open ponds to micro-organisms used in decentralized bioreactors that may be prone to leakage (Marris and Jefferson 2013).

In sum, many of the examples of organisms developed through synthetic biology can be considered as "living modified organisms resulting from biotechnology" as defined by the Convention on Biological Diversity and, as such, would be subject to its biosafety provisions as per Articles 8(g) and 19.

2.3.4 Decisions of the Conference of the Parties referring to synthetic biology

Two decisions of the Conference of the Parties refer directly to synthetic biology. The relevant paragraphs are as follows:

- Decision X/37 "Biofuels and biodiversity", paragraph 16: "The COP urges Parties and other Governments to apply the precautionary approach in accordance with the Preamble to the Convention, and the Cartagena Protocol, to the introduction and use of living modified organisms for the production of biofuels as well as to the field release of synthetic life, cell, or genome into the environment, acknowledging the entitlement of Parties, in accordance with domestic legislation, to suspend the release of synthetic life, cell, or genome into the environment."
- Decision XI/11 "New and emerging issues relating to the conservation and sustainable use of biodiversity", paragraph 4: "The COP, *recognizing* the development of technologies associated with synthetic life, cells or genomes, and the scientific uncertainties of their potential impact on the conservation and sustainable use of biological diversity, urges Parties and invites other Governments to take a precautionary approach, in accordance with the preamble of the Convention and with Article 14, when addressing threats of significant reduction or loss of biological diversity posed by organisms, components and products resulting from synthetic biology, in accordance with domestic legislation and other relevant international obligations."

A further decision that may be interpreted as referring to synthetic biology:

- Decision XI/27 "Biofuels and biodiversity", paragraph 6: "The COP, *recognizing also* the rapidly developing technology associated with biofuels, urges Parties and other Governments to monitor these developments, and recalls decision IX/2, paragraph 3(c)(i), which urged Parties and invited other Governments, inter alia, to apply the precautionary approach in accordance with the preamble of the Convention on Biological Diversity."

3. CARTAGENA PROTOCOL ON BIOSAFETY

The Cartagena Protocol on Biosafety (Cartagena Protocol) applies to the transboundary movement, transit, handling and use of all living modified organisms (LMOs) that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health (Article 4 Cartagena Protocol). Article 1 of the Cartagena Protocol explicitly refers to the precautionary approach contained in Principle 15 of the Rio Declaration on Environment and Development. The Cartagena Protocol has 167 Parties and entered into force in 2003.

In 2012, the Ad Hoc Technical Expert Group (AHTEG) on Risk Assessment and Risk Management of the Cartagena Protocol identified the risk assessment of LMOs produced through synthetic biology among a set of topics for the development of further guidance (CPB AHTEG 2012, Annex IV). This was "noted" by the sixth meeting of the Conference of the Parties serving as the meeting of the Parties to the Cartagena Protocol on Biosafety (COP-MOP 6), which also established a new AHTEG on Risk Assessment and Risk Management to "Consider the development of guidance on new topics of risk assessment and risk management, selected on the basis of the Parties' needs and their experiences and knowledge concerning risk assessment" (BS-VI/12 Annex 1(c)). In 2014, the AHTEG on Risk Assessment and Risk Management once again identified the risk assessment of LMOs produced through synthetic biology as a possible topic for the development of further guidance.[86]

This section first examines which organisms and products of synthetic biology might be considered as LMOs in the context of the Cartagena Protocol. The applicability of exemptions to certain Cartagena Protocol provisions are considered for LMOs produced through synthetic biology, as based on current and near-term research and commercialization of synthetic biology. Risk assessments undertaken pursuant to the Cartagena Protocol must be carried out in accordance with Annex III (Article 15 Cartagena Protocol); the general principles, methodology, and points to consider of Annex III are examined for application to synthetic biology.

86 Document UNEP/CBD/BS/AHTEG-RA&RM/5/6, paragraph 38(h).

3.1. LMOs and components, organisms and products of synthetic biology

The Cartagena Protocol defines LMOs as "any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology" (Article 3(g) Cartagena Protocol). To be considered LMOs, the applications of synthetic biology would thus have to: i) be a living organism, ii) possess a novel combination of genetic material, and iii) result from the use of modern biotechnology. It should be stressed that these terms are intrinsically interlinked, such that a novel combination of genetic material that did not result from the use of modern biotechnology would not be considered an LMO in the context of the Cartagena Protocol.

3.1.1. Living organisms

The Cartagena Protocol defines a "living organism" as "any biological entity capable of transferring or replicating genetic material, including sterile organisms, viruses and viroids" (Article 3(h) Cartagena Protocol). "Genetic material" is not defined in the Cartagena Protocol; in the Convention it is defined as any material "containing functional units of heredity" (Article 2). Given this definition, many areas of research in synthetic biology would be considered as producing living organisms, including microbes produced by genome-level engineering and cells altered by synthetic metabolic engineering (see section 2.3.1 above).

Two outstanding questions regarding the scope of "living organisms" in the relation to current uses of synthetic biology are: i) products of organisms resulting from synthetic biology techniques; and ii) naked DNA and constituent parts.

3.1.1.1 Products of organisms resulting from synthetic biology techniques

According to the IUCN *Explanatory Guide* to the Cartagena Protocol on Biosafety, the products of LMOs (referred to as "products thereof") were extensively discussed during the negotiations of the Cartagena Protocol (Mackenzie *et al*. 2003). "Products thereof" in the context of the Cartagena Protocol seem to primarily refer to LMOs that have been processed. They are included in notifications under Annex I and risk assessments under Annex III if they contain "detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology" (Article 20, paragraph 3(c); Annex I, paragraph (i); and Annex III, paragraph 5 Cartagena Protocol).

Organisms resulting from synthetic biology techniques that are currently used for commercial purposes are largely micro-organisms that have been altered to produce specific compounds, such as specialized chemicals, fuels, flavors, and pharmaceuticals (Wellhausen and Mukunda 2009). The compounds are not simply processed LMOs; they are the by-products of microbes or microbial fermentation of biomass. They may fall within the Protocol's definition of "products thereof" if they contain nucleic acids containing a novel combination of genetic material. However, products that are in commercial use, such as vanillin and artemisinic acid, are generally highly refined and would not be expected to contain nucleic acids.

3.1.1.2 DNA and constituent parts

The situation is less clear with regard to DNA and constituent parts. According to the IUCN *Explanatory Guide to the Carta gena Protocol on Biosafety*, the consensus decision was to not directly include plasmids or DNA in the Article 3(h) definition of living organisms (Mackenzie *et al*. 2003). DNA and parts produced for synthetic biology have been transported through postal mail for decades. For example, New England BioLabs Inc. offers the BioBrick Assembly Kit for sale over the internet. Components of the kit include destination plasmids and the upstream and downstream parts as purified DNA.[87] Purified DNA is also mailed from commercial DNA synthesis firms, often in a lyophilized (freeze-dried) form. Furthermore, because long stretches of DNA can be fragile, commercial DNA synthesis firms sometimes incorporate gene- and genome-length pieces of DNA into more stable DNA molecules (e.g. artificial chromosones) and living cells for shipment (Garfinkel *et al*. 2007). If novel DNA is inserted into living cells for shipment, those cells seem to clearly qualify as "living organisms" as per the Cartagena Protocol. Otherwise, "naked" DNA and parts may not qualify as "living organisms" under the Cartagena Protocol.

The Cartagena Protocol provisions on risk assessment and the minimum required information to be included in notifications under some of the Protocol's procedures may apply to naked DNA and its constituent parts resulting from synthetic biology techniques if they contain "detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology" (Annex I(i); and Annex III, paragraph 5 Cartagena Protocol).

87 *Ginkgo BioWorks and New England BioLabs Inc. Undated. BioBricktm Assembly Manual: Version 1.0. Available at http://ginkgobioworks.com/support/BioBrick_Assembly_Manual.pdf, accessed 6 March 2013.*

88 *Changes can be deliberate, as in "watermark" sequences of DNA or "codon optimized" sections, or accidental (see: Gibson et al. 2010).*

In practice, however, many countries do not apply the Cartagena Protocol's provisions on risk assessment and the minimum required information to naked DNA and its constituent parts because they are considered to be components rather than products of LMOs.

3.1.2. Novel combination

A "novel combination of genetic material" can result from a novel *form* or a novel *arrangement* of the functional units of heredity, regardless of whether or not this leads to a phenotypic change (Mackenzie *et al*. 2003). Most applications of synthetic biology are focused on producing novel genetic materials. Organisms resulting from synthetic biology techniques modeled after natural organisms (such as the Spanish influenza virus and the JCVI bacterial genome) are not exact copies of the originals, and thus would qualify as novel.[88] The use of directed evolution techniques that do not incorporate new genetic material, such as "gene shuffling," would likely still be considered to result in 'novel combinations' because they rearrange existing genetic material (Mackenzie *et al*. 2003).

3.1.3. Modern biotechnology

As stated in section 2.3 above, "modern biotechnology" is defined in the Cartagena Protocol as:

> "the application of:
>
> a. *In vitro* nucleic acid techniques, including recombinant deoxyribonucleic acid (DNA) and direct injection of nucleic acid into cells or organelles, or
>
> b. Fusion of cells beyond the taxonomic family,
>
> that overcome natural physiological reproductive or recombination barriers and that are not techniques used in traditional breeding and selection" (Article 3(i) Cartagena Protocol).

The negotiators of the Cartagena Protocol recognized that new techniques for modifying genetic information would continue to be developed (Mackenzie *et al*. 2003). According to the IUCN explanatory guide, although the definition gives two specific examples of *in vitro* nucleic acid techniques, other techniques cannot be excluded from the definition so long as they overcome natural physiological reproductive or recombination barriers and are not techniques used in traditional breeding and selection. The techniques and tools of synthetic biology represent an expanding frontier of biotechnology, but current applications can be considered to remain within the Cartagena Protocol's definition of modern biotechnology.

3.2. Possible exemptions to certain provisions of the Cartagena Protocol

The Cartagena Protocol applies to the transboundary movement, transit, handling and use of all LMOs that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health (Article 4 Cartagena Protocol). The text provides limited exemptions of some LMOs to some provisions, as outlined in the following subsections.

3.2.1 Exclusion from provisions of the Cartagena Protocol: pharmaceuticals for humans that are addressed by other relevant international agreements or organizations (Article 5)

The Cartagena Protocol does "not apply to the transboundary movement of living modified organisms which are pharmaceuticals for humans that are addressed by other relevant international agreements or organizations" (Article 5 Cartagena Protocol). According to the Biotechnology Industry Organization (BIO), synthetic biology is already being used to produce pharmaceuticals for humans. Synthetic biology and directed evolution technology were used by Codexis to discover and develop a transaminase to enable a biocatalytic route for the production of Sitagliptin, a treatment for type II diabetes marketed as Januvia by Merck (BIO 2013). The pharmaceutical company, DSM has also used synthetic biology to improve the process of the commercial production of the antibiotic, Cephalexin, by introducing and optimizing genes in a penicillin-producing microbial strain (*Ibid*). Furthermore Sanofi intends to produce 35 tons of "semi-synthetic"[89] artemisinin for malaria treatment in 2013 (Sanofi and PATH 2013). In 2013, researchers at Novartis and Synthetic Genomics published an approach to rapidly generate influenza vaccine viruses, using an enzymatic, cell-free gene assembly technique, producing an accurate vaccine more quickly than previously possible (Dormitzer *et al*. 2013). Another approach referred to as "SAVE" (synthetic attenuated virus engineering) (Coleman *et al*. 2008) was used to rationally redesign the genome of an influenza virus, resulting in an attenuated virus with hundreds of nucleotide changes (Mueller *et al*. 2010). Still at the research stage are synthetic biology devices that would provide therapeutic treatment, for example

89 *The term "semi-synthetic" is used because Sanofi has developed a proprietary photochemical method to convert artemisinic acid into artemisinin (Sanders 2013).*

through reprogramming mammalian cells to tackle diseases through prosthetic gene networks (see Wieland & Fussenegger 2012), controlling the timed delivery of drugs, and more controlled approaches to gene therapy (see Khalil & Collins 2010). Synthetic biology techniques are anticipated to play a major role in future pharmaceutical development and production (RAE 2009).

Where synthetic biology organisms are being used as "biofactories" to produce pharmaceuticals such as in the case of artemisinin; the organisms themselves are not pharmaceuticals. These organisms therefore are not eligible for exemption under Article 5 (see Mackenzie *et al*. 2003). Vaccines produced using synthetic biology techniques, however, would likely be considered pharmaceuticals under Article 5 of the Cartagena Protocol.[90] Future advances in synthetic biology, such as gene therapy through artificial chromosomes and modifying bacteria and viruses to identify malignant cells and deliver therapeutic agents may be considered pharmaceuticals.

LMOs that are pharmaceuticals for humans must also be addressed by other relevant international agreements or organizations to be exempted from the Cartagena Protocol. It is unclear to what extent LMOs that are pharmaceuticals for humans would need to be "addressed" by other international agreement or organization to qualify for the Article 5 exemption. In particular, it is an open question whether the agreement or organization must address the biodiversity impacts of the LMO (Mackenzie *et al*. 2003).

Currently, none of the organisms produced through synthetic biology that are intended to be used as pharmaceuticals for humans are directly addressed by other relevant international agreements or organizations. For example, a commonly invoked promise of synthetic biology is the rapid development of vaccines using viruses (RAE 2009; PCSBI 2010). Therefore, such living organisms would fall under the Cartagena Protocol's scope.

3.2.2. Exemptions from the Advanced Informed Agreement provisions

There are limited exemptions to the requirements of the Advance Informed Agreement procedure (Article 7 Cartagena Protocol).

3.2.2.1 "Contained use" (Article 6)

Under the Cartagena Protocol, provisions for Advanced Informed Agreement (AIA) do not apply to the transboundary movement of LMOs "destined for contained use undertaken in accordance with the standards of the Party of import" (Article 6, paragraph 2 Cartagena Protocol).[91] Contained use is defined as an operation, "undertaken within a facility, installation or other physical structure," in which the LMOs' contact with and impact on the external environment is "effectively limit(ed)" by "specific measures" (Article 3(b) Cartagena Protocol). Negotiations on this topic concentrated on whether chemical or biological barriers could be considered as sufficient containment, or whether physical containment was necessary (van der Meer 2002; Mackenzie *et al*. 2003). Ultimately, the text focuses on the *effectiveness* of containment measures, rather than the type of measure. The question of degree and quality of effectiveness is also left up to the Party to determine (Mackenzie *et al*. 2003).

At least three issues have been raised by some civil society groups in relation to synthetic biology and the "contained use" AIA exemption. First, the ICSWGSB (2011) argues that containment facilities that Parties consider to effectively contain LMOs may be unsuitable to contain organisms resulting from synthetic biology techniques.[92] Importing countries may need advance information in order to "judge the effectiveness of available containment" (*Ibid*). The ICSWSB calls on the Convention of the Parties serving as the meeting of the Parties to the Protocol (COP-MOP) to exclude synthetic genetic parts and LMOs produced by synthetic biology from the "contained use" exemption under the AIA provisions "at least until effective containment methods can be demonstrated" (*Ibid*). Some comments received on an earlier draft to this document strongly question the claim that containment strategies for organisms resulting from synthetic biology techniques would need to be different from those for other LMOs.

A second issue is whether specific members of the synthetic biology community should be considered able to provide for "contained use." EcoNexus, a European civil society group, has raised doubts as to whether DIYbio (do-it-yourself biology) individuals and collectives can ever be considered a "contained use" operation (EcoNexus 2011). EcoNexus does

90 *The IUCN Guide to the Cartagena Protocol reports that living modified organisms that are pharmaceuticals for humans are "principally genetically engineered vaccines" (Mackenzie et al. 2003). In comments to an earlier version of this document, one organization noted that "continued research and development of vaccines, whether for humans or animals, may be discouraged if synthetic biology is further included within the Cartagena Protocol."*

91 *The Cartagena Protocol does not require that Parties regulate such LMOs according to the AIA provisions, but Parties are still free to use national legislation to require AIA and risk assessment (Mackenzie et al. 2003).*

92 *This concern is premised on the ICSWGSB's view that organisms resulting from synthetic biology techniques, such as de novo organisms designed and constructed in the lab, may be significantly different from other organisms, including conventionally genetically-modified organisms, in that they lack analogs in the natural world (ICSWGSB 2011).*

not consider "garage biotech facilities" as contained use, and is concerned that AIA "might become close to impossible" in such instances (EcoNexus 2011). The recent WWICS report on DIYbio found that 92% of DIYers work in group spaces (not alone), that few DIYers are using "sophisticated" synthetic biology, and most work in labs that are rated as Biological Safety Level 1 (Grushkin *et al*. 2013). Considering the current status of the synthetic biology practiced by DIYers, the WWICS report finds that DIYers present a low risk to the environment. It does, however, note that future boundaries between home and group labs may be porous, leading to experiments being carried in transit and possibly spilling, and issues around the disposal of lab waste (Grushkin *et al*. 2013). These are issues around contained use, although again, Grushkin *et al*. (2013) do not see these as current problems, but possible future concerns depending on the development of synthetic biology and the DIYbio communities.

A third and more general issue, which is not limited to LMOs produced by synthetic biology, is that Parties could be faced with "regulatory arbitrage" if a laboratory imports a synthetic biology LMO for contained use and then makes a domestic application to release the synthetic biology LMO from containment (ICSWGSB 2011). Domestic standards for risk assessment may be lower than the minimums provided in the Cartagena Protocol's Annex III. The ICSWGSB recommends that the Cartagena Protocol be revised such that "any agent receiving an LMO into containment without obtaining prior informed consent may only release that LMO after it has been approved under a risk assessment process at least as strong as that specified in Annex III" (ICSWGSB 2011).

3.2.2.2 LMOs "intended for direct use as food or feed, or for processing" (Article 11)

The AIA procedure does not apply to the transboundary movement of LMOs intended for direct use as food or feed, or for processing (LMO-FFPs), although developing country Parties or Parties with an economy in transition may, in the absence of a domestic regulatory framework, declare through the Biosafety Clearing-House that their decision prior to the first import of an LMO-FFP will be taken according to a risk assessment and a decision made within a predictable timeframe (Article 7, paragraph 2 and Article 11, paragraph 6 Cartagena Protocol). Furthermore, a Party that makes a final decision regarding domestic use of an LMO that may be subject to transboundary movement for direct use as food or feed, or for processing is to inform Parties through the Biosafety Clearing-House and this information is to include a risk assessment report consistent with Annex III of the Protocol (Article 11, paragraph 1 and Annex II (j) Cartagena Protocol). LMO-FFPs must be accompanied by documentation that "clearly identifies that they "may contain" living modified organisms and are not intended for intentional introduction into the environment" (Article 18, paragraph 2(a) Cartagena Protocol). Different procedures apply, therefore, as documentation requirements vary according to the nature of the LMO concerned and its intended use in the Party of import (Mackenzie *et al*. 2003).

3.2.3. LMOs that may be identified by the COP-MOP as "not likely to have adverse effects" (Article 7(4))

The Cartagena Protocol provides opportunities for Parties to cooperate to identify LMOs that are "not likely to have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risks to human health" (Article 7, paragraph 4 Cartagena Protocol). Parties must formally identify an LMO that is "not likely to have adverse effects" through a COP-MOP decision. Such LMOs would then be exempted from the AIA procedure (Article 7, paragraph 4 Cartagena Protocol). To date, the COP-MOP has not identified any LMO that is "not likely to have adverse effects." In 2012, Parties to the Cartagena Protocol were invited to provide the Executive Secretary with "scientific information that may assist in the identification of living modified organisms or specific traits that may have or that are not likely to have adverse effects" (BS-VI/12, paragraph 11).[93] The Executive Secretary was requested to create sections in the Biosafety Clearing-House where the information could be submitted and easily retrieved (BS-VI/12, paragraph 12).

3.3. Application of Annex III Risk Assessment to synthetic biology

Under Article 15, paragraph 2, a risk assessment must be carried out for a Party of import to make a decision as per Article 10 for an intentional transboundary movement to proceed (Article 10 and Article 15, paragraph 2, Cartagena Protocol). Risk assessments must be "carried out in a scientifically sound manner, in accordance with Annex III and taking into account recognized risk assessment techniques" (Article 15, paragraph 1 Cartagena Protocol). A risk assessment as per Annex III is

93 *When considering risk management Parties shall also cooperate to identify LMOs or specific traits of LMOs that "may have adverse effects," and "take appropriate measures" regarding their treatment (Article 16, paragraph 5 Cartagena Protocol). This provision also asks Parties to make an assessment of the likelihood of impacts. As with Article 7, paragraph 4, Parties have not yet identified any LMOs or traits that fall under this category.*

Source: Macroscopic Solutions, LLC

also required if a developing country Party or a Party with an economy in transition that does not have a domestic regulatory framework decides to import an LMO-FFP and has indicated that its decision prior to import will be taken on this basis (Article 11, paragraph 6(a) Cartagena Protocol).

Annex III of the Cartagena Protocol provides general principles, methodology, and points to consider in a risk assessment. The methodology of a risk assessment as per Annex III requires: hazard identification; evaluation of likelihood of effects; evaluation of consequences of those effects if they occur; and characterization of risks based on the likelihood and consequences of effects (Annex III, paragraph 8, Cartagena Protocol). The risk assessment may take into account the characteristics of the recipient organisms, donor organisms, receiving environment, the introduced modification, and the identity of the LMO (Annex III, paragraph 9, Cartagena Protocol). The Parties have also developed further guidance on risk assessment of living modified organisms including a roadmap for risk assessment of LMOs that supplements Annex III of the Protocol as well as guidance on the risk assessment of specific types of LMOs and traits as well as the monitoring of LMOs released into the environment.[94]

Although LMOs produced through synthetic biology may present characteristics that are not common to all LMOs, Annex III of the Protocol, including its general principles, points to consider and methodology are still fully applicable to living organisms produced through synthetic biology and may also apply to "products thereof" that contain "detectable novel combinations of replicable genetic material obtained through the use of modern biotechnology" (Article 20, paragraph 3(c), Annex I(i); and Annex III, paragraph 5 Cartagena Protocol).

In addition, it could be discussed whether the risk assessment process of Annex III, which is based on the characteristics of the recipient and donor organisms and the added traits, might be adequate for synthetic biology organisms that have been developed to include genetic material from several donor organisms that may have also been optimised. In these cases, there might not be an appropriate comparator. One author considers that in this context that the risk assessment process outlined in Annex III of the Cartagena Protocol "cannot deal with such biocircuit systems" (Schmidt 2009). Unlike conventional genetic engineering techniques, synthetic biology may make the transfer of "whole systems," rather than single traits, possible. The reliance on the consideration of individual traits may be insufficient, because it is the interactions among the parts that has "no comparable counterpart in nature, making it more difficult to predict the cell's full behavioral range with a high degree of certainty" (Ibid.). Schmidt asks whether the characteristics of such a network can be predicted to a degree of certainty that would allow a "reasonable estimation" of risk (Ibid.). He identifies a number of challenges to standard risk assessment, including what will happen when one or several parts evolve to change their functions, and how to measure robustness and reliability in the case of biological circuits. Schmidt's response is not to suggest adaptations in risk assessment methods, but rather to suggest potential biosafety engineering options in designing biocircuits, such as Event Tree Analysis and Fault Tree Analysis. The ICSWGSB's analysis of the Cartagena Protocol finds that Annex III's risk assessment procedures are inadequate – particularly in cases where biological parts and devices do not have an analog in the natural world (ICSWGSB 2011).

3.4. Nagoya – Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety

The objective of the Nagoya-Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol (Supplementary Protocol) is to contribute to the conservation and sustainable use of biological diversity, taking also into account risks to human health, by providing international rules and procedures in the field of liability and redress relating to living modified organisms.

The issue of liability and redress for damage resulting from the transboundary movements of LMOs was one of the themes on the agenda during the negotiation of the Biosafety Protocol. The negotiators were, however, unable to reach any consensus regarding the details of a liability regime under the Protocol. In 2010, the Conference of the Parties serving as the meeting to the Parties to the Cartagena Protocol adopted the Supplementary Protocol. It has not yet entered into force.

This Supplementary Protocol applies to damage resulting from living modified organisms which find their origin in a transboundary movement and are (i) intended for direct use as food, feed, or for processing; (ii) destined for contained use; or (iii) intended for intentional introduction into the

94 The "Guidance on Risk Assessment of Living Modified Organisms" is available via http://bch.cbd.int/onlineconferences/guidance_ra.shtml.

Source: Macroscopic Solutions, LLC

environment (Article 3 Supplementary Protocol). It applies to damage resulting from any authorized use of the living modified organisms, damage resulting from unintentional transboundary movements as referred to in Article 17 of the Cartagena Protocol, as well as damage resulting from illegal transboundary movements as referred to in Article 25 of the Cartagena Protocol.

The Supplementary Protocol provides in Article 12 that Parties shall provide, in their domestic law, for rules and procedures that address damage. "Damage" is defined by the Supplementary Protocol (Article 2) as an adverse effect on the conservation and sustainable use of biological diversity, taking also into account risks to human health, that is measurable or otherwise observable taking into account, wherever available, scientifically-established baselines recognized by a competent authority that takes into account any other human induced variation and natural variation. Whether an adverse effect is "significant" is to be determined on the basis of factors, such as (i) the long-term or permanent change, to be understood as change that will not be redressed through natural recovery within a reasonable period of time; (ii) the extent of the qualitative or quantitative changes that adversely affect the components of biological diversity; (iii) the reduction of the ability of components of biological diversity to provide goods and services; and (iv) the extent of any adverse effects on human health in the context of the Protocol. A causal link needs to be established between the damage and the living modified organism in question in accordance with domestic law (Article 4 Supplementary Protocol).

As discussed in section 3.1 above, organisms resulting from synthetic biology techniques may fall under the definition of a "living modified organism" under the Cartagena Protocol. Further, as described in 5 of Part I of this document, it is possible that living modified organisms resulting from synthetic biology techniques could cause adverse effects on the conservation and sustainable use of biological diversity. For example, unintentionally released organisms may transfer the inserted genetic material and thus change biodiversity at a genetic level, intentionally released organisms may become invasive due to engineered fitness advantages. As has been discussed, there appears to be significant controversy as to the scope and therefore "significance" of the potential damages. The applicability of the provisions of the Supplementary Protocol would have to be assessed for particular cases.

Once entered into force, the Supplementary Protocol will require Parties to provide, in their domestic law, for rules and procedures that address damage from organisms resulting from synthetic biology techniques, where such damage falls under the definition set out in Article 2 of the Supplementary Protocol.

4. CONVENTION ON THE PROHIBITION OF THE DEVELOPMENT, PRODUCTION AND STOCKPILING OF BACTERIOLOGICAL (BIOLOGICAL) AND TOXIN WEAPONS AND ON THEIR DESTRUCTION

The Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction (Biological Weapons Convention – BWC) entered into force in 1975 and currently has 168 Parties. This agreement may apply to the use of components, organisms and products resulting from synthetic biology techniques for hostile purposes or in armed conflict.[95]

4.1. Overview of main provisions

The core provision of the Biological Weapons Convention is its Article 1 in which each Party to this Convention undertakes never in any circumstance to develop, produce, stockpile or otherwise acquire or retain: (i) microbial or other biological agents, or toxins whatever their origin or method of production, of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes; or (ii) weapons, equipment or means of delivery designed to use such agents or toxins for hostile purposes or in armed conflict.

Further, where such agents, toxins, weapons, equipment and means of delivery are in the possession or under the jurisdiction and control of a Party, the Party is obliged to destroy or divert them

95 *Relevant in this context is also the Australia Group, an informal forum of countries which, through the harmonisation of export controls, seeks to ensure that exports do not contribute to the development of chemical or biological weapons. The 41 states participating in the Australia Group are parties to the Chemical Weapons Convention and the Biological Weapons Convention. Coordination of national export control measures assists Australia Group participants to fulfil their obligations under those conventions. The Australia Group meets annually to discuss ways of increasing the effectiveness of participating countries' national export licensing measures to prevent potential proliferators from obtaining materials for chemical or biological weapons programs. Since 2007, meetings of the Australia Group have discussed synthetic biology, see www.australiagroup.net.*

Source: Macroscopic Solutions, LLC