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Abstract The modification of living agents for biological control can be collectively regarded as genetic biocontrol (GBC). Applications to invasive fish are an area of significant work in GBC, employing a diversity of techniques. Some of these techniques are governed by particular legislation, policy or treaty, (e.g., transgenesis), while others deliver agents with similar properties with minimal regulation. Together, this heterogeneity of governance and biology creates a number of challenges for effective use of GBC. In some cases, there are gaps and inconsistencies that

pose real threats to biodiversity, and the long term sustainability of oversight arrangements as they currently stand is questionable. Researchers and would-be users of GBC for invasive fish must proactively engage with a variety of stakeholders to improve governance (in fish and other taxa), which we contend may include reconfiguration of relevant national governance systems, meaningful stakeholder dialogue and the creation of a new international treaty dedicated to biological control.

Keywords Biocontrol · Sex-skewing · Autocidal · Invasive · Pest · Governance · Regulation · Policy

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Introduction

Invasive and unwanted species are increasingly recognized as serious problems of social, economic and biological concern. At the same time, our ability to understand and manipulate organisms at a genetic level is rapidly expanding. Applications to the control of invasive fish are emerging as an important area of innovation in this regard, as reflected in this special edition, although applications in other areas, especially insects, are also advancing rapidly. Aside from the technical challenges involved, genetic approaches to invasive species control are creating new challenges for regulation and oversight. Developments in one taxon in one jurisdiction likely will have implications

for work on other taxa elsewhere. To analyze this challenge and its implications for work on invasive fish, we define a new category of biotechnological endeavor that applies to all taxa, genetic biocontrol (GBC), and use it to explore the wide array of legal and policy instruments applicable to its oversight.

GBC involves the rational and intentional manipulation of a biological agent at a genetic level in order to improve its characteristics for the control of unwanted or invasive species. GBC is applied but not restricted to the classical model of biological control, in which an unmodified predator, parasite or pathogen is sought to reduce target populations. However, GBC draws on a palette of techniques to modify the biological agent, including the invasive organism itself. GBC opens up a variety of opportunities to intervene in processes of reproduction as well as disease and predation (i.e., a modified pest becomes a biocontrol agent against its unmodified brethren), enabling a diversity of strategies to control unwanted populations. GBC already has been controversially field tested for mosquito control (Benedict et al. 2011; Enserink 2010; Harris et al. 2011; Ostera and Gostin 2011), and several projects in a variety of species have been underway for some years (Angulo and Gilna 2008b).

GBC is not limited to genetically engineered agents. It can include chromosomal manipulations (e.g., Trojan Y; Cotton and Wedekind 2007; Gutierrez and Teem 2006) and sterility by triploidy (Zajicek et al. 2011) or selection (Henry et al. 2010; Lozier et al. 2008). In this volume (Thresher et al. in review), the technological options for GBC are reviewed. Kapuscinski and Patronski (2005) also describe and review GBC approaches for invasive fish. Broadly, GBC includes any rational modification of the agent in a heritable manner or that exploits our genetic understanding of heritability in order to halt reproduction or drive the unwanted population down in other ways: for example, autocidal strategies by genetic engineering (Fryxell and Miller 1995; Gong et al. 2005), mutant lines (Robinson 2002) or hybridity (Cassani and Caton 1986; Zajicek et al. 2011). Genetic engineering can include transgenic (recombination across species barriers), cisgenic (across closely related species) or intragenic approaches (engineering of host-only sequences) such as daughterless carp (Thresher 2007; Thresher and Kuris 2004). In some jurisdictions, there are distinctions of legal importance among these

approaches (see below and Nielsen 2003 for further discussion of conceptual scheme).

GBC may well offer a powerful and attractive set of management tools to deal with invasive species but, just as with invasive species themselves, its potentially far-reaching effects on ecosystems and societies demand oversight that has been slow in coming (Angulo and Gilna 2008b; Henderson and Murphy 2007). GBC follows the trend of many new technological fields in creating a new “space” for governance (Jasanoff 2005; Kuzma et al. 2009; Kuzma and Tanji 2010; Wiener 2007). GBC traverses several established conceptual boundaries, jurisdictions and legal frameworks, exacerbates existing regulatory gaps and perhaps creates new ones, creating an uneven and confusing network. Different jurisdictions may take very different views of the nature, value and risks of the species and technologies involved, and yet biology rarely conforms to culturally-imposed geographic boundaries. Regulations developed with one taxon in mind may in practice apply equally to other organisms in unanticipated ways—oversight developed for genetically engineered insects, for example, may apply to engineered fish. Oversight for GBC is therefore diffuse, complex, and context-dependent.

In this article, we first examine a range of oversight arrangements that are pertinent to GBC with particular reference to applications in fish (inclusive of other marine and aquatic organisms). We then identify major challenges emerging from these arrangements. We suggest ways in which GBC governance systems—and the GBC community—can be better prepared to deal with the array of applications and complexity from national and international perspectives.

Regimes of governance, oversight and regulation

Governance, oversight and regulation are analytical terms that refer to hierarchically distinct, interoperating phenomena in society that shape and structure its processes. “Governance” refers most broadly to these dynamics, while “oversight” is activities that entail supervision and watchfulness, and “regulation” the specific formally encoded rules and institutions that are used with governmental authority (Kuzma 2006). The variety of these elements that apply to GBC across the globe may be as numerous and diverse as their

biological particulars. A global perspective is important—like many of the invasive species at which they are targeted, GBC agents are mobile and sometimes designed to establish reproducing populations. In practice, it is often local government that undertakes management actions. Like the invasive species themselves, GBC thus evokes a daunting range of governance, from local to global.

The technology and the target species of a GBC program might be regarded very differently from one location to the next, with implications not only for risk assessment and management of a program, but also the justification for its development in the first place (e.g., Angulo and Gilna 2008b; Gilna et al. 2005). Complicating these considerations is the inherent messiness of oversight regimes—not all terms and provisions of legislation will necessarily be consistent with each other, as the processes of application and interpretation in the real world creates confusing circumstances. Finally, not all the elements of oversight are necessarily encoded in law. Politics, soft power, resource allocation, social mores and traditions can all play decisive roles in overseeing a technology.

Here, we present a selection of legal instruments at international and national levels, based on their relevance and influence, and cases particularly illustrative of the challenges that GBC oversight entails.

International

International law is a challenging area. Treaties and agreements can be rendered almost useless due to the reluctance of a minority of nations to ratify them, or watered down to achieve agreement at the expense of impact. Overlapping treaties and agreements can still leave important gaps between them, and some nations may fail to put a regime into practice on the ground. Invasive species regulation is an exemplary case (Shine 2007). Nevertheless, international agreements can unify regulatory practice across borders, and establish a general and influential understanding of important issues even when nations decide not to participate officially. The international level is therefore important to GBC for invasive fish, affecting the manner in which GBC agents are handled within a nation, and—crucially for a technology that may be able to swim across borders—structure the manner in which nations will treat each other in dealing with GBC.

Convention on biological diversity

The Convention on Biodiversity¹ (1993; CBD or Convention) is the overarching international treaty pertaining to issues of ecology and biodiversity. It aims to provide an influential platform of governance for the global challenges and tensions between the use, benefits and conservation of biodiversity. Article 8(h) explicitly instructs Parties to “[p]revent the introduction of, control or eradicate alien species which threaten ecosystems, habitats or species”, but considers genetically modified organisms (GMOs) separately. Biotechnology is defined as *any* technological manipulation of biological systems, organisms or derivatives thereof, a definition that would encompass all agents in the GBC stable.

As of mid-2012, 193 of 196 nations recognized by the United Nations are party to the Convention,² (including the European Union). The USA has signed but not ratified or acceded³ to this treaty. The CBD is broad ranging and ambitious, but despite being set up to provide a specific and binding oversight regime for biodiversity, it has mostly failed to do so (Angulo and Gilna 2008b; Harrop and Pritchard 2011; McGraw 2002). Its Protocols, however, are more substantial.

Cartagena Protocol on biosafety

The Cartagena Protocol on Biosafety⁴ to the CBD is the preeminent instrument for the regulation of the products of GM technology at the international level.⁵ Although a few nations prominent in GBC science are not party to the Protocol (e.g., the USA, Australia), 163 nations of the world have ratified this treaty as of mid-2012.⁶ Laws and regulations related to biosafety are compiled on the Biosafety Clearinghouse website.⁷ The Protocol aims to ensure the safe handling,

¹ <https://www.cbd.int/>.

² A full listing of nations and their status regards to the CBD and its Protocols can be found at <http://www.cbd.int/convention/parties/list/#tab=0>.

³ <http://www.cbd.int/world/ratification.shtml>.

⁴ <http://bch.cbd.int/protocol/text/>.

⁵ The Protocol attempts to create a minimum standard for its protection goals, specifically allowing parties to exceed its measures.

⁶ <http://bch.cbd.int/protocol/parties/#tab=0>.

⁷ <http://bch.cbd.int/database/laws/>.

transport and use of living modified organisms (LMOs) that “may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health”, with specific focus on transboundary movements.

LMOs are any living organism that possesses a novel combination of genetic material obtained through the use of “modern biotechnology” (emphasis added), defined as:

- a. In vitro nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or
- b. Fusion of cells beyond the taxonomic family, that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection;

The Protocol therefore applies unequivocally to transgenic, cisgenic and intragenic GBC agents, but not to agents produced by mutagenesis or artificial selection. The chemical and physical techniques used to manipulate chromosome number, as proposed for Trojan Y fish (Cotton and Wedekind 2007; Gutierrez and Teem 2006), likely would be excluded from its reference. The Cartagena Protocol’s particular definition of the products of biotechnology is considerably tighter than that provided in the Convention, but does not provide a mandate to oversee all forms of GBC agents.

Parties are required to minimize risks of LMOs to biodiversity and human health and to prevent unintentional transboundary movements. Other than to mandate the provision of relevant information to an affected country, the Protocol does not specify appropriate responses were a dangerous LMO to cross into another nation. In terms of compliance, the Protocol is effectively toothless and mired in ongoing negotiations on the matter.

The Cartagena Protocol is not therefore irrelevant to genetically modified fish for biocontrol, but limited to subset of applications (e.g. transgenic fish) and even then without much prescription. However, liability for damage incurred by LMOs (next section) may be more pertinent for situations where such modified fish might cross borders.

Nagoya–Kuala Lumpur supplementary protocol on liability and redress

Negotiations over contentious liability and redress matters recently culminated with the Nagoya–Kuala

Lumpur Supplementary Protocol on Liability and Redress (2011).⁸ The Supplementary Protocol establishes a set of administrative procedures for dealing with damage caused by LMOs (as defined in the Cartagena Protocol), setting out a regime of responsibilities of the “operator” (i.e., the entity using or developing the LMO) and the national “competent authority”. However, claims and lawsuits for damages from an LMO must be pursued within Party nations’ domestic laws.

Importantly, the Supplementary Protocol also defines “damage”, a phenomenon that can be considered only if caused by transboundary LMO movements, whether authorized, accidental or illegally intentional. Damage must be measurable and constitute a significant “adverse effect on the conservation and sustainable use of biological diversity”, with a clear line of causation from the LMO. The “significance” of the damage is determined by the degradation of biodiversity, goods and ecosystem services, impacts on human health, and the permanence or long-term nature of a change that will not be recovered by natural processes. These factors seem particularly relevant to a genetically modified aquatic organisms that would produce long-term changes in composition and function of the ecosystem in which it establishes.

Response measures to damages are intended to be “reasonable”, including prevention, containment and mitigation, and restoration of biodiversity. Whoever was licensed to deploy the GBC agent would bear the responsibility for any response effort under the licensing authority’s direction, or responsibility falls back to the authority if the operator fails to do so. These considerations should inform GBC programs right from the earliest stages. However, Article 6 of this Protocol allows nations to declare exemptions from and mitigations of liability “as they may deem fit”. Major invasive species and disease vectors, whose damage is acknowledged as serious and sit high on the national agenda, might well be deemed to warrant such exemption.

The Supplementary Protocol was to enter into force ninety days after the fortieth signature was deposited, (i.e., 9th of August 2011), but its status is yet to be lodged in the United Nations Treaty Collection database. As of mid-2012, 51 nations had signed the Protocol, but only two had ratified.⁹

⁸ <http://bch.cbd.int/protocol/supplementary/>.

⁹ <http://bch.cbd.int/protocol/parties/#tab=1>.

The World Trade Organization and the sanitary and phytosanitary agreement

The powerful World Trade Organization recognizes the need to manage biosecurity risks in the course of globalized trade under the Agreement on the Application of Sanitary and Phytosanitary Measures (SPS Agreement 1995). The SPS Agreement sets out conditions under which risk management measures—such as import restrictions—can be applied, with emphasis on their scientific justification (considered to be at odds with a precautionary treatment of scientific uncertainty; Peel 2007; Riley 2005) such that trade is not arbitrarily restricted.

In a controversial 2006 decision by the WTO Panel, the terms of the SPS Agreement were interpreted very broadly, inclusive of a wide range of environmental and biodiversity protection mechanisms for wild plants, animals and microorganisms (Peel 2007). The WTO hence appears to have placed the SPS Agreement superior to the Cartagena Protocol, but the issue may be far from settled (Peel 2007; Thomison 2007). For GBC in fish, the relevance of the WTO and the SPS Agreement is likely restricted to any quarantine barriers that a nation may erect to prevent invasion by a GBC agent, and in reality, then only if a disadvantaged industry has sufficient political influence to prompt its government to launch a complaint (Peel 2007). Consequently, this decision seems particularly relevant to those developing GBC agents that may affect commercially important species (e.g. commercially fished species). In addition, species subject to human consumption may invoke WTO consideration under the Codex Alimentarius (see Kapuscinski and Patronski 2005: 45).

National

A great variation can be observed across nations in governance of invasive species and measures for their control. Many biodiversity-rich countries (e.g. developing nations) severely lack capacity in this area (Shine 2007). In nations of the European Union, oversight of genetic modification is well developed, but much less so for invasive species (Hunt et al. 2008; Shine 2007). We survey a selection of some of the most informative approaches to GBC governance.

The United States of America

The United States is highly active in biotechnology, including the development of GBC for invasive fish. It distributes its governance across sectoral and sub-national jurisdictions. We give a brief overview here (readers are directed to Showater Otts 2012 in this volume for a specific review of United States legislation pertaining to biocontrol of invasive fish).

The Coordinated Framework for the Regulation of Biotechnology has drawn on existing oversight arrangements to govern biotechnology avoiding the construction of dedicated new structures. The Coordinated Framework has its strengths and weaknesses (National Research Council 2000; National Research Council 2002; Kuzma et al. 2009). One of the main issues has been the confusing nature of the interpretation of several existing laws to fit novel products. For example, GM fish are currently regulated by the Food and Drug Administration (FDA) as new animal drugs, GM microbes by the Environmental Protection Agency (EPA) as toxic chemicals, GM plants with pest-protection genes by EPA as pesticides, and most GM plants by the United States Department of Agriculture (USDA) as plant pests. The stretching of old laws has led some to criticize whether the right risk analyses are conducted, especially for ecological health and safety (Kapuscinski and Patronski 2005; National Research Council 1996; National Research Council 2000; National Research Council 2002).

National regulation of biocontrol activity, with an historically plant-health focus, largely falls to the USDA's Animal and Plant Health Inspection Service (APHIS), pursuant to the Plant Protection Act of 2000 (7 U.S.C. §§ 7701–7786). The Technical Advisory Group on the Introduction of Biological Control Agents of Weeds (TAG) of APHIS reviews petitions for candidate biocontrol agents and provides information and advice to researchers and those in APHIS responsible for issuing permits for importation, testing, and field release of biocontrol agents (USFWS 2012). APHIS's biocontrol permits must comply with other U.S. environmental laws, such as the National Environmental Policy Act and the Endangered Species Act, which require the preparation of environmental assessments and consultation with the US Fish and Wildlife Service (USFWS), respectively. Although the USFWS has significant responsibilities with respect to invasive species management and

control under the Lacey Act, the agency has a limited role in the licensing of biocontrol activities. Under a USFWS policy, the agency considers the release of exotic biocontrol organisms into National Wildlife Refuges to prevent further introduction of exotic species on refuges, except where an exotic species would have value as a biocontrol agent. Proposals requesting permission to release exotic biocontrol organisms into National Wildlife Refuges are submitted to the USFWS regional director along with an Environmental Assessment (EA) that “documents the biological need for introduction, clearly demonstrates compliance with USFWS policies, and thoroughly examines the relationship of the proposed exotic organisms to presently occurring species, as well as factors such as suitability of the available habitat, possible areas of competition, disease potential, and predation spread potential” (USFWS 2012).

State-level regimes may be quite significant for GBC in invasive fish. The California Legislature, for example, has expressly encouraged the use of biological controls for hydrilla and mosquitoes. On the other hand, California has also passed legislation to prohibit the release of transgenic fish into the environment, particularly ocean waters (California Fish and Game Code Section 15007, Van Eenennaam and Olin 2006).

New Zealand

New Zealand is a small, developed, island nation of around 4 million people, with a distinct and highly threatened biodiversity. It is party to the Cartagena Protocol, and has maintained a program on GBC to tackle invasive vertebrates that threaten both native biodiversity and primary production (Cross et al. 2011). Research on GBC for invasive fish in New Zealand is not reported in the literature to date.

Two New Zealand statutes apply to GBC, the Biosecurity Act (1993) and the Hazardous Substances and New Organisms (HSNO) Act (1996, amended 2003), under which operates the Environmental Risk Management Authority (ERMA), with inputs from the Ministry of Agriculture and Forestry and the Ministry of Environment. Together, these Acts provide the legal basis for excluding, eradicating and managing pests and unwanted organisms and, specifically under the HSNO Act, licensing and regulating a wide variety

of organisms, including “risk species” (and their subspecies and varieties) that were not present in New Zealand prior to the Act coming into force (1998), and GMOs. “Unwanted” organisms may not be released into the environment. Strict quarantine procedures are in place for “risk goods”, including living organisms that may cause unwanted harm to natural and physical resources or human health.

The HSNO Act provides the basis for declaring a species “new”, a “risk”, or licensed for contained use, full release, or “conditional release”. Because unwanted species and modified organisms are broadly defined and regulated under the same framework, New Zealand’s biosafety oversight might be uniquely well equipped to recognize and adequately manage the full suite of GBC in all taxa. New Zealand’s biosecurity arrangements establish a strong civil liabilities regime. Public participation in decision-making is mandatory, although its practice has been criticized on the grounds that it “marginalized concerns raised by the public about risk management, ethics, and ecological, economic, and cultural issues in order to give primacy to a positivist, technological worldview” (Kurian and Wright 2010: 447).

Australia

Australia is a geographically large nation with a moderate-sized, highly urbanized population. It is divided into states, territories and local governments, but governance relevant to GBC is increasingly coordinated at the national level. Australia’s experience with biocontrol (both positive and negative) is relatively prominent in the national discourse, and it maintained a long-running transgenic GBC research program, including the daughterless approach for invasive European carp (Thresher et al. this volume, and Hardy 2007; Van Leeuwen and Kerr 2007; Strive et al. 2007).

Australia has a very well developed biosecurity regime (Hunt et al. 2008), including long-standing provisions for dealing with invasive and unwanted species. At the Commonwealth level, the Quarantine Act (1908) and the Environment Protection and Biodiversity Conservation Act (1999; EPBC Act) are administered jointly by Departments of Agriculture, Forestry and Fisheries (DAFF) and of Sustainability, Environment, Water, Population and Communities (SEWPAC). These portfolios are very large and

inclusive of biocontrol.¹⁰ These departments provide not only regulatory and oversight functions for GBC, but also contribute to its research and development. States maintain lists of declared pests and protected species that are subject to prescribed action and restriction (e.g., cultivating pest species may be illegal without ministerial exemption).

Research with and release of GMOs must be authorized under the Commonwealth Gene Technology Act of 2000 (Government of Australia 2000). This act creates a definition of a GMO very similar to the “LMO” of the Cartagena Protocol (to which the country is not a party), it avoids the possible intragenic loophole of the Australian legislation affecting daughterless carp. The use of any transgenic GBC fish would be licensed under a binding risk management plan to minimize risks to human health and safety and the environment. Input from states or local governments and other Commonwealth institutions such as DAFF and SEWPAC must be taken into account, although the regime has been criticized for its limited provision for public input (Schibeci et al. 2006).

Biocontrol is specifically legislated under the Biological Control Act of 1984 (and aligning state-level acts), which establishes a mechanism whereby a cost-benefit analysis (and compensation) can be established for the introduction of a biocontrol agent should controversy (and damages) arise. An industry sector must declare impending financial loss as a result of the agent’s release, something not always applicable for conservation and public health end-points. In such cases, regulation of biocontrol introductions falls back to the Quarantine Act and EPBC Act. The Act applies only in the case of importation of the agent, which would preclude GBC applications that take a pest species already established in the country and to act as a control agent. A recent application to release a novel, heritable infection of the dengue fever vector mosquito, *Aedes aegypti*, with the intracellular commensal, *Wolbachia pipentis*, was ultimately licensed under veterinary chemicals legislation as a microbial pesticide (De Barro et al. 2011). Both organisms were already in the country, and no transgenesis was used. These characteristics are not unique to this case, (e.g. also daughterless, Trojan Y, etc.), but it is not yet clear

how satisfactory this regulatory pathway has been, and its suitability for regulation of microbial pesticides in general is under review (Hauxwell et al. 2010).

Major issues emerging in GBC oversight

GBC’s technological diversity guarantees a complex interface with the diverse palette of oversight regimes that may operate side-by-side or simultaneously. Below, we draw upon literature in science and technology policy, risk analysis, and social studies of science to examine key policy problems and issues associated with oversight for other technological systems that also apply to nascent GBC oversight frameworks.

Regulatory scope

The specificity with which many regulatory devices attempt to define genetic modification, genetic engineering or LMOs, while a necessary part of regulation, may introduce some severe limits to their application to GBC for invasive fish. The Cartagena Protocol’s definition of LMOs is globally influential—many rapidly developing nations are constructing their entire biosafety regimes around this instrument—but completely excludes powerful techniques like selection, mutagenesis, chromosomal manipulations and other novel methods to create radically modified phenotypes. Even in cases where there exists sufficient regulatory “hook” for authorities to oversee GBC fish, oversight lent from other fields may be insufficient. Kapuscinski and Patronski (2005) reviewed laws and policies that could apply to the environmental release of triploid sterilized and transgenic fish for biocontrol in the United States. They identified four primary U.S. Federal laws: the National Environmental Policy Act (NEPA), Endangered Species Act, Lacey Act, and Federal Food Drug, and Cosmetic Act (FFDCA). Under the FFDCA, transgenic fish used for GBC would likely be regulated as “new animal drugs”. However, each law has its shortcomings for promoting an adequate evaluation of ecological risks for GBC. In controversy over approval of transgenic salmon for human consumption, questions were raised over the ability of a statute designed for drugs to cover whole organisms and their ecosystems, even if NEPA review is undertaken (Pollack 2010; United States Food and

¹⁰ The agencies must arrive at consensus for the importation of biocontrol agents, something that rarely happens. New agents are thus rarely approved.

Drug Administration 2008; United States Food and Drug Administration 2009).

New Zealand's HSNO Act may be a useful template for regulating GBC fish (or indeed GBC programs in any taxa). The trigger for regulation is the novelty of an organism's presence on New Zealand territory (prior to an arbitrary date), be that organism imported (intentionally or accidentally) or created. By defining GMOs as organisms whose "genes or other genetic material... have been modified by in vitro techniques", it avoids the possible intragenic loophole of the Australian legislation affecting daughterless carp, and would capture chromosomal manipulations required for Trojan Y supermales. For many other cases in the rest of the world, several GBC approaches being pioneered in fish seem to present classes of objects that do not fit comfortably into the existing matrix of regulation and oversight. Regulatory gaps thus pose obvious risks, most obviously here regarding the adequacy of environmental protection and community consultation. At the same time, applications "shoe-horned" into regulatory frameworks originally designed for other purposes may result in unwarranted regulatory burdens that act as a *de facto* barrier to research on and deployment of GBC agents with a strong public good value (De Barro et al. 2011).

Compliance, liability and dealing with conflict

GBC has a great potential for conflict between jurisdictions, with differences in national interest arising from clashes over the means and the objectives of GBC programs. To comply with the international biosafety regime, governments must perceive a net benefit to the national interest, considering factors such as commercial incentive, protection, government reputation and legitimacy both within and between nations (Simmons 2010). These benefits must be balanced against the potential costs of compliance, including times when the immediate interest of its citizens must be forgone for longer-term, overarching benefits.

We have already seen such difficult calculations in GBC, even without the formal constraints of treaty obligations. New Zealand has and is pursuing "live" GBC agents against invasive possums that threaten industry and biodiversity (Cross et al. 2011), but such an agent would constitute serious risk to its nearby neighbor and trading partner, Australia—the origin of

possums (Gilna et al. 2005). The European rabbit is threatened in its home range, but is often a serious pest in areas to which it has been introduced. GBC agents have been researched to address the "local" rabbit "problem" in both situations, but each program effectively created one more threatening process in the other territory (Angulo and Cooke 2002; Angulo and Gilna 2008b). National governments have supported the work in each of these cases.

The Cartagena Protocol seems to be principally constructed around a notion of a controlled flow of material across national borders. "Unintentional" transboundary movements—as might be achieved by a GBC fish moving through waterways, ballast waters or even illegal introductions—are recognized as possible and risks are to be mitigated, but the assessment of such risk is fundamentally subjective, and its regulation is not prescriptive. The liability regime established by the Nagoya-Kuala Lumpur Supplementary Protocol seems particularly weak, watered down with exemptions and negotiable terms like "reasonable". Exactly what can be recognized as "damage" turns on contestable matters of valuation of biodiversity and any changes to it, likely to be seen in different lights from jurisdiction to jurisdiction. Similarly, the "reasonableness" of efforts to mitigate risk and correct damage is highly dependent on the value placed on the threatened object, and would likely be weighed against the expected benefits of the "risky" activity. Were a target species to go extinct, for example, or an unwanted GBC agent establish itself in an unintended territory, it is difficult to envisage adequate corrective measures being pursued, or even feasible.

So far, in GBC programs for which a credible trans-border risk has been articulated, formal and informal arrangements (Henderson and Murphy 2007) have resulted either in risky GBC programs being discontinued, new research objectives formed or products not yet licensed (but see Angulo and Barcena 2007; Cross et al. 2011). There has not yet been a test case in invasive fish applications. However, it is not hard to imagine situations in which local, national interest is far stronger and more urgent than the interests of distant (and perhaps unfavored) societies on the other side of a border. Even if the nations concerned were party to the Cartagena Protocol (biosafety) and the Nagoya-Kuala Lumpur Supplementary Protocol (liability and redress), the innovating nation could mount

a justification of its actions entirely consistent with the terms of these agreements.

How could such a dispute be arbitrated and resolved? Mechanisms are as yet untested and perhaps poorly developed under this regime (Sagemueller 2005). If there were sufficient negative effects on commercial interests from quarantine measures imposed as a result of the release of a GBC agent, the parties might seek arbitration in the WTO. This is not unlikely, in fact, because introduction of GBC agents via imported commodities is a plausible risk pathway (e.g. grain exports and an anti-fertility virus for mice; Williams 2007) and would rationally invoke quarantine restrictions that, in turn, could be challenged by embargoed exporting nations (Angulo and Gilna 2008b). Whether environmental impacts would be adequately dealt with under the WTO regime remains an open question (Peel 2007).

Even in cases where broad multinational consensus on the seriousness of the problem with the target species might be reached, the use of controversial technologies in GBC might be a point of conflict. Several mosquito GBC agents under development aim to tackle diseases that kill millions of people each year, sicken many millions more, and might indeed keep whole societies in an ongoing cycle of poverty and underdevelopment (Bonds et al. 2010). Few would argue with the seriousness of the problem, or the need to control vector insects. Many of these projects involve engineered “gene drive” systems, genetic elements that are designed to be invasive within the genome of the target species. Ostensibly, these transgenic elements would spread to all populations of the target mosquito species worldwide once released. Marshall (2010) observes that the Cartagena Protocol does not adequately cover the non-negligible risk of their escape from containment (in research or in transit), and that it imposes an implausible requirement to win the consent of all nations across the globe that might eventually come to host such modified genotypes. Even an experimental release could become a global release of this form of GBC. A nation that suffers badly from diseases like malaria might quite reasonably decide that the risks of violating the obligations of a poorly applicable treaty are far outweighed by the need to act to protect its people from certain suffering. Other nations that may eventually host the GBC mosquito may take decidedly different views. This major issue seems likely to come

to a head in the future, and its resolution will affect invasive forms of GBC in all taxa. The provisions of the current GBC oversight regime—particularly in compliance and arbitration—may not be up to the task of containing such a potentially fierce debate without substantial change.

Threat to existing oversight

One of the threats that inadequate oversight frameworks can produce is the collapse of regulation itself. For a nation grappling with a serious invader to which a GBC agent seems the best solution, the oversight framework itself may lose credibility if it imposes constraints that appear unjust or irrelevant. A rule that makes no sense to the regulator or the regulated community is often formally overturned, honored in the breach, or flagrantly disregarded (e.g., the political risks of a protesting constituency can work to prevent enforcement).

Consider, for instance, the oversight of Trojan Y fish. Although Trojan Y fish are designed to spread a modified genotype into populations, just like transgenic proposals for GBC in fish. However, unlike transgenic fish, the release of Trojan Y fish would appear to be largely ungoverned at the international level. This seems absurd. Absurdity is commonly used to grant exemption from laws (Jellum 2011; Manning 2003). Would the availability of this common exemption create an incentive to hastily pursue non-transgenic GBC fish, or indeed other management options (e.g. broad-spectrum piscicides, classical biocontrol), which are subject to less oversight? Such an incentive would be perverse, but perverse incentives are not unheard of in oversight regimes (Glicksman 2006; Schuyt 2005), and are often a trigger for reformulations of policy and law. The consistency of biotechnology regulation in general continues to be questioned (Kuzma and Kokotovich 2011; Rhodes 2009; Russell and Sparrow 2008; Schouten et al. 2006). Although not exclusively so, the diverse range of techniques employed in GBC for invasive fish may well exacerbate the situation. In the face of GBC innovations in other taxa, some are already calling for a new international treaty, more broadly formulated, better tailored to the full gamut of contexts in which GBC agents (derived by all means) may soon be applied (Angulo and Gilna 2008a; Marshall 2010; Oстера and Gostin 2011).

The deployment of GBC may reveal a lurking conflict within the letter of many biodiversity and biosafety laws, and their political support base. Formed with particular influence from the GM crop debate, some oversight arrangements have aligned a belief in the inherent dangerousness of transgenes with the defense of both human health and wild biodiversity. In these cases, the protection of biodiversity is conflated with the pursuit of human health (with substantial reason; Carson 1963; Frumkin 2001; McMichael et al. 2008). GBC, however, can be designed for situations in which biodiversity must be destroyed or altered to promote human well-being or the survival of other species, and often uses a technology (genetic engineering) sometimes considered inherently antithetical to such motives. GBC researchers might be conflicted themselves. Some will belong to conservation or other groups challenging or opposing the technology under biosafety, health and conservation legislation. Researchers developing GBC for invasive fish should prepare themselves to be involved in legal and policy negotiations as a result of their work, possibly to a much greater degree than they may otherwise be comfortable or deem relevant.

Public engagement

Many nations rely on “technological elites” in constructing technology policy, including risk policies. Industry developers, scientists, engineers and government regulators are called upon or given the opportunity to determine and execute the rules for decision making, a relatively small circle of people often from remarkably homogeneous backgrounds and understandings (Meghani and Kuzma 2010). Although there are benefits to this approach (e.g., technical competence), other voices may struggle to access narrow windows of opportunity for broader stakeholder and public input. In GBC, complex genetic mechanisms are typically conceived, investigated and debated in the relatively closed world of scientific journals or regulatory licensing, carrying with them a particular way of understanding both the problem to be solved and the solutions that may be viable. In at least a few instances, the inventors of particular GBC technologies have been closely involved in the establishment of policy and regulatory frameworks to govern their use (e.g., Beech et al. 2009; Mumford et al. 2009), and we are aware of undocumented examples of others.

This could be a problem, partly because science and technology are socially constructed by the actors and networks involved (Bijker and Law 1994): a practical act of politics and a material component of policy. It follows then that public participation in policy and decision-making about science and technology are warranted in a democracy (e.g., Rip et al. 1995). The absence of that participation is thought to lie behind much of the global opposition to technology like genetic modification and the institutions that promote its use. New governance models suggest roles not only for the state and markets, but also for stakeholders and citizens in technology policy processes (Wilsdon and Willis 2004). Similarly, there is a substantial body of work that recognizes the importance of community engagement in environmental risk analysis and management for improving decision-making (e.g. National Research Council 1996; National Research Council 2008). Many governance regimes in environmental management and technology specifically mandate public consultation, engagement and debate in varying degrees, including some of the legislation presented above. In other cases, governance regimes are responsive to public input via overarching political processes, like lobbying and protest. Deficiencies remain, however. There are ongoing calls to develop and improve deliberative democratic approaches to technological decision-making (Bozeman and Sarewitz 2005; Jasanoff 2003; Kuzma and Meghani 2009). These include the governance regimes that apply to GBC (Kapuscinski and Patronski 2005).

In developing a GBC strategy for control of invasive carp in Australia, researchers have collaborated with a major catchment management organization (the Murray Darling Basin Authority) and have run several public engagement events on the matter (see summary in Table 2 of Hayes et al. this volume). Early and extensive consultation with community groups throughout the watershed was influential in the decision to pursue a daughterless strategy as opposed to other GBC approaches such as modified viral pathogens (R. Thresher, pers. comm.) For the release of *Wolbachia* infected *Ae. aegypti* mosquitoes in Australia, the research group undertook significant community consultation work even though there was no legal requirement to do so (de Barro et al. 2011). Oxitec's trials of genetically modified mosquitoes have garnered much publicity; activist groups contend that community consultation was cosmetic, while the

company itself maintains that its community engagement has been appropriate in contexts of culture and government agencies (with which it often works) (Jackson 2012). In the absence of strict legal requirement, and arguably even in its presence, the will of technology developers to engage in these approaches is decisive in how much—and perhaps how well—community engagement is performed.

Precisely how to implement wide-scale deliberation and engagement and feed the results into decision making remains a question as yet without a definitive answer, although there have been a number of approaches developed in recent years (Guston and Sarewitz 2002; Kleinman et al. 2011; Powell and Colin 2008). An interesting protocol, Problem Formulation and Options Assessment (Nelson et al. 2009) seems to hold great potential for integrating a deliberative approach with the development of technical options and the even-handed assessment of their relative risks and benefits, something that may dovetail smoothly into legislative frameworks that feature both a risk assessment and management paradigm, but also, in varying degrees, mandates to permit public engagement.

Recommendations

In the face of significant deficiencies in GBC oversight (for fish and other taxa), we make several recommendations at a variety of levels.

Serious consideration should be given to a new international treaty, one that can encompass all of GBC regardless of the agent's mode of creation or its application. It is important to make the regulation of GBC distinct from the regulation of commodity-trade GMOs like crops. Trade in and production of agro-industrial commodities involves economic considerations that easily dwarf invasive and pest species issues (important as they may be), whose worth to national economies has already alienated several important governments from the preeminent international framework for biosafety regulation (the CPB). Further, GBC involves a particular combination of biological and ecological processes that have no counterpart in agro-ecological systems. The moral, social and political issues in invasive species, biodiversity conservation and exploitation invoke a different network of actors and concerns than do GM crops.

The new treaty should form another Protocol to the CBD, and should be explicitly recognized by the WTO due to its quarantine and trade restriction implications.

Although we have used the concept of *modified* biological control (i.e., GBC) as an analytical focus in this article—and we argue there is indeed something consequentially different about GBC compared to conventional biocontrol—it may not be the best concept around which to construct such a treaty. Serious consideration should be given to the inclusion of non-GBC biocontrol agents, and close interface with existing invasive species regulatory regimes makes a good deal of practical sense. New Zealand's "new organisms" approach might be a useful template upon which to establish a new regime.

Very strong consideration needs to be given to the consequences of GBC agents for other nations, who may value the target species very differently than one's own. Even within nations, different groups will have different values and visions that deserve to be considered in GBC governance. This illustrates the need for a deliberative and responsive approach in governance, and it is not unique to GBC. Some nations already have been prompted to engage in wide-reaching projects of review, reacting to the pressures and politics that contemporary and future developments in biotechnology seem to have in store (e.g., New Zealand held a Royal Commission on genetic modification; Ministry for the Environment 2001).

Options for GBC governance could profit from the intense work occurring in other technological fields to improve its own. A variety of approaches are possible (some quicker to establish than others), such as formal inter-agency coordination, a range "hard" and "soft" approaches to regulation, changes to funding priorities and incentive structures, and a variety of forms of public dialogue. A four-year review of nanobiotechnology in the United States made similar findings, advocating a dynamic approach to oversight of this rapidly developing field (Ramachandran et al. 2011).

Scientists in GBC must engage with these matters, although the legal, ethical and societal issues might not always align squarely with their natural science expertise. This is partly an interdisciplinary challenge, necessitating engagement with social science and other forms of scholarship (e.g., law, politics). Researchers must be cognizant of the interdependency between fields so apparently distant as malaria reduction, rabbit conservation and invasive fish control.

A proactive engagement with policy-makers, the public, and research sponsors (e.g., funding agencies, philanthropies and private companies) is essential. Similarly, managers and other would-be users of these technologies must also become proactive, engaging with the science and the governance systems in which they are embedded, and reaching out with meaningful engagement to the citizenry affected. The complexities of the science and the discordant heritage of the last two decades' GM crop debate mean that the potential for either or both blanket bans or defiant, deleterious releases of GBC agents remains very real.

Conclusion

GBC encompasses a wide variety of techniques to create agents to address the difficult problem of invasive and unwanted species. Progress in GBC is occurring rapidly, and application to fish is an area of intense and varied work. Developments in other taxa, however, are also advancing apace, particularly in insects. The oversight regimes applied to GBC are varied across jurisdictions, making for a complex and interconnected web of governance. The ability of GBC agents to move about an environment, such as fish migrating through waterways, makes the interface of these regimes a especially pertinent. Many gaps and deficiencies remain, and it is doubtful whether, even if significant technical challenges are overcome, the deployment of a GBC program to control invasive fish would be straightforward. GBC may even warrant the establishment of a new international treaty. GBC researchers and would-be users of the technology must take a proactive role in developing an improved oversight regime, with meaningful and constructive dialogue with stakeholders amongst the public, policy-makers, other disciplines, and even internationally.

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