Meeting of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction

10 July 2019

English only

2019 Meeting
Geneva, 3-6 December 2019

Meeting of Experts on Cooperation and Assistance, with a Particular Focus on Strengthening Cooperation and Assistance under Article X
Geneva, 29-30 July 2019
Item 4 of the provisional agenda
Review of science and technology developments relevant to the Convention, including for the enhanced implementation of all articles of the Convention as well as the identification of potential benefits and risks of new science and technology developments relevant to the Convention, with a particular attention to positive implications

Scientific and Technological Developments of Relevance to the Convention and the Assessment of Benefits and Risks

Submitted by Switzerland

I. Introduction

1. New technologies and novel technical capabilities continuously emerge as valuable tools in the life sciences across the globe. Timely identification of developments of relevance to the Biological and Toxin Weapons Convention (BTWC) is therefore central and needs to be followed by an adequate consideration of potential implications in order to outline necessary individual or collective action to address any associated benefits and risks. At the 2018 Meeting of Experts 2 (MX2), States Parties to the BTWC identified a number of scientific and technological developments that merit further review in the framework of the Convention. As set out in last year's MX2 Working Paper 4 submitted by the United Kingdom of Great Britain and Northern Ireland [1], a series of questions has been proposed to facilitate the discussion on useful approaches to risk assessment in the context of the BTWC. This Working Paper therefore highlights first some notable, recent advances in science and technology, and discusses possible avenues as well as aspects to consider when assessing the benefits and risks of advances in science and technology within the framework of the Convention. It is hoped that the examples of advances will stimulate a meaningful scientific exchange among experts at the 2019 MX2 under agenda items 4 and 5, in order to develop more clarity about useful approaches to risk-benefit assessment.

II. Scientific and Technological Developments

2. In September 2018, Switzerland organized the third iteration of the Spiez CONVERGENCE workshop to discuss scientific and technological developments of relevance to the BTWC as well as the Chemical Weapons Convention and to explore

potential implications. It brought together subject matter experts from academia, the chemical and biotech industries, as well as specialists from the arms control and policy communities. Some of the subjects covered by previous editions were revisited, which proved to be a useful approach in gaining a deeper understanding of the state of maturity of a given technology. Such an approach provides an opportunity to refine or revise earlier assumptions. The reports of all three workshops are available online [2]. What follows are notable advances in science and technology in three distinct areas.

3. Recently, researchers anticipated in a study that CRISPR technology may become a useful tool in drug screening processes for early identification of potentially emerging resistance profiles [3]. Since antibiotic resistance is an ever more prominent and concerning issue for public health on a global scale, such findings may promise much needed alternative approaches to tackle this threat for the benefit of human and animal well-being. Other researchers further explored the applicability of CRISPR technology for use as a sequence-specific, sensitive and rapid point-of-care diagnostics tool [4,5,6,7]. These applications utilize specific Cas proteins (Cas12a, Cas13a/b) that cut either RNA or single-stranded DNA and, under certain conditions, are activated to cut indiscriminately of the actual target sequence. This off-target effect could be exploited since only minute amounts of a target sequence will generate readily detectable, amplified signals when using a reporter RNA that contains a fluorophore and quencher. Current thinking postulates potential applications in e.g. early cancer diagnosis and detection of infections caused by pathogens.

4. Reading nucleic acid sequences has become ever faster and cheaper over the last several years. A similar revolution has not yet taken place for writing nucleic acid sequences, since this is primarily done through chemical synthesis, developed more than 30 years ago. This constitutes a bottleneck for applications in synthetic biology relying on the synthesis of artificial sequences. This includes applications aimed at gaining a better understanding of genome functions in order to enable programming of specific biological functions in designed organisms for industrial applications or of benefit to public health [8]. Recent advances in enzymatic nucleic acid synthesis suggest a soon to start exponential growth of the field of DNA writing, similar to the DNA reading revolution [9]. The synthesis of ever longer DNA fragments is postulated to become faster and cheaper in the form of an enzymatic oligonucleotide synthesizer [10]. This would render the current laborious procedure of stitching fragments together less cumbersome or even obsolete. Depending on further advances in the near future, this novel technology may benefit public health and industry in multiple ways through cheaper and straightforward design and testing of new genes, or could revolutionize long-term data storage by means of DNA. It is also conceivable that whole genes or even entire genomes could become more readily accessible through this novel technology and, as a consequence, may increase the risk of misuse in the future.

5. Since conducting 'wet lab' experiments in the life sciences is often repetitive and time consuming, digitization and automation is increasingly applied in biology [11,12]. Multi-tenant, fully robotic, modular cloud laboratories that have recently emerged, allow scientists to interact through computing devices with remote laboratory modules in real-time. As a consequence, biology is turned into information technology that goes beyond traditional outsourcing to contractors, because scientists are enabled to specify instructions at a granular level as opposed to giving general directions. The transition towards cloud labs serves to reduce time, effort and expertise needed to conduct experiments. At the same time, cloud labs offer increased reproducibility and accuracy through standardization, ultimately increasing productivity. This might boost creativity and innovation, but comes at the cost of potential security implications since there is no necessity for cloud lab providers to know what experiments are carried out and for what purpose. As a consequence, remote attacks against or misuse of such services is not readily detectable. Similar approaches to what nucleic acid synthesis providers have implemented may therefore constitute an option, such as customer-screening, controlled access to substances, experiment-screening for contextual understanding, as well as secured networks and firewalls.

III. Assessing benefits and risks

6. When it comes to how to assess benefits and risks, last year's MX2 Working Paper 4 submitted by the United Kingdom of Great Britain and Northern Ireland offers a useful starting point with a set of questions proposed in order to facilitate the discussion on potential avenues to risk assessment in the context of the BTWC [1]. As the above-mentioned examples of relevant scientific and technological developments suggest, it is very difficult to adequately predict and anticipate future advances – something that was already outlined in last year's MX2 Working Paper 2 submitted by Switzerland [13]. Discussions held in the 2018 MX2 suggested that not only assessing risks but equally or even more so assessing benefits of science and technology are far from obvious. For instance with regard to CRISPR technology, earlier assessments of benefits did not take into account recent findings that CRISPR effectivity in certain cells may come at the cost of increased genome instability, and thus provide a potential link to an increased probability of developing cancer [14,15,16].

7. This is exemplary for most if not all emerging technologies, since they tend to follow a hype cycle. In general, technological breakthroughs trigger a cornucopia of promises, culminating in a ‘peak of inflated expectations’. As a consequence, experiments fail to deliver and a ‘trough of disillusionment’ has to be crossed to get back on a ‘slope of enlightenment’ to eventually reach a ‘plateau of productivity’ with sustainable, commercially viable output — not just proof-of-concepts. This sequence of stages has been labeled the ‘hype cycle’ by Gartner [17,18]. In other words, it is highly likely that the benefits of nascent technologies will be overstated and thus overestimated at large in assessments, since any net added value in the form of (commercially) viable and sustainable applications will hardly ever match or exceed initial expectations.

IV. Conclusions and Recommendations

8. Potentially overstated and overestimated benefits of nascent technologies may severely bias risk-benefit analyses and assessments through blurred perceptions of the manifold possibilities and the reasonably probable. As a consequence, this renders it extremely difficult to strike the right balance between scientific, policy, ethical, environmental and security considerations in the course of developing adequate approaches to mitigate potential risks. It may therefore prove useful to discuss and determine which risk level is acceptable. In order to structure such discussions, States Parties could, among other publications, consider the UK Royal Society's "New approaches to biological risk assessment" or, as presented at last year's MX2, the US National Academies of Sciences, Engineering and Medicine's "Biodefense in the age of synthetic biology" as valuable starting points [19,20]. Both undertake to tackle the challenge of uncertainty through a robust set of non-exhaustive factors to consider when conducting risk-benefit analyses and assessments.

9. As the 'gain-of-function' (GOF) debate has demonstrated over the past several years, thorough risk-benefit assessment can be a cumbersome process, even painful at times. The process, however, demonstrated the multifaceted nature of the GOF issue, in which biosecurity was just one among several other aspects, such as biosafety and dual-use governance, under scrutiny. This implies for the BTWC, and for biological risk assessment and management in particular, the need for holistic approaches across disciplines and the need for involving stakeholders from various backgrounds. This ensures the unearthing of potentially hidden facets to the greatest extent feasible and allows for a better sense of what is most probable within the wealth of possibilities. Recalling the scientific and technological advances described in this document, a thorough consideration of intangible aspects is warranted as an increasingly important factor to include in risk-benefit assessments. When developing recommendations at an international level, in particular within the framework of the BTWC, it will remain crucial to respect national contexts, since significant differences in terms of pre-existing legal frameworks are highly likely and decrease the utility of one-size-fits-all models.

Annex

References

[1] BWC/MSP/2018/MX.2/WP.4 - Genome editing: addressing implications for the Biological and Toxin Weapons Convention - Submitted by the United Kingdom of Great Britain and Northern Ireland.

[2] https://www.labor-spiez.ch/en/rue/enruesc.htm

[3] Nyerges Á et al. Directed evolution of multiple genomic loci allows the prediction of antibiotic resistance. Proc Natl Acad Sci U S A. 2018 Jun 19;115(25):E5726-E5735.

[4] Petri K et al. SHERLOCK and DETECTR Open a New Frontier in Molecular Diagnostics. CRISPR J. 2018 Jun;1:209-211.

[5] Gootenberg JS et al. Multiplexed and portable nucleic acid detection platform with Cas13, Cas12a, and Csm6. Science 2018;360:439–444.

[6] Myhrvold C et al. Field-deployable viral diagnostics using CRISPR-Cas13. Science 2018;360:444–448.

[7] Chen JS et al. CRISPR-Cas12a target binding unleashes indiscriminate single-stranded DNase activity. Science 2018;360:436–439.

[8] Venetz JE et al. Chemical synthesis rewriting of a bacterial genome to achieve design flexibility and biological functionality. Proc Natl Acad Sci U S A. 2019 Apr 16;116(16):8070-8079.

[9] Service RF. DNA printers poised to jump from paragraphs to pages. Science. 2018 Oct 12;362(6411):143.

[10] Palluk S et al. De novo DNA synthesis using polymerase-nucleotide conjugates. Nat Biotechnol. 2018 Aug;36(7):645-650.

[11] Spiez CONVERGENCE – Report on the third workshop 11-14 September 2018 (Link Ref. [2])

[12] Lentzos F et al. Laboratories in the cloud. Bulletin of the Atomic Scientists, Disruptive Technologies. 2019 Jul 2.

[13] BWC/MSP/2018/MX.2/WP.2 - Technical Working Paper on Genome Editing and Other Scientific and Technological Developments of Relevance to the Convention - Submitted by Switzerland.

[14] Haapaniemi E et al. CRISPR-Cas9 genome editing induces a p53-mediated DNA damage response. Nat Med. 2018 Jul;24(7):927-930.

[15] Ihry RJ et al. p53 inhibits CRISPR-Cas9 engineering in human pluripotent stem cells. Nat Med. 2018 Jul;24(7):939-946.

[16] Houser K. CRISPR Could Help Us Cure Diseases; It Could Also Cause Cancer. Futurism. 2018 Jun 11.

[17] http://www.gartner.com/technology/research/methodologies/hype-cycle.jsp

[18] Invernizzi C. CRISPR and the Hype Cycle. Defence Future Technologies – What we see on the horizon (Publisher: armasuisse W+T). 2017 Nov 15;81-3.

[19] New approaches to biological risk assessment. The Royal Society. 2009.

[20] Biodefense in the Age of Synthetic Biology. National Academies of Sciences, Engineering, and Medicine. 2018.