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Mr. David Cooper
Acting Executive Secretary
Secretariat of the Convention on Biological Diversity
United Nations Environment Programme
E-mail: secretariat@cbd.int

March 14, 2022

Dear Mr David Cooper,

In response to CBD Notification CBD Notification 2023-006 "Submission of information on synthetic biology and nomination of experts to participate in the Open-ended Online Forum on Synthetic Biology," Canada is pleased to provide the Executive Secretary with relevant information on trends in new technological developments in synthetic biology to inform the horizon scanning, monitoring and assessment. Please see below for this information.

Best regards,

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New and Emerging Issues for Applications of Synthetic Biology

A horizon scan of recent literature identified key developments in synthetic biology with the potential to introduce new environmental risks. While existing risk assessment and risk management frameworks may broadly encompass new and emerging issues, variability between jurisdictions in their risk tolerance and precautionary approaches to novel technologies merits discussion and cooperation between stakeholders.[1]

The applications include synthetic constructions to express specific metabolic pathways for resilience or metabolite production, genome editing to enhance or remove specific traits, and gene drives to propagate genetic changes throughout a population with the goal of inhibiting reproduction or disease transmission.

The field of digital sequence information underpins the above-mentioned applications by harnessing bioinformatics to develop modification strategies. Digital sequences in and of themselves were not identified as posing direct environmental risks, but the decoupling of genetic information from biological materials represents an avenue for transboundary movement of genetic information and potential regulatory circumvention.[1,2]

With each modification strategy, there are concerns for unintended interactions with negative consequences for native species and biological diversity. Release of engineered organisms from laboratories or field trials or horizontal gene transfer of engineered traits in wild populations could affect natural competition and shift population ecology.[1]

Release is of particular concern for gene drives, whose velocity and extent of propagation may be unpredictable and uncontrollable. Containment strategies to reduce escape including toxin-producing safeguards, minimal genomes, auxotrophy, and engineered addiction can be designed as multilayered approaches.[3] Introducing adaptive traits could have cascading negative effects on complex ecological interactions. Unintended release to the environment could result in changes to or depletion of resources, competition with native species, and pathogenicity or toxicity.[4]

Escape detection using signaling and sensing with targeted antimicrobial secretion can provide mitigation to some concerns from uncontrolled release.[3] Risk assessment should consider potential irreversible propagation with lack of detection and traceability tools, weighed against potential benefits.[5] For example, the introduction of synthetic soil microbiome inoculants in reforestation for reduced fertilizer inputs and improved environmental tolerance should be weighed against expansion and disruption of natural ecosystems, or the potential for unintended interactions or spread of modified monoculture traits into the surrounding environment.[6]

Regulation should focus on the products themselves rather than the processes used to create them.[7] Assessing new products may require defining additional pathways and identifying new risk assessment endpoints.[2] To assess and manage these potential risks, jurisdictions can develop specific risk assessment guidance, define what constitutes harm with specific criteria, and ensure a dynamic approach between risk assessment (pre-release modeling) and management (post-release monitoring).[5]

Using a phased, modular approach to regulatory authorizations could fit product development phases to regulatory steps.[5]

Risk assessment should weigh potential risks against potential benefits including non-action and alternative approaches.[5] Advanced ecological and evolutionary modeling is required to anticipate consequences, but uncertainties will remain.[8] Biosafety and biosecurity concerns will broaden as development in these fields continues, and there is the potential to overwhelm risk assessment regulatory programs.[9] Periodic iterative reexamination of the results of foresight / horizon scanning exercises as developments in synthetic biology progress will increase their utility.[10]

1 Rabitz et al (2020) Emerging Technologies in Biodiversity Governance: Gaps and Opportunities for Action

2 Keiper and Atanassova (2020) Regulation of Synthetic Biology: Developments Under the Convention on Biological Diversity and Its Protocols

3 Ke et al (2021) Microbiome Engineering: Synthetic Biology of Plant-Associated Microbiomes in Sustainable Agriculture

4 Hewett et al (2016) Human health and environmental risks posed by synthetic biology R&D for energy applications: a literature analysis

5 Devos et al (2022) Risk management recommendations for environmental releases of gene drive modified insects

6 Sutherland et al (2023) A global biological conservation horizon scan of issues for 2023

7 Karoui et al (2019) Future Trends in Synthetic Biology—A Report

8 Coleman and Goold (2019) Harnessing synthetic biology for kelp forest conservation

9 Wang and Zhang (2019) Synthetic biology: Recent progress, biosafety and biosecurity concerns, and possible solutions

10 Nelson et al (2021) Foresight in Synthetic Biology and Biotechnology Threats

General synthetic biology reviews

Synthetic biology 2020–2030: six commercially-available products that are changing our world | Nature Communications

Synthetic biology: a new frontier in food production - ScienceDirect

Plant synthetic biology innovations for biofuels and bioproducts: Trends in Biotechnology (cell.com)

Synthetic biology landscape and community in Germany - ScienceDirect

Synthetic chromosomes, genomes, viruses, and cells (Venter et al., 2022)

Controlling the Implementation of Transgenic Microbes: Are We Ready for What Synthetic Biology Has to Offer? (Stirling and Silver, 2021)

Biotechnology for secure biocontainment designs in an emerging bioeconomy (Arnolds et al., 2021)

Genome editing

Frontiers | The application of CRISPR /Cas mediated gene editing in synthetic biology: Challenges and optimizations (frontiersin.org)

Synthetic Biology and Genome-Editing Tools for Improving PHA Metabolic Engineering: Trends in Biotechnology (cell.com)

CRISPR technology: A decade of genome editing is only the beginning | Science

Harnessing synthetic biology to engineer organoids and tissues - ScienceDirect

Enabling technology and core theory of synthetic biology | SpringerLink

Unlocking the magic in mycelium: Using synthetic biology to optimize filamentous fungi for biomanufacturing and sustainability - ScienceDirect

Metabolic engineering

Role of Metabolic Engineering and Synthetic Biology in the Development of Microbes for Biofuel Production | SpringerLink

Metabolic engineering and synthetic biology of plant natural products – A minireview - ScienceDirect

Systems biology, synthetic biology, and metabolic engineering - ScienceDirect

De novo biosynthesis of berberine and halogenated benzylisoquinoline alkaloids in Saccharomyces cerevisiae | Communications Chemistry (nature.com)

Metabolic engineering for sustainability and health - ScienceDirect

Leveraging synthetic biology and metabolic engineering to overcome obstacles in plant pathway elucidation - ScienceDirect

Genome recoding

Synthetic Genome Recoding: New genetic codes for new features (nih.gov)

Synonymous genome recoding: a tool to explore microbial biology and new therapeutic strategies | Nucleic Acids Research | Oxford Academic (oup.com)

With 'recoded' synthetic genome, scientists give life new dictionary - STAT (statnews.com)

Development of safe and highly protective live-attenuated SARS-CoV-2 vaccine candidates by genome recoding (Trimpert et al., 2021)

Artificial Cells

Bottom-Up Synthesis of Artificial Cells: Recent Highlights and Future Challenges(Ivanov et al., 2021)

Interfacing Living and Synthetic Cells as an Emerging Frontier in Synthetic Biology (Yuval Elani 2021)

Vesicle-based artificial cells: materials, construction methods and applications. (Lu Y et al., 2022)

Gene drive

Gene drives gaining speed (Ethan Bier 2022)

Base editing technology

A novel base editor SpRY-ABE8eF148A mediates efficient A-to-G base editing with a reduced off-target effect. (Li G et al., 2022)

PhieABEs: a PAM-less/free high-efficiency adenine base editor toolbox with wide target scope in plants (Tan J et al., 2022)

Artificial intelligence (AI) and machine learning (ML) in Synthetic Biology

Perspectives for self-driving labs in synthetic biology (Martin et al., 2023)

Metabolomics and modelling approaches for systems metabolic engineering (Khanijou et al., 2022)

Cybergenetic identification

Recent advances, opportunities and challenges in cybergenetic identification and control of biomolecular networks (Caringella et al., 2023)

Cybergenetic control of microbial community composition. (Lee TA, Steel H. 2022)

Dynamic cybergenetic control of bacterial co-culture composition via optogenetic feedback (Mena et al., 2022)

GM viruses for F&DA biologics

Synthetic and systems biology principles in the design of programmable oncolytic virus immunotherapies for glioblastoma (Monie et al., 2021)

Synthetic biology in the clinic: engineering vaccines, diagnostics, and therapeutics (Tan et al., 2021)

Combating Infectious Diseases with Synthetic Biology (Khan et al., 2022)

Synthetic Biology Design as a Paradigm Shift toward Manufacturing Affordable Adeno-Associated Virus Gene Therapies (Collins et al., 2023)

Trends and industrial applications of synthetic biology

Future Trends in Synthetic Biology—A Report (El Karoui et al 2019)

Trends in Synthetic Biology Applications, Tools, Industry, and Oversight and Their Security Implications (Carter and Warner 2018)

Advanced materials for industrial application

A living foundry for Synthetic Biological Materials: A synthetic biology roadmap to new advanced materials (Le Feuvre and Scrutton 2018)

Developing synthetic biology for industrial biotechnology applications (Clarke and Kitney 2020)

Synthetic biology: applications come of age (Khalil and Collins 2010)

Applications, challenges, and needs for employing synthetic biology beyond the lab (Brooks and Alper 2021)