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Convention on Biological Diversity

Multidisciplinary Ad Hoc Technical Expert Group on Synthetic Biology to Support the Process for Broad and Regular Horizon Scanning, Monitoring and Assessment
First meeting
Montreal, Canada, 11–14 July 2023
Item 3 of the provisional agenda[*]
Implementation of the mandate

Considerations on synthetic biology pursuant to decision 15/31

Note by the Secretariat

I. Introduction

1. In its decision 15/31, the Conference of the Parties to the Convention on Biological Diversity established a process for broad and regular horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology and agreed to start its work for one intersessional period.

2. In the same decision, the Conference of the Parties also established the multidisciplinary Ad Hoc Technical Expert Group on Synthetic Biology to Support the Process for Broad and Regular Horizon Scanning, Monitoring and Assessment and requested the Executive Secretary to convene the Open-ended Online Forum on Synthetic Biology to support the work of the Expert Group.

3. The Conference of the Parties invited Parties, other Governments, indigenous peoples and local communities, and relevant organizations to provide the Executive Secretary with relevant information on trends in new technological developments in synthetic biology to inform the process of horizon scanning, monitoring and assessment.

4. The Conference of the Parties requested the Subsidiary Body on Scientific, Technical and Technological Advice to consider, among other things, the outcomes of the horizon scanning process contained in the report of the Expert Group and to make recommendations for consideration by the Conference of the Parties at its sixteenth meeting.

5. Pursuant to the above, the Executive Secretary issued notification 2023-006, in which she invited Parties, other Governments, relevant organizations and indigenous peoples and local communities to submit information relevant to the intersessional process on synthetic biology and requested the submission of nominations of experts for participation in the Open-ended Online Forum.

6. A total of 16 submissions were received by the Secretariat: 5 from Parties, 1 from indigenous peoples and local communities and 10 from organizations.[1]

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[*] CBD/SYNBIO/AHTEG/2023/1/1.

[1] The original submissions are available at https://bch.cbd.int/en/submissions-to-notifications?schema=submission&currentPage=1&notification=2023-006.

7. The Open-ended Online Forum on Synthetic Biology was convened from 20 to 31 March 2023. A total number of 87 people registered, of whom 87 actively participated. A total of 194 interventions were made, of which 97 were made by 24 Parties, 5 by one non-Party, 88 by 36 organizations and 4 by one representative of indigenous peoples and local communities.[2]

8. The present document has been prepared to facilitate the deliberations of the Expert Group and is organized according to the elements in the terms of reference for the Group, as adopted in the annex to decision 15/31. Section II thus outlines the methodologies and steps to be taken for broad and regular horizon scanning, monitoring and assessment; section III addresses the trends in synthetic biology and the scope of the process; and section IV details the work to be undertaken by the Expert Group. The information in those sections is drawn from the submissions on synthetic biology, the discussions in the Online Forum and the compilation of literature made by the Secretariat. Group members are encouraged to review the original submissions and online discussions for further information.

9. In addition, the following background documents containing detailed information to support the discussions have also been prepared:

(a) Synthesis of submissions on synthetic biology (CBD/SYNBIO/AHTEG/2023/1/INF/1);

(b) Summary of discussions of the Open-ended Online Forum on Synthetic Biology (CBD/SYNBIO/AHTEG/2023/1/INF/2).

10. The report of the Ad Hoc Technical Expert Group on Synthetic Biology on its meeting in 2019 (CBD/SYNBIO/AHTEG/2019/1/3) and the publication *CBD Technical Series No. 100: Synthetic Biology*[3] could also represent complementary sources of information.

11. In undertaking its deliberations, the multidisciplinary Ad Hoc Technical Expert Group should bear in mind paragraph 4 of decision XIII/17, in which the Conference of the Parties acknowledged the outcome of the work of the Ad Hoc Technical Expert Group on Synthetic Biology on the operational definition of synthetic biology (see annex II, footnote 2) and considered it useful as a starting point for the purpose of facilitating scientific and technical deliberations under the Convention and its Protocols.

II. Process for broad and regular horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology

12. In paragraph 1 (a) of its terms of reference, the multidisciplinary Ad Hoc Technical Expert Group is tasked with making use of existing tools and approaches to enable a participatory process to review and assess the information to be gathered through the process for broad and regular horizon scanning, monitoring and assessment. To facilitate the process and to fulfil its mandate, the Group may wish to consider examples of other horizon scanning and foresight exercises, as they contain specific elements that could relate to the steps agreed by the Conference of the Parties in decision 15/31. Section A below details specific methodologies, approaches and examples of similar excises, while section B provides options and details related to the steps outlined in decision 15/31.

[2] The discussions held in the Open-ended Online Forum are available at www.cbd.int/synbio/current_activities/open-ended_online_forum/.

[3] Secretariat of the Convention on Biological Diversity, *Synthetic Biology*, CBD Technical Series No. 100 (Montreal, 2022). Available at www.cbd.int/doc/publications/cbd-ts-100-en.pdf.

A. Methodologies, approaches and examples from other horizon scanning and foresight activities

13. There are a number of methodologies for carrying out the process for broad and regular horizon scanning, monitoring and assessment of the most recent technological developments on synthetic biology, which were identified during the discussions of the Open-ended Online Forum on Synthetic Biology.[4] A summarized list of methodologies for performing horizon scanning either collected during the Open-ended Online Forum or identified by the Secretariat, as well as considerations for the participation of indigenous peoples and local communities in that process, can be found in annex I.

14. In decision 15/31, the Conference of the Parties decided that the process for horizon scanning, monitoring and assessment consisted of the following steps: (a) information gathering; (b) compilation, organization and synthesis of information; (c) assessment; and (d) reporting on outcomes.

15. On that basis, when referencing the steps defined by Conference of the Parties and the methodologies detailed in annex I, two categories of methodologies can be established:

(a) Expert-driven methodologies, which involve guidance from and the submission of information by experts, for example, through surveys and questionnaires. Examples of such methodologies with steps similar to those decided by the Conference of the Parties include:

(i) Expert-driven horizon scanning;

(ii) The "investigate, discuss, estimate and aggregate" protocol;

(iii) Expert panel discussions;

(b) Research-driven methodologies, which are based on extensive information-gathering. Examples of such methodologies with steps similar to those decided by the Conference of the Parties include:

(i) Processes for scanning emerging science and technology issues;

(ii) The European Environment Information and Observation Network horizon scanning;

(iii) Six-stage horizon scanning;

(iv) The National Institute for Health and Care Research Innovation Observatory horizon scanning;

(v) The Patient-Centered Outcomes Research Institute Horizon Scanning System.

16. For expert-driven horizon scanning, it would be important to ensure that a broad range of expertise and diverse groups of experts are involved in the process, especially during the submission of topics for consideration for the horizon scan. The initial steps involving the submission of topics for consideration and first scoring could be performed through virtual means, while a final assessment and re-scoring could be conducted at a later in-person meeting. For expert-driven horizon scanning and the investigate, discuss, estimate and aggregate protocol, modified Delphi techniques are applied to build consensus around topics. There may also be a need for further consideration of participatory approaches to feed into such a process.

17. For research-driven horizon scanning, there is usually a framing or scoping step to focus or set the context for the information-gathering step. This appears to improve the effectiveness of the information-gathering process. In addition, there are often additional steps for filtration and prioritization to assist in the management of the information during the compilation, organization and synthesis of information and assessment steps.

[4] See CBD/SYNBIO/AHTEG/2023/INF/2.

18. Predefined criteria or a structure to the discussions are often set up for the assessment step of horizon scans to facilitate a standardized approach.

19. Furthermore, there could be a need to consider an approach specific to indigenous peoples and local communities, as outlined in section II of annex I, to facilitate their participation and assessment.

20. The Expert Group may wish to consider the information above and the additional details in annex I and discuss the options for methodologies, with a view to identifying a methodology or the specific elements of a methodology to be applied for horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology.

B. Steps for broad and regular horizon scanning, monitoring and assessment

21. One of the aforementioned methodologies could be adapted or elements from various methodologies could be borrowed to customize the process, if needed, to enable the Expert Group to fulfil its mandate and follow the steps decided by the Conference of the Parties in its decision 15/31. The individual steps are considered below.

1. Information gathering

22. The Conference of the Parties specified that the coordinating actors for the "information-gathering" step would be the Secretariat, with the support of consultants, as appropriate. Furthermore, the coordinating actors should make use of digital tools for disseminating and collecting information, including submissions of information, outreach to relevant institutions and organizations, online forums and collaborative activities, as necessary.

23. The following entities and sources could therefore inform the information-gathering process: Governments, academia, private institutions, industry associations, civil society, indigenous peoples and local communities, experts, committees, media, peer-reviewed literature, patent registries, surveys, information provided through submissions, meetings, conferences and grey literature databases.

24. Methodologies for gathering information could include literature searches and reviews, surveys, questionnaires, interviews, open forums, workshops, exploratory scanning, issue-centred scanning and the "petal flower framework".

25. If an expert-driven process, such as the expert-driven horizon scanning or the investigate, discuss, estimate and aggregate protocol, is considered, questionnaires and surveys would be the primary means of information gathering. There could also be opportunities to complement those with other methodologies. The list of applications provided in annex II could be a starting point for recent developments in the field of synthetic biology.

26. If a research-based process is chosen, a more specific scope may be needed to carry out the mandate given by the Conference of the Parties in the time available. The list of trends in synthetic biology, as presented in section III of the present document, will be discussed under agenda item 3 (c) and may provide ideas for information gathering.

2. Compilation, organization and synthesis of information

27. The Conference of the Parties specified that the coordinating actors for the "compilation, organization and synthesis of information" step would be the Secretariat, with the support of consultants, as appropriate.

28. If an expert-driven process is considered, the submission of topics would need to be organized so as to facilitate scoring and ranking during the assessment step.

29. If a research-based horizon scan is considered, filtration criteria may assist with managing the quantity of information gathered and support its compilation, organization and synthesis. Filtration criteria may be similar to the assessment criteria detailed in section II.B.3 below. Information on those criteria could also be provided to inform the assessment step. Furthermore, this could be

assisted by a small group of experts to oversee the filtration step, confirm the pre-grouping of the applications or signals and organize the various inputs against new or existing trends, if necessary.

30. With regard to the organization of the information gathered, section III of the present document contains a list of trends in synthetic biology compiled from trends identified by the Ad Hoc Technical Expert Group on Synthetic Biology in 2019 and new trends identified in the online discussions. The trends provide a potentially helpful organizational structure to categorize the information in a way that will facilitate a synthesis. However, the applications of synthetic biology might be best organized more granularly for ease of scoring or assessment. Similarly, the publication *CBD Technical Series No. 100: Synthetic Biology* also provides an organizing frame that categorizes the applications in synthetic biology as follows:

(a) Synthetic biology applications in unmanaged or wild settings (commercially available, near term and research);

(b) Synthetic biology applications in semi-managed, managed or urban settings (commercially available, near term and research);

(c) Synthetic biology applications in containment, industrial processes or laboratory settings (commercially available, near term and research).

3. Assessment

31. The Conference of the Parties specified that the coordinating actors for the "assessment" step would be the Expert Group, the Subsidiary Body on Scientific, Technical and Technological Advice, the Conference of the Parties to the Convention and the Conference of the Parties serving as the meetings of the Parties to the Cartagena Protocol on Biosafety and of the Parties to the Nagoya Protocol on Access to Genetic Resources and the Fair and Equitable Sharing of Benefits Arising from their Utilization.

32. The compiled information from step 2 above will be presented to the experts for their assessment. The method for conducting the assessment could include structured debates, breakout groups, surveys, scoring and ranking and re-ranking. Participatory approaches will be an integral part of the assessment step. Specific methodologies used could include the Delphi method, scenarios and scenario planning, expert panels, multi-criteria decision analysis, a participatory action research approach and game playing.

33. If an expert-driven process is considered, the assessment step could consist of scoring, shortlisting, the consideration of information related to shortlisted topics, discussions, re-scoring and the finalization of a prioritized list. Further deliberations might be necessary to create the final list of prioritized topics and inform reporting in step 4 below. For such a process, it would be important to have predefined criteria, scales for scoring and a methodology for ranking (e.g. thresholds and set sizes of shortlist).

34. If a research-based methodology is considered, the Expert Group would participate in deliberations to assess the compiled information from step 2. It might be helpful to have some agreed areas or criteria for assessment or structure in the discussions, to facilitate an equal understanding of and participation in the assessment, while also ensuring time effectiveness.

35. To enable a standardized or methodological assessment, potential evaluation criteria could be the stage of development, the time frame to release or commercialization, barriers to market, potential impacts, the magnitude of potential impacts, the spatio-temporal scale, risk, novelty, available evidence, sources of information, the plausibility of application, the level of interest, desirability, ethical issues, socioeconomic considerations and the level of available expertise, among others.

36. Given the multidisciplinary nature of the Expert Group, further potential considerations for the assessment could include ethical, socioeconomic and cultural impacts; gaps in knowledge; the need for technology assessments; and the identification of capacity-building, technology transfer and

knowledge-sharing needs. There may also be a need to consider how to facilitate contributions through an indigenous people-led process.

37. In the light of the aforementioned information and the assessment, trends in synthetic biology may need to be redefined and prioritized, as necessary, for reporting in step 4 below.

4. Reporting on outcomes

38. The Conference of the Parties specified that the coordinating actors for the "reporting on outcomes" step would be the Expert Group, the Subsidiary Body on Scientific, Technical and Technological Advice, the Conference of the Parties to the Convention and the Conference of the Parties serving as the meetings of the Parties to the two Protocols.

39. The reports resulting from the Expert Group meetings will be submitted to the Subsidiary Body on Scientific, Technical and Technological Advice to enable it to make recommendations on specific issues that may require further consideration by the Conference of the Parties to the Convention and the Conference of the Parties serving as the meetings of the Parties to the two Protocols.

40. It was suggested that the Expert Group focus its final report to the Subsidiary Body on Scientific, Technical and Technological Advice on a subset of high-priority technological developments, such as the most significant 15 to 20 developments, identified from a longer list. The reports could contain a brief summary of potential impacts, gaps in knowledge and state of development, among others. They will be complemented by an additional report outlining the capacity-building, technology transfer and knowledge-sharing needs on the basis of priorities determined by Parties on issues related to synthetic biology and in the light of the outcomes of the horizon scanning process.

41. The Expert Group may wish to consider the information above and the additional details in annex I and discuss the most appropriate options for each step decided by the Conference of the Parties, with a view to constructing a methodology for horizon scanning, monitoring and assessment of the most recent technological developments in synthetic biology.

III. Trends in synthetic biology and clarification of the scope of the broad and regular horizon scanning, monitoring and assessment process

42. In the report on its meeting held in 2019, the Ad Hoc Technical Expert Group on Synthetic Biology compiled the following non-exhaustive list of trends in the field of synthetic biology:

(a) Increased field testing of organisms, components and products derived from new developments in synthetic biology;

(b) Increased development of technologies that genetically modify organisms directly in the field;

(c) A shift to the development of synthetic biology for environmental, conservation, agricultural and health uses;

(d) Increasing sophistication of methods, including, for example, new genome editing techniques, more complex metabolic engineering, the recoding of genomes and the use of artificial intelligence/machine learning for the redesign of biological systems;

(e) The use of transient modification of organisms, including, for example, through the use of synthetic double-stranded RNA molecules, nanoparticles and genetically modified viruses;

(f) Ability to produce new synthetic biomolecules using non-canonical nucleotides and amino acids;

(g) The use of synthetic biology for non-biological purposes, for example in data storage.

43. When providing information on the trends, several additional technological developments and applications of synthetic biology were shared. Annex II contains a list of applications and recent developments in the field of synthetic biology compiled from the submissions of information, discussions of the online forum and the publication *CBD Technical Series No. 100: Synthetic Biology*.

44. When considering the aforementioned trends and technological developments in synthetic biology, it can be seen from the submissions and discussions in the online forum that some applications of synthetic biology may fall under more than one of the trends listed in paragraph 42. Furthermore, it can be noted that the majority of synthetic biology applications that are in the later stages of research and development are for use in contained or industrial settings. In contrast, applications for use in the environment largely appear to be at a research and development stage.

45. In addition to the trends identified by the Ad Hoc Technical Expert Group on Synthetic Biology, a number of potential trends and issues were also raised for consideration in the submissions of information and during the discussions of the Open-ended Online Forum on Synthetic Biology,[5] namely:

(a) Engineering photosynthetic pathways;

(b) Engineered gene drives, including anti-clustered regularly interspaced short palindromic repeats-associated (CRISPR-Cas) and anti-drives;

(c) Modified algae applications under semi-contained or open-release conditions;

(d) The technological convergence of synthetic biology with other fields, such as nanotechnology and artificial intelligence;

(e) Paratransgenesis;

(f) Novel protein engineering;

(g) Transgenic and foliar applications based on RNA interference;

(h) Transient expression;

(i) Viral and nanoparticle delivery systems;

(j) Modified microorganisms, such as viruses, synthetically synthesized viruses (e.g. horsepox virus) and self-spreading vaccines;

(k) Complex applications of genome editing, such as de novo domestication and ribonucleoprotein complexes;

(l) Engineered sterility to enable the widespread use of non-native plants (e.g. non-native fast-growing trees for plantation use that would otherwise become invasive);

(m) Null or negative segregants;

(n) Plastid engineering and organelle modification (e.g. through genome editing);

(o) Living materials;

(p) Xenobots;

(q) Biosensors for environmental applications;

(r) Bioelectronics, such a DNA digital storage and bioactive cells;

(s) The increased complexity of genetic (DNA and RNA) circuits;

(t) Artificial chromosomes;

[5] See also CBD/SYNBIO/AHTEG/2023/INF/1 and CBD/SYNBIO/AHTEG/2023/INF/2.

(u) Hachimoji DNA (expanded DNA and RNA bases);

(v) Cell-free systems;

(w) Biofoundries;

(x) The use of big data;

(y) The dual-use nature of synthetic biology and biosecurity (e.g. microorganisms, horizontal environmental genetic alteration agents, engineered gene drives and "do-it-yourself" biology);

(z) Interaction of synthetic biology organisms in the environment and cumulative effects;

(aa) The increased scale of synthetic biology techniques and their use in series;

(bb) Transboundary movements into and use of applications developed in non-Party territories on other territories, especially for countries without the ability to detect and identify the applications and their impacts on the environment;

(cc) Field-testing applications outside the national jurisdiction of the developers or funders;

(dd) Changes in ethical standards, such as "norm erosion";

(ee) Regulatory documents and final projects not made public in a timely manner;

(ff) The exponential growth of the synthetic biology market without significant participation of developing countries;

(gg) The adoption of the Kunming-Montreal Global Biodiversity Framework and its support to the implementation of Articles 16 to 19 of the Convention on Biological Diversity;

(hh) Public engagement, awareness and communication.

46. In considering the proposed new trends in synthetic biology, it was suggested that new technological developments might not always be indicativ of imminent applications or of new trends. However, it may also be important to adopt a broad process to capture applications that could have an impact on the objectives of the Convention.

47. For the purposes of the horizon scanning process, the Expert Group may need to re-examine the trends at its second meeting as part of the "assessment" or "reporting on outcomes" steps and in the light of the results of the process.

48. With respect to the information above and the discussions under agenda items 3 (a) and 3 (b) (see sects. II.A and II.B), the Expert Group may wish, as necessary and appropriate, to discuss the identified trends in synthetic biology in order to set the scope of the process of broad and regular horizon scanning, monitoring and assessment for the intersessional period. Alternatively, the Expert Group could address the trends in synthetic biology at its second meeting.

IV. Programme of work for the multidisciplinary Ad Hoc Technical Expert Group on Synthetic Biology to Support the Process for Broad and Regular Horizon Scanning, Monitoring and Assessment

49. Two meetings of the Expert Group are planned during the current intersessional period, one in July 2023 to decide how to perform the process for broad and regular horizon scanning, monitoring and assessment of the most recent developments in synthetic biology (see sect. II), and one in the first quarter of 2024 to finalize the work.

50. It is expected that the Expert Group will set the methodology for the first cycle of the process and evaluate the trends in the field of synthetic biology to set the scope for the process (see sect. III) at the present meeting. The steps of "information gathering" and "compilation, organization and

synthesis of information", as defined by Conference of the Parties in decision 15/31, will be addressed between the two meetings of the Group on the basis of the report of the present meeting.

51. It is also expected that the Expert Group will complete its mandate at its second meeting by conducting the "assessment" and "reporting on outcomes" steps, as well as identifying capacity-building, technology transfer and knowledge-sharing needs on the basis of the priorities determined by Parties on issues related to synthetic biology and in the light of the outcome of the horizon scanning process. At the same meeting, the Group will also prepare recommendations for consideration by the Subsidiary Body on Scientific, Technical and Technological Advice at its twenty-sixth meeting.

52. The table below provides an overview of the timeline for the work of the Expert Group.

Timeline for the 2023/24 period

Activity	*Dates*
Submissions of information on synthetic biology	February–March 2023
Open-ended Online Forum on Synthetic Biology	20–31 March 2023
First meeting of the Expert Group	11–14 July 2023
Information gathering (step 1)	17 July 2023–end of 2023
Compilation, organization and synthesis of information (step 2)	
Second meeting of the Expert Group Assessment (step 3) and reporting on outcomes (step 4)	First quarter of 2024 (tentative)
Peer-review of the Expert Group report (step 4)	First quarter of 2024 (tentative)
Twenty-sixth meeting of the Subsidiary Body on Scientific, Technical and Technological Advice (steps 3 and 4)	13–17 May 2024 (tentative)
Sixteenth meeting of the Conference of the Parties	Third or fourth quarter of 2024 (tentative)

Annex I

Horizon scanning and foresight methodologies

I. Specific methodologies for performing horizon scanning

1. When considering the mandate to begin a first cycle of horizon scanning, assessment and monitoring and to inform the overall process, it could be useful to consider previous examples of horizon scans and foresight activities. As such, several methodologies were highlighted during the discussions of the Open-ended Online Forum on Synthetic Biology,[1] such as:

(a) **The Delphi method**. This method is a consensus-based approach that involves iterative rounds of surveys and feedback from experts in the field. It can be used to identify emerging technologies, assess their potential impacts, and prioritize them for further analysis. Delphi studies are widely used to pool knowledge and build consensus around emerging issues. They often involve two or more rounds. In the first round, participants identify relevant issues, which are then pooled and ranked; in the second round, the issues are discussed and re-ranked. This process is iterated until a consensus is reached. An example of a Delphi method is the Foresight programme of the United Kingdom of Great Britain and Northern Ireland;[2]

(b) **Investigate, discuss, estimate and aggregate (IDEA) protocol**. Under this protocol, a diverse group of experts is convened to answer questions with probabilistic or quantitative responses. The experts investigate the questions and clarify their meaning before providing estimations and credible intervals. They are then provided with the anonymous answers to the questions, if possible with a visual summary of the responses. Following a discussion, the experts are then requested to provide another, anonymous estimation. The answers are aggregated, and a mean value is calculated as the final output. Further discussion and clarifications may be also provided following the aggregation of the responses. The IDEA protocol is aimed at improving expert judgements and reducing linguistic ambiguity. An example of a horizon scan performed using the IDEA protocol is the World Health Organization (WHO) publication on emerging trends and technologies for public health of 2022.[3] WHO performed its horizon scan using a diverse group of experts who identified issues on the basis of predefined criteria. The issues were then compiled into one list and scored anonymously, also on the basis of predefined criteria. After that, z-scores[4] were calculated and a shortlist based on ranking was produced. The participants received the shortlist with z-scores, and a commentary period was opened for their deliberation at workshops and in online discussions. At a final workshop, they were asked to submit comments and re-score at least half of the shortlisted issues for a calculation of the final z-scores. A final prioritized list of 15 topics was then submitted for analysis;

(c) **Scenarios and scenario planning**. Scenarios are plausible extrapolations about the future that explore various possible outcomes on the basis of various drivers of change. Scenarios can be used to identify key uncertainties, explore alternative futures and inform strategic planning. It was suggested that scenarios that explore the intersection of technological developments and social contexts should also be developed. Examples of scenarios used for horizon scanning are the Small Island Developing States Global Business Network scenarios for synthetic biology, which explored four possible futures based on different levels of public acceptance and regulatory oversight, and the Synthetic Biology Roadmap developed by the United Kingdom;

[1] See CBD/SYNBIO/AHTEG/2023/INF/2.

[2] See www.gov.uk/government/collections/foresight-projects.

[3] WHO, *Emerging Trends and Technologies: A Horizon Scan for Global Public Health* (Geneva, 2022).

[4] A z-score measures exactly how many standard deviations above or below the mean a data point is.

(d) **Environmental scanning**. This method involves systematically gathering and analysing information from a wide range of sources to identify trends, emerging issues and potential threats and opportunities. It can be used to identify emerging technologies, assess their potential impacts and inform policymaking and decision-making. An example of environmental scanning used for horizon scanning is the state of the environment report for 2020 published by the European Environment,[5] in which emerging environmental risks and opportunities in Europe were identified;

(e) **Expert panels**. Expert panels are groups of experts in a particular field that are convened to provide insights and recommendations on emerging trends and issues. Expert panels can be used to identify emerging technologies, assess their potential impacts and prioritize them for further analysis. Examples of expert panels used for horizon scanning are the Emerging Frontiers in Research and Innovation programme of the National Science Foundation, the horizon scan on genome editing and synthetic biology of the National Committee on Biosafety of the Philippines and the horizon scan for synthetic biology of the Australian Council of Learned Academies;

(f) **Literature review and synthesis**. This method consists of a comprehensive review and synthesis of scientific literature for identifying and assessing the potential impacts of synthetic biology on biodiversity, gaps in knowledge and areas for further research;

(g) **Multi-criteria decision analysis**. This method is used for evaluating and ranking various options or scenarios on the basis of multiple criteria that can be useful for identifying and evaluating potential policy or management options for synthetic biology and biodiversity. Examples of such an analysis include a review on sustainable manufacturing decision-making[6] and an analysis performed for vegetable oils to produce bio-based plastics;[7]

(h) **The European Environment Agency horizon scanning guide**.[8] This guide uses the following steps: (i) signal spotting (locating signals); (ii) signal scanning (collecting signals); (iii) sense-making; and (iv) communicating output. The protocol usually starts with an initial framing step;

(i) **Participatory action research**. These are a set of approaches originally developed by people who were in, or worked in close collaboration with, communities experiencing oppression. People who had previously been marginalized are able to designate the focus of the participatory and dialogue processes themselves. Participatory action research approaches have been adopted by Red de Evaluación Social de Tecnologías en América Latina, Espace citoyen d'interpellation démocratique in Mali and Prajateerpu in India;

(j) **Game playing.** This method consists of playing through scenarios. In the field of cybersecurity, there are two types of entities: players and intruders. The players communicate or operate with one another while the intruders attempt to steal their information or intercept their secrets. The simulation continues as the players and intruders are changed. With respect to synthetic biology, it was suggested that the players could be physical (e.g. cells, biochemical pathways, entire organisms or the environment) or social (e.g. religious beliefs). Examples of game playing are the European Union Agency cybersecurity projects for understanding the overlaps between cybersecurity and biotechnology.

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[5] European Environment Agency, *The European Environment – State and Outlook 2020: Knowledge for Transition to a Sustainable Europe* (Luxembourg, Publications Office of the European Union, 2019).

[6] Anbesh Jamwal and others, "Review on multi-criteria decision analysis in sustainable manufacturing decision-making", *International Journal of Sustainable Engineering*, vol. 14, No. 3 (December 2020).

[7] Laura Äkräs and others, "A multi-criteria decision-making framework and analysis of vegetable oils to produce bio-based plastics", *Industrial Crops and Products*, vol. 188, part A (November 2022).

[8] Tanja Schindler and others, *Horizon Scanning: Tips and Tricks – A Practical Guide*, (European Environment Agency, 2021). Available at https://eionet.kormany.hu/download/2/bf/b2000/Horizon_Scanning_Guide.pdf.

2. To complement this information, the Secretariat also has identified the following approaches and methodologies that could be considered for facilitating horizon scanning, monitoring and assessment:

(a) **Expert-driven horizon scanning**. This method involves convening a group of participants who identify the areas or signals to be evaluated. It consists of the following steps: (i) identifying topics through submissions; (ii) collating topics; (iii) conducting a first scoring of topics; (iv) selecting the highest-scoring topics; (v) having participants produce a commentary on the shortlisted topics; (vi) discussing and rescoring topics; and (vii) establishing a final list of the 15 (or other number) highest-ranking topics. A global biological conservation horizon scan of issues for 2023[9] used this methodology, which was based on a Delphi-style technique. Experts were invited to request members of their networks to contribute to the process and to submit two to five topics for consideration. The submitted topics were then organized by theme before being scored anonymously. The scores were converted to a ranking to create a shortlist of topics. Participants were then invited to examine up to four topics not submitted by them ahead of a final workshop. At the final workshop, the shortlisted topics were opened for comment, discussed and re-scored (assessment). The result was a final list of 15 topics (reporting);

(b) **Exploratory scanning**. This method consists of the following steps: (i) setting up a (slightly focused) search profile; (ii) conducting a broad scanning for signals;[10] (iii) conducting a preliminary assessment, filtration and selection; and (iv) clustering signals.[11] This process can be also thought of as “hypothesis generation”;

(c) **Issue-centred scanning**. This method consists of the following steps: (i) framing and conceptualization; (ii) seeking of signals to build a narrative with an impact, using reliable sources and assessments based on predefined criteria; and (iii) conducting a second search to confirm or oppose constructed narratives. The process starts with existing or emerging topics and proceeds with searches for signals to strengthen or weakened the topic. It could be seen for hypothesis evaluating;[12]

(d) **Emerging science and technology issue scanning process**. This method consists of the following steps: (i) selecting a broad area of issues to be examined; (ii) clustering weak signals; (iii) assessing the significance of the clustered issues; (iv) framing connected weak signals in clustered issues; (v) conducting a tentative modelling of emerging issues into possible emerging issues; and (vi) selecting significant issues. Exploratory and issue-centred scanning can be used to contribute to providing information during this protocol. Assessment of the list of emerging issues and the refinement of the issues into the specific context could be assisted by an expert workshop;[13]

(e) **Six-stage horizon scanning**. This method consists of the following steps: (i) scoping the issue (through interviews or issue trees); (ii) gathering information (through literature searches, online sources and activities); (iii) spotting signals (through a Delphi questionnaire); (iv) watching trends (through a trend analysis); (v) making sense of the future (through scenarios or system maps); and (vi) agreeing on the response (“backcasting”). The final step is designed to explore how the vision of the future could be met on the basis of the current situation;[14]

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[9] William J. Sutherland and others, “A global biological conservation horizon scan of issues for 2023”, *Trends in Ecology and Evolution*, vol. 38, No. 1 (January 2023).

[10] Signals in this sense could mean data points, new developments, indications of changes or new information, among others.

[11] See, for example, Effie Amanatidou and others, “On concepts and methods in horizon scanning: Lessons from initiating policy dialogues on emerging issues”, *Science and Public Policy*, vol. 39, No. 2 (March 2012).

[12] Ibid.

[13] Ibid.

[14] See, for example, William J. Sutherland and Harry J. Woodroof, “The need for environmental horizon scanning”, *Trends in Ecology and Evolution*, vol. 24, No. 10 (October 2009).

(f) **The National Institute for Health and Care Research Innovation Observatory horizon scanning methodology**.[15] This method requires the involvement of two institutions and consists of the following steps: (i) identification of emerging technologies and production of a briefing report, where the first institution seeks to identify emerging technologies with the assistance of consultations and organizes information; (ii) filtration, which is first performed by the first institution using predefined criteria, followed by another filtration carried out by the second institution; and (iii) prioritization of products by the second institution, using predefined criteria, to form a list of products for technology briefing;[16]

(g) **Patient-Centred Outcomes Research Institute horizon scanning methodology**.[17] This method consists of the following steps: (i) broad scanning led by guiding questions to identify information related to potential topics and trends; (ii) reviewing information and topics and identifying trends, using inclusion criteria; (iii) topic vetting, possibily through the use of experts; (iv) topic and trend nomination, performed by a team of horizon scanners; (v) topic and trend profile development, which will form the basis for stakeholder comments; and (vi) stakeholder engagement and surveys.

II. Examples and considerations for including indigenous peoples and local communities

3. In addition to the methodologies for horizon scanning, monitoring and assessment, there could also be specific approaches and considerations for including indigenous peoples and local communities. Some important points include defining how indigenous peoples and local communities could contribute to the process and how to incorporate their perspective; share, protect and respect their knowledge; allow for reflexivity; and facilitate dissemination back to the people in a culturally appropriate manner.[18] In addition, the Secretariat published in 2004 the Akwé: Kon Voluntary Guidelines for the Conduct of Cultural, Environmental and Social Impact Assessments regarding Developments Proposed to Take Place on, or which are Likely to Impact On, Sacred Sites and On Lands and Waters Traditionally Occupied or Used by Indigenous Peoples and Local Communities, which contain principles that could be relevant to horizon scanning, monitoring and assessment and the inclusion of indigenous peoples and local communities.

4. The following suggestions for or examples of inclusion of indigenous peoples and local communities have also been shared during the submission of information or identified by the Secretariat:

(a) Establishing an informal advisory group consisting of indigenous people and local community members from the seven eco-regions. The group would ensure respect for and the recognition and inclusion of knowledge systems, innovation, human rights and innovations of indigenous peoples and local communities, as well as indigenous sciences and free prior and informed consent, in the overall process. As a matter of fact, steering committees[19] have already been established to foster grass-roots decision-making. The work of the informal advisory group would be

[15] www.io.nihr.ac.uk/horizon-scanning.

[16] See, for example, Ashleigh Prest, Katrina Lapham and David Grainger, "Horizon Scanning: strengthening Australia's approach to horizon scanning for new therapies", round table report, 2021. Available at www.biointelect.com/wp-content/uploads/2022/08/Horizon-Scanning-Strengthening-Australias-approach-to-horizon-scanning-for-new-therapies.pdf.

[17] Randy Hulshizer and others, *Horizon Scanning Protocol and Operations Manual*, revised ed. (Washington, D.C., Patient-Centred Outcomes Research Institute, 2022). Available at www.pcori.org/sites/default/files/PCORI-Health-Care-Horizon-Scanning-System-Protocol-Operations-Manual.pdf.

[18] See Jelena Porsanger, "An essay about indigenous methodology", *Nordlit*, No. 15 (2004); and Jo-ann Archibald, "Coyote learns to make a story basket: the place of First Nations stories in education", PhD dissertation, Simon Fraser University, April 1997.

[19] See Grassroots Connect at https://grassrootsconnect.org/structure/#:~:text=Steering.

based on active listening, a shared purpose, preparations, deliberations and a focus on issues and solutions;

(b) The approach to recognizing and working with indigenous and local knowledge in the Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services,[20] which presented a framework of considerations, best practices, understanding and general challenges. The approach consists of: (i) the collaborative definition of problems and goals for the assessment; (ii) the synthesis and incorporation of related data from multiple sources of indigenous and local knowledge; (iii) engagement with indigenous peoples and local communities; and (iv) sharing knowledge and insights gained through the assessment with the indigenous peoples and local communities;

(c) Guidelines for Indigenous-centred artificial Intelligence Design, version 1,[21] which can be applied to initiating, maintaining and evolving relationships with other human beings or with non-humans, such as animals, rocks and wind. The Guidelines offer as an example the comparison of the building of a sweat lodge with that of a physical computing device. The protocol provided in the Guidelines consists of the following steps: consultation, identifying stakeholders, identifying raw materials, compensation, construction, preparing internal components, running the programme, transforming, welcoming, managing the life cycle and preparing for the death cycle;

(d) The publication *Kaandossiwin: How We Come to Know*,[22] written with respect to the Anishinaabe word *Kaandossiwin*, which describes the process of acquiring knowledge. The author suggested three steps: (i) a review of literature, including thesis projects, from indigenous scholars and researchers; (ii) individual conversations with indigenous scholars and researchers; and (iii) a group-learning circle with scholars and researchers from indigenous peoples and local communities;

(e) The petal flower framework,[23] in which the leadership and scholarship of indigenous peoples and local communities are acknowledged and validated. The components of the framework are interrelated. The framework consists of: (i) roots (foundational elements); (ii) a flower at the centre (self as central to the search); (iii) leaves (the journal, process and transformation); (iv) a stem (methodological backbone and supports); (v) petals (diverse ways of searching for knowledge); and (vi) the environment (context);

(f) The CARE Principles for Indigenous Data Governance,[24] which are based on collective benefit, authority to control, responsibility and ethics. These principles could complement the existing data-centric approach represented in the findable, accessible, interoperable and reusable (FAIR) guiding principles for scientific data management and stewardship;

(g) The First Nations principles of ownership, control, access and possession,[25] designed by the First Nations Governance Centre in Canada, which are aimed at ensuring that indigenous peoples and local communities have control over data collection processes in their communities and that they own and control how this information is stored, interpreted, used or shared.

[20] Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services decision IPBES-5/1, annex II.

[21] https://spectrum.library.concordia.ca/986506

[22] Kathleen Elaine Absolon (Minogiizhigokwe), *Kaandossiwin: How We Come to Know*, 2nd ed. (Winnipeg, Fernwood Publishing, 2022).

[23] Kathleen Elaine Absolon, "Kaandossiwin, this is how we come to know! Indigenous graduate research in the academy: world views and methodologies", PhD dissertation, University of Toronto, 2008, fig. 10. Available at www.collectionscanada.gc.ca/obj/thesescanada/vol2/002/NR39770.PDF?is_thesis=1&oclc_number=646562811.

[24] Stephanie Russo Carroll and others, "The CARE Principles for Indigenous Data Governance", *Data Science Journal*, vol. 19, No. 43 (November 2020).

[25] See https://fnigc.ca/ocap-training/.

Annex II

Recent technological developments in synthetic biology

1. Several examples of applications and developments in synthetic biology were shared during the Open-ended Online Forum on Synthetic Biology held from 20 to 31 March 2023 and through the submissions of information on synthetic biology.[1] In addition, various applications were also detailed in the publication *CBD Technical Series No. 100: Synthetic Biology*. All applications of synthetic biology from those resources have been listed by time frame of commercial or environmental release in sections I to V below.
2. It should be noted that, when considering the technological developments in synthetic biology outlined below, it could be difficult to predict the time frame for the release of an application, as there could be other factors that influence a larger-scale deployment (e.g. performance during field trials or challenges in scaling up the application).
3. Furthermore, it is important to recall that, in its decision XIII/17, adopted in 2016, the Conference of the Parties to the Convention on Biological Diversity acknowledged the operational definition of "synthetic biology"[2] proposed by the Ad Hoc Technical Expert Group on Synthetic Biology and considered it useful as a starting point for the purpose of facilitating scientific and technical deliberations under the Convention and its Protocols. However, there remains diverging views on whether some applications could be considered applications of synthetic biology

I. Forecast commercial developments or environmental release over the next five years

- Engineered microbes (bacteria and algae) for remediation or waste-recycling
    - Microbes degrade or metabolize contaminants into upcycled, high-value materials (developed by Allonia; commercialization stage)
- Use of synthetic biology for producing petrochemical precursors and industrial chemicals
    - Metabolic engineering of bacteria for biofuel precursors and high-value fine chemicals
        - Microbial chassis for petrochemical precursor synthesis (e.g. limonene) (developed by Global Bioenergies and LanzaTech; commercially available)
        - Farnesene, bisabolene, isobutene, methyl ketones or polycyclopropanated hydrocarbons (limited tests with marine biofuels)
        - Lignocellulosic biofuels based on soy, sugar or wood biodiesels (limited tests)
    - Metabolically engineered bacteria to capture greenhouse and waste gases to convert them into soil fertilizers (developed by Kiverdi; commercially available)
    - Engineered algae for chemical, protein, enzyme, lipid, hydrogen and alcohol production (near term)
- Unconfined cultivation of engineered algae
- Biosensors and synthetic biology-based diagnostics, for example for use in medicine and environmental water monitoring
- Living modified organisms containing engineered gene drives
    - Mosquitoes (could be longer than five years)
    - Mice (could be longer than five years)
    - Components of the system

[1] See CBD/SYNBIO/AHTEG/2023/INF/1 and CBD/SYNBIO/AHTEG/2023/INF/2.

[2] Synthetic biology is 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.

- Sterile insects
  - Field trial of sterile male mosquitoes (in 2019)
  - Mosquitoes (*Aedes aegypti*, *Anopheles albimanus* and *Anopheles stephensi*) or agricultural pests (fall armyworm, soybean looper, medfly, spotted-wing drosophila, diamondback moth) (developed by Oxitec; near term – field trials for mosquitoes and diamondback moth)
- Genome-edited agricultural crops
  - Tomato with increased γ-aminobutyric acid levels (commercially available)
  - *Camelina sativa* for improved oil quality for potential biofuel use (application for release)
  - High-oleic acid soybean (developed by Calyxt; previously approved, current market status not clear)
- Genome-edited button mushroom to prevent enzymatic browning (previously approved, current market status not clear)
- Genome-edited animals
  - Beef cattle with short, slick coats for heat tolerance (no objections to application raised)
  - Sea bream modified for increased growth rate and muscle mass (commercially available)
  - Pufferfish modified for increased growth rate and muscle mass (commercially available)
  - Pigs modified for xenotransplantation (near term)
- Genetically engineered bacteria as a nitrogen fertilizer in maize systems (developed by Pivot Bio; commercially available)
- EVO2106A – double-stranded RNA spray pesticide for use in agricultural settings
- Field trial of *Nicotiana tabacum* with synthetic glycolate pathway (in 2016)
- Field trial of modified poplar trees with increased photosynthetic capacity (developed by Living Carbon; ongoing)
- Self-spreading vaccines
  - To control Lassa fever in rats, rabies in bats and Ebola virus in primates
  - Field trial of self-spreading viral vaccines, such as modified raccoon poxvirus vaccine against *Pseudogymnoascus destructans* (in 2019)
- Biomaterials, such as mycelium-based leather products (developed by Bolt Threads), biosynthetic indigo dye for denim (developed by Huue), and microbial production of spider silk (developed by Spiber and AMSilk) (commercially available)
- Cosmetics, flavours and fragrances (commercially available)
  - Animal-free collagen substitutes (developed by Geltor)
  - Synthetic squalene production by fermentation (developed by Amyris)
  - Vanilla (developed by Conagen)
  - Nootkatone and valencene (developed by Evolva)
  - Metabolically engineered yeast (e.g. terpenes and proteins from rare or extinct plants; developed by Gingko Bioworks)
  - Other fragrances and flavours (0–10 years, mixed development)
- Biopharmaceuticals
  - Chimeric antigen receptors T-cell immunotherapies (developed by Novartis; commercially available)
  - Sitagliptin (re-engineered (R)-selective transaminase for diabetes) (developed by Merck; commercially available)
  - Semi-synthetic artemisinin (developed by Amyris; commercially available)
  - Synthetic recombinant factor C replacement for horseshoe crab blood (*Limulus* amoebocyte lysate) (developed by Lonza and bioMérieux; commercially available)

  - Cannabinoid production in yeast and bacteria (developed by Gingko Bioworks; commercially available)
  - Viral-vector vaccines, such as those for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and ebola virus (developed by AstraZeneca, Janssen, CanSinoBio and Gamaleya Research Institute; commercially available)
  - Synthetic RNA vaccines against SARS-CoV-2 (developed by Pfizer-BioNTech and Moderna; commercially available)
  - Engineered phages as antimicrobials (developed by Eligo Biosciences; near term)
  - Engineered probiotics for the production and in vivo delivery of therapeutics (developed by Precigen, Azitra and Synlogic; near term)
  - *Bacillus subtilis* ZB183™, a modified bacteria for the breakdown of acetaldehyde following alcohol consumption (commercially available)
  - BioElixOne – *Escherichia coli* expressing Cas9 and guiding RNAs to target genes in *Salmonella* sp. to prevent its growth in the intestine
  - *Escherichia coli* strain Nissle 1917 engineered as a therapeutic for infectious diseases, metabolic disorders, inflammatory bowel diseases and cancer
- Olfactory detection devices based on a microelectrode array, a microfluidics layer and engineered neurons (developed by Koniku; commercially available)
- Products produced from biofoundries (some available on the market)
- Chemical synthesis of viruses (e.g. horsepox, poliovirus, 1918 influenza virus and ectromelia virus)
- Genome editing using codon-optimized or rewritten DNA inserts
- Cell-free biology
- Expanded clustered regularly interspaced short palindromic repeats-associated (CRISPR-Cas) systems for genome editing and diagnostics (developed by Mammoth Biosciences; commercially available)

II. Forecast commercial developments or environmental release in the near term[3]

- Genetically engineered sorghum to produce a new synthetic protein to improve digestibility in food and feed
- Genetically engineered oilseed rape to enhance resource use efficiency of existing cropland
- Biofabricated wildlife products (e.g. ivory; developed by Pembient and Ceratotech)
- Plant-based vaccines (e.g. virus-like particle production)
- Microbial production of proteins for human consumption (developed by Motif FoodWorks, Clara Foods and Impossible Foods)
- Bacterial protein for food and feed generated by renewable energy and direct air capture of CO_2 (developed by Air Protein and CO2 Aquafeed developed by Kiverdi)
- Meat from cultured cells (developed by Memphis Meats, Meatable and Higher Steaks)
- Genome-edited hens that lay allergen-free eggs

III. Forecast commercial developments or environmental over the next 5 to 10 years

- Engineered plants and animals for remediation or waste-recycling
- Sugarcane-based fermentation to produce bioidentical molecules, such as plastics
- Soybeans with modified oil qualities for use as biofuels

[3] According to *CBD Technical Series No. 100: Synthetic Biology*, if not otherwise specified.

- Environmental use of double-stranded RNA sprays as herbicides and insecticides, as well as for delayed senescing
- Use of genome editors to create null segregants
- Use of genome editors for use in veterinary medicine and rodent control
- Genome editing gene therapy based on lentivirus or adeno-associated virus vectors to treat genetic disorders, including the delivery of CRISPR to brain tissues
- Retrobiosynthesis[4] using designed and optimized gene circuits for product synthesis
- Projects resulting from the International Genetically Engineered Machine competition

IV. Forecast commercial developments or environmental release beyond the next 10 years

- Engineered chytridiomycosis resistance in Australian frogs (e.g. corroboree frogs)
- Use of synthetic biology applications as sensors for disease-associated biomarkers or to modify intestinal microbiota composition
- New functional organisms as a result of artificial genome synthesis

V. Unspecified timeline or new technological developments

- Living modified organisms containing engineered gene drives
  - Thirty-two proposals for six insect orders, of which mosquito (*Anopheles gambiae* and *Aedes aegypti*) applications are the most advanced
  - Forty-two non-insect proposals, of which mice applications are the most advanced
  - Technical refinements, such as artificial speciation, efficiency of the engineered gene drive system in *Aedes aegypti* and temperature-dependent “cleave and rescue” selfish elements in *Drosophila*
  - Gene drive therapy for human immunodeficiency virus in high-risk population groups
- CRISPR-mediated transactivation in mosquitoes
- Modified viruses
  - Horizontal environmental genetic alteration agents
  - Viral vectors for contained use and *in planta* modifications (early research and development)
  - Engineered phages to combat antibiotic resistance
  - Novel viral delivery methods for genome editing plants and bacteria
  - Vaccines based on viral genomic recoding
  - Incorporation of gene circuits in oncolytic viral vectors for the treatment of glioblastoma multiforme
- Plant applications
  - Metabolically engineered to produce vitamin B12
  - Engineered to have C4 photosynthesis
  - Expression of plant-incorporated protectants
  - Fixation of their own nitrogen (distant future)
  - *In planta* production of recombinant polyclonal antibodies against snake venom, and other anti-venoms
  - New sterility systems to control invasive species or allow for forestation with exotic (non-native) species for lumber and pulp production
- Increased carbon capture in plants (possible on a research scale but not a large scale)
  - Engineering ribulose-1,5-bisphosphate carboxylase-oxygenase (Rubisco)
  - Utilizing synthetic pathways

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[4] The synthesis of organic chemicals from inexpensive precursors and evolved enzymes.

    - Improving the ability to capture light and tolerate dynamic lighting conditions more efficiently
    - Engineering carbon concentrating mechanisms
- Photosynthetic engineering (limited progress):
    - Rubisco
    - Mechanisms for concentrating carbon dioxide to Rubisco
    - Synthetic photorespiratory bypasses
    - Creation of novel carbon fixation pathways, including in minimal and synthetic cells, as well as in the development of artificial photosynthesis
- Genome-edited organisms
    - More than 400 applications (as at July 2022)
        - Majority cereal crops
        - High representation of the following traits: modified composition, biotic stress tolerance and plant yield and architecture
        - Pre-commercialization stage: six for herbicide tolerance, five for modified composition, two for improved storage performance, two for biotic stress tolerance and one for modified yield or architecture
        - Sorghum (striga resistance), teff (reduced lodging and grain shatter) and *Brassica carinata* (improved oil quality)
    - Abiotic resilience in coral and kelp (early research)
    - Pathogen resistance in amphibians and black-footed ferret (early research)
    - To prevent the spread of tick-borne Lyme disease in mice (early research)
- Hens engineered with photo-induced male lethality for use in egg production
- CRISPR-based nucleic acid detection and quantification of environmental DNA for identifying invasive species or providing insights in the distribution of threatened species
- Open-air use of proteins for modifying genetic materials
- Use of double stranded RNAs, including new formulation chemistries, such as clay nanoparticles (laboratory and greenhouse testing, potentially field trials)
- Use of synthetic DNA for transient modifications (e.g. using carbon nanotubules) (research stage)
- Increased field testing
- Engineered microbiomes
    - Coral microbiome for abiotic stress tolerance (early research and development)
    - Honeybee microbiome for biotic and pesticide tolerance
    - Engineered plant-microbe interactions for nitrogen-fixation or efficient phosphorus use
    - Use of viruses to change the genome of bacteria in intestinal microbiomes
    - Antibody treatments to modify the microbial composition of the intestinal track of livestock to reduce methane emissions
- Synthetic biology to mitigate environmental pollution
    - Degradation of plastics, petrochemicals and oil, pesticides, antibiotics, nutrients in agriculture or aquaculture run-off and cleaning by fluorinated compounds
    - Halotroph applications for water treatment
    - Bacteria modified to degrade nitrobenzene
    - Bacteria for mercury and phosphate absorption (research)
    - Biomining using engineered bacteria (e.g. gold, cobalt and nickel) (research stage)
- Microorganisms engineered to capture industrial emissions:
    - Chemotrophs using various carbon sources (e.g. engineered acetogens, hydrogenogens or methanotrophs) or through the creation of de novo synthetic carbon dioxide fixation pathways

  - Conversion into bioplastics, precursors to acrylic glass, cellulose, biofuels or carbonates
- Cell-free systems designed to capture carbon and for the production of high-value pharmaceuticals
- Organisms for industrial and pharmaceutical use
  - Microbial production of plant metabolites, e.g. stevia-derived sugar rebaudioside M
  - Microbial production of chitooligosaccharides, using microbial cell factories expressing highly specific and selective enzymes to produce defined chitooligosaccharides, also improved yield
  - Mycological production platforms for enzymes, pharmaceuticals, foods and materials
- Other biomedical and biopharmaceutical applications
  - Engineered organoids
  - Synthetic tissues
  - Cost-efficient platforms for detecting and preventing infectious diseases (e.g. SARS-CoV-2)
  - Expanded antibiotic chemical diversity (e.g. through engineering biosynthetic pathways through polyketide synthase and non-ribosomal peptide synthetase)
  - New ability to synthesize natural products
  - Development of new vaccines (e.g. to combat cancers)
  - Modified plasmodium parasites as potential strategy for malaria vaccination
- Bio-inspired and "living" materials
  - Bacterial strain as a chassis for sensor-containing genetic circuits to interact with fungal mycelium to direct activity, influence growth or morphology of the fungus (FUNGATERIA project)
  - Biofilms and engineered living materials with the capability to self-repair and self-replicate, sense local and distant disturbances in their environment and respond with functionalities (early research and development)
  - New biodegradable materials, such as bioplastics and marine degradable plastics
- Containment systems for engineered organisms (laboratory stage)
  - Kill switches
  - Incorporation of non-canonical amino acids
  - Engineered auxotrophies
  - Toxin-producing safeguards
  - Minimal genomes
  - Engineered addiction methodologies
  - Anti-CRIPSR technology
  - *Escherichia coli* with a re-programmed codon usage (replacing two of six serine for leucine codons) to prevent viral infection and gene transfer
- Applications containing non-canonical nucleotides (early research)
  - Enzymatic addition of metal ions to nucleic acids
  - *Escherichia coli* with the ability to biosynthesize and incorporate modified base
  - Hachimoji DNA and RNA
  - Mammalian cells containing logic gates controlled by unnatural amino acids
- De-extinction of animal species with active projects for the quagga (*Equus quagga quagga*), the aurochs (*Bos taurus primigenius*), the Floreana Island giant tortoise (*Chelonoidis elephantopus*), the woolly mammoth (*Mammuthus primigenius*), the passenger pigeon (*Ectopistes migratorius*) and the heath hen (*Tympanuchus cupido cupido*) and an effort to restore various moa species (order Dinornithiformes) (research stage)
- Non-biological uses of synthetic biology
  - Digital information storage using DNA molecules (e.g. biocomputing) (early research)

  - DNA-enable biobatteries[5]
- Increased sophistication of genome editing
  - CRISPR RNA-guided protease
  - Organism and locus-specific genome editing of microbial communities
  - Prime editing
  - Base editors (e.g. to induce C-to-A transversions in *Escherichia coli* and C-to-G transversions in mammalian cells, reduce off-targets by adenine base editor in A-to-G conversions and increase the efficiency of adenine base editors in plant systems)
  - Multiplex RNA-guided CRISPR activation systems
  - Systems with light-induced degradation of single guide RNA
  - Ultrafiltration to remove excess RNA
  - Crapase (CRISPR-guided caspase)
  - In-field delivery methods
  - Inhalable or powder formulations
- Genome editing and engineering of organelles and plastids
- Replacing mitochondrial haplotype with one from a closely related species for conservation or resilience to climate change, abiotic stress or pathogen resistance
- De novo construction of berberine and halogenated benzylisoquinoline alkaloid biosynthetic pathways in *Saccharomyces cerevisiae*
- Increasingly complex genetic circuits
  - Self-regulating, reconfigurable DNA circuit
  - Recombinase-based circuits in plant systems
  - Integrase-mediated differentiation circuits in *Escherichia coli*
  - Inducible plasmid copy number control in *E. coli*
  - Gene switches for *Mycoplasma*
  - Genetic circuits for algal systems
  - Bacteria engineered for modified behaviour through the expression of the plasmid-encoded neutral network
- Protocells and minimal cells for basic research (research stage)
- Karyotype engineering of 16 yeast chromosomes into a single functional chromosome
- Improved manufacturing of long (> 200 nucleotide length) oligonucleotides with higher fidelity (e.g. by Twist Bioscience, Integrated DNA Technologies, DNA Script and Camena)
- Improved assembly of large DNA fragments (e.g. optimized Golden Gate assembly, open-source pipelines, standards for plasmid construction)
  - Synthesis and assembly of four yeast chromosomes
- Automation and machine learning
  - “Self-driving” (fully automated) laboratories for drug discovery, experiment optimization, auxotrophic experiments and gene deletions
  - Machine learning-informed and synthetic biology-enabled semi-continuous algal cultivation
  - Cybergenetics (aimed at developing digital and biological controllers for living organisms)
  - Low-cost DNA and RNA circuits designed through machine learning
- Machine learning and artificial intelligence algorithms
  - Interactions and forces between atoms (e.g. SIRAH 2.0)
  - Design of novel proteins with new functionalities

[5] See Katherine E. Dunn and Alistair Elfick, “Harnessing DNA Nanotechnology and Chemistry for Applications in Photonics and Electronics”, *Bioconjugate Chemistry*, vol. 34, No. 1 (2023); and Mireia Buaki-Sogó and others, “Enzymatic Glucose-Based Bio-batteries: Bioenergy to Fuel Next-Generation Devices”, *Topics in Current Chemistry*, vol. 378, No. 49 (2020).

- Protein folding
- Design metabolic pathways
- Inform genetic circuit design
- Influence choice of bacterial strain, carbon sources
- Incorporate metabolic data
- Understand cellular regulation
- Use of metabolomics in computational modelling to understand metabolic dynamics
- New machine learning algorithms resulting from synthetic biology research

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