Chapter 5:
The International Governance of Engineered Gene Drives

As set out in the first chapter, recent advances in molecular biology include the development of *synthetic gene drives*, which make it possible to quickly disseminate genetic modifications to populations of wild species.[1] Research into these techniques is justified, *inter alia*, by the potential to obtain a long sought-after tool to control infectious diseases.[2] However, others have warned that releases of engineered gene drives could be irreversible and could have major effects on ecosystems or human health on a transboundary or even global level.[3]

The present chapter[4] assesses the current debate on the regulation of gene drive techniques in international law. The most relevant treaties in this context are the *Convention on Biological Diversity* (CBD)[5] and its *Cartagena Protocol on Biosafety*.[6] In 2018, the parties to the CBD adopted a first substantive decision on the issue of engineered gene drives (A.). While the decision is not legally binding in a formal sense, it still has a normative effect as 'soft law' (B.). This is also because the decision does not stipulate new obligations but rather confirms the applicability of already-existing

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1 See chapter 1, section C.

2 Cf. *Stephanie James* et al., Pathway to Deployment of Gene Drive Mosquitoes as a Potential Biocontrol Tool for Elimination of Malaria in Sub-Saharan Africa: Recommendations of a Scientific Working Group, 98 (2018) Am. J. Trop. Med. Hyg. 1; *Austin Burt* et al., Gene Drive to Reduce Malaria Transmission in Sub-Saharan Africa, 5 (2018) Journal of Responsible Innovation S80.

3 Cf. *John M. Marshall*, The Cartagena Protocol and Genetically Modified Mosquitoes, 28 (2010) Nature Biotech. 896, 896; *Kenneth A. Oye* et al., Regulating Gene Drives, 345 (2014) Science 626; *Kevin M. Esvelt/Neil J. Gemmell*, Conservation Demands Safe Gene Drive, 15 (2017) PLOS Biology e2003850; *Virginie Courtier-Orgogozo* et al., Agricultural Pest Control with CRISPR-based Gene Drive, 18 (2017) EMBO Reports 878.

4 Parts of earlier versions of this chapter were contributed to an unpublished study on gene drives by *R. Guy Reeves* et al. (2020), which was commissioned by the German *Bundestag*. The chapter was substantially revised thereafter.

5 Convention on Biological Diversity (05 June 1992; effective 29 December 1993), 1760 UNTS 79.

6 Cartagena Protocol on Biosafety to the Convention on Biological Diversity (29 January 2000; effective 11 September 2003), 2226 UNTS 208; see chapter 3, section A.

rules and principles on gene drives (C.). However, the decision does not address potential transboundary spreads (D.).

A. The Development of COP Decision 14/19

Due to its near-universal membership,[7] the *Conference of Parties* (COP) to the CBD has emerged as the principal forum for discussing the regulation of gene drives at the global level.[8] However, parties to the CBD have been deeply divided over whether engineered gene drives should be developed at all, and if so, whether their release into the environment should be allowed.[9]

In the context of the CBD, the issue of engineered gene drives has been part of a broader discussion about the international regulation of *synthetic biology*.[10] In 2014, COP 12 established an *Ad Hoc Technical Expert Group* (AHTEG) on this issue,[11] which defined the term 'synthetic biology' as

> *'a further development and new dimension of modern biotechnology that combines science, technology and engineering to facilitate and accelerate the understanding, design, redesign, manufacture and/or modification of genetic materials, living organisms and biological systems.'*[12]

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7 See chapter 3, section B.

8 See *Natalie Kofler* et al., Editing Nature: Local Roots of Global Governance, 362 (2018) Science 527, 527; *Hung-En Lai* et al., Synthetic Biology and the United Nations, 37 (2019) Trends in Biotechnology 1146; *Heidi J. Mitchell/Detlef Bartsch*, Regulation of GM Organisms for Invasive Species Control, 7 (2020) Front. Bioeng. & Biotechnol. 927, 4.

9 See *Jesse L. Reynolds*, Governing New Biotechnologies for Biodiversity Conservation: Gene Drives, International Law, and Emerging Politics, 20 (2020) Global Environmental Politics 28; *Florian Rabitz*, Gene Drives and the International Biodiversity Regime, 28 (2019) RECIEL 339.

10 For an overview, see *Felicity Keiper/Ana Atanassova*, Regulation of Synthetic Biology: Developments Under the Convention on Biological Diversity and Its Protocols, 8 (2020) Front. Bioeng. & Biotechnol. 310.

11 CBD COP, Decision XII/24. New and Emerging Issues: Synthetic Biology, UN Doc. UNEP/CBD/COP/DEC/XII/24 (2014), para. 4.

12 AHTEG on Synthetic Biology, Report of the Ad Hoc Technical Expert Group on Synthetic Biology: Montreal, Canada, 21–25 September 2015, UN Doc. UNEP/CBD/SYNBIO/AHTEG/2015/1/3 (2015), para. 24. The definition was formally acknowledged by the states parties in CBD COP, Decision XIII/17. Synthetic Biology, UN Doc. CBD/COP/DEC/XIII/17 (2016), para. 4.

In its decision of 2014, the COP also adopted a first set of principles on the use of synthetic biology.[13] Parties were urged to take a precautionary approach and to

> *'establish, or have in place, effective risk assessment and management procedures and/or regulatory systems to regulate environmental release [sic!] of any organisms, components or products resulting from synthetic biology techniques'.*[14]

In this regard, the decision explicitly referred to Article 3 CBD, which enshrines the obligation of states to ensure that activities within their jurisdiction or control do not cause transboundary harm.[15] Moreover, the decision called upon governments to approve field trials of organisms resulting from synthetic biology only after appropriate risk assessments have been carried out in accordance with national, regional and/or international frameworks.[16]

Two years later, at COP 13 in 2016, the parties to the CBD reiterated these principles and noted that they 'can also apply to some living modified organisms containing gene drives'.[17] At the same time, they rejected language that would have urged parties to 'obtain consent from other governments whose biodiversity could be affected by any proposed gene drive before approval of its release'.[18] The meeting also rejected a moratorium on the further development of gene drives,[19] which was called for by some parties and non-governmental organizations (NGOs).[20]

In the lead-up to COP 14 in 2018, the members of the CBD's *Subsidiary Body on Scientific, Technical and Technological Advice* (SBSTTA) disagreed

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13 CBD COP, Decision XII/24 (n. 11).
14 *Ibid.*, para. 3(a).
15 *Ibid.*
16 *Ibid.*, paras. 3(b) and (c).
17 CBD COP, Decision XIII/17 (2016) (n. 12), para. 2.
18 Cf. CBD COP, Synthetic Biology: Draft Decision Submitted by the Chair of Working Group II, UN Doc. UNEP/CBD/COP/13/WG.2/CRP.22 (2016), para. 2.
19 IISD, Summary of the UN Biodiversity Conference: 2–17 December 2016, ENB Vol. 9 No. 678 (2016), 17; *Ewen Callaway*, 'Gene Drive' Moratorium Shot Down at UN Biodiversity Meeting, Nature News (21 December 2016), available at: http://www.nature.com/news/gene-drive-moratorium-shot-down-at-un-biodiversity-meeting-1.21216 (last accessed 28 May 2022).
20 See SynBioWatch, Common Call for a Global Moratorium on Genetically-Engineered Gene Drives (05 December 2016), available at: http://www.synbiowatch.org/gene-drives/gene-drives-moratorium/?lores (last accessed 28 May 2022).

on whether states should be called upon to apply a precautionary approach with regard to the release of gene drives or whether they should be called to refrain from such releases altogether.[21] At the COP meeting, some states parties and a number of NGO representatives again demanded a moratorium, although this time no longer on the development of gene drives but only on their release.[22] Other parties and NGOs opposed a moratorium, arguing that the technique should not be abandoned before its potential costs and benefits could be fully evaluated.[23] After controversial negotiations,[24] the parties adopted decision 14/19, which recognises that

> *'as there could be potential adverse effects arising from organisms containing engineered gene drives, before these organisms are considered for release into the environment, research and analysis are needed, and specific guidance may be useful, to support case-by-case risk assessment'.*[25]

The decision also 'calls upon' upon parties and other governments[26] to apply a precautionary approach, and to

> *'only consider introducing organisms containing engineered gene drives into the environment, including for experimental releases and research and development purposes, when:*

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21 CBD SBSTTA, Recommendation 22/3. Synthetic Biology, UN Doc. CBD/SBSTTA/REC/22/3 (2018), para. 10; see *Reynolds* (n. 9), 36–40.

22 Cf. SynBioWatch, A Call to Protect Food Systems from Genetic Extinction Technology: The Global Food and Agriculture Movement Says No to Release of Gene Drives (16 October 2018), available at: http://www.etcgroup.org/sites/www.etcgroup.org/files/files/etc_ftfsignonletter113018engweb_1.pdf (last accessed 28 May 2022); European Parliament, Resolution on the 15th Meeting of the Conference of Parties (COP15) To the Convention on Biological Diversity, P9_TA(2020)0015 (2020), para. 13; IISD, UN Biodiversity Conference Highlights: Sunday, 18 November 2018, ENB Vol. 9 No. 716 (2018), 2.

23 Cf. IISD (n. 22), 2; Outreach Network for Gene Drive Research, Open Letter: Research on Gene Drive Technology Can Benefit Conservation and Public Health (14 November 2018), available at: https://genedrivenetwork.org/open-letter (last accessed 28 May 2022); Royal Society, Gene Drive Research: Why It Matters (2018).

24 See IISD, Summary of the UN Biodiversity Conference: 13–29 November 2018, ENB Vol. 9 No. 725 (2018), 16–17; *Natalie Kofler*, Gene Drives: Yelling Match Drowns Out Marginalized Voices, 565 (2019) Nature 25.

25 CBD COP, Decision 14/19. Synthetic Biology, UN Doc. CBD/COP/DEC/14/19 (2018), para. 9.

26 This refers to governments of states not party to the CBD, namely the United States and the Holy See.

> *(a) Scientifically sound case-by-case risk assessments have been carried out,*
> *(b) Risk management measures are in place to avoid or minimise potential adverse effects, as appropriate;*
> *(c) Where appropriate, the "prior and informed consent", the "free, prior and informed consent" or "approval and involvement" of potentially affected indigenous peoples and local communities is sought or obtained, where applicable in accordance with national circumstances and legislation'.*[27]

Regarding the issue of contained use, the decision calls to develop and implement measures to prevent or minimise potential adverse effects from exposing the environment to organisms, components, and products of synthetic biology in contained use.[28]

B. Legal Status of COP Decision 14/19

COP decision 14/19 lays down specific principles for the research of gene drives techniques and spells out concrete preconditions that shall be met before engineered gene drives are released, even experimentally. Before further exploring the meaning and consequences of this decision, it ought first to be determined whether, and in which way, states are bound to it.

I. Functions of COP Decisions

The Conference of the Parties is an organ established by the CBD[29] in which all parties are represented and which is mandated to adopt decisions relating to the operation and further development of the treaty.[30] The COP is charged to 'keep under review the implementation' of the CBD and, to this end, may adopt and amend protocols and annexes.[31] It may also establish procedures and subsidiary bodies carrying out specific functions.[32]

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27 CBD COP, Decision 14/19 (n. 25), para. 11.
28 *Ibid.*, para. 12.
29 Article 23 CBD.
30 *Ibid.*; cf. *Jutta Brunnée*, COPing with Consent: Law-Making Under Multilateral Environmental Agreements, 15 (2002) Leiden J. Int'l L. 1, 16.
31 Articles 23(4)(c)-(f) CBD.
32 Articles 18(3), 20(2), 21(1), 23(2), 23(4)(a), 23(4)(b), 23(4)(g) CBD.

The COP usually meets biannually.[33] It also serves as the 'meeting of the Parties' (MOP)[34] to the protocols adopted under the auspices of the CBD, including the Cartagena Protocol[35] and its Supplementary Protocol on Redress and Liability.[36]

With regard to their legal nature, decisions adopted by the COP can be classified into three categories.[37] In some aspects, primarily concerning matters of internal governance, the COP is mandated by the CBD to adopt decisions that have direct legal effect.[38] The second category concerns the adoption of protocols and annexes to the CBD as well as amendments to these instruments and the CBD itself.[39] Such additions or amendments are first decided upon by the COP and must subsequently be ratified by the parties concerned to become legally binding upon them.[40]

The third category includes decisions on matters concerning the CBD and its implementation, which are not expressly assigned a legal status. Pursuant to Article 23(4)(j) CBD, the range of these decisions comprises 'any additional action that may be required for the achievement of the purposes of this Convention in the light of experience gained in its operation'. Hence, these decisions often address new or persisting challenges to the implementation of the CBD.[41]

Insofar as analysed here, decision 14/19 belongs to the third of the aforementioned categories, since it neither addresses matters of internal governance nor adopts changes to the treaty text.[42]

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33 CBD COP, Rules of Procedure for the Conference of the Parties, UN Doc. UNEP/CBD/COP/DEC/I/1 (1995), Rule 4(1).

34 The difference in name between COP and MOP does not indicate a substantive difference in function; see *Robin R. Churchill/Geir Ulfstein*, Autonomous Institutional Arrangements in Multilateral Environmental Agreements: A Little-Noticed Phenomenon in International Law, 94 (2000) AJIL 623, 629–630.

35 Cf. Article 29 Cartagena Protocol.

36 Cf. Article 14 Supplementary Protocol, which provides that the CBD COP, serving as the MOP to the Cartagena Protocol, shall serve as the meeting of the Parties to the Supplementary Protocol.

37 Similar typologies have been proposed by *Churchill/Ulfstein* (n. 34), 626; *Brunnée* (n. 30), 15–33.

38 See, e.g., Articles 23(3), 24(2), and 28(3) CBD.

39 See *supra* n. 32.

40 Cf. Articles 29(4), 30(3) CBD.

41 All decisions adopted by the CBD COP are available at https://www.cbd.int/cop/.

42 But see CBD COP, Decision 14/19 (n. 25), paras. 14–15, extending the mandate of subsidiary bodies, and *ibid.*, paras. 17–18, requesting the Executive Secretary and a subsidiary body to gather additional information. These parts of the decision concern self-governance and thus belong to the first category.

II. COP Decisions as 'Soft Law'

Unlike some other multilateral environmental agreements (MEAs), the CBD does not provide for the adoption of binding 'secondary law' by the COP that creates new obligations for the parties or extends existing ones.[43] Hence, except for the relatively rare cases of decisions in the first and second categories mentioned above – internal governance and the adoption or amendment of treaty provisions – decisions adopted by the COP are not legally binding upon the parties to the CBD. However, this does not mean that such decisions have no normative effect. Instead, it is widely acknowledged that decisions adopted by COPs of MEAs exert some form of normative influence concerning the obligations of their parties and can be seen, as argued here, as international 'soft law'.[44]

Two reasons justify this assumption. First, COP decisions are usually adopted by consensus.[45] The Rules of Procedure, which govern the conduct of meetings of the CBD COP,[46] provide that every effort shall be made to reach a consensus on all matters of substance.[47] Only if all efforts to reach consensus have been exhausted may decisions be taken by a two-thirds majority.[48] Thus, despite the lack of formal ratification, every COP decision is carried by the (at least implied[49]) consent of all parties. If a state agrees to a COP decision but later rejects or negates its content, it acts at least in a self-contradictory manner and may even face accusations of *bad faith*.[50]

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43 See, e.g., Montreal Protocol on Substances that Deplete the Ozone Layer (16 September 1987; effective 01 January 1989), 1522 UNTS 3, as last amended by the Meeting of Parties in 2018, Article 2(9); for further examples, see *Churchill/Ulfstein* (n. 34), 638–641.

44 See, e.g., *Churchill/Ulfstein* (n. 34); *Brunnée* (n. 30); *Annecoos Wiersema*, The New International Law-Makers? Conferences of the Parties to Multilateral Environmental Agreements, 31 (2008) Mich. J. Int'l L. 231; *Daniel Bodansky*, Thirty Years Later: Top Ten Developments in International Environmental Law (2020) Yearbook of International Environmental Law 1, 12–13.

45 *Churchill/Ulfstein* (n. 34), 642–643.

46 Cf. Article 23(3) CBD.

47 Cf. CBD COP Rules of Procedure (n. 33), Rule 40.

48 Cf. *ibid.*

49 In practice, many parties are not actively taking part in negotiations, but are represented through 'blocks' of states with mutual or (supposedly) congruent interests. In the negotiations on decision 14/19, relevant blocks were the European Union and an 'African Group', see IISD (n. 24), 16–17.

50 Cf. *Hartmut Hillgenberg*, A Fresh Look at Soft Law, 10 (1999) European Journal of International Law 499, 505–506; *Daniel Thürer*, Soft Law, in: Wolfrum/Peters

The second reason why COP decisions have normative force is closely related to the first. To reach a consensus, decisions are often negotiated in great detail and intensity.[51] Especially the 'operative clauses', which express the intent of the parties, are of fundamental importance for the normative effect of a decision: When a decision 'invites' or 'encourages' certain action, it implies a lower degree of expectation that parties will actually comply than when a decision 'urges' states to adhere to or refrain from a particular conduct.[52] As a result, the wording of decisions and resolutions is often negotiated with the same commitment and vigour as that of binding treaties or protocols.[53]

For these reasons, although decisions and declarations adopted by consensus are – except for the aforementioned first and second categories – not legally binding in a formal sense, they still have a 'de facto' normative power that influences the conduct of states and is therefore often characterized as 'soft law'.[54] In addition, decisions adopted by COPs to multilateral treaties stand in the specific context of the respective treaty and therefore closely relate to the 'hard law' provisions of that treaty. Consequently, it can be argued that COP decisions have the effect of 'thickening' the treaty obligations by adding to its text through interpretation and guidance.[55] Depending on the circumstances, COP decisions could even be regarded as subsequent practice by the parties to the treaty, which, pursuant to Article 31(3) of the *Vienna Convention on the Law of Treaties* (VCLT),[56] shall be taken into account when interpreting the treaty.[57] On

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(ed.), MPEPIL, MN. 26–27; also see *Thomas Cottier/Jörg P. Müller*, Estoppel, in: Wolfrum/Peters (ed.), MPEPIL, MN. 12.

51 In the context of the UN climate change negotiations, see *Antto Vihma*, Climate of Consensus: Managing Decision Making in the UN Climate Change Negotiations, 24 (2015) RECIEL 58.

52 Cf. *Wiersema* (n. 44), 253–254; also see University of Joensuu et al., Multilateral Environmental Agreement Negotiator's Handbook (2nd ed. 2007), 3.67 – 3.71.

53 See *Brunnée* (n. 30), 7–15.

54 *Hillgenberg* (n. 50), 514–515; *Brunnée* (n. 30), 51; also see *Silja Vöneky*, Recht, Moral und Ethik (2012), 383 et seq.; but see *Wiersema* (n. 44), 261–264, arguing that the tripartite notion of hard law, soft law, and non-law was insufficient to capture the legal significance of COP decisions.

55 *Wiersema* (n. 44), 245.

56 Vienna Convention on the Law of Treaties (23 May 1969; effective 27 January 1980), 1155 UNTS 331.

57 Cf. *Churchill/Ulfstein* (n. 34), 641; *Wiersema* (n. 44), 278; see ILC, Draft Conclusions on Subsequent Agreements and Subsequent Practice in Relation to the Interpretation of Treaties, with Commentaries (2018), UN Doc. A/73/10, p. 12, Conclusion 11 and Commentary thereto.

the other hand, even a consensus decision may mask remaining substantive disagreements, which is why the circumstances of its adoption and the text of the decision must be carefully analysed.[58]

III. Soft Law Status of Decision 14/19 for Parties to the CBD

Coming back to decision 14/19, it can be concluded that it represents 'soft law' in the aforementioned sense. Not only was it adopted by the parties to the CBD by consensus.[59] The fact that parties were 'called upon'[60] – and not merely 'invited' or 'encouraged'[61] – to observe the stated principles indicates that there is indeed a mutual expectation that the parties will adhere to the decision. At the same time, parties were not 'urged', which would have indicated an even higher level of commitment.[62]

IV. Effect on Non-Parties

The provisions of decision 14/19 not only address the 'parties' to the CBD but also 'other Governments'.[63] This refers to the governments of non-parties to the CBD, namely the United States and the Holy See.[64] Although these governments attend the CBD COP as observers,[65] they do not formally participate in its decision-making. Therefore, the above conclusions about the decision's 'soft law' status do not apply with regard to the United States. Nevertheless, the decision is a clear political call of the international community to the United States, where a significant

58 *Brunnée* (n. 30), 41 and fn. 204.
59 See CBD COP, Report of the Conference of the Parties to the Convention on Biological Diversity on Its Fourteenth Meeting, UN Doc. CBD/COP/14/14 (2019), para. 399. While the report does not expressly state that the decision was carried by consensus, the exception of a majority vote would have been noted.
60 Cf. CBD COP, Decision 14/19 (n. 25), paras. 11–12.
61 See, e.g., CBD COP, Decision XIII/17 (2016) (n. 12), paras. 8–9.
62 See, e.g., CBD COP, Decision XII/24 (n. 11), para. 3; on this provision, see *infra* section C.I.
63 CBD COP, Decision 14/19 (n. 25), paras. 11–12.
64 See *supra* n. 7.
65 Cf. Article 23(5) CBD and Rule 6 of the CBD COP Rules of Procedure (n. 33). The United States regularly participate in the meetings of the CBD COP and its subsidiary bodies, and also make interventions from time to time.

share of the world's research on gene drives takes place,[66] to observe the adopted principles.

C. Substance, Context, and Consequences of COP Decision 14/19

The quasi-normative status of decision 14/19 is supported by the fact that it does not introduce new concepts and rules, but rather applies principles to gene drives that are already established in international (environmental) law.[67] First, states are called to apply a precautionary approach (I.). Then, the decision sets out three conditions that shall be met before any environmental release of engineered gene drives is 'considered' (II.). Finally, the decision calls for effective containment standards while engineered gene drives are still under development in the laboratory (III.).

I. Precautionary Approach (or Principle)

Decision 14/19 calls upon parties and other governments,

> *'taking into account the current uncertainties regarding engineered gene drives, to apply a precautionary approach, in accordance with the objectives of the Convention'.*[68]

According to its Article 1, the objectives of the CBD are the conservation of biological diversity, the sustainable use of its components, and fair benefit-sharing with regard to genetic resources. An iteration of the precautionary principle is laid down in the preamble to the CBD, which notes that

> *'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 minimise such a threat'.*[69]

Although the preambles of international treaties do not have the function of laying down legal obligations, they often reiterate already-established

66 See *Kelsey L. Warmbrod* et al., Gene Drives: Pursuing Opportunities, Minimizing Risk (2020), 51; *Reynolds* (n. 9), 40–41.
67 CBD COP, Decision 14/19 (n. 25), paras. 11–12.
68 *Ibid.*, para. 11.
69 Cf. Preamble to the CBD, recital 9.

principles or rules of custom and also serve as 'context' that must be taken into account when interpreting the treaty pursuant to Article 31(2) VCLT.[70] In this way, preambles may become legally binding, especially when they are cast in clear and specific terms.[71]

1. References to Precaution in Earlier COP Decisions

A footnote to the term 'precautionary approach' in COP decision 14/19 refers to an earlier decision on synthetic biology adopted by COP 13 in 2016.[72] This decision, in turn, refers to two decisions adopted in 2012[73] and 2014[74], which had already urged parties and other governments to take a precautionary approach with regard to synthetic biology and gene drives. In this context, the decisions also referred to Article 3 of the CBD, which enshrines the obligation to prevent transboundary harm,[75] and to Article 14, which requires the parties to the CBD to minimize adverse impacts on biodiversity, including through environmental impact assessments of proposed projects that may have such impacts.[76]

Taken together, the decisions leave no doubt that the parties to the CBD view the precautionary approach as an essential guardrail in regulating engineered gene drives.

2. Early Deployment of Gene Drives as a Precautionary Measure?

According to some scholars, the precautionary approach may not unambiguously militate *against* the release of engineered gene drives in situations of scientific uncertainty. It has been argued that it could also be inter-

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70 Cf. *Makane M. Mbengue*, Preamble, in: Wolfrum/Peters (ed.), MPEPIL.

71 *Ibid.*, MN. 11–13; see ICJ, Rights of Nationals of the United States of America in Morocco (France v. United States of America), Judgment of 17 August 1952, ICJ Rep. 176, 183–184.

72 CBD COP, Decision XIII/17 (2016) (n. 12).

73 CBD COP, Decision XI/11. New and Emerging Issues Relating to the Conservation and Sustainable Use of Biodiversity, UN Doc. UNEP/CBD/COP/DEC/XI/11 (2012), para. 4.

74 CBD COP, Decision XII/24 (n. 11), para. 3.

75 Cf. *ibid.*

76 Cf. CBD COP, Decision XI/11 (n. 73), para. 4. On the restrictive interpretation of this provision by the ICJ, see chapter 3, section B.VI.1.

preted as *permitting* such releases to mitigate biodiversity loss caused by other factors, such as invasive alien species.[77] According to this reading, the lack of scientific certainty about the environmental impacts of engineered gene drives should not be used as a reason to postpone their deployment for reducing harmful impacts on biological diversity from other sources.[78]

However, this interpretation is based on a misconception of the precautionary approach.[79] The principle refers to scientific uncertainty not in relation to the potential hazards of mitigation measures, but to the causes of biodiversity loss or other forms of environmental degradation that shall be mitigated.[80] The precautionary principle can, therefore, not be invoked to justify hazardous measures simply because they are motivated by the mitigation of harm resulting from other causes.

No different result follows from the wording of the precautionary approach in the *Rio Declaration*, which provides that scientific uncertainty shall not be used as a reason for postponing 'cost-effective measures to prevent environmental degradation'.[81] In particular, it cannot be inferred from this wording that the use of engineered gene drives may be acceptable despite scientific uncertainty but simply because they are potentially cheaper than conventional biocontrol measures.[82] The precautionary approach does not require using the *most cost-effective* measure to prevent environmental degradation. All the less can it be invoked to justify hazardous measures that are (allegedly) more cost-effective than others.

This reading is also supported by the aforementioned COP decisions, which show that the parties to the CBD understand the precautionary principle as calling for restraint in the use of gene drive techniques rather than their premature deployment.

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77 Cf. *Rabitz* (n. 9), 343; also see *Tina Rulli*, CRISPR and the Ethics of Gene Drive in Mosquitoes, in: David Boonin (ed.), The Palgrave Handbook of Philosophy and Public Policy (2018) 509, 511–513.

78 *Rabitz* (n. 9), 343–344.

79 On the misconceptions and (philosophical) dilemmas involved when the precautionary principle is used to choose among different policy options, see *Daniel Steel*, Philosophy and the Precautionary Principle (2015), 17–43.

80 See *Lyle Glowka* et al., A Guide to the Convention on Biological Diversity (1994), 11, who argue that the precautionary principle could place a burden on those who propose a new project to prove it will not significantly reduce or cause significant loss of biological diversity.

81 Cf. Rio Declaration on Environment and Development (14 June 1992), UN Doc. A/CONF.151/26/Rev.1 (Vol. I), Principle 15.

82 But see *Rabitz* (n. 9), 346.

3. Assessment

As noted above, decision 14/19 not only calls upon states to take a precautionary approach but, in the same paragraph, also sets out conditions for potential environmental releases.[83] These conditions can be construed as describing specific manifestations of precaution in the context of engineered gene drives.[84] At the same time, they show that there is a – at least theoretical – pathway to releases consistent with the precautionary approach. Consequently, it cannot be assumed that the precautionary principle does, by itself, result in a general prohibition of releasing engineered gene drives into the environment.

II. Preconditions for Environmental Releases of Engineered Gene Drives

After referring to the precautionary principle, decision 14/19 calls upon parties and other governments 'to only consider introducing organisms containing engineered gene drives into the environment' when three given criteria are met.[85] First, a scientifically sound case-by-case risk assessment must have been carried out (1.). Second, risk management measures must be in place to avoid or minimize potential adverse effects (2.). Third, the prior and informed consent of potentially affected indigenous peoples and local communities must have been sought and obtained, where required (3.). These criteria also apply to experimental releases as well as releases for research and development purposes.[86]

1. Scientifically Sound Case-by-Case Risk Assessment

The first condition for environmental releases of engineered gene drives is that 'scientifically sound case-by-case risk assessments have been carried

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83 Cf. CBD COP, Decision 14/19 (n. 25), para. 11; see the following section.

84 A similar approach has also been used in earlier COP decisions on genetic use restriction technologies in agriculture, see CBD COP, Decision V/5. Agricultural Biological Diversity: Review of Phase I of the Programme of Work and Adoption of a Multi-Year Work Programme, UN Doc. UNEP/CBD/COP/5/23, p. 74 (2000), para. 23.

85 CBD COP, Decision 14/19 (n. 25), para. 11.

86 *Ibid.*

out'.[87] This reiterates an obligation that is already established in international law (a)). In the context of the CBD, risk assessment was primarily addressed in the framework of the Cartagena Protocol (b)).

a) Status of the Obligation Under International Law

It was already shown above that states are obliged to carry out environmental impact or risk assessments of LMOs that may have adverse effects on biodiversity. Article 14(1)(a) CBD provides that parties shall 'introduce appropriate procedures requiring environmental impact assessment' of projects likely to have significant adverse effects on biodiversity.[88] According to Articles 10(1) and 15 of the Cartagena Protocol, a 'scientifically sound' risk assessment is a necessary part of the *Advance Informed Agreement* procedure that applies prior to intentional transboundary movements of LMOs.[89] Annex III to the Cartagena Protocol establishes methodological standards for carrying out such assessments.[90] In addition to these treaty law provisions, the duty to carry out an environmental impact assessment before authorizing hazardous activities that may have adverse transboundary effects is also part of universal customary international law.[91]

Consequently, by requiring risk assessments, the decision merely restates an obligation that is already binding upon states as 'hard law'. However, it also clarifies that this obligation applies to all releases of engineered gene drives, and thus regardless of whether there are specific indications of a risk to biodiversity in an individual case.

b) The Cartagena Protocol's AHTEG on Risk Assessment

Within the CBD framework, the issue of risk assessment was predominantly addressed by the meeting of the parties to the Cartagena Protocol (COP-MOP). In 2008, COP-MOP 4 established a dedicated *Ad Hoc Technical Experts Group (AHTEG) on Risk Assessment and Risk Management*,[92] which is

87 *Ibid.*
88 See chapter 3, section B.VI.1.
89 See chapter 3, section A.II.1.c).
90 See *ibid.*
91 See chapter 4, section D.II.
92 Note that the AHTEG on Risk Assessment discussed here should not be confused with the AHTEG on Synthetic Biology discussed in *supra* section A.

composed of experts nominated by the parties.[93] The AHTEG developed a guidance document on risk assessment and monitoring of LMOs (aa)). Recently, it considered the need for additional guidance on risk assessments of LMOs containing engineered gene drives (bb)).

aa) Guidance on Risk Assessment and Monitoring of LMOs

By request of the parties to the Cartagena Protocol, the AHTEG on Risk Assessment developed a 'Guidance' on the risk assessment and monitoring of LMOs, which was completed in 2016.[94] The Guidance consists of three parts. The first part contains a general 'roadmap' for assessing the risks of LMOs, which elaborates, *inter alia*, individual steps of the assessment process set out in Annex III to the Cartagena Protocol.[95] The second part contains guidelines for assessing the risks of specific types of LMOs, including a chapter on living modified (LM) mosquitoes that act as disease vectors.[96] The third part contains guidelines for monitoring LMOs once released into the environment.[97]

The chapter on risk assessment of LM mosquitoes addresses various approaches of using biotechnology to reduce the transmission of vector-borne human pathogens.[98] It begins by introducing different techniques, including population suppression and population replacement strategies, such as engineered gene drives.[99] Subsequently, the chapter discusses a range of potential problems and concerns, including potential unintended effects of LM mosquitoes on biodiversity, vertical and horizontal gene transfer, and evolutionary responses in target species or pathogens.[100] With regard to unintentional transboundary movements, the chapter notes that mosquitoes have a very broad geographical distribution, and describes the risk of dispersal due to anthropogenic activities, such as transport and

93 CP COP-MOP, Decision BS-IV/11. Risk Assessment and Risk Management, UN Doc. UNEP/CBD/BS/COP-MOP/4/18, p. 80 (2008), para. 4.
94 AHTEG on Risk Assessment, Guidance on Risk Assessment of Living Modified Organisms and Monitoring in the Context of Risk Assessment, UN Doc. UNEP/CBD/BS/COP-MOP/8/8/Add.1, Annex (2016).
95 *Ibid.*, 8–51.
96 *Ibid.*, 52–94.
97 *Ibid.*, 95–112.
98 *Ibid.*, 80–94.
99 *Ibid.*, 80–83; see chapter 1, section C.III.1.
100 *Ibid.*, 84–90.

trade of potential breeding sites.[101] Finally, the chapter discusses potential risk management and containment strategies.[102]

The value of the Guidance has been controversial, particularly regarding the 'roadmap' contained in the first chapter.[103] Criticism was also voiced about the composition of the AHTEG, which allegedly lacked experts with actual experience in conducting risk assessments of LMOs.[104] Moreover, the process was criticised for attempting to merge irreconcilable points of view, including on many non-technical issues, which allegedly resulted in political negotiations on the contents of a technical document.[105]

Consequently, the roadmap was criticized for not reflecting the process usually followed during risk assessments, therefore being neither practical nor useful.[106] Yet, in a survey on the utility of the Guidance, many governments with little or no experience in conducting risk assessments of LMOs stated that they actually found the roadmap to be useful and practical as well as consistent with the Cartagena Protocol.[107] Governments with more experience in conducting risk assessments were more hesitant to agree with these conclusions.[108] This could be explained by the quality of the Guidance, but also by the fact that these governments simply saw no need for further advice on their already-established procedures.

In a decision adopted by COP-MOP 8 in 2016, the parties to the Cartagena Protocol 'took note' of the Guidance.[109] They described it as a 'voluntary tool' while acknowledging that other guidance documents and national approaches could also assist in conducting risk assessments in accordance with the Protocol.[110] Notably, the decision did neither 'welcome'

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101 *Ibid.*, 91; see *Marshall* (n. 3), 896.

102 AHTEG on Risk Assessment, Guidance on Risk Assessment and Monitoring of LMOs (n. 94), 91–94.

103 See *Helmut Gaugitsch*, Under the Cartagena Protocol on Biosafety – Where Is the Roadmap for Risk Assessment Taking Us?, 3 (2015) Front. Bioeng. & Biotechnol. 212, 2; *Karen E. Hokanson*, When Policy Meets Practice: The Dilemma for Guidance on Risk Assessment Under the Cartagena Protocol on Biosafety, 7 (2019) Front. Bioeng. & Biotechnol. 82, 2.

104 *Hokanson* (n. 103), 5; also see *Keiper/Atanassova* (n. 10), 18.

105 *Hokanson* (n. 103), 10.

106 *Ibid.*, 16.

107 *Ibid.*, 11–15; cf. CBD Secretariat, Analysis of the Results of the Testing of the "Guidance on Risk Assessment of Living Modified Organisms", UN Doc. UNEP/CBD/BS/COP-MOP/7/INF/3 (2014).

108 Cf. *Hokanson* (n. 103), 11–15.

109 CP COP-MOP, Decision VIII/12. Risk Assessment and Risk Management, UN Doc. CBD/CP/MOP/DEC/VIII/12 (2016), para. 2.

110 *Ibid.*, para. 3.

nor 'endorse' the Guidance, which are terms commonly used in COP decisions approving reports.[111] Consequently, in light of the aforementioned criteria,[112] the Guidance is neither legally binding nor constitutes quasi-normative 'soft law'. It is even doubtful whether the document provides a real added value to states seeking to improve their risk assessment procedures. A better approach would be to encourage bilateral partnerships where experienced governments assist others in need of support.[113]

bb) Additional Guidance on Risk Assessment of Engineered Gene Drives

In 2015, even before concluding its work on the general guidance document, the AHTEG recommended developing additional guidance on the risk assessment of LMOs developed through synthetic biology.[114] An outline of potential issues to be covered by such a document notes that gene drives could pose serious threats to human health and ecosystems.[115] It argues that existing risk assessment methodologies may need to be adapted to fully reflect these potential adverse effects.[116]

At COP-MOP 9 in 2018, parties had diverging views about the need to develop additional guidance on specific questions of risk assessment, including gene drives.[117] As a compromise, it was decided to launch a process to identify and prioritise specific issues on which further guidance should be developed.[118] The CBD Secretariat[119] was requested to commis-

111 Cf. University of Joensuu et al. (n. 52), p. 3–71; see CBD COP, Decision 14/19 (n. 25), para. 1, which 'welcomes' the outcomes of the AHTEG on Synthetic Biology.
112 See *supra* section B.II.
113 *Hokanson* (n. 103), 17.
114 AHTEG on Risk Assessment, Report of the Ad Hoc Technical Expert Group on Risk Assessment and Risk Management, Brasilia, 16–20 November 2015, UN Doc. UNEP/CBD/BS/RARM/AHTEG/2015/1/4 (2015), para. 37.
115 AHTEG on Risk Assessment, Outline of Guidance on Risk Assessment of Living Modified Organisms Developed Through Synthetic Biology, UN Doc. UNEP/CBD/BS/COP-MOP/8/8/Add.3, Annex (2016), 4.
116 *Ibid.*
117 Cf. CP COP-MOP, Decision 9/13. Risk Assessment and Risk Management (Articles 15 and 16), UN Doc. CBD/CP/MOP/DEC/9/13 (2018), para. 2.
118 *Ibid.*, para. 6.
119 According to Article 31(1) of the Cartagena Protocol, the Secretariat established by Article 24 CBD shall also serve as the secretariat to the Protocol.

sion a study informing this process,[120] which was subsequently prepared by a private contractor.[121]

The study noted that various aspects essentially distinguish engineered gene drive-bearing organisms from other LMOs.[122] It held that these differences involve methodological challenges that will likely render the risk assessment of such organisms more detailed and more complex than assessments of conventional LMOs.[123] Traditional risk assessment techniques, such as 'stepwise' releases, could not be applied since the smallest scale introduction of an LMO with a low-threshold gene drive could result in a spread and thus permanently impact the environment.[124] The study also noted the potential of cross-border dissemination. While this was assumed to be a characteristic of the host organism rather than the gene drive technique itself, the fact that most applications currently under development target non-domesticated species meant that there would be little to no possibility of preventing transboundary movements.[125]

Based on the study, the AHTEG concluded in April 2020 that additional guidance for the risk assessment of LMOs containing engineered gene drives should be developed.[126] This was endorsed in March 2022 by the Subsidiary Body on Scientific, Technical and Technological Advice,[127] which unlike the AHTEGs is a standing body under the CBD.[128] The draft COP decision envisages renewing the mandate of the AHTEG on Risk Assessment and asking it to develop 'additional voluntary guidance materials for conducting case-by-case risk assessments of living modified organisms containing engineered gene drives in accordance with annex III of the [Cartagena] Protocol', with a special focus to be placed on

120 CP COP-MOP Decision 9/13 (2018) (n. 117), para. 11.
121 *Greet Smets/Patrick Rüdelsheim*, Study on Risk Assessment: Application of Annex I of Decision CP 9/13 to Living Modified Organisms Containing Engineered Gene Drives, UN Doc. CBD/CP/RA/AHTEG/2020/1/4, Annex (2020).
122 *Ibid.*, 31.
123 *Ibid.*, 31–32.
124 *Ibid.*, 32; also see *Keiper/Atanassova* (n. 10), 15.
125 *Smets/Rüdelsheim* (n. 121), 33.
126 AHTEG on Risk Assessment, Report of the Ad Hoc Technical Expert Group on Risk Assessment, UN Doc. CBD/CP/RA/AHTEG/2020/1/5 (2020), Annex I, para. 42.
127 CBD SBSTTA, Recommendation 24/5. Risk Assessment and Risk Management, UN Doc. CBD/SBSTTA/REC/24/5 (2022), para. 5.
128 Cf. Article 25 CBD.

engineered gene drive mosquitoes and existing national and regional risk management experiences.[129]

It appears likely that the COP will follow this recommendation at its next face-to-face meeting.[130] However, the experience of developing the 'general' guidance document on risk assessment discussed above shows that the usual format and composition of the AHTEGs may hinder a clear separation between scientific advice and political negotiations. Parties should keep in mind the mandate of the Cartagena Protocol, which is primarily to regulate transboundary movements of LMOs. The potential of engineered gene drives to spread across borders is undisputed.[131] Therefore, any additional guidance should focus on how this potential can be adequately considered in pre-release risk assessments.

c) Assessment

Insofar as decision 14/19 makes releases of engineered gene drive contingent upon scientifically sound risk assessments, it only restates an obligation firmly anchored in international environmental law. However, as shown above,[132] the scope and methodologies of such assessments are much less regulated. Therefore, the efforts of the AHTEG on risk assessment to develop further guidance on how to conduct risk assessments of LMOs are laudable. At the same time, it seems that this standard-setting effort is welcomed only half-heartedly by those states that already have well-established procedures for assessing the risks of biotechnology products. Future work on risk assessment of gene drives should, therefore, focus on the challenges to which all frameworks must be adapted, especially potential transboundary spreads.

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129 CBD SBSTTA (n. 127), Annex, para. 1(d).

130 CBD COP 15 was was originally scheduled to take place in October 2020 in Kunming, China, but its face-to-face segment was postponed several times due to the COVID-19 pandemic. As of May 2022, the conference is scheduled for the third quarter of 2022; see CBD Secretariat, Calendar of SCBD Meetings (25 May 2022), available at: https://www.cbd.int/meetings/ (last accessed 28 May 2022).

131 See *infra* section D.

132 See chapter 4, section D.II.

2. Appropriate Risk Management Measures

The second condition for releases of organisms containing engineered gene drives set out in COP decision 14/19 is that 'appropriate risk management measures are in place to avoid or minimise potential adverse effects, as appropriate'.[133]

Again, this restates an already-existing obligation of states under international law (a)). A number of risk management strategies for gene drives have already been proposed, which could be relevant because states must use the 'best available techniques' to prevent damage (b)).

a) Status of the Obligation Under International Law

Like the obligation to carry out risk assessments, the obligation to apply appropriate risk management measures is already established in international law. Article 8(g) CBD provides that states must regulate, manage or control the risks associated with the release of LMOs.[134] Article 16 of the Cartagena Protocol further specifies this obligation by providing, *inter alia*, that states shall prevent unintentional transboundary movements.[135] In customary international law, risk management is inherent in the general obligation to act with due diligence to prevent transboundary harm. This entails a duty to use the 'best available technologies' to prevent such damage.[136]

b) Proposed Risk Management Strategies for Gene Drives as 'Best Available Techniques'?

The risk management measures required in a particular case will largely depend on the result of the risk assessment in that case. However, a number of general risk management strategies for gene drives have already been proposed, which could arguably contribute to an emerging 'best available technology' (BAT) standard. These include a 'stepwise' approach

133 CBD COP, Decision 14/19 (n. 25), para. 11(b).
134 See chapter 3, section B.III.
135 See chapter 3, section A.II.2.a)cc).
136 See chapter 4, section D.III.

to the deployment of gene drives (aa)) and the use of self-limiting gene drives (bb)).

aa) Phased Pathway to the Deployment of Gene Drives

Several authors and governmental as well as non-governmental organizations have proposed a 'phased pathway' or 'stepwise approach' to releasing engineered gene drives into the environment. According to these concepts, a gene drive would first be tested in cage trials and confined releases before being deployed on a larger scale.[137] It has been argued that the generation of release-relevant data requires a gradual reduction of the containment in order to expose the gene drive to increasingly realistic conditions.[138] The experience and data gained during the preceding steps would be used as a basis for risk assessment of the following, less confined step.[139] Moreover, the development of approaches that fail to fulfil pre-defined criteria on efficacy and safety could be terminated.[140]

These proposals have, however, faced strong opposition. The main contention against 'phased' testing pathways is that even confined releases could be irreversible and lead to an uncontrolled spread of the gene drives, especially when low-threshold, invasive drive systems are released.[141] Consequently, it has been argued that 'semi-field testing' in outdoor cages or under environmental confinement should not be considered as contained use but as an environmental release.[142]

The stepwise approach was also controversial within the AHTEG on Synthetic Biology. While some experts noted that a stepwise approach could be appropriate to gather the information needed to fill knowledge gaps, others warned that any environmental release could be irre-

137 NASEM, Gene Drives on the Horizon (2016), 86–111; *James* et al. (n. 2), 22–25; *Keith R. Hayes* et al., Identifying and Detecting Potentially Adverse Ecological Outcomes Associated with the Release of Gene-Drive Modified Organisms, 5 (2018) Journal of Responsible Innovation S139-S158; WHO-TDR/FNIH, Guidance Framework for Testing of Genetically Modified Mosquitoes (2nd ed. 2021), 13–17.

138 *Hayes* et al. (n. 137), S141.

139 *Smets/Rüdelsheim* (n. 121), 25.

140 *Hayes* et al. (n. 137), S141.

141 *Samson Simon* et al., Synthetic Gene Drive: Between Continuity and Novelty (2018) EMBO Reports e45760, 2–3; *Li C. Lim/Li L. Lim*, Gene Drives: Legal and Regulatory Issues (2019), 109–110; *Keiper/Atanassova* (n. 10), 15.

142 *Esvelt/Gemmell* (n. 3), 4; *Lim/Lim* (n. 141), 74.

versible.[143] Hence, strategies involving stepwise or phased releases currently do not constitute an internationally accepted standard.[144] At the same time, it seems that even opponents of the technique would agree that large-scale deployments should at least be preceded by confined trials and small-scale releases. Consequently, if gene drives were to be released into the environment, strategies of phased or stepwise releases should be seen as part of the best technologies currently available.

bb) Self-Limiting Gene Drives

It has been warned that developing a standard, self-propagating gene drive system could become highly invasive and cause severe ecological damage.[145] To mitigate this risk, scientists have proposed to develop drive systems that only have a limited capacity to spread.[146]

One approach is so-called 'daisy-chain' gene drives, which successively lose their capacity to spread and therefore stop after a certain number of generations.[147] A similar proposal uses non-invasive or high-threshold gene drives that do not become permanently established in the target population but require repeated subsequent releases of drive-bearing individuals.[148] Another approach is to develop 'prevision drives', which refers to drive systems programmed for specific genetic sequences that are unique to the target population but do not occur in other populations of the same species elsewhere in the world.[149]

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143 AHTEG on Synthetic Biology, Report of the Ad Hoc Technical Expert Group on Synthetic Biology: Montreal, Canada, 5–8 December 2017, UN Doc. CBD/SYNBIO/AHTEG/2017/1/3 (2017), para. 45.

144 See CP COP-MOP, Decision 9/12. Transit and Contained Use of Living Modified Organisms (Article 6), UN Doc. CBD/CP/MOP/DEC/9/12 (2018), para. 2(c), reminding parties that confined field trial were to be regarded as intentional introduction into the environment when the criteria for contained use under Article 3(b) were not met.

145 *Esvelt/Gemmell* (n. 3), 2; *Charleston Noble* et al., Current CRISPR Gene Drive Systems Are Likely to Be Highly Invasive in Wild Populations, 7 (2018) eLife e33423.

146 Cf. *James* et al. (n. 2), 5–6.

147 Cf. *Charleston Noble* et al., Daisy-Chain Gene Drives for the Alteration of Local Populations, 116 (2019) PNAS 8275.

148 Cf. *John Min* et al., Harnessing Gene Drive, 5 (2018) Journal of Responsible Innovation S40, S41.

149 Cf. *ibid.*, S48.

Critics of gene drive techniques argue that these confinement strategies still lack proof of concept and thus are not viable solutions to mitigate the risk of an uncontrolled spread.[150] Nevertheless, the obligation to use the best available technologies will require states to consider these strategies as alternatives to highly invasive, low-threshold drive systems. Deploying the latter when less hazardous alternatives are available would violate the obligation to act with due diligence. At the same time, the effectiveness of confinement strategies must still be established in risk assessment and, potentially, in phased testing.

c) Assessment

As a corollary to risk assessment, the obligation of states to employ appropriate risk management measures is also well-established in international law. However, since the required measures depend on the risks identified in the assessment, the content of this obligation is more difficult to define. This is also because there is no practical experience with releasing gene drives into the environment. However, if such releases were envisaged, proposals by researchers to limit the potential risks by stepwise testing and using self-limiting techniques should not be disregarded. They arguably constitute the 'best available technologies' that states are bound to use should they decide to move forward with environmental releases.

3. Free, Prior and Informed Consent

According to decision 14/19, the third prerequisite for releases of engineered gene drives is that

> *'[w]here appropriate, the "prior and informed consent", the "free, prior and informed consent" or "approval and involvement" of potentially affected indigenous peoples and local communities is sought or obtained, where applicable in accordance with national circumstances and legislation'.*[151]

150 Cf. *Simon* et al. (n. 141), 3; *Lim/Lim* (n. 141), 3; see *Sumit Dhole* et al., Invasion and Migration of Spatially Self-Limiting Gene Drives, 11 (2018) Evolutionary Applications 794.

151 CBD COP, Decision 14/19 (n. 25), para. 11(c).

This provision refers to the consent of potentially affected *indigenous peoples and local communities* (a)). Besides, consent could also be required from potentially affected *individuals* (b)).

a) Status of the Obligation Under International Law

Neither the CBD nor the Cartagena Protocol expressly provides that states shall obtain the consent of indigenous peoples and local communities before releasing LMOs into the environment. However, a set of guidelines previously adopted by the CBD COP could potentially be applied to the present issues (aa)). An obligation to obtain the prior consent of indigenous peoples could also be derived from general human rights law (bb)).

aa) CBD Mo'otz Kuxtal Voluntary Guidelines

A footnote in COP decision 14/19 refers to the *Mo'otz Kuxtal Voluntary Guidelines* adopted by COP 13.[152] This soft law instrument establishes principles for obtaining the free, prior and informed consent (FPIC) of indigenous peoples and local communities when accessing their traditional knowledge. It serves the implementation of Article 8(j) CBD, which requires obtaining 'the approval and involvement of the holders of such knowledge' when promoting its wider application.

According to the Mo'otz Kuxtal Guidelines, *consent* or *approval* is understood as the agreement of the indigenous peoples and local communities concerned or their respective competent authorities, which presupposes that such consent may also be denied.[153] *Free* implies that the approval is obtained without coercing or unduly influencing the group concerned.[154] *Prior* means that the consent is obtained sufficiently in advance of any authorization and respecting the customary decision-making processes and time requirements of the indigenous peoples and local communities in

152 Cf. CBD COP, Decision XIII/18. Article 8(J) and Related Provisions: Mo'otz Kuxtal Voluntary Guidelines, UN Doc. CBD/COP/DEC/XIII/18 (2016). The Voluntary Guidelines as well as decision 14/19 refer to three different concepts, namely 'prior and informed consent', 'free, prior and informed consent' and 'approval and consent', which shall apply 'depending on national circumstances', although none of the instruments seem distinguish between them.

153 Cf. *ibid.*, para. 7(d).

154 Cf. *ibid.*, para. 7(a).

question.[155] Finally, *informed* consent presupposes that information is provided that covers all relevant aspects, including potential risks.[156]

By their terms, neither Article 8(j) nor the Mo'otz Kuxtal Guidelines apply to releases of LMOs in general or engineered gene drives in particular. However, the section on 'procedural considerations', which discusses the modalities of how FPIC should be obtained when it is required,[157] could also be applied to other areas. Consequently, the fact that the Guidelines are cited by decision 14/19 suggests that the parties to the CBD intended to endorse their application to releases of engineered gene drives.[158]

bb) United Nations Declaration on the Rights of Indigenous Peoples

An obligation to seek the consent of indigenous peoples could also be derived from general international law. An important role in this context is played by the *United Nations Declaration on the Rights of Indigenous Peoples* adopted by the UN General Assembly in 2007.[159] Although not legally binding in a formal sense, the Declaration is an important soft law document that has already been relied upon by several treaty bodies when interpreting pre-existing human rights treaties.[160]

The Declaration provides that states shall obtain the free and informed consent of indigenous peoples before relocating them from their lands or territories,[161] or before adopting legislative or administrative measures that may affect them.[162] Although the principle of FPIC originally concerned land use interventions,[163] it appears justifiable to also apply it to technological interventions such as engineered gene drives, at least where indigenous

155 Cf. *ibid.*, para. 7(b).
156 Cf. *ibid.*, para. 7(c).
157 *Ibid.*, paras. 17–21.
158 Cf. *Lim/Lim* (n. 141), 20.
159 UNGA, United Nations Declaration on the Rights of Indigenous Peoples, UN Doc. A/RES/61/295, Annex (2007). While only 144 states initially voted in favour of the Declaration, all states that had voted against it (Australia, Canada, New Zealand, and the United States, all having large indigenous populations) and some that had abstained endorsed it later, see *Benedict Kingsbury*, Indigenous Peoples, in: Wolfrum/Peters (ed.), MPEPIL, MN. 9.
160 See *ibid.*, MN. 15, with further references.
161 UN Declaration on the Rights of Indigenous Peoples (n. 159), Article 10.
162 *Ibid.*, Article 19.
163 Also cf. *ibid.*, Articles 28(1), 29(2), 32(2).

peoples are affected in their particular lifestyles or relationship with their environment.[164]

cc) Assessment

Although the concept of FPIC is widely recognized, it is still fraught with uncertainties and controversies, especially about the situations in which it applies and the modalities of how consent shall be obtained.[165] Consequently, the implementation and effectiveness of this right still largely depend on pertinent domestic laws.[166] This is also reflected in decision 14/19, which limits the application of FPIC to situations 'where appropriate' and 'where applicable in accordance with national circumstances and legislation'.[167]

Nevertheless, there appears to be broad support in favour of a requirement to obtain the FPIC of indigenous peoples and local communities potentially affected by releases of engineered gene drives.[168] The UN Declaration on the Rights of Indigenous Peoples makes clear that the particular lifestyles of indigenous peoples shall be protected as a human right.[169] If their lifestyles are likely to be affected by an engineered gene drive, their FPIC should be obtained prior to authorizing its release. But even beyond the scope of 'indigenous peoples and local communities',[170] the consent

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164 *Dalton R. George* et al., Articulating 'Free, Prior and Informed Consent' (FPIC) For Engineered Gene Drives, 286 (2019) Proc. R. Soc. B 20191484; also see *Kofler* et al. (n. 8).

165 *George* et al. (n. 164), 3; see *David Szablowski*, Operationalizing Free, Prior, and Informed Consent in the Extractive Industry Sector? Examining the Challenges of a Negotiated Model of Justice, 30 (2010) Canadian Journal of Development Studies 111.

166 See *Szablowski* (n. 165).

167 CBD COP, Decision 14/19 (n. 25), para. 11(c).

168 Cf. Report of the AHTEG on Synthetic Biology 2017 (n. 143), para. 25; *Kofler* et al. (n. 8); AHTEG on Synthetic Biology, Report of the Ad Hoc Technical Expert Group on Synthetic Biology: Montreal, Canada, 4–7 June 2019, UN Doc. CBD/SYNBIO/AHTEG/2019/1/3 (2019), Annex, para. 1; *George* et al. (n. 164).

169 UN Declaration on the Rights of Indigenous Peoples (n. 159), Article 5.

170 Note that Article 8(j) CBD refers 'indigenous and local communities embodying traditional lifestyles'. On request by the UN Permanent Forum on Indigenous Issues, the COP decided in 2014 to instead refer to 'indigenous peoples and local communities' in the future, see CBD COP, Decision XII/12 F. Terminology "Indigenous Peoples and Local Communities", UN Doc. UNEP/CBD/COP/DEC/XII/12 (2014), paras. 1–2. This shows that in the present

of potentially affected populations should become a standard precondition for any gene drive release.[171]

b) Excursus: Consent of Individuals as a Human Rights Requirement?

The aforementioned requirement to obtain 'free, prior and informed consent' refers to the consent of entire communities rather than potentially affected individuals.[172] Thus, the concept must be distinguished from the 'informed consent' commonly required from individuals participating in medical trials.[173] The latter is derived from Article 7 of the *International Covenant on Civil and Political Rights*,[174] which provides that

> *'no one shall be subjected without his free consent to medical or scientific experimentation'.*

In the context of engineered gene drives in mosquitoes, there appears to be a scientific consensus that the drive components should be assessed for their toxicity and allergenicity potential.[175] It also seems undisputed that potential alterations in the disease transmission of modified mosquitoes should be considered.[176] However, it is controversial whether this entails a requirement to obtain the consent of all potentially affected individuals.

According to one view, '[t]here are, strictly speaking, no human subjects of field trials' and, consequently, regulations requiring the informed consent of every participant do not apply.[177] According to a more differentiat-

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context, 'local communities' means such that embody traditional lifestyles in the sense of Article 8(j) CBD.

171 Cf. *Silja Vöneky*, International Standard Setting in Biomedicine – Foundations and New Challenges, 61 (2019) German YBIL 131, 141; see *Joanna Buchthal* et al., Mice Against Ticks: An Experimental Community-Guided Effort to Prevent Tick-Borne Disease by Altering the Shared Environment, 374 (2019) Philos. Trans. R. Soc. B 20180105.

172 *George* et al. (n. 164), 3–4.

173 See *Onora O'Neill*, Informed Consent and Public Health, 359 (2004) Philos. Trans. R. Soc. B 1133.

174 International Covenant on Civil and Political Rights (16 December 1966; effective 23 March 1976), 999 UNTS 171.

175 *Andrew Roberts* et al., Results from the Workshop "Problem Formulation for the Use of Gene Drive in Mosquitoes", 96 (2017) Am. J. Trop. Med. Hyg. 530, 531.

176 *Ibid.*

177 *Carolyn P. Neuhaus/Arthur L. Caplan*, Ethical Lessons from a Tale of Two Genetically Modified Insects, 35 (2017) Nature Biotech. 713, 716.

ed view, informed consent must be obtained from individuals when blood or other clinical data are collected from them, when they participate in behavioural or social science research involving the completion of surveys or questionnaires, or when their home or property is accessed or the location recorded as a spatial variable for the release or collection of organisms.[178]

If Article 7 ICCPR was held to be applicable, the free consent of every potentially affected individual would be required. This seems impossible to achieve, especially considering that many mosquito species have a wide geographical range. To solve this impasse, it has been proposed to apply 'opt-out' models of consent to large-scale field trials.[179] However, this approach is questionable because there is no real possibility for individual residents to opt out from the potential effects of a gene drive on their environment or even health.[180]

According to another proposal, individual consent should be replaced by a form of community consent given by a representative of the potentially affected population. This could especially be applied to experiments that may affect individuals but do not constitute medical research *strico sensu*.[181] In effect, this would extend the FPIC requirement for indigenous peoples[182] beyond this specific target group to all potentially affected communities. In any case, the validity of such community consent should be contingent upon a scientifically sound risk assessment and a transparent consultation process.[183]

This appears to be in line with the – soft law – *Universal Declaration on Bioethics and Human Rights* adopted in 2005 by the General Conference of

178 *Pamela A. Kolopack/James V. Lavery*, Informed Consent in Field Trials of Gene-Drive Mosquitoes, 1 (2017) Gates Open Research 14, 4; WHO-TDR/FNIH, Guidance Framework for Testing GM Mosquitoes (n. 137), 94; see *Andrew D. McRae* et al., Who Is the Research Subject in Cluster Randomized Trials in Health Research?, 12 (2011) Trials 183.

179 Cf. *James* et al. (n. 2), 32.

180 Cf. *O'Neill* (n. 173).

181 *Vöneky* (n. 171), 141; *Delphine Thizy* et al., Providing a Policy Framework for Responsible Gene Drive Research: An Analysis of the Existing Governance Landscape and Priority Areas for Further Research, 5 (2020) Wellcome Open Research 173, 5; WHO-TDR/FNIH, Guidance Framework for Testing GM Mosquitoes (n. 137), 94.

182 See *supra* n. 170 and accompanying text.

183 *Vöneky* (n. 171), 141.

the UN Educational, Scientific and Cultural Organization (UNESCO).[184] It provides that, in principle, scientific research should only be carried out with the FPIC of the person concerned, but that exceptions may be made in accordance with ethical and legal standards adopted by states.[185] Moreover, the Declaration provides that in appropriate cases of research carried out on a group of persons or a community, additional agreement of the legal representatives of the group or community concerned may be sought.[186] However, it also makes clear that such a collective agreement should in no case substitute an informed consent of an individual where required.[187]

Whether the consent of individuals is required primarily involves scientific questions. When a modified mosquito exhibits no tangible changes in biting patterns, disease transmission, and the salvia transferred to the host during the bite, it makes no difference for individuals whether they are bitten by a drive-bearing mosquito or a wild type. However, when there are such changes, it seems difficult to argue that a human bit by such a mosquito is not subjected to (medical or) scientific experimentation[188] in the sense of Article 7 ICCPR. At least when such experiments may be detrimental to their health, the free consent of all potentially affected persons must be obtained.[189] Community consent can only complement but not substitute the individual consent that may, depending on the circumstances, be required under Article 7 ICCPR.[190] This is even more true when modified insects are used to disperse vaccines.[191]

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184 UNESCO General Conference, Universal Declaration on Bioethics and Human Rights (19 October 2005), Records of the General Conference, 33rd session, Vol. 1: Resolutions, p. 74.

185 *Ibid.*, Article 6(2).

186 *Ibid.*, Article 6(3).

187 *Ibid.*

188 The Human Rights Committee did not consider it necessary to draw up a list of prohibited acts or to establish sharp distinctions between the different treatments prohibited by Article 7 ICCPR, cf. Human Rights Committee, CCPR General Comment No. 20 (Article 7), UN Doc. HRI/GEN/1/Rev.1, p. 30 (1992), para. 4.

189 Cf. *ibid.*, para. 7.

190 Also see *ibid.*, pointing out that Article 7 ICCPR requires the 'free consent *of the person concerned*' (emphasis added).

191 *Vöneky* (n. 171), fn. 38 on p. 140; see *D. S. Yamamoto* et al., Flying Vaccinator; a Transgenic Mosquito Delivers a Leishmania Vaccine via Blood Feeding, 19 (2010) Insect Molecular Biology 391.

4. Conclusions

The three criteria for environmental releases of engineered gene drives set out in CBD COP decision 14/19 seem to be ordered by decreasing clarity. First, the obligation to carry out risk assessments is well established in international law.[192] Despite remaining national differences, whether an assessment is 'scientifically sound' can be determined through peer review.[193]

Second, the obligation to apply risk management measures is derived from the obligation of states to act with due diligence and to employ the best available technologies. While there are specific proposals to reduce the risks inherent in gene drive techniques, the measures actually required will largely depend on the result of the risk assessment and can, therefore, not be defined abstractly.[194]

Third, the requirement to obtain the FPIC of affected indigenous peoples and local communities is the least concise of the conditions. It is clearly made subject to 'national circumstances and legislation',[195] which gives states many grounds for not applying the requirement. The consent of individuals, which may be required under international human rights law, is not addressed by the decision. Probably it will be upon human rights jurisprudence to determine whether the FPIC requirement applies to engineered gene drives under human rights law.

After the decision was adopted, views diverged on whether these criteria resulted in a *de facto* moratorium or rather showed a clear path toward responsible releases.[196] In any event, it should be noted that the fulfilment of these criteria does not automatically make releases permissible. Decision 14/19 calls upon states 'to only consider' releases when the criteria are met. This clearly indicates that they are meant as preconditions and that releases should not even be considered as long as they are not met. Moreover, other

192 See *supra* section C.II.1.

193 See *R. Guy Reeves* et al., Scientific Standards and the Regulation of Genetically Modified Insects, 6 (2012) PLOS Neglected Tropical Diseases e1502.

194 See *supra* section C.II.2.

195 CBD COP, Decision 14/19 (n. 25), para. 11(c).

196 See *Ewen Callaway*, UN Treaty Agrees to Limit Gene Drives but Rejects a Moratorium, Nature News, 29 November 2018, available at: https://www.nature.com/articles/d41586-018-07600-w (last accessed 28 May 2022).

rules of international law must also be observed,[197] including with regard to potential transboundary spreads.[198]

III. Safety of Synthetic Biology in Contained Use

As far as is known, no engineered gene drive has so far been released into the environment. Instead, research is currently carried out in containment, particularly in laboratories and insect cages.[199] However, due to the inherent properties of gene drives, any accidental release could have unpredictable ecological consequences.[200]

Against this background, decision 14/19 addresses the prevention of harm from 'organisms, components and products of synthetic biology in contained use', which, in CBD COP parlance, includes engineered gene drives.[201] The decision calls upon parties, other governments[202] and relevant organizations to develop or implement

> *'measures to prevent or minimize potential adverse effects arising from exposing the environment to organisms, components and products of synthetic biology in contained use, including measures for detection, identification and monitoring, in accordance with domestic circumstances or internationally agreed guidelines, as appropriate, with special consideration to the centres of origin and genetic diversity'.*[203]

There are no binding international rules on the contained use of LMOs (1.). The notion 'internationally agreed guidelines' apparently refers to a non-binding manual on laboratory biosafety developed by the World Health Organization (2.). A coherent framework is also missing in the European Union, and some of its member states have begun to adopt uni-

197 See chapter 3.
198 Also see *infra* section D.
199 See chapter 1, section C.III.1.c). For a systematic overview of the research currently performed, see *Smets/Rüdelsheim* (n. 121), 19–20; *Ethan Bier*, Gene Drives Gaining Speed, 23 (2022) Nature Rev. Genet. 5.
200 *Omar S. Akbari* et al., Safeguarding Gene Drive Experiments in the Laboratory, 349 (2015) Science 927.
201 Gene drives are considered to be one particular application of synthetic biology since CBD COP, Decision XIII/17 (2016) (n. 12), para. 2.
202 See *supra* section B.IV.
203 CBD COP, Decision 14/19 (n. 25), para. 12.

lateral approaches (3.). Besides, scientists have made proposals to improve the safety of laboratory research on gene drives (4.).

1. No Binding International Rules on LMOs in Contained Use

The CBD does not expressly address LMOs in contained use. In this respect, only the general obligation to control the risks associated with LMOs applies.[204] The Cartagena Protocol applies to contained use since it covers all handling and use of LMOs.[205] According to its Article 3(b), 'contained use' is defined as

> *'any operation, undertaken within a facility, installation or other physical structure, which involves living modified organisms that are controlled by specific measures that effectively limit their contact, and their impact on, the external environment.'*

Article 6(2) provides that LMOs destined for contained use are not subject to the *Advance Informed Agreement* mechanism under the Cartagena Protocol. In any case, the Cartagena Protocol does not contain any specific provisions regulating the contained use of LMOs.

Binding international rules on the contained use of LMOs or other hazardous biological materials are not laid down in other instruments either. Although there exist various international standards and guidelines on laboratory biosafety,[206] including the ISO Standard for Laboratory Biorisk Management,[207] the OIE Manual for Diagnostic Tests and Vaccines for Terrestic Animals,[208] and the WHO's Laboratory Biosafety Manual discussed below,[209] none of these documents create binding rules of international law.

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204 Cf. Article 8(g) CBD.
205 Article 4 Cartagena Protocol.
206 For a collection of relevant documents, see *Michael P. Owen*, Lab Rat's Web Portal for Laboratory Biorisk Management (04 January 2020), available at: https://www.seanet.com/~owenmp/biosafety/lab-biorisk-mgmt.html (last accessed 28 May 2022).
207 ISO, Biorisk Management for Laboratories and Other Related Organisations, ISO 35001:2019 (2019).
208 OIE, Manual of Diagnostic Tests and Vaccines for Terrestrial Animals (8th ed. 2018), ch. 1.1.4.
209 See *infra* section C.III.2.

Consequently, there are currently no dedicated binding rules on risk assessment and minimal control measures applicable to LMOs in contained use.[210] This is particularly striking in the context of engineered gene drives and modified viruses, since even small releases could result in extensive dissemination.[211] An accidental laboratory release has also been discussed as a possible origin of the SARS-CoV-2 coronavirus that caused the COVID-19 pandemic in 2020.[212]

2. The WHO Laboratory Biosafety Manual

Decision 14/19 calls upon states to act 'in accordance with […] internationally agreed guidelines'. This appears to refer to the *Laboratory Biosafety Manual*, which was developed under the auspices of the World Health Organization (WHO).[213] Although not adopted by governments, the Manual is widely regarded as 'a de facto standard that represents best practices' for laboratory biosafety.[214]

Earlier editions of the Manual have introduced four different risk groups, ranging from organisms unlikely to cause harm to pathogens that cause serious disease and can be readily transmitted.[215] These risk groups corresponded to four biosafety levels (BSL), ranging from BSL-1 as the lowest to BSL-4 as the highest level.[216] Most domestic frameworks on the contained use of microorganisms or LMOs have adopted this sys-

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210 *Cécile J. B. van der Vlugt* et al., A Framework for the Risk Assessment and Management of Gene Drive Technology in Contained Use, 23 (2018) Appl. Biosaf. 25, 25.

211 *Marshall* (n. 3), 897; *Lim/Lim* (n. 141), 76; see Report of the AHTEG on Synthetic Biology 2017 (n. 143), para. 51(c).

212 Cf. *Kristian G. Andersen* et al., The Proximal Origin of SARS-CoV-2, 26 (2020) Nature Medicine 450; *Matt Field*, Experts Know the New Coronavirus Is Not a Bioweapon. They Disagree on Whether It Could Have Leaked from a Research Lab, Bulletin of the Atomic Scientists, 30 March 2020, available at: https://thebulletin.org/2020/03/experts-know-the-new-coronavirus-is-not-a-bioweapon-they-disagree-on-whether-it-could-have-leaked-from-a-research-lab/ (last accessed 28 May 2022); *Paul Rincon*, Coronavirus: Is There Any Evidence for Lab Release Theory?, BBC News, 01 May 2020, available at: https://www.bbc.com/news/science-environment-52318539 (last accessed 28 May 2022).

213 WHO, Laboratory Biosafety Manual (4th ed. 2020).

214 *Kazunobu Kojima* et al., Risk-Based Reboot for Global Lab Biosafety, 360 (2018) Science 260.

215 WHO, Laboratory Biosafety Manual (3rd ed. 2004), 1.

216 *Ibid.*, 2.

tem.[217] However, the requirements applicable for each level vary significantly under different national or regional biosafety regulations.[218] In addition, the classification of works varies significantly, as shown by the fact that basic research involving SARS-like coronaviruses was routinely carried out in medium-safety BSL-2 laboratories,[219] despite reports about such viruses escaping even from BSL-3 facilities and infecting laboratory workers.[220] It has also been argued that most regimes currently do not address the specific risks involved with the use of self-propagating biological agents such as gene drives.[221]

In the latest edition of the Manual published in 2020, the system of biosafety levels was waived in favour of a more differentiated approach.[222] The Manual now proposes to determine the actual risk of working with biological agents on a case-by-case basis.[223] Nevertheless, it still differentiates between 'core requirements',[224] 'heightened control measures'[225] and 'maximum control measures',[226] which shall be applied depending on the previously-established degree of risk.

Gene editing and gene drives are identified as 'emerging biological risks' in a chapter on laboratory biosecurity, which refers to the potential for

217 See, e.g., Directive 2000/54/EC on the Protection of Workers from Risks Related to Exposure to Biological Agents at Work (18 September 2000), OJ L 262, p. 21; Directive 2009/41/EC on the Contained Use of Genetically Modified Micro-Organisms (06 May 2009), OJ L 125, p. 75; U.S. Centers for Disease Control and Prevention, Biosafety in Microbiological and Biomedical Laboratories (6th ed. 2020); Government of Canada, Canadian Biosafety Standard: For Facilities Handling or Storing Human and Terrestrial Animal Pathogens and Toxins (2nd ed. 2015); Gentechnikgesetz (Genetic Engineering Act) (16 December 1993), last amended by Article 8 of the law of 27 September 2021 (Bundesgesetzblatt, Pt. I, p. 4530), Section 7(1).

218 *Barbara Johnson/Rocco Casagrande*, Comparison of International Guidance for Biosafety Regarding Work Conducted at Biosafety Level 3 (BSL-3) and Gain-of-Function (GOF) Experiments, 21 (2016) Appl. Biosaf. 128; *Rincon* (n. 212).

219 *Andersen* et al. (n. 212), 451–452.

220 Cf. *Poh L. Lim* et al., Laboratory-Acquired Severe Acute Respiratory Syndrome, 350 (2004) N. Engl. J. Med. 1740; see *Field* (n. 212).

221 Cf. *Jeantine E. Lunshof/Angela Birnbaum*, Adaptive Risk Management of Gene Drive Experiments, 22 (2017) Appl. Biosaf. 97, 99; *van der Vlugt* et al. (n. 210), 26–27.

222 WHO (n. 213), xvii.

223 *Ibid.*, 5–27.

224 *Ibid.*, 27–47.

225 *Ibid.*, 49–57.

226 *Ibid.*, 59–64.

deliberate misuses.[227] In this regard, the Manual recommends not to focus on any particular issue or technology, but rather to use a single framework to assess and manage risks regardless of the technology involved.[228] Consequently, the Manual does not specifically address gene drives or other types of LMOs.

In sum, the Manual's recognition as a 'de facto standard' mainly roots in its legacy of introducing the four biosafety levels with corresponding minimum requirements for laboratory hardware and the performance of works. However, its value for ensuring laboratory biosafety (and biosecurity) for engineered gene drives appears to be rather limited.

3. Excursus: Regulation of Gene Drives in Contained Use in the European Union

Uniform rules for the contained use of engineered gene drives are not only missing on the global level but also in the European Union.[229] While there is an EU-wide authorization system for the release of GMOs into the environment,[230] the EU Directive on contained use only applies to genetically modified microorganisms[231] and therefore does not cover gene drives in other organisms, such as in plants, arthropods, or mammals. Consequently, the responsibility for regulating the contained use of most gene drive techniques lies with the EU member states.[232]

In the absence of a coherent international framework, a number of EU member states have already begun to adopt unilateral approaches. For example, in the Netherlands, the *GMO Regulation* was amended in July

227 As opposed to biosafety, laboratory biosecurity refers to measures that are not aimed at preventing accidental escapes but rather the loss, theft, misuse, diversion or intentional release of biological agents, cf. *ibid.*, 83.

228 *Ibid.*, 88.

229 See *Marion Dolezel* et al., Beyond Limits – The Pitfalls of Global Gene Drives for Environmental Risk Assessment in the European Union, 15 (2020) BioRisk 1.

230 See Directive 2001/18/EC on the Deliberate Release into the Environment of Genetically Modified Organisms (12 March 2001), OJ L 106, p. 1; see chapter 3, section A.IV.

231 Directive 2009/41/EC on the Contained Use of Genetically Modified Micro-Organisms (n. 217), Article 1.

232 *Mitchell/Bartsch* (n. 8), 5.

2016.[233] It now provides that activities involving gene drives are classified in *containment category IV*, which is the strictest containment level.[234] Consequently, laboratory works with gene drives require prior authorization, which involves an assessment of the proposed activity and specification of the required containment level on a case-by-case basis.[235]

In Germany, the *Ordinance on Safety Levels and Measures for Genetic Engineering Works* was revised in August 2019.[236] The ordinance now provides that laboratory works aimed at producing genetic elements that promote their own dispersal in populations of sexually reproducing organisms[237] shall, in principle, be subject to biosafety level 3.[238] This means that, as in the Netherlands, these works require prior authorization by the competent authority.[239] During the authorization process, the competent authority may, based on the risk assessment to be submitted by the operator, also assign the works to a different biosafety level.[240]Moreover, the competent authority shall obtain an opinion on the specific safety measures required for the proposed works from the *Central Biosafety Committee* (ZKBS), an expert commission established under the German *Gene Technology Act*.[241] Notably, the revised ordinance overturns an earlier opinion by the ZKBS, which had concluded that the production and handling of gene drive

233 Cf. Dutch State Secretary for Infrastructure and the Environment, Regeling Genetisch Gemodificeerde Organismen Milieubeheer 2013 (GMO Regulation) (01 January 2018).

234 *C. van der Vlugt* et al., Risk Assessment Method for Activities Involving Organisms with a Gene Drive Under Contained Use, RIVM Letter report 2018–0090 (2018), 11–12.

235 *Ibid.*

236 Verordnung über die Sicherheitsstufen und Sicherheitsmaßnahmen bei gentechnischen Arbeiten in gentechnischen Anlagen (Ordinance on the security levels and safety measures for genetic engineering operations in genetic engineering facilities) (12 August 2019; effective 01 March 2021), Bundesgesetzblatt Pt. I, p. 1235 (hereinafter 'Genetic Engineering Safety Ordinance 2021').

237 It remains unclear whether this also applies to other self-propagating genetic elements that do not rely on the sexual reproduction of their host organism, such as genetically modified viruses.

238 Genetic Engineering Safety Ordinance 2021 (n. 236), Section 10(5) (for microorganisms) and Section 11(6) (for animals and plants).

239 Gentechnikgesetz (Genetic Engineering Act) (n. 217), Sections 8(1) and 9(3). According to Section 31, the *Länder* (the federated states in Germany) shall be responsible for designating the respective competent authorities responsible for implementing the Act.

240 Genetic Engineering Safety Ordinance 2021 (n. 236), Sections 10(5)(2) and 11(6)(2).

241 *Ibid.*, Sections 10(5)(3) and 11(6)(3).

systems should only be subject to biosafety level 2.[242] This level applies to works that merely involve a 'low risk' to human health or the environment and requires that the works must be notified to, but not authorized by, the competent authority.[243]

In 2018, members of the competent authorities in Belgium, Germany, the Netherlands and the United Kingdom proposed a framework for risk assessment and risk management of gene drive technology in contained use.[244] The paper identifies three risk classes of gene drives organisms, which depend on the likelihood of occurrence and the level of severity of potential adverse effects in case of an unintentional release.[245] The paper argues that these classes largely correspond to the biosafety levels identified in the WHO's Laboratory Biosafety Manual, but should be complemented by additional control measures to take account of the particular risks involved with gene drives.[246]

The paper, as well as the aforementioned national regimes, demonstrate the low level of harmonization concerning biosafety for laboratory research on gene drives. Domestic regulators even disagree on whether such research should be subject to a general requirement of prior authorization or whether a case-by-case determination is sufficient. Moreover, although the system of biosafety levels is broadly recognized and applied, the lack of coherent standards for laboratory hardware and the performance of works under these levels show that it would be insufficient to simply agree on harmonized biosafety or risk levels for different types of gene drives.

4. Containment Standards for Gene Drives Formulated by Researchers

In the absence of international standards on contained use agreed by governments, guidelines developed by scientists may become more relevant in defining minimum requirements. In a paper published in 2015, leading researchers in the area of engineered gene drives recommended that laboratory studies of gene drives use a combination of multiple confine-

242 ZKBS, Position Statement of the ZKBS on the Classification of Genetic Engineering Operations for the Production and Use of Higher Organisms Using Recombinant Gene Drive Systems, Az. 45310.0111 (2016), 4.
243 Gentechnikgesetz (Genetic Engineering Act) (n. 217), Section 7(1), subpara. 2.
244 *Van der Vlugt* et al. (n. 210).
245 *Ibid.*, 29; see *supra* section C.III.2.
246 *Ibid.*, 29–30.

ment strategies.[247] Potential strategies identified by the authors include the molecular level (e.g. targeting synthetic DNA sequences not present in wild organisms), the ecological level (e.g. performing experiments in an area lacking wild populations), the reproductive level (i.e. using a laboratory strain that cannot reproduce with wild organisms), and physical barriers that should only be removed when the organisms are inactive.[248] Because these strategies operate independently from each other, the authors assume that using a combination could result in 'multiplicative' safety improvements.[249]

The paper is still widely regarded as describing the current state of knowledge and 'best practice' in preventing unintentional releases of engineered gene drives.[250] It could even be seen as a description of the 'best available technologies' in this context. As shown earlier, international law obliges states to ensure that the best available techniques are used to prevent damage,[251] and decision 14/19 even refers to 'internationally agreed guidelines'. Until states develop and adopt such guidelines themselves,[252] there appears to be a certain leeway for the scientific community to define by itself what the 'best available technologies' are.[253]

IV. Conclusions

Since it articulates a first set of concise principles on the use of engineered gene drives, decision 14/19 represents a leap forward in international standard-setting on this matter. At the same time, the decision does not create any new obligations, but rather clarifies the application of already-established rules of international law to gene drives. This is not only true for the precautionary approach, but also for the obligation to ensure that appropriate risk assessment and risk management measures are in place.

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247 *Akbari* et al. (n. 200).
248 *Ibid.*, 927–928.
249 *Ibid.*, 928.
250 See, e.g., NASEM, Gene Drives on the Horizon (n. 137), 160; *Lunshof/Birnbaum* (n. 221), 100; *van der Vlugt* et al. (n. 210), 29; *Simon* et al. (n. 141), 1; *Noble* et al. (n. 147), 8276; *Warmbrod* et al. (n. 66), 33.
251 See chapter 4, section D.III.
252 See *supra* section C.II.1.b)bb).
253 Cf. NASEM, Gene Drives on the Horizon (n. 137), 166–169; *Warmbrod* et al. (n. 66), 31.

By mentioning the principle of 'free, prior and informed consent' of indigenous peoples and local communities, the decision takes account of an emerging collective human right that is increasingly accepted. However, one should not underestimate the role of human rights of individuals, especially when drive-bearing organisms interact with humans (e.g., through biting). Lastly, the call to ensure the biosafety of contained use applications of synthetic biology appears to be rather uncontroversial. However, international harmonization in this regard is far less advanced than one might think.

D. Governance of (Potential) Transboundary Spreads

An issue left unaddressed by decision 14/19 is potential transboundary spreads of engineered gene drives. This is surprising, especially considering that the potential of drive-bearing organisms to spread across political borders once released is generally recognized.[254]

It has been suggested that that before releasing any gene drive system that may spread across borders, potentially affected states should be consulted or even asked to approve the release.[255] An obligation to do so could result from the Cartagena Protocol (I.) as well as from the general obligation to prevent significant transboundary harm (II.).

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254 See, e.g., *Marshall* (n. 3), 896; *Oye* et al. (n. 3), 628; NASEM, Gene Drives on the Horizon (n. 137), 149; AHTEG on Risk Assessment, Guidance on Risk Assessment and Monitoring of LMOs (n. 94), 91; *Esvelt/Gemmell* (n. 3), 4; *James* et al. (n. 2), 41; *Warmbrod* et al. (n. 66), 33; *John B. Connolly* et al., Systematic Identification of Plausible Pathways to Potential Harm via Problem Formulation for Investigational Releases of a Population Suppression Gene Drive to Control the Human Malaria Vector Anopheles Gambiae in West Africa, 20 (2021) Malaria Journal 170, 61; WHO-TDR/FNIH, Guidance Framework for Testing GM Mosquitoes (n. 137), 125; also see *Elena Angulo/Ben Gilna*, When Biotech Crosses Borders, 26 (2008) Nature Biotech. 277.

255 *John M. Marshall*, Commentary: The Cartagena Protocol in the Context of Recent Releases of Transgenic and Wolbachia-Infected Mosquitoes, 19 (2011) Asia-Pacific Journal of Molecular Biology and Biotechnology 91, 97; NASEM, Gene Drives on the Horizon (n. 137), 157; *Esvelt/Gemmell* (n. 3), 4; *Kent H. Redford* et al., Genetic Frontiers for Conservation (2019), 41; *Robyn R. Raban* et al., Progress Towards Engineering Gene Drives for Population Control, 223 (2020) Journal of Experimental Biology, 1–4; WHO-TDR/FNIH, Guidance Framework for Testing GM Mosquitoes (n. 137), 125.

I. Regulation of Transboundary Movements Under the Cartagena Protocol

1. 'Likely' Transboundary Movements as 'Intentional' Transboundary Movements?

As shown above, organisms containing engineered gene drive systems constitute living modified organisms (LMOs) in the sense of the Cartagena Protocol.[256] The Protocol provides that *intentional* transboundary movements require the 'advance informed agreement' (AIA) of the receiving state,[257] whereas *unintentional* transboundary movements shall be prevented.[258]

Against this background, it has been argued that the release of an engineered gene drive that is known to be highly invasive and likely to spread across national borders should be considered to constitute an *intentional* transboundary movement, even when the initial release is only carried out domestically.[259] This would result in an obligation to obtain the AIA of all potentially affected states before authorizing the release.[260] Such an interpretation finds support in the Protocol's two-coined objective, which is to protect not only biological diversity but also the sovereign decision-making of each party whether to admit a particular LMO into its territory.[261]

However, it seems questionable whether an interpretation that equates *potential* or even *likely* transboundary movements with *intentional* transboundary movements is permissible. According to Article 31(1) VCLT, the primary reference for interpreting the terms of a treaty is their 'ordinary meaning'. In its ordinary meaning, the term 'intentional' means 'done on purpose'[262] or 'done with the aim of carrying out the act'.[263] Thus,

256 See chapter 3, section A.I.1.e)bb).
257 Article 7(1) Cartagena Protocol; see chapter 3, section A.II.1.
258 Article 16(3) Cartagena Protocol, see chapter 3, section A.II.2.a)cc).
259 Cf. *Marshall* (n. 255), 97; *Rabitz* (n. 9), 346; *Lim/Lim* (n. 141), 99–103.
260 Cf. *Marshall* (n. 3), 896; *Rabitz* (n. 9), 346; *Redford* et al. (n. 255), 41; *Florian Rabitz*, The International Governance of Gene Drive Organisms (2021) Environmental Politics 1, 13.
261 See chapter 3, section A.III.
262 Cf. 'intentional, adj.', in: *James Murray* et al., Oxford English Dictionary, Online Edition, available at: http://www.oed.com/ (last accessed 28 May 2022).
263 Cf. 'intentional, adj.', in: *Bryan A. Garner* (ed.), Black's Law Dictionary (11th ed. 2019), 965.

the notion of 'intentional transboundary movement' implies that such a movement is carried out deliberately. Consequently, movements that occur unintentionally or accidentally do not constitute intentional but *unintentional* transboundary movements. This is in line with a decision adopted by the parties to the Cartagena Protocol, which provides that unintentional transboundary movements are such where an LMO 'inadvertently crosses the national borders of a Party where the living modified organism was released'.[264]

In the alternative, it could be assumed that the obligation to prevent *unintentional* transboundary movements, which requires states to take 'all appropriate measures' to that end, results in a prohibition to release gene drives whenever their transboundary spread is difficult or even impossible to prevent.[265] Ultimately, this would have the same effect of requiring the prior consent of potentially affected states into such releases.

While this interpretation appears to accord with the terms and spirit of the Cartagena Protocol, its practical effectiveness is questionable. As shown earlier, the obligation to take 'all appropriate measures' is one of due diligence and does therefore not require to guarantee that unintended transboundary movements do not occur under any circumstances.[266] This is in line with general international law, which does not generally prohibit ultra-hazardous activities but only requires that adequate safeguards are put in place to prevent adverse transboundary effects.[267] On a factual basis, however, there will often be differing perceptions about the risk of a transboundary spread as well as the potential resulting damage.[268]

As a result, there is a considerable likelihood that transboundary spreads of gene drives are neither regarded as *intentional* transboundary movements – which would trigger the AIA mechanism – nor constitute a violation of the due diligence standard that applies to *unintentional* transboundary movements.

264 CP COP-MOP, Decision VIII/16. Unintentional Transboundary Movements and Emergency Measures (Article 17), UN Doc. CBD/CP/MOP/DEC/VIII/16 (2016), Annex.
265 *Marshall* (n. 3), 896.
266 See chapter 3, section A.II.2.a.cc)(2).
267 See chapter 4, section C.
268 *Marshall* (n. 255), 97.

2. Proposal for a Clarification

To close the gaps currently left by the Cartagena Protocol, it has been proposed to develop a new multilateral instrument that expressly acknowledges that any release of organisms containing self-propagating genetic elements, including gene drives, requires the consent of all affected states.[269] However, given that the first environmental releases are expected to take place already in the next few years, the process of negotiating and ratifying a new instrument – if it were successful at all – would likely take too long.[270] For this reason, it appears more sensible to make use of the existing frameworks.

A fairly straightforward approach to strengthen the effectiveness of the Cartagena Protocol could be to clarify that any release of an engineered gene drive *likely* to spread across borders is considered to constitute an *intentional* transboundary movement, thus requiring the AIA of all potentially affected states prior to the release.[271] This could be accomplished through a decision adopted by the meeting of the parties to the Cartagena Protocol (COP-MOP). As shown above, such a decision would not be formally binding, but could clarify the obligations under the Protocol as quasi-normative soft law.[272]

Such a step would not be unprecedented. In a decision adopted at COP-MOP 9 in 2018, the parties to the Cartagena Protocol addressed the issue of confined field trials. As noted earlier, such confined trials have been proposed as part of 'stepwise' approaches to releasing gene drives.[273] However, the decision 'reminds parties' that

> *'[a] field trial, confined field trial or experimental introduction is to be regarded as intentional introduction into the environment when the conditions specified in Article 3, paragraph b, of the Protocol are not met'*.[274]

Admittedly, when making this decision, the parties could rely on the definition of 'contained use' in Article 3(b) of the Cartagena Protocol, while

269 *Graciela R. Ostera/Lawrence O. Gostin*, Biosafety Concerns Involving Genetically Modified Mosquitoes to Combat Malaria and Dengue in Developing Countries, 305 (2011) Journal of the American Medical Association 930, 931; *Marshall* (n. 3), 896.
270 Cf. *Marshall* (n. 255), 97; also see *Angulo/Gilna* (n. 254), 281.
271 *Marshall* (n. 255), 97–98; *Rabitz* (n. 9), 347; *Rabitz* (n. 260), 13–14.
272 See *supra* section B.II.
273 Cf. *James* et al. (n. 2), 22–25; *Hayes* et al. (n. 137); see *supra* section C.II.2.b)aa).
274 CP COP-MOP Decision 9/12 (2018) (n. 144), para. 2(c).

there is no such definition of what constitutes an 'intentional' transboundary movement. Nevertheless, a potential decision could, for instance, call upon parties to

> *'consider the intentional release of any living modified organism that is likely to traverse political borders after its release to constitute an intentional transboundary movement of that organism to the potentially affected Parties, thus requiring their advance informed agreement in accordance with Article 7, paragraph 1, of the Protocol'.*

If the consensus usually required for such a decision could not be achieved, an alternative approach would be to 'call upon parties to voluntarily obtain the AIA of the potentially affected states', or at least to 'notify, consult and cooperate with potentially affected states'. This would merely institutionalize an already-existing obligation, namely to notify and consult with potentially affected states about hazardous activities that may have transboundary effects.[275]

II. Transboundary Spreads and the Obligation to Prevent Significant Transboundary Harm

Ambiguities also exist with regard to the obligation to prevent significant transboundary harm. As shown earlier, states are obliged to ensure that activities within their jurisdiction do not cause damage to the environment of other states or areas beyond national jurisdiction.[276] However, this obligation only applies to harm that is 'significant', which requires that it must lead to a 'real detriment' to matters such as human health, property, or the environment.[277] This poses no problems when a gene drive causes such detriment through unintended side-effects on untargeted species, ecosystems, or human health. It also seems to be undisputed that the deliberate eradication of a species in its native habitat range contravenes the CBD and therefore constitutes significant harm.[278]

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275 Article 5 CBD; Article 17(4) Cartagena Protocol; see chapter 4, section D.IV.

276 Article 3 CBD, see chapter 3, section B.II., and chapter 4.

277 Cf. ILC, Draft Articles on Prevention of Transboundary Harm from Hazardous Activities, with Commentaries (2001), YBILC 2001, vol. II(2), p. 148, Commentary to Article 2, para. 4; also see chapter 4, section B.IV.

278 Cf. *Axel Hochkirch* et al., License to Kill?, 11 (2018) Conservation Letters e12370, 2–3; *Reynolds* (n. 9), 34.

Establishing a 'real detriment' could be more difficult when a gene drive exceeds its intended target range but, apart from this, functions as intended and does not cause any injury.[279] For instance, consider a (hypothetical) case where a modification drive designed to reduce the potential of a mosquito species to transmit a human pathogen spreads to a neighbouring state and replaces the local population there, resulting in a substantial reduction of transmission rates in that state.[280] In such a case, it could be argued that there is no case of significant transboundary harm because the neighbouring state does not suffer any 'real detriment' but rather benefits from an improvement of its public health.

However, such an understanding would ignore that the modification or replacement of an entire species severely interferes with the territorial integrity of the affected state. It also disregards the concept of 'biological diversity', which is not limited to individual species but also encompasses ecosystems and the greater ecological complexes of which they are part.[281] Arguably, this even includes the pathogen addressed by the gene drive and its interactions with vector and host organisms.[282] Moreover, it is recognized that damage to biological diversity can take many forms and is not limited to cases of 'biodiversity loss'.[283] Finally, the notion of 'significant harm' is not meant to exclude certain types of harm but rather cases of tolerable nuisance.[284] However, when a gene drive has a lasting effect on an entire species, it can hardly be said to be insignificant.

Consequently, the transboundary spread of an engineered gene drive will most probably constitute 'significant transboundary harm'.[285] When such a spread is known to be likely, a release is therefore only permissible with the consent of all affected states. However, there will often be differing perceptions of the risks related to the release of a particular gene drive

279 See chapter 4, section B.VII.2.
280 See chapter 1, section C.III.1.a).
281 Cf. Article 2 CBD; see chapter 6, section B.II.1.
282 *Hochkirch* et al. (n. 278), 3–4.
283 CBD COP, Synthesis Report on Technical Information Relating to Damage to Biological Diversity and Approaches to Valuation and Restoration of Damage to Biological Diversity, as Well as Information on National/Domestic Measures and Experiences: Note by the Executive Secretary, UN Doc. UNEP/CBD/COP/9/20/Add.1 (2008), paras. 8–19.
284 Cf. *K. Sachariew*, The Definition of Thresholds of Tolerance for Transboundary Environmental Injury Under International Law: Development and Present Status, 37 (1990) Netherlands International Law Review 193.
285 See chapter 4, section B.VII.2.

and the probability that it will have transboundary effects.[286] This became evident in 2016 when the parties to the CBD rejected language that would have urged states to obtain the consent of potentially affected states before approving any proposed release of a gene drive.[287]

Moreover, as shown earlier, the jurisprudence of the International Court of Justice indicates that a violation of the obligation to prevent significant transboundary harm cannot be assumed unless such harm has actually occurred, which limits the options of a potentially affected state to object to a particular release.[288] *Vice versa*, a breach is not assumed solely because damage has occurred, but there must be proof that the releasing state has breached its obligation to employ due diligence.[289] Therefore, it remains questionable whether the obligation to prevent significant transboundary harm under general international law effectively prevents unilateral releases of gene drives that may disseminate into the territory of other states.

E. Summary and Outlook

Although no engineered gene drive systems have been released into the environment so far, it is assumed that the first field trials could commence as early as 2023.[290] Therefore, it is no surprise that the debate on the international regulation of this emerging technology has rapidly gained momentum in recent years. In 2018, this culminated in the adoption of the first substantive decision on gene drives by the parties to the CBD. The fact that virtually all countries except for the United States carried this decision by consensus awards it a high degree of normative authority. This is also because the decision does not attempt to establish new principles, but rather endorses the application of certain already-established rules of international law to the issue of gene drives. However, the present chapter has shown that this is still prone to various uncertainties and grey areas.

For instance, the decision recalls 'the current uncertainties regarding engineered gene drives' and calls upon states to apply a precautionary approach. Contrary to what a few authors have contended, this cannot be used to justify premature releases in order to address other environmental

286 *Marshall* (n. 255), 97.
287 Cf. CBD COP, UN Doc. UNEP/CBD/COP/13/WG.2/CRP.22 (n. 18), para. 2.
288 See chapter 4, section E.II.
289 See chapter 4, section E.I.
290 *Mitchell/Bartsch* (n. 8), 8.

threats that require rapid action. Instead, the precautionary principle calls for restraint in using gene drive techniques as long as their risks and benefits cannot be fully evaluated.

The decision calls on states 'to only consider' releasing engineered gene drives when three conditions are met, namely when a scientifically sound risk assessment has been carried out, appropriate risk management measures are in place, and, where applicable, the free, prior and informed consent of indigenous peoples and local communities has been obtained.[291] The analysis in this chapter shows that these criteria have been previously recognized by the parties to the CBD, although their consequences in the context of gene drives may be less clear than it seems at first sight. In this regard, the benchmarks for what constitutes the 'best available technologies' are currently not defined by the states but rather by the researchers involved in the development of gene drives. The same is true for the call to ensure the safety of gene drive in contained use, where the decision even suggests a level of international harmonization that actually does not exist.

Unsurprisingly, the consequences of the conditions articulated by decision 14/19 are already controversial among states and various stakeholders. While opponents of the gene drive technique argue that the decision's language comes close to a moratorium, scientists involved in the development of gene drives claimed that it did not necessitate changes in their ongoing activities.[292] However, it seems that neither assessment is correct. The criteria are not impossible to fulfil, but they also do not constitute a comprehensive 'checklist' for future releases. Therefore, the decision should be seen as a carefully balanced compromise between both ends of the spectrum, which does not answer the question as to whether responsible gene drive releases are possible under the current rules of international law.

An issue left unaddressed by decision 14/19 is the potential for engineered gene drives to spread across borders. Considering that this problem is so broadly recognized, one might wonder why the states chose to ignore the proverbial 'elephant in the room'. However, the likeliness of such spreads will often be controversial between the state planning a release and potentially affected neighbouring states, which makes it difficult to agree on general rules.

A way forward could be to clarify that releases that are likely to result in a transboundary spread constitute 'intentional transboundary movements'

291 CBD COP, Decision 14/19 (n. 25), paras. 11–12.
292 Cf. *Callaway* (n. 196).

under the Cartagena Protocol. This could be done through a decision adopted by the parties to the Cartagena Protocol, which would not be unprecedented. Although the Cartagena Protocol lacks the participation of several key actors in the area of gene drives, such a decision would still constitute an important step in clarifying that the pertinent obligation of universal customary law, namely not to cause undue environmental interference to other states, applies no less to proposed releases of engineered gene drives.