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

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Meeting of Experts on Review of developments in the field of science and technology related to the Convention
Geneva, 31 July and 2 August 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

Review of Developments in the Field of Science and Technology Related to the Convention – Synthetic biology

Submitted by Australia

I. Overview

1. The rapid advances in genome engineering technology, in particular, the emergence of genome editing and synthetic biology and more recently, DNA origami have the potential to revolutionise human, animal, plant and ecosystem health. Genome editing can be used for altering genetic loci through insertions, deletions and point mutations in virtually any organism. DNA origami assembles single-stranded DNA template molecules (typically M13 phage) into target structures by annealing templates with hundreds of short synthetic DNA oligonucleotides designed to perform specific mechanical functions or biological interactions. Synthetic biology is the ability to design and build artificial biological systems or reengineer existing biological systems for research, engineering and medical applications. Rapid advances over recent years have resulted in improved efficiency, relatively high precision and low cost, making these technologies now mainstream methods, accessible to academic, government or industry laboratories and potentially even civilian run laboratories. These characteristics have also led to some concern over how quickly applications for beneficial or harmful uses will be developed and spread.

2. BWC MX2 on "Review of Developments in the Field of Science and Technology Related to the Convention" offers the opportunity to discuss emerging technologies and consider potential risks and benefits relevant to the Convention. The current paper provides an overview of synthetic biology, an update on the capabilities and regulations associated with new technologies in Australia and the implications for Australia and the Indo-Pacific region, and some comments on codes of conduct. Increased transparency and sharing of information on the experiences of States Parties in managing the risks associated with new technologies, including through regulation, is a useful way to strengthen the BWC and keep it relevant to contemporary challenges.

II. Synthetic Biology – what are the opportunities and potential risks?

3. Newer technologies including genome editing, synthetic biology and DNA origami have a variety of applications in human health and have yielded important scientific findings. Synthetic biology has applications in the biotechnology and biomanufacturing industries and is expected to have broadening impacts to address ongoing issues of human health, food supply, and in the production of biofuels, chemicals and enzymes[1]. Examples in the human health space include the recoding of viruses to produce attenuated versions that can serve as vaccines which has already been demonstrated to protect animals against a lethal dose of wild type virus in the case of influenza and polioviruses[2]. Synthetic biology can also be used to produce antibiotics and other molecules for which routine synthesis is too complex or economically unfeasible. The synthesis of vaccines and improved antimicrobial agents hold significant promise for improved health systems[3].

4. While the majority of applications for new technologies are beneficial, there are always opportunities for misuse. Dual use concerns have been focused around the ability to generate microorganisms with altered virulence, increased transmissibility, the ability to remain infectious for longer, enhanced ability to infect or spread among hosts or evade therapeutic or diagnostic methods, resistance to antimicrobial agents, weaponisation and the generation or reconstitution of an eradicated or extinct agent or toxin. The latter includes recreation of known pathogens such as the highly virulent 1918 Spanish flu whose sequence is publicly available or polio virus[2]. Another example which has raised recent concern is the publication of a method to reconstruct horsepox virus by gene synthesis[4]. Given the close relationship between horsepox and smallpox virus, implications for the transfer of the techniques used for horsepox have clear implications for public health and biosecurity if they were applied to the synthesis of the smallpox virus.

5. A number of companies provide DNA synthesis services, allowing a client to order synthesised DNA material as short oligonucleotides of less than 100 nucleotides or DNA sequences of between 200-3000 nucleotides in length. Although there are a number of ways of producing a synthetic viral genome using either short oligonucleotides or longer DNA sequences, the technical challenges associated with creating a functional genome are still significant. As with other genome engineering techniques, the extensive knowledge and technical expertise and specialist facilities required for synthetic biology applications may restrict its misuse, at least in the short term. Although the risk remains small at this stage, the potential consequences of the misuse of synthetic biology are considerable. A malevolent actor or agency foolish enough to resurrect or alter a deadly pathogen may not be able to control its subsequent evolution and thus spread and impact if containment is breached, the consequences of which cannot be over-emphasised. Managing the risks by appropriate oversight of materials, including the distribution of synthetic DNA and methods for generating novel organisms, will be assisted by international consideration and cooperation in the BWC framework.

III. Regulations in Australia

6. Australia's statutory officer who regulates activities with genetically modified organisms, the Gene Technology Regulator (GTR) within the Australian Government Department of Health is responsible for administering the *Gene Technology Act 2000* and corresponding state and territory laws. The GTR oversees all activities with genetically modified organisms in Australia, both in contained research settings and the open environment.

7. In Australia, scientists working with defined genetically modified organisms can only do so if authorised under the *Gene Technology Act 2000*. Much low-risk contained work is, project by project, assessed by Institutional Biosafety Committees (IBCs) and notified to the GTR. Higher risk work requires a licence from the GTR, supported by a case-specific scientific risk assessment. The GTR maintains a national record of activities with GMOs

(past, present and planned). The role of the GTR is to protect the health and safety of the Australian people and the Australian environment.

8. Although different agencies and institutions may vary, at CSIRO's Australian Animal Health Laboratory (AAHL), the IBC plays a role in ensuring that individual scientists are aware of their obligations, legal and moral. The IBC informs scientists of the higher rating of certain proposed activities and the requirements of containment of those dealings to ensure the safety of the Australian people and the Australian environment. Records of material storage is also an obligation under this system.

9. It is important to note that changes in the Gene Technology Regulations 2001, commencing in October 2019, will deem organisms modified using gene editing that does not use a template to guide modifications outside the scope of regulation (i.e. not GMOs). As such organisms modified using transgenic approaches and synthetic biology, the subject of discussion of MX2, remain within scope of the gene technology regulatory scheme. This will help ensure any risks to humans and the environment associated with current and future work will be managed appropriately.

10. One concern that was raised as part of the Third Review of the National Gene Technology Scheme was the emergence of "DIY biology", so called "bio-hackers." The GTR is active in engaging with the Australian DIY biology community, providing advice and education to ensure compliance with the gene technology regulatory scheme, and the review recommended continued monitoring of DIY biology activity (also see attached appendix). Other review recommendations included clarifying regulation of environmental release of genetically modified gene drive organisms and maintaining a watching brief on synthetic biology (5).

IV. An ethical code of conduct for biological scientists

11. A strong theme that has emerged in previous BWC meetings is the concept of a voluntary code of conduct for biological scientists, which would also apply to the use of technologies such as genome engineering, including synthetic biology. In many countries, including Australia, codes of conduct are outlined by funding bodies and national organisations as a prerequisite for funding. The GTR also has a National Framework of Ethical Principles in Gene Technology which provides useful guidance in this regard (6).

12. In a BWC context, a voluntary code of conduct developed by scientists would help to ensure these values were instilled into the working culture. Various models have been proposed in working papers and BWC discussions, although the scope of such a code of conduct has yet to be agreed. In practical terms, a code of conduct could encourage scientists to undergo structured training and mentoring specific to their area of expertise to instil a culture and commitment to work for the wellbeing of humanity, animals and the environment.

13. Australia's education systems for students of science introduce these moral and cultural values. As those students progress to learning the practicalities of conducting science the bio-safety and biosecurity frameworks in place within science institutions, described above, will reinforce these ethical messages and guide appropriate conduct. While other agencies may have different views, CSIRO's AAHL, which has responsibility for maintaining and handling Security Sensitive Biological Agents (SSBAs) and considerable expertise in gene technology, has a keen interest in implementing a self-governed code of conduct that is obligatory under law.

14. As is the case with more traditional techniques used for genetic modification, the burden of closely monitoring the use of new technologies in microorganisms falls to separate institutions, be they scientific, medical, academic or government. Although microorganisms that are already considered harmful are generally considered the highest risk for weaponisation, innocuous microorganisms are not exempt from this risk and can also be modified to do harm. Institutions that conduct gene technology research (such as universities, medical schools, state or federal government agencies and private companies) have an ethical and legal responsibility to ensure that biosecurity standards are maintained for all work taking place at the institution and for instilling a positive and transparent culture in the workplace.

15. Most organisations in Australia undertaking dealings with GMOs undergo accreditation to assess whether they have the resources and the internal processes in place to enable effective oversight of this work. This includes access to an appropriately constituted IBC. Many organisations require staff undertaking work with GMOs to undertake training to ensure they are aware of the regulations and requirements.

16. Australia is currently grappling with how best to support and encourage innovation, international cooperation and the peaceful use of biological science while appropriately managing dual use and proliferation risks. Despite our best efforts and the robust systems we have in place, there will always be the risk that staff members who have access to harmful or innocuous microorganisms and the expertise to use genome engineering techniques on them may use this material and their expertise for harmful purposes, even if these activities are illegal. Furthermore, as gene technologies are now so pervasive, our scientists need to ensure they are not facilitating proliferation through intangible technology transfer (knowledge transfer). Strict screening and oversight of visitors is therefore essential to ensure gene technology skills are transferred only to those who will use them for peaceful applications. Scientists and researchers should make best possible efforts to know with whom they are collaborating and the source of any funding, including for international collaboration.

V. Resources for Capability building in the Indo-Pacific region

17. The AAHL in Geelong, Victoria is the largest high containment lab in the Southern hemisphere with laboratory and animal capacity to work with pathogens up to the highest level of containment, biosecurity level 4 (BSL4). The lab also has significant expertise in genome engineering, synthetic biology and diagnostics. To this end, genome engineering is being used for a variety of applications, including projects involving the engineering of animals to confer improved disease resistance, control invasive species, and in mosquitoes to decrease disease transmission.

18. Although the high containment lab was originally built to contain dangerous pathogens, it also provides the opportunity to contain genetically modified or gene edited organisms, including animals, microorganisms and insect vectors of disease without the risk of accidental release. In the event of a natural incursion or intentional release of a harmful agent, this laboratory is well placed in the Indo-Pacific region to perform diagnostics and coordinate a response plan. In addition, this laboratory is an ideal place to test potential therapeutics against novel pathogens using animal models at high biocontainment.

19. In addition to laboratory capacity in Australia, training and capacity building in other countries in the Indo-Pacific region is critical for disease preparedness against outbreaks due to naturally occurring and intentionally released organisms. To this end, the Australian Government launched the A$300 million, five-year Indo-Pacific Health Security Initiative on 8 October 2017. The Initiative's work at the at the country and sub regional level aims to strengthen regional capacity to prevent, detect and respond to emerging and re-emerging infectious disease threats with the potential to cause social and economic harm on a national, regional or global scale. Amongst the range of activities programmed, laboratory strengthening activities across the region will include twinning between AAHL and veterinary laboratories in Indonesia (Wates, Central Java) and Myanmar (Yangon and Mandalay) to improve the capacity of these labs and others across the region to support responses to disease outbreaks. This assistance will at the same time build laboratories' capacity to detect and respond to a threat posed by a deliberately released, modified or synthesised microorganism. Training of scientists and laboratory workers in biosafety, biosecurity and laboratory diagnostics will also be conducted. The basic laboratory biosafety training component will include topics in bioethics to cover more general ethical behaviours of scientists including plagiarism, irresponsible gene manipulation and unethical treatment of animals, all of which are of concern to the international science community. Elements of any code of conduct agreed by BWC States Parties could also be incorporated.

VI. References

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7. http://www.ogtr.gov.au/internet/ogtr/publishing.nsf/Content/gtecccethicalprinciples2012-toc/$FILE/gtecccethicalprinciples2012.pdf[1]

Prepared by Michelle Baker[1,2], Mark Tizard[2] and Trevor Drew[3].
1. Indo-Pacific Centre for Health Security, Department of Foreign Affairs and Trade, Canberra, ACT, Australia. CSIRO, 2. Health and Biosecurity Business Unit, Australian Animal Health Laboratory, Geelong, Vic, Australia. 3. Australian Animal Health Laboratory, Geelong, Vic, Australia.

Annex I

Australian Government
Department of Health
Office of the Gene Technology Regulator

Biohacking and community science

There is a growing community of individuals in Australia who are conducting do-it-yourself biology which is also sometimes known as biohacking or community science.

Community science or biohacking covers a wide range of possible experiments and activities, some of which may involve genetically modified organisms.

In Australia there are strict laws to regulate activities involving GMOs. The laws are in place to make sure any risks to human health, safety and the environment are managed appropriately. Significant fines, and even jail time, can result from non-compliance.

Before you start

If you are planning to use GMOs in do-it-yourself biological research in Australia, your first port of call should be the OGTR website to find out your obligations.

There are also community science groups around Australia who can assist you.

What are the rules?

If you are considering working with or creating genetically modified organisms (GMOs) in Australia, you need to understand your obligations under the legislation.

Some work involving GMOs in Australia is classified as **exempt** dealings. The legislation includes scientific descriptions of GMO work which is exempt. If you're using a kit such as those used in Australian schools which enable you to insert a fluorescent colour into a harmless laboratory strain of bacterium, then there's a good chance that your work is **exempt** provided you follow good laboratory practice and don't release your GMO into the environment.

It is illegal to import, create or work with GMOs, unless:

- what you are doing is classed as exempt, or
- what you are doing is classed as a notifiable low risk dealing, or
- you are licensed by the Gene Technology Regulator, or
- the materials are already included on the GMO Register, or
- the relevant government Minister has issued a temporary approval for a GMO (such as a vaccine) to respond to a public health or environmental emergency.

The next level is **Notifiable low risk dealings** (NLRD). This mostly covers research in universities and other research organisations that poses minimal risk to health and safety of people and the environment provided they meet specified conditions. The work must be conducted in certified containment facilities and assessed by an Institutional Biosafety Committee (IBC) before work commences. NLRDs must be reported to the OGTR annually.

Some universities are providing support to community groups to enable them to conduct work at this level.

If you want to import, use, or create GMOs in other ways then you must apply to the OGTR for a licence. You can read more about all the classifications of GMO dealings at Who needs to apply to import or use (deal with) a GMO?

Keeping GMOs in the lab

The OGTR has developed notes on how to avoid releasing a GMO into the environment: containment of exempt dealings.

These cover **exempt** dealings – the lowest risk category. Working at higher levels requires certified facilities and/or a licence from the OGTR.

The guidance notes do not provide comprehensive guidance for laboratory safety, good laboratory practice or broader occupational health and safety issues. You should seek additional guidance on these matters.

Related Factsheets

Genetically modified organisms in Australia

How are genetically modified organisms (GMOs) regulated in Australia?

Who needs to apply to import or use (deal with) a GMO?

Version 1	December 2009
Version 2	June 2018

Contact us: ogtr@health.gov.au, www.ogtr.gov.au, phone 1800 181 030,
or post: Office of the Gene Technology Regulator MDP 54, GPO Box 9848, Canberra ACT 2601.