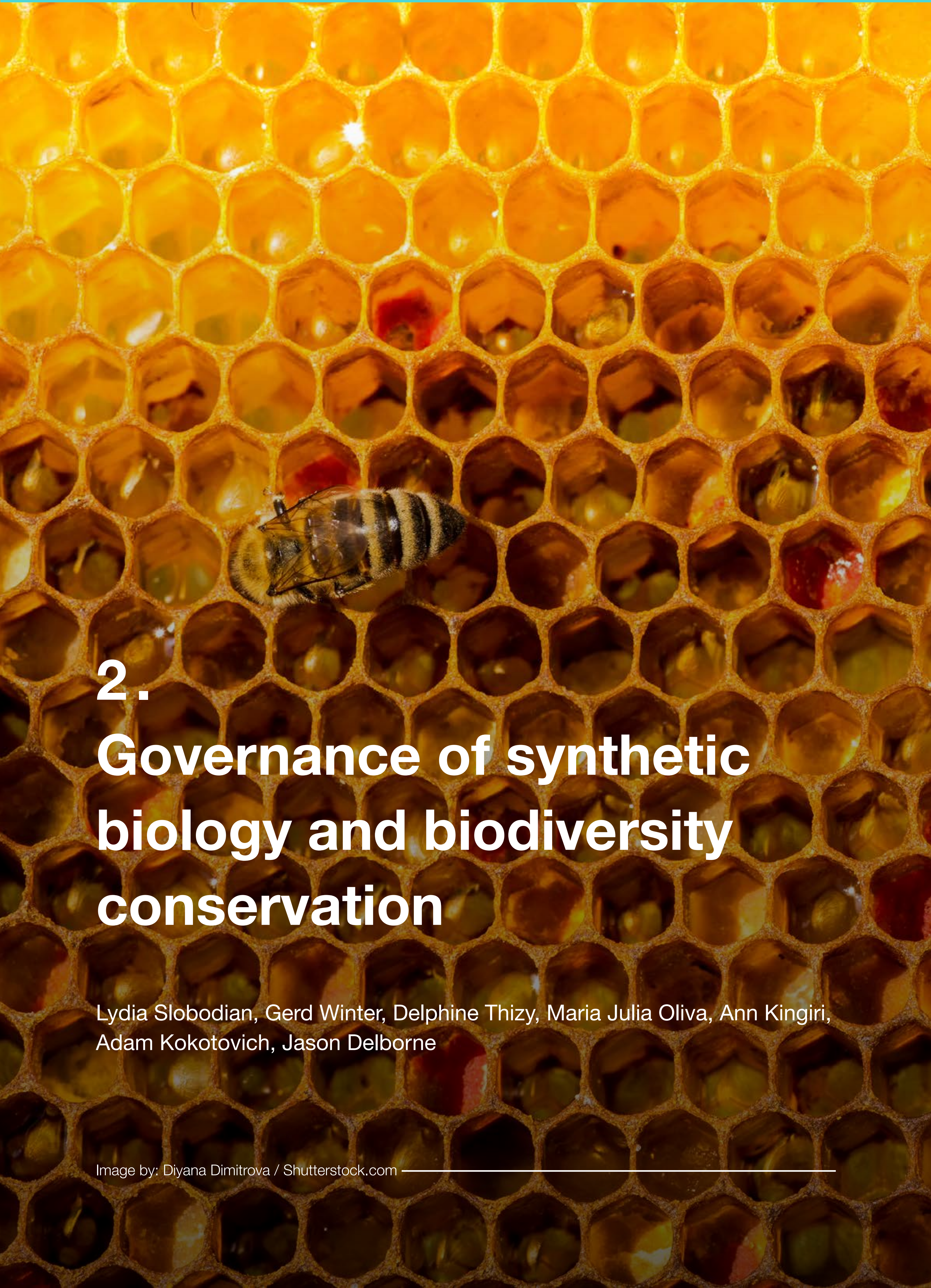

# 2. Governance of synthetic biology and biodiversity conservation

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Understanding the potential implications of synthetic biology for conservation and sustainable use of biological diversity entails examination of the existing governance frameworks applicable to this area, as well as the special governance challenges raised by synthetic biology, including engineered gene drive systems.

This chapter first describes principles relevant to governance of synthetic biology. It then assesses existing governance frameworks and tools applicable to synthetic biology, including international and national law, indigenous, customary and religious governance, and governance by industry and communities of practice. Finally, it discusses challenges raised by synthetic biology, including challenges associated with synthetic biology techniques and practices as well as challenges in engaging with different communities and perspectives.

## 2.1 Principles

This section highlights principles relevant to the governance of synthetic biology that have featured in the discourse: the precautionary principle; the principle of state sovereignty and state responsibility; principles of access to information, participation and access to justice in decision making; principles associated with indigenous peoples' rights to self-determination and free prior informed consent; and principles of inclusivity and non-discrimination. This is not an exhaustive list of principles, but a selection of principles that appear frequently in ongoing governance discussions on synthetic biology.

### 2.1.1 Precautionary principle/approach

Scientific uncertainty is a persistent characteristic of environmental governance. The precautionary principle or approach provides a tool for addressing uncertainty in decision making (Wiener & Rogers, 2002; Peterson, 2006). As formulated in the Rio Declaration on Environment and Development, it states:

*Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation [Rio Declaration, Principle 15].*

This has been reformulated in the preamble of the Convention on Biological Diversity, which reads:

*Where there is a threat of significant reduction or loss of biological diversity, lack of full scientific certainty should not be used as a reason for postponing measures to avoid or minimize such a threat.*

The CBD has been ratified by 196 states, with the exception of the United States (Table 2.1). Precaution has been referenced in the preamble of the Cartagena Protocol and applied in the articles relating to decision-making procedures. CBD COP Decision XI/11 explicitly applies the approach to synthetic biology, stating:

*Recognizing the development of technologies associated with synthetic life, cells or genomes, and the scientific uncertainties of their potential impact on the conservation and sustainable use of biological diversity, urges Parties and invites other Governments to take a precautionary approach, in accordance with the preamble of the Convention and with Article 14, when addressing threats of significant reduction or loss of biological diversity posed by organisms, components and products resulting from synthetic biology, in accordance with domestic legislation and other relevant international obligations [CBD Decision XI/11 para. 4].*

In November 2018, the CBD COP further called upon Parties to apply a precautionary approach with regard to engineered gene drives [COP/14/L.31].

Precaution as a legal requirement is multiform and controversial (Marchant, 2003). It has been incorporated into international instruments as well as national constitutions and laws (Fisher, Jones and von Schomberg, 2006; Hanson, 2014). The European Union (EU), for example, has elaborated guidelines on application of the precautionary principle which include a preliminary evaluation of risks and uncertainties to determine when the principle is triggered [EU, 2000]. Other countries, like the United States, have not explicitly included the precautionary principle in their legal system and have resisted codification of the principle in international treaties, though in practice they may still have adopted measures to manage risk in the context of uncertainty (Hammitt et al., 2005; Hanson, 2014).

While the principle has not yet achieved the status of an international customary rule, it is accepted as an "approach" that guides the interpretation of existing treaty or customary rules (Birnie, Boyle & Redgwell, 2009, p. 163). Whether as a binding principle or approach, there is wide agreement that precaution includes the following core elements (Wiener, 2018, p. 179):

1. a threat of serious or irreversible or catastrophic risk or damage;
2. a stance on knowledge, providing that scientific uncertainty about such risks does not preclude policy measures;
3. a stance on timing, favouring earlier measures to anticipate and prevent the risk;
4. a stance on stringency, favouring greater protection (such as prevention or burden-shifting that prohibits risky activities until they are shown to be safe or acceptable); and
5. a qualifying stance on the impacts of the precautionary measures themselves, calling for them to be cost-effective or weigh costs and benefits, and to be provisional and hence involve reassessment and improvement over time as knowledge is gained (Wiener, 2018, p. 179).

As detailed in Chapters 5 and 6, applications of synthetic biology carry risk that is uncertain and potentially irreversible, making the precautionary principle or approach applicable. There is no consensus on what this means in terms of regulatory measures. Some proponents of synthetic biology claim that some or all of the new techniques should be exempted from current genetically modified organism (GMO) regulation, while others insist that all techniques should be covered by administrative oversight, which may allow for some simplified procedures (ENSSER, 2017). Some civil society and scientific organisations have argued that the precautionary principle or approach necessitates a "moratorium on the release and commercial use of synthetic organisms, cells, or genomes until government bodies, with full participation of the public" have conducted assessments and developed international oversight mechanisms (Friends of Earth (FOE), 2012; https://genedrivenetwork.org/open-letter; http://www.etcgroup.org/content/over-200-global-food-movement-leaders-and-organizations-reject-gene-driveshttp://www.etcgroup.org/content/over-200-global-food-movement-leaders-and-organizations-reject-gene-drives). Others claim that a moratorium on synthetic biology could cripple the field and block potentially beneficial advances, while a more nuanced interpretation of the principle that allows for some, well-regulated risk, could help manage the tension between a desire for caution regarding the risk of intervention and worry about the risks of non-intervention (Wareham & Nardini, 2015).

### 2.1.2 State sovereignty and state responsibility for international harm

A basic principle of international law is that states have sovereignty over natural resources in their territory as well as responsibility for activities within their jurisdiction or control that cause damage to the environment of other states or areas beyond the limits of national jurisdiction [Stockholm Declaration 1972, Principle 21]. State sovereignty provides the basis for states to make decisions regarding genetic resources and biological diversity within their territory. This includes decisions regarding access to genetic resources that states may subject to requirements for permits and benefit-sharing contracts or make freely available for access and utilisation (Section 2.2.4). State sovereignty also includes decisions relating to activities affecting natural resources in their territory, including decisions on introduction of modified organisms into the environment (Section 2.2.1). Many fora are working on regional and even global harmonisation of state-based standards for risk assessment and management (Tung, 2014).It has been argued, though, that a plurality of approaches may be more realistic and even preferable (Winter, 2016a).

States also have responsibility for transboundary harm. There is an international customary rule that a state must prevent and provide compensation for damage wrongfully caused from its territory to other states [ICJ Pulp Mills 2010]. The International Law Commission has concretised the general rule by developing Draft Articles on Responsibility of States for Internationally Wrongful Acts, which provide an obligation to make reparation for "any damage, whether material or moral, caused by the internationally wrongful act of a State"[ILC Draft Articles 2001, art. 31].The obligation has been partly applied to biosafety issues by the Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress, which had only 42 Parties as of 2018.

In addition to the "ex post" liability approach, the principle of state responsibility for transboundary harm implicates an "ex ante" approach in the form of a responsibility to conduct environmental impact assessments where there is potential for significant transboundary adverse impact [ICJ Pulp Mills 2010; UNCLOS art. 206]. Depending on scope, this could apply in cases where synthetic biology or engineered gene drives cross boundaries. The Cartagena Protocol further stipulates that export of GMOs requires prior informed consent of the importing state. However, as of 2018, some of the most active states in biotechnology are not among the 171 Contracting Parties of the Protocol, including the United States, Australia, Canada, Russia, Israel and Chile. Failure to comply with prior informed consent and EIA obligations would possibly qualify as a wrongful act in the sense of the international customary rule and Draft Articles described above.

Recognising the potential for harm in the absence of wrongful activities, the International Law Commission of the United Nations developed Draft Principles on the Allocation of Loss in the Case of Transboundary Harm Arising out of Hazardous Activities [2006], which would require states to impose strict liability on operators of hazardous activities, and require operators to have financial security, such as insurance, to cover compensation claims [ILC Draft Principles 2006]. It is however open to debate whether synthetic biology could be considered a "hazardous activity" as understood by the Draft Principles (see Section 2.2).

### 2.1.3 Access to information, public participation and access to justice in environmental matters

Procedural norms of good governance apply to decision making on activities related to or potentially impacting biodiversity and the natural environment. These include three key components: access to information; public participation in decision-making processes; and access to justice [SDG 16; Rio Declaration Principle 10]. These components have a long tradition in several legal systems, including the United States (Stewart, 2003). They were further elaborated in the Aarhus Convention on Access to Information, Public Participation in Decision-making and Access to Justice in Environmental Matters [1998]. The Aarhus Convention, while European in scope, provides guidance on interpretation of the three aspects, that have been recognised as globally relevant (Morgera, 2005). According to the Aarhus Convention, the principle of access to information requires that any person has the right of access to environmental information held by public authorities, including private actors with public functions, notwithstanding exceptions concerning the protection of privacy, trade secrets and certain public interests [Aarhus art. 4].The principle of public participation provides for a right of the public at large and particularly concerned persons to participate early in decision-making processes in relation to certain hazardous activities or environment-related plans, programmes and executive regulations [Aarhus arts. 6-8]. The principle of access to justice in environmental matters states that any person – which includes any environmental organisation – who considers their rights violated or interests affected by an environmental decision has access to a court or other independent and impartial review procedure to challenge the substantive and procedural legality of the decision [Aarhus art. 9]. The Aarhus Convention explicitly applies these principles to matters related to genetically modified organisms [Aarhus art. 2(3)(a), art. 6(11)].

### 2.1.4 Peoples' rights to self-determination and free prior and informed consent

Synthetic biology decision making can implicate rights of indigenous peoples and local communities in relation to natural resources and culture. The principle of self-determination of peoples, recognised in the Charter of the United Nations, the International Covenant on Civil and Political Rights, the International Covenant on Economic, Social and Cultural Rights, entails a right to control over natural wealth and resources [UN

Charter art. 55; ICCPR art. 1; ICESCR art. 1]. The UN Declaration on the Rights of Indigenous Peoples and International Labour Organization (ILO) Convention 169 elaborate the rights of indigenous and tribal peoples to participate in the use, management and conservation of resources pertaining to their lands. ILO Convention 169 requires governments to "respect the special importance for the cultures and spiritual values of the peoples concerned of their relationship with the lands or territories, or both as applicable, which they occupy or otherwise use..." [ILO Convention 169 art. 14]. A series of international human rights cases have highlighted the special relationship between indigenous peoples and their traditional territory and resources and found that interference with rights of communities related to their natural resources can implicate the human right to culture [e.g. HRC "Lubicon Lake Band" 1984; IACHR "Awas Tingni" 2001; ACHPR "Endorois" 2009].

In practice, these rights are realised through procedural requirements for involvement of communities in decision making. The UN Declaration on Rights of Indigenous Peoples provides that indigenous peoples shall not be relocated from their lands or territories without their free, prior and informed consent [art. 10]. The concept of free prior and informed consent (FPIC) has been extended to apply to any decision making related to activities affecting the territory or natural resources of indigenous peoples or communities. For instance, financial institutions have included FPIC in the Equator Principles, a risk management framework for determining, assessing and managing environmental and social risk in projects (Amalric, 2005). Human Rights Tribunals have found that FPIC entails good faith and culturally appropriate consultation, sufficient sharing of information including environmental and social impact studies in advance of decisions, and appropriate monitoring [IACHR "Saramaka" 2007; ACHPR "Ogoni" 2001; IACHR "Maya" 2004].

Free, prior and informed consent has been largely discussed in the context of conservation for decisions impacting indigenous peoples and local communities. In its recent report, the CBD's Ad Hoc Technical Expert Group on Synthetic Biology noted that "free, prior and informed consent of indigenous peoples and local communities, might be warranted in the development and release of organisms containing engineered gene drives" (Ad Hoc Technical Expert Group on Synthetic Biology, 2017, para. 25). The AHTEG also stated that the development of synthetic biology technologies "should be accompanied by the full and effective participation of indigenous peoples and local communities" (para. 26). In 2018, the CBD COP called upon Parties and other Governments to obtain, as appropriate, free, prior and informed consent or approval and involvement of potentially affected indigenous peoples and local communities as a prerequisite to introducing engineered gene drives into the environment, in accordance with national circumstances and legislation [COP/14/L.31 para. 9, 11].

### 2.1.5 Inter-generational equity and sustainable development

Synthetic biology has potential benefits and adverse effects that could affect resource management and economic development now and for future generations. The concept of sustainable development is defined as development that "meets the needs of the present without compromising the ability of future generations to meet their own needs" (World Commission on Environment and Development, 1987). It recognises that economic and social development and environmental conservation are interdependent [Rio Declaration, Principle 4]. It is linked to the principles of intergenerational equity, which entails an obligation of stewardship of the natural environment for future generations, and intragenerational equity which emphasises the need to meet the basic needs of current generations across circumstances and regions (Brown Weiss, 1993; [ICJ Nuclear Test Case, 1995, Weeramantry dissenting; ICJ Gabcikovo-Nagymaros, 1997, Weeramantry concurring; Minors Oposa, 1993]).

The Sustainable Development Goals (SDGs) adopted in 2015 provide globally agreed upon targets for alleviating poverty, ensuring food security, combating climate change and conserving biological diversity. Certain applications of synthetic biology are intended to provide a means for realising sustainable development goals. For example, applications to address invasive species could contribute to goals related to terrestrial and marine conservation [SDGs 14 and 15], while applications addressing human disease vectors such as mosquitos support achievement of goals on human health and well-being as well as alleviation of poverty [SDGs 1 and 3]. At the same time, some of the risks associated with synthetic biology could affect attainment of these goals in a different way (see Section 2.2). The potential benefits and risks of synthetic biology are discussed in more detail in Chapters 5 and 6.

## 2.2 Governance frameworks relevant to synthetic biology impacts on biodiversity

Synthetic biology engages existing normative systems, including legal, customary and industry systems, at the international, regional, national and subnational levels. These include frameworks governing risk assessment and management, liability for harm, intellectual property and ownership, and sharing of benefits. Table 2.1 provides a summary of relevant international legal regimes.

Many of the existing governance frameworks were developed in the context of "traditional" genetic engineering and may have to be revised in order to cope with challenges raised by synthetic biology (Wynberg & Laird, 2018). These challenges are addressed in depth in Section 2.3.

This section first explores international and national legal instruments and approaches in relation to risk assessment, liability, intellectual property, and access and benefit sharing. It then briefly discusses indigenous, customary and religious governance, followed by governance by industry and communities of practice.

**Table 2.1** International legal frameworks.

| Instrument | Description | Relevance for synthetic biology |
|---|---|---|
| **Convention on Biological Diversity (CBD)**<br>Adopted: 1992<br>Entered into force: 1993<br>Parties: 196 | Global legal framework addressing conservation, sustainable use and sharing of benefits of biodiversity | Creates obligations for each Party to manage risks associated with living modified organisms that could have a negative impact on biological diversity (art. 8(g)) and framework for access and benefit sharing relating to genetic resources (art. 15). |
| **Cartagena Protocol on Biosafety to the Convention on Biological Diversity (Cartagena Protocol)**<br>Adopted: 2000<br>Entered into force: 2003<br>Parties:171 | Protocol to CBD intended to ensure the "safe transfer, handling and use of living modified organisms resulting from modern biotechnology that may have adverse effects on biological diversity..." (art. 1) | Requires sharing of risk related information between exporting and importing Parties and provides guidelines on methodology for environmental risk assessments and considerations in decision-making. |
| **Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety (Supplementary Protocol)**<br>Adopted: 2010<br>Entered into force: 2018<br>Parties: 42 | Supplementary Protocol to Cartagena Protocol intended to provide rules and procedures for liability and redress relating to living modified organisms | Provides for national frameworks requiring response measures and assigning civil liability in event of damage resulting from living modified organisms which find their origin in transboundary movement. |
| **Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization to the Convention on Biological Diversity (Nagoya Protocol)**<br>Adopted: 2010 | Protocol to CBD providing international framework for access to genetic resources and sharing of benefits arising from their utilisation | Applies to genetic resources that serve as source material for synthetic biology research. Creates ABS framework based on traceability and transfer of material that could be undermined by use of digital sequence information. |

| Instrument | Description | Relevance for synthetic biology |
|---|---|---|
| Entered into force: 2014<br>Parties: 105 | | |
| **International Treaty for Plant Genetic Resources for Food and Agriculture (ITPGRFA)**<br>Adopted: 2001<br>Entered into force: 2004<br>Parties: 144 | International regime recognising sovereign rights over plant genetic resources for food and agriculture, and establishing multilateral system to facilitate access to and sharing of benefits from listed plants | Creates ABS system that could be undermined by new techniques using digital sequence information that enable development of new plant varieties without access to the original genetic material. |
| **Agreement on Trade-related Aspects of Intellectual Property Rights (TRIPS)**<br>Adopted: 1994<br>Entered into force: 1995<br>Parties: 164 | WTO Agreement defining obligations to grant and respect patents, including exceptions for patenting of plants, animals and biological processes | Provides forum for ongoing discussions on patentability of genetic resources. |
| **Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES)**<br>Adopted: 1973<br>Entered into force: 1975<br>Parties: 183 | Multilateral Environmental Agreement establishing regulations and permitting system covering trade in listed species | Hosts discussions related to 1) synthetic products that substitute or resemble products from a CITES listed species in international trade; and 2) status of genetically modified species and "de-extinction" under CITES. |
| **UN Convention on the Law of the Sea**<br>Adopted: 1982<br>Entered into force: 1994<br>Parties: 168 | Codification of law of the sea including activities and resources in areas beyond national jurisdiction | Provides basis for ongoing negotiation of international agreement on marine biodiversity in areas beyond national jurisdiction, including sharing of benefits from marine genetic resources. |
| **Convention on the Prohibition of Military or Any Other Hostile Use of Environmental Modification Techniques (ENMOD)**<br>Adopted: 1976<br>Entered into force: 1978<br>Parties: 78 | Multilateral instrument prohibiting use of military or hostile environmental modification techniques having widespread, long-lasting or severe effects | Potentially applies to military use of synthetic biology techniques with potential to significantly modify ecosystems. |

### 2.2.1 Risk assessment and regulation

Most countries have national regulatory frameworks for risk assessment and management in relation to genetically modified organisms. The Cartagena Protocol requires Parties to "establish and maintain appropriate mechanisms, measures and strategies to regulate, manage and control risks" connected with the use, handling and transboundary movement of living modified organisms (LMOs), including "possible adverse effects of living modified organisms on the conservation and sustainable use of biological diversity" [Arts. 15, 16]. Where LMOs are intended for introduction into the environment, the decision to allow import must be based on a risk assessment and apply precaution [Arts. 7, 10(6), 15]. Annex III of the Protocol outlines the methodology of risk assessment, including identification of potential adverse effects, evaluation of the likelihood of the effects, evaluation of the consequences of the effects and estimation of overall risk. It also lists points to consider, including the characteristics of the recipient or parental organism, the donor organism, the vector and the insert or modification, as well as a comparison of the unmodified with the modified

## 131 countries
with national laws on risk assessment and management

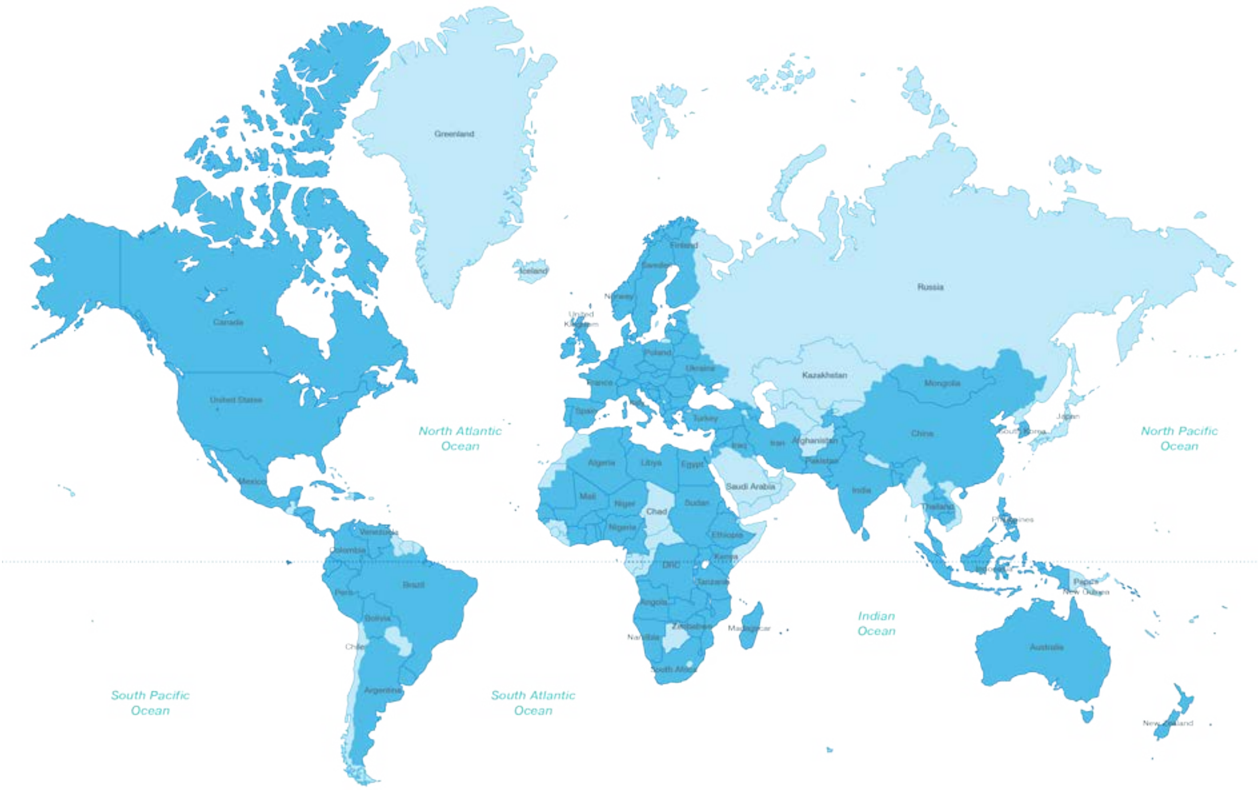


**Figure 2.1** Countries with national laws on risk assessment and management related to genetically modified organisms. This map shows only those countries whose laws show up in the CBD Biosafety Clearing House or ECOLEX legal database. Lack of inclusion on this map does not mean that the country has no biosafety regulation. Adapted from CBD Biosafety Clearing House; ECOLEX.

recipient or parental organism. National biosafety regulation may provide that certain activities require prior authorisation or notification, containment procedures or other forms of administrative oversight.

The Cartagena Protocol has 171 Parties, but was not ratified by several countries active in biotechnology, as discussed above. Nonetheless, many countries have biosafety legislation in place that fully or partly follows the risk assessment framework outlined in the Protocol. A search of the CBD Biosafety Clearing House and the ECOLEX legal database found 131 countries with national laws on risk assessment and management (Figure 2.1). This includes countries such as the United States, Canada and Argentina that are not Parties to the Protocol.

National risk management legislation applicable to synthetic biology may include a range of legal instruments addressing different sectors and products. In addition to specific biosafety regulations, this may include legislation covering plant-breeding, food and drug safety, pesticides, toxic substances, sanitary and phytosanitary measures, and environmental protection. Some countries may have multiple laws that potentially cover synthetic biology products, as discussed below.

### 2.2.1.1 Scope of application of regulatory oversight

At COP13 in Mexico in 2016, the CBD Parties noted that it is not clear whether or not some organisms of synthetic biology would fall under the definition of LMO under the Cartagena Protocol [COP13 Decision 17, para. 7]. They stated that the Cartagena Protocol and existing biosafety frameworks provide a starting point for addressing synthetic biology but may need to be updated and adapted for current and future developments and applications, and directed the Synthetic Biology AHTEG to continue deliberating on the matter [COP13 Decision 17, para. 6]. In 2017, the AHTEG concluded that “most living organisms already developed or currently under research and development through techniques of synthetic biology, including organisms containing engineered gene drives, fell under the definition of LMOs as per the Cartagena Protocol" (Ad Hoc Technical Expert Group on Synthetic Biology, 2017, para. 28). In November 2018, CBD COP14 extended the AHTEG, and emphasised the need for case-by-case risk assessments before organisms containing engineered gene drives are considered for release into the environment and recognised that specific guidance on such risk assessment could be useful [COP/14/L.31 para 9(a), 10].

National regulatory regimes take different approaches in addressing scope of applicability. These are often discussed in terms of "product" or "process" approaches. A "product" approach means that oversight is triggered by certain characteristics of products that are considered to pose a risk, no matter by what processes the product was generated, where a "process" approach means that the product that is subject to oversight is defined by the process of its generation. The United States, Argentina, Canada, the Philippines and Bangladesh have been categorised as having product-based approaches, while Brazil, India, China, Bolivia, Australia, Burkina Faso, the EU and New Zealand have been counted as process-based (Ishii & Araki, 2017). In reality, product-based approaches to regulation often rely upon process-based distinctions, and process-based approaches often consider a combination of product and process-based factors. The usefulness of the product/process dichotomy has therefore been questioned (Kuzma, 2016).

The United States applies what is frequently considered a product approach under the Plant Protection Act (PPA), Federal Insecticide, Fungicide and Rodenticide Act, the Federal Food, Drug and Cosmetics Act, and the Toxic Substances Control Act (Bergeson et al., 2015). However, in some cases agencies may consider process in their decision making. For example, applications for permits for introduction of genetically modified plant pests require a "detailed description of the molecular biology of the system (e.g., donor-recipient-vector) which is or will be used to produce the regulated article" [US 7 CFR 340.4] (Kuzma, 2016). The Toxic Substances Control Act applies to genetically modified micro-organisms defined as "intergeneric" but not physically or chemically mutagenised micro-organisms (Wozniak et al., 2013). Likewise, the Food and Drug Administration (FDA) regulates genetically engineered animals under the "new animal drug" provisions of the Federal Food, Drug and Cosmetics Act, considering manufacturing methods and facilities in its review process (FDA, 2017b). There have been claims that the combination of product and process approaches can open the door for industry to lobby for whichever approach suits their interest. According to Kuzma, "[i]ronically the same GE developers who once claimed that the process of GE does not matter for regulatory purposes are now arguing that changes to the engineering process justify looser regulatory scrutiny" (Kuzma, 2016, p. 166).

Canada likewise bases its regulatory approach on the characteristics of genetically modified products, embedded within its overall framework for regulating "novel products." The trigger for regulatory review of products intended for introduction into the environment is "novelty," whether it derives from genetic modification or other techniques, though the determination of "novelty" may entail process considerations (Montpetit, 2005; McHughen, 2016). For example, the Food and Drug Regulations define "novel food" to include "a food that is derived from a plant, animal or micro-organism that has been genetically modified such that … one or more characteristics of the plant, animal or microorganism no longer fall within the anticipated range for that plant, animal or microorganism" [Canada Food and Drug Regulations B.28.001]. The Seeds Regulations define "Novel Trait" as one that "is not substantially equivalent, in terms of its specific use and safety both for the environment and for human health, to any characteristic of a distinct, stable population of cultivated seed of the same species in Canada" [Seeds Regulations 107(1)].The "substantial equivalence" test has raised criticisms of ambiguity and susceptibility to regulatory capture (Moran, Ries and Castle, 2009). Others have lauded the "novelty" trigger as more practical and scientifically sound than other regulatory approaches (McHughen, 2016).

In contrast, the EU applies what is considered a process approach, under which the process of genetic modification of an organism is the main trigger for oversight. A genetically modified organism (GMO) is defined as an organism "in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination" (2001/18/EC Art. 2(2)). This definition implies that the application of the recombination technique must result in a changed organism, and hence in a modified product (Callebaut, 2015). Certain techniques are listed as being – among others – genetic modification. They are considered to include not only the transfer of genes between species (transgenesis) but also the reorganisation of genes within a species (cisgenesis) [ECJ Case 528/16, 2018, paras 27–38].

### 2.2.1.2 Regulatory stages and requirements

Most regulatory systems require prior authorisation for certain types of genetic engineering or release of GMOs into the environment. For activities considered to be low or negligible risk, notification or reporting obligations are used as a form of more lenient oversight. Synthetic biology applications are often subject to step-by-step or staged regulation and monitoring at different levels, from the laboratory to full deployment/release of the organism through potentially other stages such as confined field trials (Figure 2.2). For example, EU Directive 2001/18 sets out a step-by-step approach for introduction of a GMO into the environment, with evaluation of impacts on human health and the environment required at each step. Its preambular consideration 24 explains this as follows:

*The introduction of GMOs into the environment should be carried out according to the 'step by step' principle. This means that the containment of GMOs is reduced and the scale of release increased gradually, step by step, but only if evaluation of the earlier steps in terms of protection of human health and the environment indicates that the next step can be taken.*

Likewise, in Canada, plants with novel traits, including genetically modified plants, must go through multiple regulatory stages to be approved for environmental release. Stages include, as applicable: import (subject to permit); contained use in a laboratory or greenhouse (subject to biosafety guidelines); confined environmental release (subject to risk management conditions); unconfined environmental release (subject to risk assessment and management and monitoring); variety registration; and commercialisation ([http://www.inspection.gc.ca/plants/plants-with-novel-traits/eng/1300137887237/1300137939635]).

Oversight tools typically distinguish between GMOs made or used in containment and GMOs released to the environment (Prabhu, 2009). For example, Japanese legislation distinguishes between "Type 1 Use" and "Type 2 Use" where "Type 2 Use" describes use where measures are taken to prevent release outside the facility, and "Type 1 Use" refers to all other use where such measures are not taken. Type 1 Use requires ministerial determination that the use will result in no adverse effect if the approved procedures are followed, while Type 2 Use requires confirmation of measures for containment [Japan, Act no. 97 of 2003, arts. 4–15].

In some cases, the areas where the GMO may be released are restricted. In the EU, even if a genetically modified plant was authorised for the EU market, the member states have powers to "opt out" and close areas and even the whole country to its release (Winter, 2016a) [2001/18/EC Art. 26b]. In addition, nature protection, seed protection and other laws may prevent the release of GMOs for specified areas. For instance, in an area under special nature protection the introduction of GMOs may be categorically excluded for reasons of maintaining GM free reference sites, or of preserving the pristine nature. In Germany and


**Figure 2.2** Typical stages in risk regulation applicable to synthetic biology.

other states, farmers have agreed to declare regions as to be held GMO-free (GMO Free Europe, 2016).

### 2.2.1.3 Factors in assessing risks

In assessing risk, national decision makers may be legally required or allowed to take different factors into consideration. Many countries' laws institute administrative bodies and provide them with broadly discretionary powers of oversight [see, e.g. (Saegusa, 1999); Nordrhein-Westfalen Nature Protection Law s. 54]. Other countries' laws set out material yardsticks for oversight in an endeavour to bind administrative decision makers and provide legal certainty for operators [see, e.g. EU Directive 2001/18/EC, Article 4; German Genetic Engineering Act sec. 16]. Commonly, laws provide that impacts on human health and the environment are to be considered.

In addition, some countries include socio-economic concerns as well as impacts on indigenous and local communities. Art. 26 of the Cartagena Protocol states:

*The Parties, in reaching a decision on import under this Protocol or under its domestic measures implementing the Protocol, may take into account, consistent with their international obligations, socio-economic considerations arising from the impact of living modified organisms on the conservation and sustainable use of biological diversity, especially with regard to the value of biological diversity to indigenous and local communities.*

There are many possible socio-economic considerations that could be relevant to biotechnology regulation, and the ways in which they are taken into account vary across countries (Ludlow, Smyth & Falck-Zepeda, 2014). For example, there are arguments that use of biotechnology can drive change in agricultural practices, and even influence the change of whole regions from sustainable peasant agriculture to industrialised agriculture, as has been observed in Argentina and other countries (Robin, 2010). This type of socio-economic impact could potentially be captured in systems like the EU, which considers impacts on cultivation, management and harvesting techniques.

In some countries, moral values are also considered in risk regulation. Poland, for instance, referred to religious beliefs of its population when prohibiting the cultivation of genetically modified plants, though bringing such plants onto the market was previously authorised by the Commission. The European Court of Justice found the reason not sufficiently substantiated [ECJ Case C-165/08, paras 57–59].

### 2.2.1.4 Weighing risks against benefits

Many risk assessment frameworks do not allow for analysis of benefits. Some legal systems, including that of the EU, have separate systems for risk assessment – which does not consider costs – and risk management – which can consider regulatory costs and other concerns, depending on the wording of the applicable law (Winter, 2016b).

The United States applies cost-benefit analysis in many, but not all, processes of environmental decision making. In reviewing pesticides, the US Environmental Protection Agency (EPA) considers economic, social and environmental costs to determine whether any adverse effects on the environment are "unreasonable" (NASEM, 2016b). Conversely, in determining safety of food additives, the FDA can only consider whether there is a "reasonable certainty of no harm," and may not take into account other factors (NASEM, 2016b). Cost-benefit analysis has been proposed as an alternative to the precautionary principle as a means for guiding decision makers and ensuring the best outcomes, taking into consideration all possible benefits and risks (Sunstein, 2005).

There are different methodologies for weighing risks and benefits. One example can be found in the EU chemicals regulation [1907/06 "REACH"]. According to Art. 60, an authorisation of marketing of a substance is possible, even if the substance is highly dangerous or considered not to be adequately controlled, "if it is shown that socio-economic benefits outweigh the risk to human health or the environment arising from the use of the substance and if there are no suitable alternative substances or technologies." This is a type of risk-inclined approach, which allows benefits to outweigh any risk, even a serious one. Other systems are risk-averse, allowing only residual risks to be outweighed by benefits (Winter, 2016b).

Those states that allow for the weighing of risks and benefits of products for synthetic biology must consider how to define benefits. The EU chemicals regulation suggests a broad range of concerns including economic interests of suppliers, employment, consumer demand, benefits for human health and the environment, etc. [Annex XVI of the REACH Regulation]. Other approaches would limit benefits to justifiable use values that are expressed in qualitative terms rather than through market prices or survey-based pricing (Ackerman & Heinzerling, 2004; Winter, 2018).

The CBD COP in 2016 invited parties "in accordance with their applicable domestic legislation or national circumstances, to take into account, as appropriate, socio-economic, cultural and ethical considerations when identifying the potential benefits and potential adverse effects of organisms, components and products resulting from synthetic biology techniques in the context of the three objectives of the Convention" [CBD COP13 Decision 7, 2016]. The present study describes certain ways that synthetic biology can be intended to create benefits for biodiversity conservation and sustainable use (Chapter 5) and socio-economic benefits and benefits for human health (Chapter 6), as well as potential negative impacts. For example, the effect of a new product (such as "natural" vanillin produced through synthetic biology) on existing supply chains (such as vanilla supply chains in Madagascar) may have to be weighed against socio-economic benefits of synthetic production (Chapter 6).

Another component of risk-benefit weighing is the testing of alternatives, to determine which could achieve the intended benefit with lowest environmental risks. For example, in evaluating a proposal for modification of a mosquito to eradicate human malaria, decision makers would need to consider alternatives such as vaccination and use of pesticides. Under this concept, it would not be necessary to assess the value of human lives saved and compare them with the loss of biodiversity. It may suffice to examine which of the alternatives – the synthetic biology technique and the application of chemicals – have less harmful impacts on the environment (Winter, 2018).

#### 2.2.1.5 Risk assessment methodologies

The methodology of risk assessment has a common structure throughout national systems, but differs somewhat in terms of depth and width of analysis (Paoletti et al., 2008). One of the most detailed examples is the EU Environmental Risk Assessment methodology (Box 2.1). Most risk assessment methodologies are based on two main components: (1) evaluation of intended and unintended effects, including probability and potential significance of the effects; and (2) comparison of the modified product with existing counterparts (Paoletti et al., 2008). In evaluating potential effects, decision makers can consider information relating to, inter alia, toxicity, persistence and gene transfer, and evaluate potential intended and unintended impacts on target and non-target populations as well as associated social and cultural effects. The comparison of the modified product with counterparts is at the heart of risk assessment. Many countries exempt products from risk assessment where they have a history of safe use. Traditionally the comparison has been between modified and "natural" products, but as genetic modification becomes more common, the definition of "conventional" may change (Paoletti et al., 2008; Pauwels et al., 2013).

**Box 2.1**

**Environmental risk assessment in the EU**

The environmental risk assessment (ERA) required by the EU Directive on deliberate release into the environment of genetically modified organisms is defined as "the evaluation of risks to human health and the environment, whether direct or indirect, immediate or delayed, which the deliberate release or the placing on the market of GMOs may pose and carried out in accordance with Annex II" [EU Directive 2001/18/EC, arts. 2(8), 4(2)]. In relation to agricultural plants a Guidance Paper of the European Food Safety Authority (EFSA) distinguishes between seven paths of possible impact (EFSA, 2010):

- Persistence and invasiveness of the GM plant, or its compatible relatives, including plant-to-plant gene transfer

- Plant-to-microorganism gene transfer
- Interaction of the GM plant with target organisms
- Interaction of the GM plant with non-target organisms
- Impact of the specific cultivation, management and harvesting techniques[2]
- Effects on biogeochemical processes
- Effects on human and animal health

Each specific path must be examined following six steps of ERA [EU Directive 2001/18/EC Annex II sec. C.2].


**Figure 2.3** Six steps in the EU environmental risk assessment. Adapted from Directive 2001/18/EC.

Under the EU regulations, different types of information are to be submitted and considered in risk assessment, including information on the molecular and cellular level, the organism and population level, and the ecosystem level, as well as technical information. The information must reveal how the donor organism differs from the recipient organism in terms of functions, reproduction, dissemination, survivability, etc. [EU Directive 2001/18/EC, Annex III].

### 2.2.1.6 Monitoring

Legislation may provide for monitoring of regulated activities. The United States provides post-market oversight authority to multiple agencies in relation to biotechnology products. The FDA requires reporting from manufacturers and conducts post-market risk assessment and safety inspections in relation to animal drugs, foods and other biotechnology products (NASEM, 2017b). The EPA is required to re-evaluate pesticide products every 15 years, though in practice it has been re-evaluating biotechnology products every 5–6 years. In contrast, genetically engineered organisms that could act as plant-pest can be deregulated upon evidence that they are unlikely to pose a risk, in which case there is little follow-up monitoring or oversight (NASEM, 2017b).

Under EU law, monitoring requirements are different depending on whether a GMO is experimentally released into the environment, or if it is brought to the market with subsequent general release. In the latter case, for instance, the operator is obliged to comply with the authorisation conditions, and in particular with regard to the monitoring scheme, and to continuously report to the competent authority about unexpected

[2] An example for such effects on cultivation practices would include the change of whole regions from sustainable peasant to industrialised agriculture, as has for example been observed in Argentina (Robin, 2010).

incidents during the market placement or release into the environment, be it through case specific or general observations. Likewise, the competent authority is obliged to supervise the monitoring and intervene in case of emergencies [EU Directive 2001/18/EC Article 20]. It has however been found that the monitoring requirements are not well implemented in practice and need to be revised in order to produce more scientifically usable information (Züghart et al., 2011).

### 2.2.2 Liability

National and international legal systems may provide for liability for environmental damage attributable to synthetic biology. As described in Section 2.1.2, there is an international legal principle of state responsibility for international harm. However, there are few international frameworks that explicitly provide for liability – either on the part of states or on the part of operators – in the context of biosafety. The Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress [Supplementary Protocol] to the Cartagena Protocol provides for states to establish national frameworks for liability in cases of environmental harm caused by living modified organisms. Under the Supplementary Protocol, Parties should require operators to take certain actions in the event of damage, including informing the competent authority, evaluating the damage, and taking reasonable actions to restore affected biodiversity [art. 2, 5]. Where the operator fails to take appropriate response measures, the competent authority may implement such measures and recover from the operator the associated costs. States should also provide for rules and procedures that address damage, including as appropriate, civil liability. Parties may apply existing general rules and procedures on civil liability and/or develop specific civil liability rules and procedures. In either case, under the Protocol they shall, as appropriate address (a) damage; (b) standard of liability (strict or fault-based); (c) channelling of liability; and (d) the right to bring claims. The Supplementary Protocol provides little in the way of binding obligations for civil liability, and has only 42 Parties to date.

European legal instruments apply a principle of strict liability, or no-fault liability, for damage to the environment resulting from certain dangerous activities. The European Convention on Civil Liability for Damage Resulting from Activities Dangerous to the Environment [Lugano Convention] imposes liability on the operator of a dangerous activity for any damage caused by the activity, regardless of fault [art. 6]. Dangerous activities are those which create significant risk for man, the environment or property, and include the production, storage, use disposal or release of genetically modified organisms [art. 2]. The EU Liability Directive applies strict liability to environmental damage caused by a set of listed activities "in order to induce operators to adopt measures and develop practices to minimise the risks of environmental damage so that their exposure to financial liabilities is reduced" [preambular para 2, art. 3(1)(a)]. Listed activities include: "Any contained use, including transport, involving genetically modified micro-organisms" and "Any deliberate release into the environment, transport and placing on the market of genetically modified organisms" [Annex III (10 and 11)].

In Tanzania, the 2009 Biosafety Regulations provide for strict liability in relation to GMOs, including synthetic organisms [§ 3]. The Regulations state:

*Any person or his agent who imports, transits, makes contained or confined use of, releases, carries out any activity in relation to GMOs or products thereof or places on the market a GMO shall be strictly liable for any harm, injury or loss caused directly or indirectly by such GMOs or their products or any activity in relation to GMOs [§ 56(1)].*

Damage to the environment or biological diversity is explicitly included as a type of harm covered by this provision [§ 56(2)]. In these cases, compensation includes the cost of restoration and the cost of preventive measures, where applicable [§ 56(4); 58]. It also applies to harm or damage caused to "the economy, social or cultural principles, livelihoods, indigenous knowledge systems, or indigenous technologies" [§ 59]. The Regulations require operators to take out a policy of insurance against liability [§ 35(1)].

Harm caused by synthetic biology could lead to civil liability under common law principles of tort, or civil law delict. For example, intrusion of modified organisms onto private property could give rise to claims of nuisance or trespass (Strauss, 2012). In the United States and Canada, farmers have brought lawsuits against biotechnology companies alleging contamination of their fields with genetically modified crops which rendered their yield less valuable or made it impossible for them to achieve organic accreditation (Rodgers, 2003). To bring a tort suit alleging environmental harm from synthetic biology, claimants would need to show standing, causation and damage, as well as fault or strict liability. Each of these elements could be challenging in the context of synthetic biology. Where damage is to an environmental interest rather than a private person, it may be difficult to prove standing. Some of the potential damage from synthetic biology is extremely attenuated; even where it is possible to show "but for" causation, there may not be a sufficiently close causal link between the activity and the damage to show liability. Fault-based liability may be difficult to prove and ineffective; if significant harm occurs despite best safety practices, the cost may lie with the state. Strict liability is typically reserved for particularly hazardous activities or activities listed in statute, and may not be available for harm caused by synthetic biology in many jurisdictions.

### 2.2.3 Intellectual property

There are differences in how countries deal with inventions and discoveries linked to genetic resources. These can promote or limit development or use of synthetic biology in conservation. While intellectual property decisions are made mainly at national and regional levels, international law, including bilateral treaties on trade and intellectual property, has played a role, e.g. through the harmonisation of patent and plant variety rights.

In general, industrialised countries allow the patentability of genes and gene sequences (Kumar & Rai, 2007). For example, in 1998, the EU harmonised patent law relating to biotechnological inventions and – though excluding the discovery of a gene or gene sequence from patentability – allowed for an isolated gene or gene sequence to constitute a patentable invention, if it met other patentability criteria. In the US, a recent Supreme Court decision found isolated genomic DNA not to be patentable, based on the law of nature exception to patentability [Association for Molecular Pathology v Myriad Genetics, Inc]. However, the Supreme Court maintained non-naturally occurring molecules may be patented, which may limit the impact of the finding in fields such as synthetic biology (Holman, 2014). Developing countries, for example in Latin America, tend not to allow the possibility of patenting genes and gene sequences (Bergel, 2015). For example, in Brazil, biological material, including the genome or germplasm of living organisms, found in nature or isolated therefrom, is not considered an invention [Industrial Property Law, art. 10].

Intellectual property in organisms, including genetically modified ones, are also treated differently by different states. While the United States provides for patent rights in plants and animals under certain conditions (Rimmer, 2008), the EU allows patenting of microorganisms but excludes patenting of plant and animal varieties [EU Directive 98/44/EC Art. 4; Regulation (EC) 2100/94 Art. 1]. In the EU, intellectual property in plant varieties is only possible in the form of plant variety protection. Farmers are allowed to further propagate their plants and develop new breeds (farmers' and breeders' exemptions) [Regulation (EC) 2100/94 Arts. 13 and 14]. The EU does not provide for intellectual property rights in animals, so that in practice trade secrecy protection is used as a substitute [EU Directive 98/44/EC Art. 4 (1) (1); Winter, 2016]. This means for products of synthetic biology that, for example, the malaria vector mosquito that is engineered to be non-reproductive (Case study 6) would be patentable in the United States but not in the EU; the engineered blight resistant chestnut (Case study 4) would be suitable for patent as well as plant variety protection in the US, but only for plant variety protection in the EU. Modified microorganisms would be patentable in both systems. Methods of plant and animal production are also suitable for patenting. This is however excluded in the EU if the processes are "essentially biological" [EU Directive 98/44/EC Art. 4 (1) (2)].

Proponents of intellectual property protection view it as a tool indispensable to promote innovation in synthetic biology (Calvert, 2012). J. Craig Venter, co-founder of Synthetic Genomics, views intellectual property as fundamental for "a vital and robust science and biotechnology industry"(Nelson, 2014). Others in the field of synthetic biology worry about negative impacts of intellectual property and advocate for more open innovation, in line with experiences in engineering and computer science. For proponents of open innovation, intellectual property in the context of synthetic biology may create a "perfect storm" (Rai & Boyle, 2007). As in other fields, patents may be both too broad (e.g. foundational patents) and too narrow (e.g. patent thickets) that stifle innovation (Martin, 2008; Winter, 2016b).

Openness in synthetic biology is often adopted also as a fundamental principle – though such principle is not always interpreted in the same way (Calvert, 2012). Several initiatives are promoting the synthetic biology commons. For example, the iGEM Registry of Standard Biological Parts is a growing collection of genetic parts that can be accessed to build synthetic biology devices and systems (Section 6.6). This Registry is an open community with a "Get & Give (& Share)" philosophy. Users get parts, samples, data and tools – and give back the new parts they have made. They also share experiences in the open community.

Commentators have compared these efforts to the open-source software model, as an alternative to proprietary rights (Kumar & Rai, 2006). Unlike software, though, copyright does not apply to synthetic biology products. Moreover, the modularity of synthetic biology makes it difficult to mediate how its parts are shared and re-shared (Pottage & Marris, 2012). As a result, the BioBricks Foundation, created in 2006, has developed tools such as BioBricks Public Agreement and OpenMTA, which facilitate access to synthetic biology parts as a public access resource, but impose no obligation on users to 'return' derivative products to the common pool. This is due, in part, to uncertainties as to the existing ownership status of parts, but also to a recognition that different forms of property may not only coexist in synthetic biology, but also contribute to mutual flourishing (Calvert, 2012; Pottage & Marris, 2012).

In terms of intellectual property rights, synthetic biology has been characterised as a tug-of-war between open and proprietary approaches. It may be that such dichotomy is not so clear, but rather that tools such as the BioBricks Public Agreement and OpenMTA are leading to a "diverse ecology" of both proprietary and open systems (Calvert, 2012; Grewal, 2017). Such a system may see a role for patents, particularly for more complex inventions. As explained in *Nature* through a Lego analogy, "the bricks would be free but a design for a complex rocket ship made of hundreds of Lego pieces would be patentable"(Nelson, 2014).

Intellectual property may also be one of the tools used to safeguard synthetic biology commons. As products of synthetic biology do not have copyright protection, it may be possible to create patent-based commons such as the one established by the group Biological Innovation for Open Society (BIOS). Cost may be a hindering factor (Kumar and Rai, 2006). *Sui generis* intellectual property systems may be developed, such as has been done for plant varieties, databases and – in some countries – traditional knowledge. Contracts may also be used to guarantee access to synthetic biology parts and – possibly after some time – to resulting products.

### 2.2.4 Access and benefit sharing

The CBD recognises that the sovereign rights of countries over natural resources extend to genetic resources, and access to such resources is subject to national authority and regulation. The Nagoya Protocol to the Convention on Biological Diversity affirms that these sovereign rights entail the right to regulate access to genetic resources and negotiate terms for the fair and equitable sharing of benefits from their utilisation. Both instruments recognise rights of holders of traditional knowledge associated with genetic resources to provide approval for and be involved in utilisation of such knowledge and to share in resulting benefits. These provisions are relevant to synthetic biology insofar as it is based on genetic resources accessed for their utilisation (UN CBD, 2015).

Under the Nagoya Protocol, access to genetic resources should be based on prior informed consent and mutually agreed terms, subject to legislative and regulatory requirements established by the countries where these resources are accessed. Many countries, including, for instance, the UK and Germany have decided not to introduce restrictions on access to their own resources, though, as described below, these countries have requirements on compliance with access rules in other countries. An increasing number of countries, however, have established national frameworks to regulate access to genetic resources within their territories.

Ownership of genetic resources is defined through national laws and regulations. Most countries that have introduced national frameworks for access and benefit sharing distinguish between biological resources, generally owned by private or public persons, and genetic resources, generally owned by the state [absch.cbd.int]. In some countries, such as in South Africa, the state is a trustee of biodiversity, but it does not have ownership over genetic resources, unless these resources occur in public land [South African National Environmental Management Biodiversity Act, 2004]. The landowner or local communities in South Africa own both the biological and genetic resources on their property. Nevertheless, bioprospecting in South Africa requires not only prior informed consent from the owner of the land where plant material is collected, but also the competent authorities, and benefits arising from utilisation of genetic resources are channelled through the state [South African National Environmental Management Biodiversity Act, 2004, art. 3, 81, 85]. In both cases, access to genetic resources is predicated on permits from competent authorities and agreements for sharing of benefits. These requirements would apply to genetic resources accessed for the purpose of synthetic biology.

The Nagoya Protocol aims at ensuring compliance with provider state requirements through corresponding user state obligations. User states are obligated to take “appropriate, effective and proportionate legislative, administrative or policy measures” to ensure that researchers utilising genetic resources within their jurisdiction have accessed them in accordance with the provider state requirements [art 15]. Such requirements also apply to synthetic biology involving genetic resources obtained from a provider state.

Disclosure requirements in patent law provide a mechanism for ensuring compliance with ABS regulations, by requiring patent applicants to disclose the origin of genetic resources on which the invention was based, facilitating confirmation that ABS procedures were followed. A 2017 study published by the World Intellectual Property Organization found that over 30 countries have established specific disclosure requirements related to genetic resources and/or traditional knowledge for patent applications (WIPO, 2017). For example, Article 26 of the Chinese Patent Law requires that the applicant for a patent on an invention-creation accomplished by relying on genetic resources indicate the direct and original source of the genetic resources. Under the Chinese Patent Law, patent rights may not be granted for inventions that are accomplished by relying on genetic resources that are obtained or used in violation of the provisions of laws and administrative regulations [Chinese Patent Law, art. 26].

There is an ongoing negotiation on a new international agreement on marine biodiversity in areas beyond national jurisdiction, including questions of sharing of benefits from genetic resources originating in the high seas or the deep seabed [UNGA Res. 72/249, 2017]. The implications of synthetic biology and associated tools such as digital sequence information have become part of the discussion.

Synthetic biology tools such as digital sequence information challenge ABS frameworks by impeding traceability, as discussed in Section 2.3.4. There are also questions of how to address benefit-sharing questions where inventions involve genetic elements from multiple organisms including organisms both within and beyond national jurisdiction, elements which are functionally identical in different organisms, and elements which are used in the research process but not found in the resulting invention (Bagley & Rai, 2013; Bagley, 2016). The global ABS mechanism is based on the premise that benefit sharing is an important incentive and source of funding for conservation. The challenges raised by synthetic biology could impact this intended contribution to conservation and sustainable use.

### 2.2.5 Indigenous, customary and religious frameworks

Statutory frameworks are not the only sources of law relevant for synthetic biology. Legally binding norms and authorities governing research and use of synthetic biology can derive from religious, indigenous or customary systems. Multiple legal and normative systems may overlap in the same geographical space, community or subject field (Figure 2.4; Meinzen-Dick & Pradhan, 2002). This legal pluralism is important for synthetic biology, as researchers, regulators and users of synthetic biology may be faced with a maze of legal rules from different sources. Failure to navigate these rules can result in violations that lead to conflict.

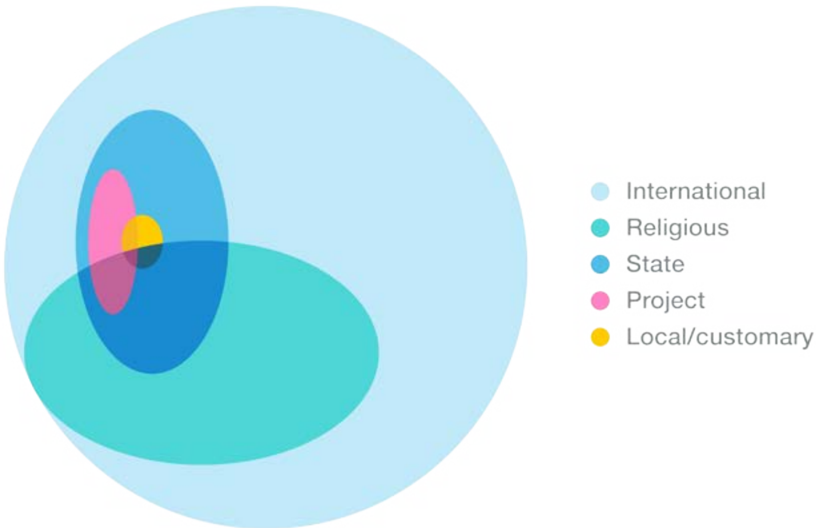


**Figure 2.4** Overlaps in normative systems. Adapted from Meinzen Dick and Pradhan, 2002.

Many countries formally recognise indigenous, customary or religious law as well as civil and common law in national legal systems. An IUCN analysis in 2011 found that 60 per cent of the world's countries have constitutional provisions relevant to customary law, ranging from provisions that protect cultural practices to provisions that define customary law and its legal weight (Cuskelly, 2011). In other countries, legal principles or norms from customary or religious systems can be incorporated into legislation. Indigenous or religious authorities can be legally granted exclusive or shared jurisdiction over specific territory or subject matter, or granted the right to participate in national decision making (Cuskelly, 2011). Even where non-statutory law is not formally recognised, it has legal weight within the communities and territories where it is practiced.

The CBD AHTEG has noted that customary law of indigenous peoples and local communities should be taken into account in implementing risk management measures for synthetic biology [CBD/SBSTTA/22/4, 2018, para. 47]. However, there have been few analyses of application of indigenous or customary law to synthetic biology or genetic engineering more broadly. Some of the most advanced research addresses Maori perspectives of synthetic biology and its products and processes. A recent report explored how moving genes between species, introduction of genes from non-native species, extraction of genetic material from an organism and other practices associated with synthetic biology would have direct implications for Maori values, concluding that there are differing positions and interpretations, and that the perceived potential benefits of the technology may vary according to the intended use of the techniques (Mead, Hudson & Chagne, 2017).

Several groups of indigenous peoples have developed formal statements and declarations on the topic of genetic technologies. Many of these assert the right to free, prior and informed consent for research relating to their biological resources, and restrict patenting of such resources (Mead & Ratuva, 2007). The Statement of Bioethics Consultation from the Tonga National Council of Churches establishes the principle that "scientific and commercial advances should not be allowed to proceed past the deliberations necessary to provide for their social, moral and ethical control" (Tonga National Council of Churches, 2001).

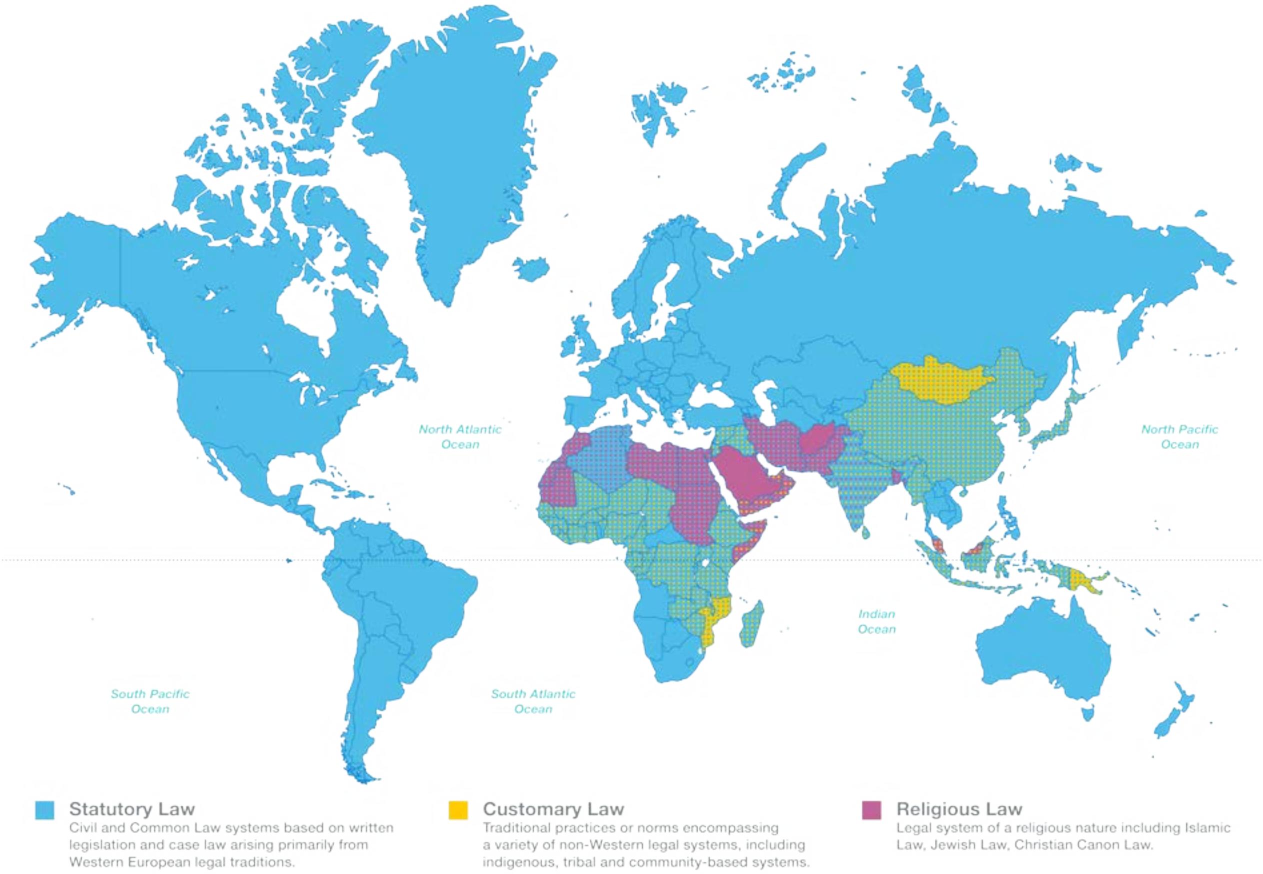


**Figure 2.5** World legal systems. Adapted from a map by the University of Ottawa.

There has been some examination of the interaction between customary law and intellectual property aspects of biotechnology. While traditional knowledge is legally protected under the Nagoya Protocol, in practice legal frameworks for ABS and patenting of genetic material focus on statutory law and may exclude customary legal systems relating to property rights and the status of genetic resources (Vermeylen, 2010).

Synthetic biology has spurred active discussion by religious legal experts, raising questions ranging from whether modern biotechnology amounts to "playing God" to whether laboratory meat can be considered kosher or halal (Dabrock, 2009; Gross, 2014). While these discussions influence ethical perspectives on synthetic biology, as discussed in Section 2.3.9, they also relate to applicability of religious law to synthetic biology and constitute a form of governance separate from the role they play in influencing governance under statutory structures. In his 2015 *Encyclical*, Laudato Si, Pope Francis called for "a broad, responsible, scientific and social debate" regarding genetic modification, which he characterised as a "complex environmental issue," recognising both the potential benefits and the ethical questions (Francis, 2015). In 2010, the Church of Scotland produced a report finding that "synthetic biology does not put humanity on a par with God," as synthetic biology techniques do not amount to "ex nihilo creation," but should be guided by humankind's special responsibility for the rest of creation under the doctrine of "Imago Dei" (Church of Scotland, 2010). The Catholic Commission of the Bishops' Conferences of the European Union (COMECE) issued an opinion on synthetic biology in 2016, also finding that synthetic biology techniques do not amount to "playing God" and recognising the potential benefits arising from synthetic biology while calling for appropriate governance measures and public participation (COMECE, 2016; Heavey, 2017). These documents do not constitute sources of binding canon law, but they do provide a sense of how the Catholic system may view synthetic biology activities and products.

Use of synthetic biology implicates religious law particularly in the context of food. Synthetic meat production could reduce land and water use, with positive benefits for conservation, but there are questions as to how such meat would fit into religious dietary systems (Wolinsky & Husted, 2015). Rabbis at Yeshiva University in Israel have argued that, depending on the circumstances, even artificial pig could be kosher, and could be eaten with dairy ([https://www.ynet.co.il/articles/0,7340,L-5185466,00.html]). Cultured meat could potentially also be halal, depending on the origin of the source cells and the medium used (Hamdan et al., 2018).

### 2.2.6 Governance by industry and communities of practice

Non-state actors can play an important role in regulating new technologies where the technologies develop rapidly, risks and benefits are uncertain, and there is a need for specialised knowledge (Abbot, 2012). In relation to synthetic biology, there is a growing body of standards created and imposed by industry, researchers and communities of practice. The emerging private sector of synthetic biology uses so-called 'soft' standards, which can facilitate norms and behaviour within the sector, and impact how synthetic biology is perceived by the society (Parks et al., 2017). The soft standards applied by the industry are not binding or legally enforced; instead they rely on personal values and are often 'borrowed' from other relevant standards and more established industries, such as biotechnology and genetic engineering.

Scientists working on engineered gene drive applications have had numerous conversations on self-governance and good practices for safe and responsible research. In 2015, prominent engineered gene drive researchers working on different projects published recommendations for safeguards to contained experiments of engineered gene drive (Akbari et al., 2015). There are ongoing attempts to organise a more formal coordination of researchers working on engineered gene drive technology. For example, the Foundation for the National Institutes of Health convenes the Gene Drive Research Consortium to discuss communication, safe testing and engagement in relation to gene drive technology (FINH, 2018a). The safety board of the International Genetically Engineered Machine (iGEM) international student competition has established a policy specifically discussing safety of their projects and developed a separate policy on work related to engineered gene drive systems and how to prevent accidental gene drive release. These guidelines were established after a team of students attempted to reproduce a scientific paper discussing engineered gene drive development, though discussion of an engineered gene drive policy preceded the incident (iGEM, 2017). The do-it-yourself biology community has developed a code of conduct, which generally draws from good practices applied by the scientific community (DIYbio, 2011).

The role of funding organisations is also important for the governance of research. In its report on gene drive the American National Academies of Sciences, Engineering and Medicine recommended several actions to the funders of research, including the need to collaborate with scientists and regulators to "to develop oversight structures to regularly review the state of gene drive science and its potential for misuse" [recommendation 8.7] (NASEM, 2016a). In addition, the Presidential Commission for the Study of Bioethical Issues established the responsibility of funders to promote some key principles for a responsible research and use of synthetic biology (Weiss, Gutmann and Wagner, 2010). In response to these calls, a number of organisations sponsoring or supporting gene drive research have agreed to a set of principles for responsible research (Emerson et al., 2017). Beyond the key principles, this forum of supporters and sponsors holds regular meetings to discuss key issues around gene drive research, including topics like data sharing, regulatory capacity, etc. (FINH, 2018b).

Several academies of sciences have been looking at synthetic biology or engineered gene drive, trying to establish some recommendations for researchers but also beyond this community proposing guidance for regulators, decision-making authorities and more generally the public (Table 1.1).

## 2.3 Governance challenges raised by synthetic biology and conservation

Synthetic biology challenges existing governance systems in many respects, of which only a few will be addressed here. New techniques of genetic modification and characteristics of novel organisms create questions relating to the applicability of existing regulations and the methodology of risk/benefit assessment. The potential intended and unintended spread of synthetic biology products, including engineered gene drive, raise challenges for mitigation, liability and compensation systems relating to transboundary harm. Tools and practices associated with synthetic biology, such as use of digital sequence information and the growing "Do-it-yourself Biology" (DIYbio) community, potentially undermine enforcement approaches predicated on monitoring, regulating and tracking genetic material and researchers. Different countries may have different levels of capacity to engage in synthetic biology research and provide effective regulatory frameworks and oversight. A multitude of social, ethical and practical concerns also surround synthetic biology, including the question of moral hazard and concern about sources of funding for research. Engaging with these questions and perspectives creates challenges of its own. There may be particular challenges for developing countries related to research and governance capacity.

### 2.3.1 Applicability of existing regulations to new techniques

There is a debate over whether existing regulations developed to manage genetic engineering are also applicable to new techniques of synthetic biology. This question goes to the heart of concerns that existing legislation is not adequate to address changing genetic technology. Many regulatory systems were developed for the paradigm of transfer of genetic material (DNA, RNA, etc.) between species – transgenesis. Such systems may not apply to mutagenesis – techniques for modifying the genome without introducing foreign DNA (Duensing et al., 2018). Engineered gene drives may fall into an area of regulatory ambiguity, uncertainty or even overlap – it may not be clear how they fit into existing frameworks addressing pest control, animal drugs, toxins or environmental protection (Oye et al., 2014).

As outlined above (see Section 2.2.1), in the EU, the definition of GMOs and thus the scope of regulatory oversight is very broad, but certain techniques are excluded if they "have conventionally been used in a number of applications and have a long safety record" [2001/18/EC]. Mutagenesis was initially classified as one of those techniques [2001/18/EC Art. 3 with Annex I]. In July 2018, the EU Court of Justice decided that while physical and chemical mutagenesis qualifies as having a sufficient safety record this is not so for new genome editing techniques. They are therefore not covered by the mutagenesis exemption [ECJ Case 528/16 paras 46–53]. This means that in the EU all new synthetic biology techniques involving transgenesis and non-physical and non-chemical mutagenesis are within the scope of the regulatory oversight. The EU legislator has the possibility to modify the exemptions and decide what applications of synthetic biology are safe enough to be listed as exempted techniques, or subject certain techniques to less stringent tools of oversight, such as prior notification or ex post monitoring and reporting instead of prior authorisation.

In the United States, certain synthetic biology products may not be covered by existing product-related legislation. The US Plant Protection Act, for instance, only covers plants if a plant pest, such as an agrobacterium, was used to introduce the genetic material. This would not cover new synthetic biology techniques which use CRISPR-Cas9 or other pathways to insert a gene or otherwise modify the organism (Bergeson *et al.*, 2015, 45). The US Department of Agriculture issued a statement in March 2018 that it would not regulate plants developed through genomic editing techniques which are indistinguishable from plants that could be developed through traditional breeding techniques ([https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/brs-news-and-information/2018_brs_news/pbi-details][https://www.usda.gov/media/press-releases/2018/03/28/secretary-perdue-issues-usda-statement-plant-breeding-innovation]).

Another example is the dengue transmitting mosquito *Aedes aegypti* into which a lethal gene was inserted that through reproduction could lead to a reduction in populations. The modified mosquito was initially determined to be covered by the US Federal Food, Drug and Cosmetic Act (FFDCA) as an animal drug, analogous to other drugs used for animal population control. However, unlike other such drugs, the mosquito was intended to be released in the wild and used for the purpose of addressing human disease, raising questions about the appropriateness of FDA jurisdiction (Bergeson *et al.*, 2015, 20). In 2017, the FDA announced that products "intended to function as pesticides by preventing, destroying, repelling, or mitigating mosquitoes for population control purposes" would not be considered "drugs" under the FFDCA, but would instead be regulated as "pesticides" by the EPA (FDA, 2017a). In 2018, the EPA opened public comment on an application for an experimental use permit for genetically engineered *Aedes aegypti* mosquitos ([https://www.epa.gov/pesticides/epa-reopens-public-comment-period-application-experimental-use-permit-combat-mosquitoes]).

In Japan, the Advisory Panel of GMOs of the Minister for the Environment has proposed that any product not categorised as genetically engineered under the Cartagena Protocol shall be exempted from the existing regulation. The Panel suggested that this would include any product created through genome editing that does not involve introduction of foreign nucleotides, such as deletions, as well as any product developed through introduction of material from species which could naturally cross with the host organism. The proposal is open for public comment and has not been formally adopted (USDA, 2018a).

In New Zealand in 2014, the Environmental Protection Authority decided that plants produced via gene editing methods, where no foreign DNA remained in the edited plant, would not be covered by GMO legislation. However, this decision was successfully appealed to the High Court, which overturned the decision on the basis that creating exceptions to the GMO regulations was a political decision and not within the power of the Authority [Sustainability Council v EPA, 2014, 69] (Kershen, 2015). In reaching its decision, the Court affirmed the applicability of the precautionary approach based on the scientific uncertainty related to environmental effects of rapid changes caused by the technology [Sustainability Council v EPA, 2014, 68]. Following this decision, all products of gene editing are currently captured within the scope of legislation in New Zealand (Fritsche et al., 2018).

A number of additional countries are currently considering what applications of genetic modification fall within the scope of risk assessment frameworks for GMOs. Chile, Brazil, Israel, Argentina and Australia, among others, have adopted or introduced regulations clarifying whether products of genome editing can be considered GMOs for the purpose of risk assessment regulation (Duensing *et al.*, 2018). In general, the likelihood of biotechnology products falling within the scope of existing regulation relates to the use of recombinant DNA and the degree of change to the host DNA sequence.

### 2.3.2 Risk/benefit assessment of novel organisms

Synthetic biology applications challenge existing risk assessment paradigms due to their potential to express novel traits, persist in the environment, and cross geographic and political boundaries (NASEM, 2016a). Existing risk assessment paradigms for genetically engineered organisms have largely been developed and used to assess the risks from two novel traits in plants: insect resistance and herbicide tolerance. Novel synthetic biology and gene drive applications will have traits that differ quite drastically from these. While the overarching risk assessment process may not change, specific steps within risk assessment will need to be tailored to these new applications. Decisions will have to be made concerning how to change risk assessment approaches to adequately assess the potential harm caused by organisms that have not previously existed (NASEM, 2016a; Hayes et al., 2018). New concerns may arise, for example relating to the uncertainty and difficulty of conducting a complete environmental risk assessment without environmental release. Furthermore, the values-laden judgments inherent to the risk assessment process (Section 3.4.3) will receive extra scrutiny, given the novel and controversial nature of synthetic biology (Stirling, Hayes & Delborne, 2018; Thompson, 2018).

A major characteristic of risk assessment for traditional GMOs is the familiarity or comparison approach. This has been described as a "comparison of the characteristics of the GMO(s) with those of the non-modified organism under corresponding conditions of the release or use" and is intended to help identify "the particular potential adverse effects arising from the genetic modification" [Directive 2001/18/EC Annex II sec. B. 1st indent and sec. C. 2.1]. There are suggestions that the comparison with parental and/or non-modified organisms loses validity where synthetic biology does not only marginally modify an organism but can create essentially new ones (Winter, 2016b). A proposed alternative to the comparison approach is use of a set of tests following a step-by-step and case-by-case approach to information generation before the release of the modified or new organism is approved (see above Section 2.2.1.3).

Applications of synthetic biology can create irreversible effects. In some cases, as in use of engineered gene drives to eradicate a species from a certain habitat, irreversibility could be seen as part of the intent. There have been calls for development of effective reversal drives as part of regulatory requirements for engineered gene drives (Oye et al., 2014). Such risk management measures could provide a means to address indirect or unintended environmental impacts, but even if effective, they would not address intended impacts. Moreover, permanent damage could be caused before the reversal drive reached all members of the population (Esvelt et al., 2014).

### 2.3.3 Transboundary movement

International and national law have established mechanisms for managing transboundary movement of genetically modified organisms and potentially hazardous substances as well as principles for addressing transboundary harm (see Section 2.1.2). To some extent these existing structures provide a framework applicable to transboundary impacts of synthetic biology. However, certain applications of synthetic biology, including engineered gene drive systems, create questions related to coverage and implementation of these frameworks.

Two types of transboundary movements can be envisaged when considering synthetic biology: unintended and intended. Some applications of synthetic biology focus on particular geographies, contained within country borders. This is the case for applications against invasive species that intend to suppress those species locally but are not intended to have such effect on a global scale. If those applications were to be moved across borders, it would be an unintended or illegal transboundary movement [for definitions of unintended or illegal transboundary movement, refer to Decision VIII/16 of the Cartagena Protocol on Biosafety and its annex Operational definitions of the terms "unintentional transboundary movement" and "illegal transboundary movement"]. This could happen through natural dispersal of modified individuals, or through human transport (intentional or unintentional). For unintended transboundary movement, there are existing governance frameworks. Under Article 17, the Cartagena Protocol requires countries to notify other countries that might be affected by an unintentional transboundary movement that may have an adverse effect on biodiversity.

Another set of the technologies, approaches and tools are intended to move across boundaries. For example, the vector control applications of engineered gene drive for malaria (see Chapter 6) are intended to address vector movement across different countries, as this would be an important factor for success. Several recent reports looking at engineered gene drive for malaria control have raised the importance of regional approaches (James et al., 2018), or coordination and communication between neighbouring countries (NASEM, 2016a). The Cartagena Protocol requires states from whose territory organisms are intentionally moved across borders to obtain advance informed agreement from the importing state. However, this provision was developed in the context of transboundary import and export, and it is not clear how it applies to intended or anticipated spread of modifications across borders (NASEM, 2016a).

Transboundary damage can create particular problems for compensation or restitution. The Supplementary Protocol applies to damage resulting from both intentional and unintentional transboundary movement as well as illegal transboundary movement, and requires Parties to mandate response measures in the event of damage [Arts 3, 5]. However, the application of civil liability in the event of transboundary damage is largely left to be determined under domestic law. This can raise questions relating to proving causality and quantifying harm, particularly where the modified organism does not cause direct economic or environmental damage.

These issues are in some ways analogous to the governance of biological control agents. In that context, they have been addressed through discussion and harmonisation of measures at the regional level (Bateman, Sulaiman & Ginting, 2014). The African Union has started looking at regional harmonisation around the possible use of engineered gene drive for malaria control (NEPAD, 2018).

In addition to the regulatory question, the potential of intended or unintended transboundary movement raises challenges for stakeholder engagement, to ensure that public consultation can be carried out at the appropriate level.

### 2.3.4 Digital sequence information

The growing use of genetic information derived from digital sequencing in synthetic biology creates uncertainty for access and benefit-sharing regimes (see Section 6.6.1 for a description of technological advances in digital sequence information). There have been numerous studies examining the impact digital sequence information and synthetic biology may have on access and benefit-sharing agreements around genetic material (Bagley & Rai, 2014; Bagley, 2016; Welch et al., 2017; Wynberg & Laird, 2018b; *see also* Table 1.1).

At the CBD, where "genetic resources" were primarily envisioned and defined as genetic material, a process is now underway to respond to the potential implications of the use of digital sequence information on CBD objectives [CBD COP13 Decision 16; COP14/L.36].

An *ad hoc* technical expert group on digital sequence information on genetic resources was established to consider the potential implications of the use of digital sequence information on genetic resources for the CBD.

Submissions from countries and other stakeholders to the CBD expert group show the range of perspectives on considering digital sequence information "genetic resources." For certain non-governmental organisations, such as the Third World Network, not regulating such information under the CBD could "economically and culturally undermine indigenous peoples and local communities, thereby negatively impacting the conservation and sustainable use of biodiversity." They point to the use of synthetic biology to produce vanilla and vetiver as examples of the potentially disruptive impact on farmers and other local actors (AHTEG, 2018b). For research organisations such as the UK Natural History Museum, Royal Botanic Gardens Kew, and Royal Botanic Gardens Edinburgh, there are potentially negative implications in regulating access to digital sequence information. They highlight the value of digital sequence data in the public domain for biodiversity conservation and sustainable management and the impracticability of asking open-access international databases to regulate the use of digital sequence data. It is also put forth that the current mechanism for sharing digital sequence information might already be considered the equivalent of a global multilateral benefit-sharing mechanism (AHTEG, 2018a). Some researchers have argued that including digital sequence information under the Nagoya Protocol would create a global damper on research(Kupferschmidt, 2018).

A scoping study commissioned by the CBD found that the use of information on genetic resources, including in synthetic biology, could create opportunities for new forms of non-monetary and monetary benefit-sharing (Wynberg & Laird, 2018). At the same time, the study noted the risk that access to digital sequence information would allow researchers to look at the genetic or biochemical composition of genetic resources without having to physically access the resources themselves, which could undermine existing approaches to access and benefit sharing.

If the genetic information is deemed to fall within the scope of "genetic resources" in the CBD, the challenge will be defining whether and how the principle of sovereignty over genetic resources and the system of access and benefit-sharing based on this principle can address these vastly different dynamics. In his book on genetic resources as natural information, Ruiz (2015) notes that: "Inasmuch as information constituents can be stripped from their physical medium in biological samples, attempting to institutionalize controls over the flow of information, disembodied at different moments, by different actors, and in different places, is not only impossible but absurd." Ruiz advocates a conceptual framework for ABS based on the economics of information, as well as an alternative mechanism for ABS that is multilateral, non-contractual and focused on fairness and equity in the sharing of monetary benefits. Such a multilateral benefit-sharing mechanism is possible under Article 10 of the Nagoya Protocol. In discussions under this article, at least one country – Argentina – has noted that a global multilateral mechanism may be useful for the use of digital sequence information (SBI, 2018).

The evolving technological, legal and institutional context surrounding the exchange and use of digital sequence information (DSI) for synthetic biology and genomic research may affect access to ABS frameworks under the ITPGRFA (Welch et al., 2017). The availability of sequence data through decentralised data libraries and organisations may challenge the multilateral system set up by the ITPGRFA (Welch et al., 2017). Other factors including partial sequence combinations, and the fact that the same sequence may occur in multiple organisms create further questions for ABS (Welch et al., 2017).

### 2.3.5 "Do-it-yourself" (DIY) biology

The tools associated with synthetic biology are becoming increasingly accessible to private actors, including actors who may not have the backing of an established institution. This raises governance questions as well as some public concern (Charo & Greely, 2015). Many of these concerns may be based on an inaccurate understanding of the activities and capabilities of community laboratories (Kuiken, 2016). However, as with any decentralised activity, the DIY aspects of synthetic biology research create certain challenges to traditional models of governance.

One concern centres on safety. DIY biologists may not be held to the same standards of safety as formally trained biologists (Garrett, 2013). In some jurisdictions, licensing requirements on laboratory biologists, including training in safety and ethics, may not apply to community laboratories (Kolodziejczyk, 2017). However, in Germany and other countries in Europe, community laboratories, like other laboratories, need licenses to undertake experiments involving genetic engineering (Seyfried, Pei & Schmidt, 2014). In all countries, biosafety regulations and risk assessment and management procedures covering synthetic biology activities – including requirements relating to notification, authorisation, containment, transfer and monitoring – would apply to DIY biologists as well as formal labs. The DIY biology community has also developed its own safety standards (Guan et al., 2013) as discussed above, and continues to evaluate their effectiveness and develop additional resources associated with biosafety and biosecurity (Yassif, 2017).

Where they are held to the same or similar licensing standards as formal laboratories, community laboratories will also be required to obtain insurance. In some countries, such as Tanzania, all operators engaging in activities involving genetic modification are required to carry insurance [Tanzania Biosafety Regulations, 2009, § 35(1)]. In other countries, DIY biologists operating outside an institutional setting may not have explicit insurance requirements, though many of the labs may carry this type of insurance regardless. This creates a potential problem if something does go wrong, as community biologists may not have the resources to cover costs of compensation or remediation.

As DIY biology becomes more accessible to users not associated with a particular institution, this may raise challenges for enforcement of biosafety and environmental regulations against actors with bad intent. While the community's own regulations may support safe practices among well intentioned operators, informal or illegal operators with bad intent may be difficult to identify and hold liable (Garrett, 2013). However, there are still limits on the capability of community laboratories to create organisms that would cause significant environmental damage, and to date there has been no evidence of attempts or intent to do so (Lentzos, 2016).

Much of the concern around DIYbio centres relates to questions of biosecurity. These questions are outside the scope of this assessment, though there has been some thinking in the biosecurity context that could be relevant to governance of DIYbio to prevent environmental impacts. Kelle (2009) proposes a “5P” strategy that outlines five points of intervention for managing risks: principal investigator, project, premises, provider (of genetic material) and purchaser. At each of these points, measures ranging from awareness raising and education to industry codes of conduct to national and international laws and regulation could be used to prevent misuse (Kelle, 2009).

An issue hardly discussed is the application of ABS regulations to DIY biology. Any rules user states may have established to ensure compliance with pertinent provider state regulation also apply to DIY synthetic biologists. But DIY biologists may not be aware of this, and it could be difficult for user state authorities to supervise their research and development in termsof ABS.

### 2.3.6 Research and governance capacity

Emerging economies represent significant potential markets and research centres for synthetic biology as well as providers of genetic material that may be used. However, capacity varies across jurisdictions, with implications for both research and governance.

In emerging economies, research capacities across disciplines and departments with regards to synthetic biology are underdeveloped. Developing and upgrading research and development facilities represents significant capital investment. There is consensus that emerging economies require support in this regard [Cartagena Protocol art. 22] but the form and nature of capacity needed is still unclear. Advanced applications require advanced skills and capital which can delay synthetic biology development and the deployment process. The African Union recognises the need for strengthening the capacity on the continent in order to harness the potential benefits of these developments while being able to ensure that those are co-developed with African scientists (African Union, 2018). Recent growth in digital innovation in Africa and Asia indicate potential for technological entrepreneurship. In 2018, teams from Uganda, Egypt, Singapore and Pakistan, among others, participated in the International Genetically Engineered Machine Championship (iGEM.org).

Emerging economies also represent potential markets for synthetic biology applications and products. Certain types of technology may be nationally or regionally prioritised based on context and needs (African Union, 2018). In Africa for instance, production of synthetic biofuels may have immediate environmental, social and economic benefits (Stafford et al., 2018).
There is evidence of gaps in legal frameworks and capacity for regulatory oversight in many developing countries. Few countries have enacted biosafety laws that could act as reference points for synthetic biology development and diffusion (Figure 2.1). Of significance is the lack of or inadequate provisions for post-release phases. Governments also faced the challenge of balancing a precautionary approach with the potential economic benefits of synthetic biology applications (Kingiri & Hall, 2012).

Reduced technical and regulatory capacity made worse by porous national and regional borders raise questions of biosafety and potential misuse of synthetic biology. There have been calls for harmonisation of biosafety- and trade-related policies with clear guidelines for deployment of synthetic biology applications and products at respective national levels to enhance responsible and productive synthetic biology piloting, products release, monitoring and surveillance (Escaler et al., 2012).

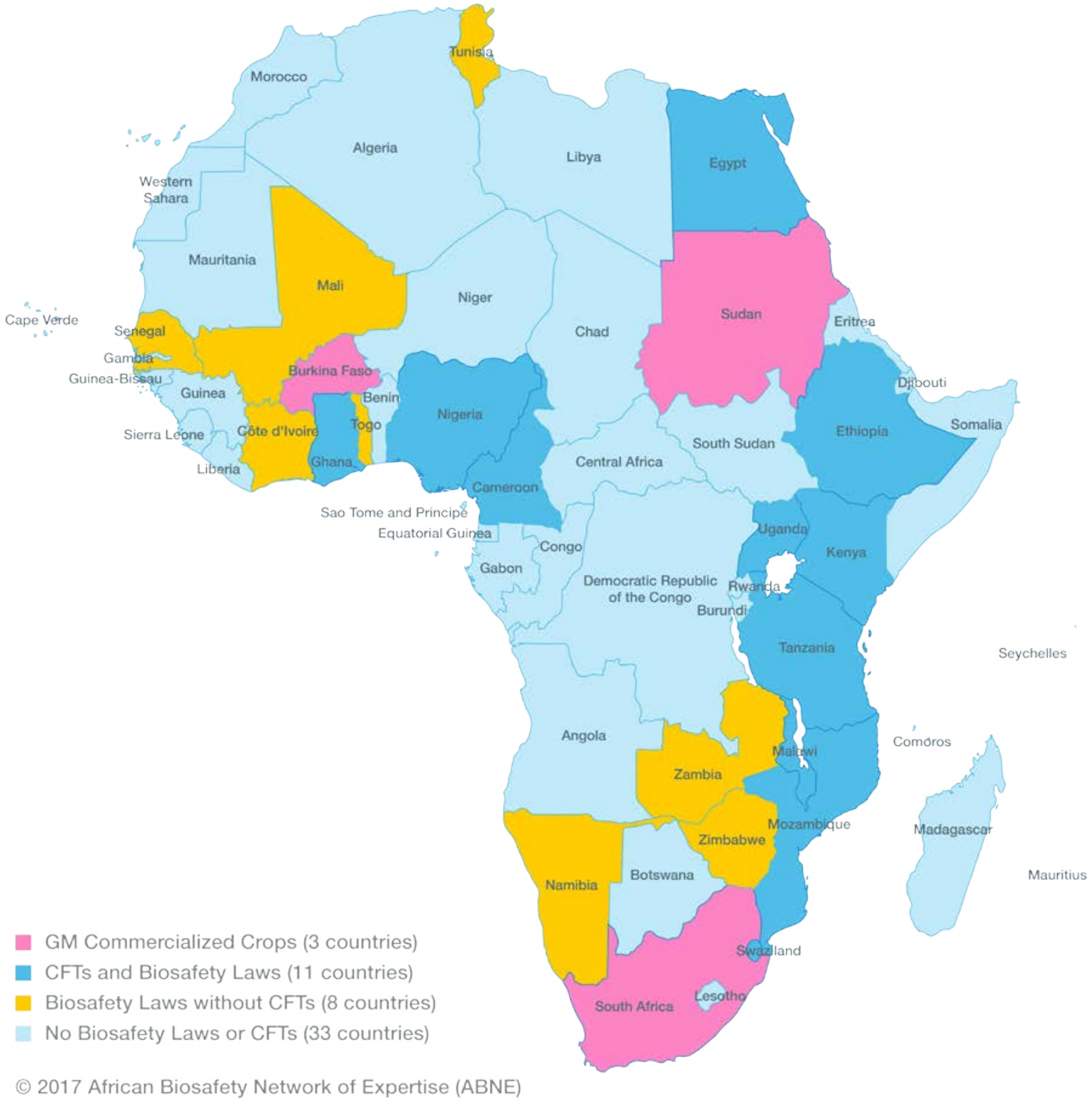


**Figure 2.6** Biosafety Laws in Africa. Adapted from a graphic by the African Biosafety Network of Expertise.

### 2.3.7 Funding and financial flows

The funding sources and financial flows associated with synthetic biology (Section 1.6) have influenced the discourse around governance. Availability and access to funding drives innovation. While some private organisations, such as the Gates Foundation-funded Target Malaria project, fund work pursuing the safe and effective use of engineered gene drive systems, most funding comes from public sources.

In Europe, funding for synthetic biology has primarily come from public funding organisations such as the Swiss National Science Foundation, UK Research Councils and the Netherlands Organisation for Scientific Research (Pei, Gaisser & Schmidt, 2012). In the United States, there are few publicly funded research programmes outside military programmes, such as the US DARPA Safe Genes Program (DARPA, 2018d). Before 2008, the US federal government invested relatively small amounts in synthetic biology. By 2014, it had invested approximately US$ 819 million in synthetic biology research (WWC, 2015). Since 2012, the majority of that funding came from Department of Defense initiatives (see Chapter 1). A recent exception is approximately US$ 2 million from the US Department of Agriculture's National Institute of Food and Agriculture (NIFA) for research on the implications of gene edited technologies, including one project explicitly focused on engineered gene drive systems in agriculture (USDA, 2018b).

There have been calls for increased funding for research into ethical, legal and social issues relating to synthetic biology. A 2012 review of European public funding organisations showed that where such funding is available, there can be problems in linking funding opportunities with the research community (Pei et al., 2012).

Concerns have been raised about synthetic biology funding patterns, partly regarding the agenda behind the funding, and the purpose, or alternate purposes, to which the technology and its applications might be used (Lentzos, 2015; Kuiken, 2017; Reeves et al., 2018). Concerns range from the power funders have to determine the trajectory of research to problems of conflict of interest in scientific research, whereby the objectivity of researchers is compromised – or perceived to be compromised – by sources of funding or other institutional commitments (Krimsky, 2004, 2013). In addition, synthetic biology's technical and institutional connections to agricultural biotechnology create discursive links to critiques of the political economy of first-generation genetically-modified organisms (Charles, 2001; Schurman, Kelso and Kelso, 2003; Worthy et al., 2005; Kleinman & Vallas, 2006; Delborne, 2008; Kinchy, 2012). As such, concerns have been raised that synthetic biology will benefit private over public interests, continue enclosures of genetic commons through aggressive intellectual property practices, concentrate power in the hands of elites, and undermine more holistic and traditional approaches to sustainability (e.g. ETC Group, 2018). More research is required to understand where and under what conditions these concerns may actualise, and how to prevent them from doing so (Pottage, 2006; Calvert, 2008; Lawson & Adhikari, 2018).

### 2.3.8 Moral hazard

Synthetic biology creates a fundamental challenge for risk assessment and conservation governance more broadly in the form of what is called moral hazard. "Moral hazard" means that new technologies may correct the symptoms of, and provide an excuse not to address, more fundamental socio-political failures which caused the symptoms in the first place. For example, climate change caused by increased emissions of greenhouse gases into the atmosphere is projected to cause changing weather patterns including increased droughts potentially affecting food production. Fundamental change would require that emissions are drastically reduced. Moral hazard occurs if new technologies, such as drought-resistant crops, create excuses for decision makers not to implement mitigation policies to prevent droughts. In this example, even if synthetic biology can lessen the severity of certain consequences from climate change-induced droughts, the vast number of consequences caused by such droughts simply cannot be addressed through synthetic biology alone – the fundamental problem needs to be addressed. The same applies to engineered gene drive technology. If applied as a means of nature conservation it may foster a vision that traditional habitat and species protection can be replaced by just making species and habitats resilient to new stresses.

### 2.3.9 Engaging with multiple perspectives and ethics

As has been highlighted in Chapter 1, there are a number of ethical questions raised by synthetic biology. Ethics are value systems that shape the perception, assessment and management of a technology. Ethics also shape governance systems in multiple ways. Many governance systems are based on norms and concepts deriving from ethics. Ethical considerations are behind calls for limits on certain applications of synthetic biology, such as use of gene editing on human beings, which can influence national and international law (e.g. Convention on Human Rights and Biomedicine of the Council of Europe; Grubb, 1994). Ethical considerations will influence the scrutiny of risk assessment, the determination of acceptable risk, and the weighing of benefits and risks in decision making related to synthetic biology research and introduction into the environment.

There is wide recognition that ethical arguments are important to take into consideration when considering synthetic biology applications and they need to be clearly framed when responding to the concerns of different cultural traditions and political orientations within and between particular communities or regions (Winter, 2016a; Zetterberg & Edvardsson Björnberg, 2017). The ethical debate about science and technology is often done in absolute terms at a given time, but increased experience and exposure can change perspectives, sometimes in favour of technology and sometimes against it (UNESCO, 2015). The diversity of moral perspectives and values inform decision making, but also creates a challenge for regulation.

Scientists themselves have questioned their practice in response to ethics with normative instruments such as the UNESCO World Conference on Science Declaration on Science and the Use of Scientific Knowledge [1999] that calls for responsible science and its interaction with society's values. Synthetic biology researchers are becoming increasingly cognisant of the ethics and value-based discussion about synthetic biology and how its potential application as well as the research itself can question values in society. This recognition has been translated to action with the integration of "ethical, legal and social implications" (ELSI) into research networks and programmes (Synbiosafe, 2018) and a growing interaction between ELSI experts and synthetic biology researchers (DARPA, 2018d).

Even in the absence of guidelines or regulatory requirements, researchers and scientific associations drawing on field experience and literature argue that transparency and openness are the foundation for ethical engagement (Esvelt et al., 2014; NASEM, 2016a; Resnik, 2018). They agree that engagement should ensure that evidence and uncertainties about both potential risks and benefits are shared with the public.

Engagement also needs to be responsive to input and information received from stakeholders. The Royal Society dialogue on gene editing (Van Mil, Hopkins & Kinsella, 2017) showed the importance for stakeholders of ensuring the engagement was not a box-ticking exercise and was going to be taken into consideration by policy makers (Van Mil, Hopkins & Kinsella, 2017). Organisations such as LEAP Synthetic Biology made calls to use deliberative dialogues to ensure that communities' perspectives would be taken into consideration seriously during policy-making processes (Ritterson, 2012).

While the dialogue might enable discussion of different values, perspectives and understanding of evidences, researchers recognise that it is important to build mutual understanding in order to achieve a meaningful dialogue (UNESCO, 2015). Practitioners also recognise the need for a structured and continuous engagement and the establishment of clearer engagement pathways (NASEM, 2016a).

Although researchers' commitment to engagement is critical, it is not sufficient. There is also a need for national governance mechanisms to provide guidelines about the remits and scope of the engagement and of stakeholders' participation in decision making so that engagement can be aligned (NASEM, 2016a). While there are existing guidelines for public consultation (EFSA, 2018), there have been criticisms from concerned NGOs and scholars about bias in engagement, particularly where it is undertaken by the proponent of the technology, as well as limited identification of who is entitled to give consent and how consent is sought (Unknown, 2014; Bäckstrand et al., 2010).