-than-usual resources for engagement (ECCC, 2022c). These examples suggest the need for Canadian regulators to consider experimentation, which may prove practical for tailoring requirements and processes according to the risks, stakeholders, and contexts involved.

Box 6.4 Salmon Lice in the Pacific Northwest

Salmon is highly valued throughout the Pacific Northwest for economic and cultural reasons. It is also a significant driver of economic activity and a lucrative financial export product generating $1.12 billion in 2021, over $600 million of which was exported by British Columbia (DFO, 2022). The practice of salmon farming is contentious but also viewed as necessary by many, including some Indigenous communities that own, manage, and rely on hatcheries to maintain their traditional ways of life (Braun, 2022). Salmon lice (*Lepeophtheirus salmonis*) are a significant pest in this domain (Guragain *et al.*, 2021; Lavoie, 2022). The lice have a damaging impact on wild salmon populations and are even more damaging in salmon hatcheries, where they can proliferate due to the high density of hosts. A range of pest management control measures have been deployed to counter the lice, but these tools are failing, leading stakeholders to consider genomic alternatives (Guragain *et al.*, 2021).

Gene editing using CRISPR/Cas9 (Box 2.2) has been proposed as a means for enabling effective control of salmon lice (Guragain *et al.*, 2021). Approaches could be used to target the lice themselves using mechanisms discussed in Chapter 2, since the genome of the salmon louse has been sequenced (Skern-Mauritzen *et al.*, 2021). Alternatively, genetic characterization projects on salmon populations to monitor for susceptibility to lice are taking place in British Columbia, through a joint effort among academic researchers, federal scientists, and several Indigenous communities and organizations (Genome BC, 2021b).

(Continues)

48 This process has only been used in the context of notification for transgenic ornamental aquarium fish, thus far (CSAS, 2022).

(Continued)

These activities could inform ongoing work to apply gene editing to salmon themselves, in order to reduce their susceptibility to lice (Nofima, 2022). The existing alignment of stakeholders in the context of this pest could represent fertile ground for partnerships to develop a genetic pest-control program (Section 3.2), including its objective, design, implementation, monitoring, and evaluation.

Canada can only participate in defining and operationalizing standards and leading practices if it possesses capacity for regulatory science and partnerships

Regulating gene-edited organisms is complicated by our limited experience with these products and accompanying uncertainty in assessing their safety and efficacy. In the absence of dedicated legislative frameworks, establishing standards and guidelines will be vital soft-law tools for product developers, scientists, and regulators alike (NASEM, 2016). Standards provide regulators with greater certainty about pre-market evidence, and they can inform post-market monitoring by defining limits or thresholds for regulatory action. Proactively establishing standards and other soft policy tools will facilitate risk management while broader regulatory structures (or legislation) take shape (Millett *et al.*, 2022). The existence of harmonized standards in this area can also facilitate commerce and trade among jurisdictions (Marchant & Allenby, 2017).[49]

Two closely linked issues remain unanswered with respect to the definition and use of standards or guidelines for genetic pest control in Canada, and both draw attention to domestic regulatory capacity. First, the optimal way to implement emerging standards in Canada's regulatory environment is not yet clear. Incorporation by reference is one possible process, one used by the federal government to directly link regulations to standards (both national and international), allowing regulations to be updated as standards evolve (HC, 2022b).[50] This process places significant trust in standards-setting organizations; this may not be feasible for gene-edited organisms in the same way it might be for food safety, due to a still-limited evidence base, even internationally. However, in the absence of domestic R&D activities or field trials in this area, Canada may need to rely on international efforts, since no domestic standards or guidelines based on Canadian data currently exist.

49 At a global scale, the WHO is active in setting and disseminating standards and guidelines in this field (including a guidance framework for genetically modified mosquitoes) as a way to share best practices in the use of these organisms for the benefit of public health (WHO, 2021a).

50 CFIA makes use of this process in the context of food safety, with 50 standards being incorporated by reference into regulatory legislation (CFIA, 2022c).

This speaks directly to the second issue, namely participation in standards-setting. Canada participates in novel pest-control agent standards-setting initiatives mounted by the OECD (HC, 2020) but is not, at present, directly involved in major international R&D activities for genetic pest control involving live modified organisms (Section 3.1). In fact, in areas adjacent to this topic, such as agri-food and aquaculture, some CFIA stakeholders have recently reported that Canada is insufficiently visible at an international level with respect to defining standards (CFIA, 2021). There is no remedying these issues without increasing the involvement of researchers from Canada in projects underway in these fields. Effective governance will require the scientific capacity to understand and work with these technologies in a regulatory setting. The potential consequence is that Canada may need to accept standards from other jurisdictions, even though ecological, physical, and sociocultural factors specific to Canada will influence the safety and efficacy of genetic pest-control programs carried out domestically.

Proactive collaboration with the United States will allow Canada to begin addressing capacity deficits; to do so, however, Canada will need to present a value proposition

In the long term, Canada risks being unprepared to harness the use of these technologies should their safety and efficacy be demonstrated; in the shorter term, Canada may also be unprepared to manage the risks of gene-edited organisms appearing domestically following U.S. deployment.

In the United States, regulators have carried out assessments of several technologies, including a number of genetically modified insects and mosquito species infected with *Wolbachia* (USDA APHIS, 2015; Waltz, 2017b; Oxitec, 2020, 2022; US EPA, 2023). The approval of trials for these modified organisms has resulted in their release into the U.S. environment to explore their potential for tackling pest problems in public health and agriculture. In contrast, Canada does not possess any direct, relevant experience working with modified organisms for pest control (outside of SIT), unlike the United States or Mexico (Ramsey *et al.*, 2014). As these technologies continue to mature, a persistent lack of experience could translate to a lack of preparedness. In the long term, Canada risks being unprepared to harness the use of these technologies should their safety and efficacy be demonstrated; in the shorter term, Canada may also be unprepared to manage the risks of gene-edited organisms appearing domestically following U.S. deployment.

Pests are not impeded by borders, and jurisdictional issues in federal systems are known to be challenging (Section 6.1); collaboration among neighbours is therefore necessary. Given the intensity of U.S. R&D on this topic, Canada may face pressure to increase regulatory harmonization with the United States for political and trade purposes. Precedents exist for such alignment as a result of trade agreements (see, for example, GAC, 2020a, 2020b) and through relationships among related federal agencies; PMRA and the U.S. EPA, for instance, have a long history of cooperation on new pest-control products (PMRA, 2002, 2016). Data requirements are, in fact, harmonized between the United States and Canada for microbials, and joint reviews with U.S. agencies are common for these products (PMRA, 2001). Effective transnational collaboration also occurs in the context of biological control but from the standpoint of soft law; standards and guidelines established through the North American Plant Protection Organization (NAPPO) are used to guide oversight of these programs (CFIA, 2017, 2022b) and depend on the work of numerous expert scientific working groups in Canada, Mexico, and the United States (NAPPO, n.d.).

Put simply, it is the Panel's view that, if Canada wishes to influence the governance of these technologies on the continent, it will need to offer a contribution to the framework.

Canada will need to leverage these existing networks for cross-border cooperation in genetic pest control, as well as others occurring in the contexts of common environmental interests along the border (US EPA, 2022b). It will also, however, need to contribute expertise and knowledge if it is to participate and influence discussions in these areas. Put simply, it is the Panel's view that, if Canada wishes to influence the governance of these technologies on the continent, it will need to offer a contribution to the framework. For this aim, investments in regulatory science could offer potential returns as strong or stronger as those in discovery science, given ongoing debates on effective governance. For example, the United States has funded proposals with approximately US$5.8 million over the past three years to support research in risk assessment for gene-edited organisms (USDA, 2022c). Risk assessment is a key element of governance where significant efforts are being carried out in the context of adapting standard processes to genetic pest control. Funding streams such as those dedicated to climate change adaptation could arguably be leveraged for this purpose in the Canadian context, in order to overcome the structural challenges in supporting genetic pest control within the R&D funding landscape, as described in Section 3.1 (ECCC, 2019).

The Panel stresses that regulatory harmonization or alignment does not imply joint approvals for release. Canada cannot relinquish sovereignty on this point. Alignment impacts various regulatory activities across the lifecycle (Figure 6.3) beyond approval, including standards, inspections, and certification, among others (GC, 2018a). Ongoing initiatives in Africa toward regional governance of genetically modified (and eventually gene-edited) mosquitoes to curb the transmission of malaria could also inform future approaches in North America (Box 6.5). Effective collaboration with Canada's neighbours, and the adoption of leading practices in transnational governance established elsewhere, will be essential to disentangle jurisdictional issues, including sovereignty, and effectively coordinate regulatory activities for regional pest problems.

Box 6.5 Regional Governance for Malaria Control in Africa

Work undertaken by the African Union and the New Partnership for Africa's Development has initiated approaches to leverage capacity across borders in R&D, regulation, guideline harmonization, and stakeholder engagement, with an emphasis on regional alignment (AUDA-NEPAD, n.d.; Pare Toe *et al*., 2022b). A similar network has been established to focus on technology specifically (AGBC, 2022). These organizations have provided several recommendations for member states proceeding with gene-drive programs to fight malaria. The objectives, in part, allow other countries that could find themselves involved in the area-wide control program to benefit, without needing to repeat or duplicate regulatory or scientific efforts (AUDA-NEPAD, n.d.). The strategy involves a staged release with adaptive and evolving risk assessment to reflect the changing risk landscape as the project moves through different phases (AUDA-NEPAD, n.d.). This regional approach aims to avoid fragmented decision-making given the shared disease burden among countries, while also accounting for the reality that ecological and epidemiological processes do not stop at national borders.

7

Panel Reflections

Gene-editing technology is enabling the design of new pest control tools at a time when pest threats are changing and current tools are failing. However, their effectiveness and appropriateness remain matters of intense debate and reflection. It follows that regulators face a daunting challenge in overseeing the safe and effective use of these tools across the wide range of application areas where pest control is needed. The Panel's assessment of the Sponsor's charge explored the numerous considerations related to the governance of gene-edited organisms, from R&D barriers to challenges in jurisdictional oversight and risk management, as well as other pivotal issues such as ethics and public engagement. Taking these findings together, the Panel observed three main themes for the path ahead.

7.1 Shifting Landscapes

The failure to adapt can exacerbate public health crises while also placing biodiversity and food security at risk.

Over the course of deliberations, the Panel came to conclude that current discussions surrounding the application of gene-editing tools for pest control are taking place in the context of shifting landscapes. International trade, climate change, and resistance to pesticides are three of several major and evolving sources of concern in pest management. These factors are leading to the establishment or worsening of pest problems and the diminishing effectiveness of commonly used pest control tools. Technology can help meet new pest problems and address areas where existing tools are no longer useful. The failure to adapt can exacerbate public health crises while also placing biodiversity and food security at risk. Fortunately, technology is developing in ways that offer new approaches to addressing these needs. It is adapting so quickly, however, that understanding how best to harness it is challenged by numerous unknowns and a lack of evidence.

Gene editing provides new tools to meet the above threats, but are they the correct ones? Can they be implemented in an appropriate manner that benefits those in need without causing adverse impacts for others? The measurement of efficacy and safety, and the quantification of uncertainties, will help to address these questions, but the answers also go beyond science-based considerations. These technologies are developed, used, and governed in a social context, and the appropriateness of their use will also hinge on social acceptability. Social values and priorities will influence the perception of these technologies and their associated risks.

From a practical standpoint, broadening risk governance outward from biosafety considerations to include more holistic approaches that incorporate sociocultural and other risks marks a departure from conventional governance practices. To this end, effective risk assessment and communication will rely on active public engagement practices that, by including outside perspectives earlier in the process, will run counter to current approaches. To strengthen input and participation capacity, consideration of diverse equity-deserving actors is needed; these include Indigenous peoples in Canada, who possess a wealth of ecosystem knowledge and experience. These practices will require careful assessment and re-examination to allow for participatory approaches to governing genetic pest-control interventions. In this environment of shifting landscapes, regulatory bodies have the greatest potential for success if they can be proactive, reflexive, and nimble. Generating and maintaining trust in programs remains paramount and can be achieved by working toward increased accountability and transparency. Although genetic pest-control approaches that recognize these underlying shifting landscapes exist, they have yet to be internalized in regulatory practices. Doing so will rely on strategic and timely investments along with a desire to implement and evaluate new approaches.

7.2 A Need for Preparedness

Policy development typically chases the rapid evolution of technology. The resourcing for regulatory innovation pales in comparison to the corresponding investments in scientific innovation. Moreover, it can take many years for scientific discoveries to be translated and diffused into society. There remains a crucial need for regulators to proactively identify gaps in capacity and resourcing to meet the arrival of new pest-control products and tools. Canadian representation among the major R&D initiatives in genetic pest control is meager, and experimental trials are not operating domestically. As the Panel indicated throughout this report, deficits in R&D capacity will translate to challenges for regulatory science.

These challenges are exacerbated by the fact that such activities are proceeding intensively in the United States. It is plausible that gene-edited organisms could be deployed close enough to Canada that they may spread across the border prior to a regulatory framework being established domestically. Moreover, as trials advance, some stakeholders in Canada could begin to question why these technologies are unavailable to them for solving pest problems shared with counterparts in the United States. A successful method in one jurisdiction will generate desires to access its benefits in others. This in turn will create regulatory pressures to accommodate demand. Overcoming fragmentation across the Canadian R&D funding environment will be an important step for building

domestic capacity. However, it is also imperative that Canada establishes a means for working with partners in the United States to remediate the current lack of experience.

The many national interests at stake underscore the need for preparedness. Failure to do so is itself a decision that will expose Canada to unnecessary risk. Training highly qualified personnel, establishing partnerships for R&D and risk governance, and investing in understanding risk factors specific to Canada, as reflected by individuals across all segments of society, will all be needed for effectively establishing and operationalizing regulations and policy.

7.3 Opportunities for Canadian Leadership

Despite the deficits mentioned above, the Panel emphasizes that many of the necessary ingredients for preparedness are present in Canada and need only to be properly leveraged. Decision-makers will nevertheless be required to make investments and pursue strategic choices to achieve both short- and long-term objectives. For example, policy decisions unrelated to regulatory practices in pest control underlie Canada's limited R&D activity and directly impact domestic regulatory capacity. There will be real costs and risks in developing the capacity needed to govern genetic pest control. Although it is not possible to unequivocally predict future threats and needs, actions taken in the near term will build solid foundations in governance. Doing so will play an enabling role that is essential in shaping future readiness, allowing Canada to better navigate this space.

In fact, there are areas where Canada could go beyond preparedness and establish a leading position in this growing field. Risk assessment, for example, represents one area where significant opportunities exist to not only bolster readiness in the regulation of gene-edited organisms but also to build capacity in engagement with stakeholders and Rights-holders, which is central to the ethical development and deployment of these technologies. Establishing methods for cooperative and inclusive public engagement that are sensitive to budgetary and logistical realities could be modelled by jurisdictions around the world. Genetic pest-control technologies do not necessarily need to be held to a separate or exceptional set of standards compared to other pest control tools; rather, the emergence of these technologies offers a setting for improving decision-making processes more widely in pest control and other environmental interventions. Leadership in previously underdeveloped areas of risk assessment that touch on social and cultural dimensions could translate into a holistic governance approach for gene-edited organisms for pest control that is both effective and predictable while also being mindful of sociocultural and ethical dimensions.

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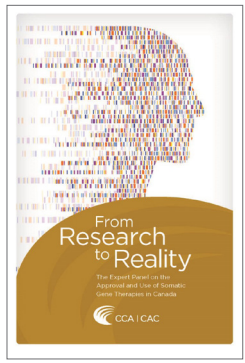
CCA Reports of Interest

The assessment reports listed below are accessible through the CCA's website (www.cca-reports.ca):



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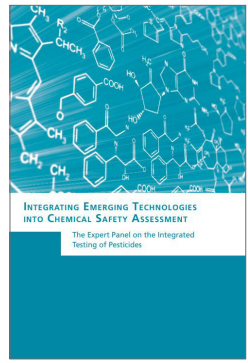

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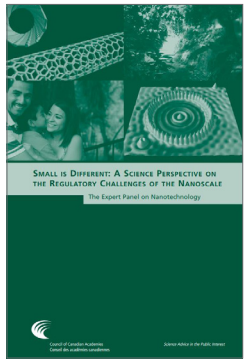

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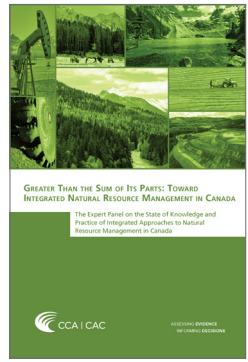

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