iGEM

Horizon scanning

Dr. Piers Millett

Vice President, Safety and Security

Red Cross

COMITE INTERNATIONAL GENEVE

ICRC

ICRC - Process

https://www.icrc.org/eng/resources/documents/misc/5vdj7s.htm

ICRC – Horizon scanning

ICRC – Key challenge

Scientific and Technical Update – 31 March 2004

Interspecies transmission of influenza viruses (Update on Superflu articles in February update).

The Structure and Receptor Binding properties of the 1918 Influenza Hemagglutinin
Science, Vol.303, 19 March 2004, pp1838-42

The article reviews that the influenza virus Hemagglutinin (HA), a membrane glycoprotein, mediates receptor binding and membrane fusion. Thus, it controls the first stages of such viral infections. This is achieved by recognizing the sialic acids of the cell-surface glycoproteins and glycolipids. These sialic acids are usually found in two structural linkages to galactose molecules. These have been named ∝2,3 and ∝2,6. The structural presentation and the associated binding preferences of the HAs of these biochemicals plays a crucial role in determining the species specificity of the virus. All of the HAs of the 15 subtypes of avian influenza viruses preferentially bind to the ∝2,3 form. Swine influenza viruses bind to both the ∝2,3 and ∝2,6 forms, whilst human influenza viruses preferentially bind the ∝2,6 form. Thus, in order for an avian influenza virus to be able to infect humans (which is what is being reportedly attempted in last months update) it would be necessary for the avian HA to undergo changes resulting in different binding specificities. It has been indicates that most human influenza viruses (H2 and H3 subtypes – which are not generally associated with highly pathogenic infections) have achieved this through genetic mutation. To date the mechanism by which H1 subtype viruses (including the one responsible for the 1918 outbreak) have overcome this hurdle. This article postulates that the H1 subtype HA has achieved this through a structural change as opposed to a genetic one. It includes the a detailed description of the structure and properties of associated viral HAs and establishes the binding properties of the 1918 strain but fails to elucidate its actual structure

Structure of the Uncleaved Human H1 Hemagglutinin from the Extinct 1918 Influenza Virus
Science, Vol.303, 19 March 2004, pp1866-70

Following on from the previous article the researchers who published this paper did succeed in establishing the structure of the 1918 influenza virus HA.

These two papers in combination represent a considerable step toward developing the capability to produce highly pathogenic avian influenza viruses capable of infection and reproduction in humans. It is especially important because the research is specifically targeted the 1918 influenza virus which caused the most deadly pandemic on record. This research by itself does not confer the ability to produce 'superflu' viruses, as it does not detail a mechanism by which the necessary structural alterations could be conferred, not does it deal with any other alterations which may be necessary to ensure successful replication and assemble when the host cell has been breached. This situation will be closely watched for further development and especially for the publication of the actual conversion mechanism.

There will be no smoking gun

BWC

Biological Weapons Convention

BWC - Process

BWC/CONF.VII/INF.3

Seventh Review Conference 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 October 2011

Original: English

Geneva, 5–22 December 2011
Item 10 of the provisional agenda
Review of the operation of the Convention as provided for in its Article XII

New scientific and technological developments relevant to the Convention

I. Overview of scientific and technological developments

Prepared by the Implementation Support Unit

GE.11-64010

BWC/MSP/2013/MX/INF.1

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

3 June 2013

Original: English

2013 Meeting
Geneva, 9–13 December 2013

Meeting of Experts
Geneva, 12–16 August 2013
Item 6 of the provisional agenda
Standing agenda item: review of developments in the field of science and technology related to the Convention

I. Advances in science and technology

A. Introduction

GE.13-61197

Advances in science and technology related to the Convention

Background information document submitted by the Implementation Support Unit

https://bit.ly/2LBMtdU

BWC – Horizon scanning

BWC – Key challenge

Importance of translating for audience

Biosecure

Biosecu.re

Biosecure - Process

biosecu.re

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Annotated bibliography of developments in science & technology with potential risks for the Biological Weapons Convention

A background paper commissioned by the Royal Society

DISCLAIMER: *The advances identified in this paper are indicative of developments since 2011 and are not exhaustive. There are other whole fields of research which could be of relevance other than those covered in this paper. The advances discussed provide an overview of the speed and direction of research and can be used to identify relevant trends. Given the number of sciences and disciplines of possible relevance, the geographic distribution of scientists, the number of languages in which they publish and the increasing pace of research, there are other specific advances which could have been captured in this report.*

Introduction

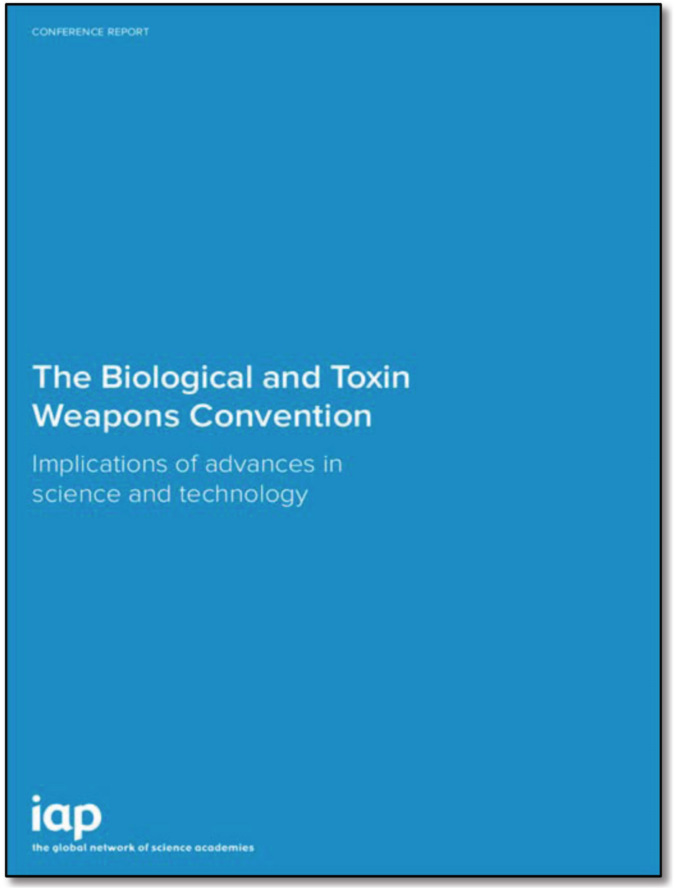
The Biological Weapons Convention (BWC) will hold its Eighth Review Conference late in 2016 which will consider 'new scientific and technological developments relevant to the Convention'.[1] This review will draw upon work undertaken in a standing agenda item in the BWC's 2012-2015 work programme. Each year, States Parties have reviewed developments in science and technology relevant to the BWC, focusing on advances that could have benefits for, or which could possibly be used in contravention to this international instrument. During the course of their work, States Parties supported by international organizations, scientific bodies, companies and individual experts, have reviewed developments in: enabling technologies; for dealing with disease; in the understanding of pathogenicity, virulence, toxicology, immunology and related issues; as well as production, dispersal and delivery technologies.

The international scientific community has held a series of meetings prior to past review conferences to assist States Parties in identifying advances and considering their implications. In 2006, the Royal Society, IAP: Global Network of Science Academies, and the International Council for Science organised an international workshop on science and technology developments relevant to the Biological and Toxin Weapons Convention.[2] In 2010, The US National Academies of Sciences, in cooperation with the Chinese Academy of Sciences, the IAP: Global Network of Science Academies, the International Union of Biochemistry and Molecular Biology and the International Union of Microbiological Societies held a workshop to identify trends relevant to the Biological Weapons Convention.[3]

The Royal Society, the IAP: Global Network of Science Academies and the US National Academies of Sciences have organized a workshop to review relevant developments in September 2015. This background document provides a partial overview of relevant advances. It draws upon the background information documents compiled by the BWC since 2012, presentations, statements and other contributions by States Parties, international organizations and Guests of the Meeting at meetings of the BWC, reports and outputs from other significant international scientific and technical workshops, as well as original research.

In order to provide the greatest utility in preparing for the review conference, this report focuses on developments with potential for immediate to short-term application for purposes contrary to the BWC. In line with the approach adopted for the review prior to the most recent review conference of

[1] http://bit.ly/1MHg3g3
[2] https://royalsociety.org/~/media/Royal_Society_Content/policy/publications/2006/8245.pdf
[3] http://bit.ly/1ljEF8k



https://royalsociety.org/topics-policy/projects/biological-toxin-weapons-convention/

Biosecure – Key challenge

Seeing the wood
for the trees

Biosecure – Science advice


MEETING SUMMARY

The Biological and Toxin Weapons Convention

Considerations for a science advisory mechanism

iap SCIENCE RESEARCH HEALTH

the interacademy partnership

Why…

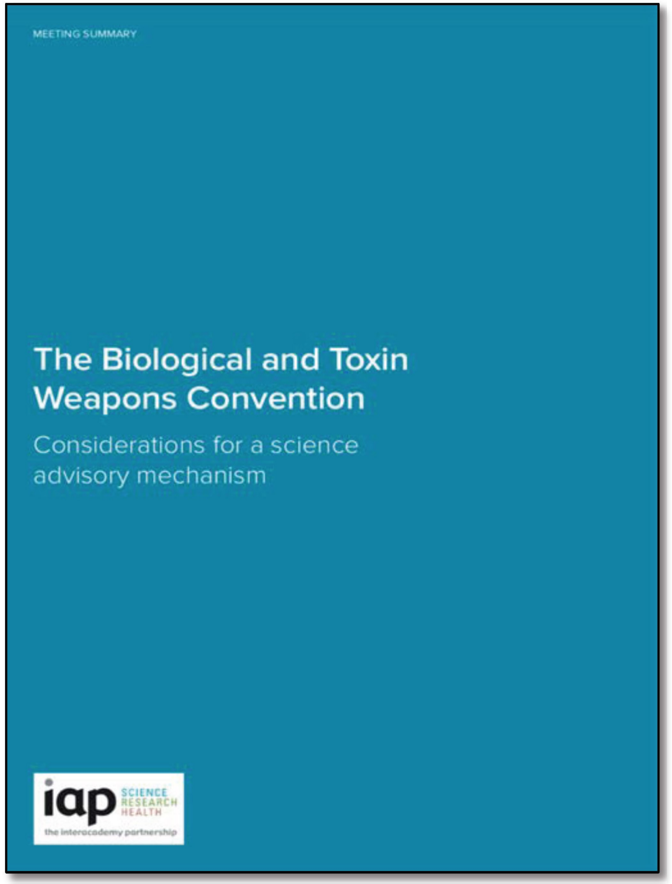
- Have a science advice process?
- change existing arrangements?

Who…

- Should be involved?
- Should govern it?
- Should fund it?
- Should support it?

https://royalsociety.org/topics-policy/projects/biological-toxin-weapons-convention/

Biosecure – Science advice


MEETING SUMMARY

The Biological and Toxin Weapons Convention

Considerations for a science advisory mechanism

iap SCIENCE RESEARCH HEALTH
the interacademy partnership

What…

- Should it include?
- Format should it adopt?
- Should be the target audience?

How…

- Should output be structured?
- Will all views be included?
- Could success be measures?

https://royalsociety.org/topics-policy/projects/biological-toxin-weapons-convention/

Biosecure – Science advice iGEM


MEETING SUMMARY

The Biological and Toxin Weapons Convention

Considerations for a science advisory mechanism

iap SCIENCE RESEARCH HEALTH

the interacademy partnership

When…

- Should it meet & how often?
- During BWC work programmes?

Where…

- Should it be based?
- Should it meet?

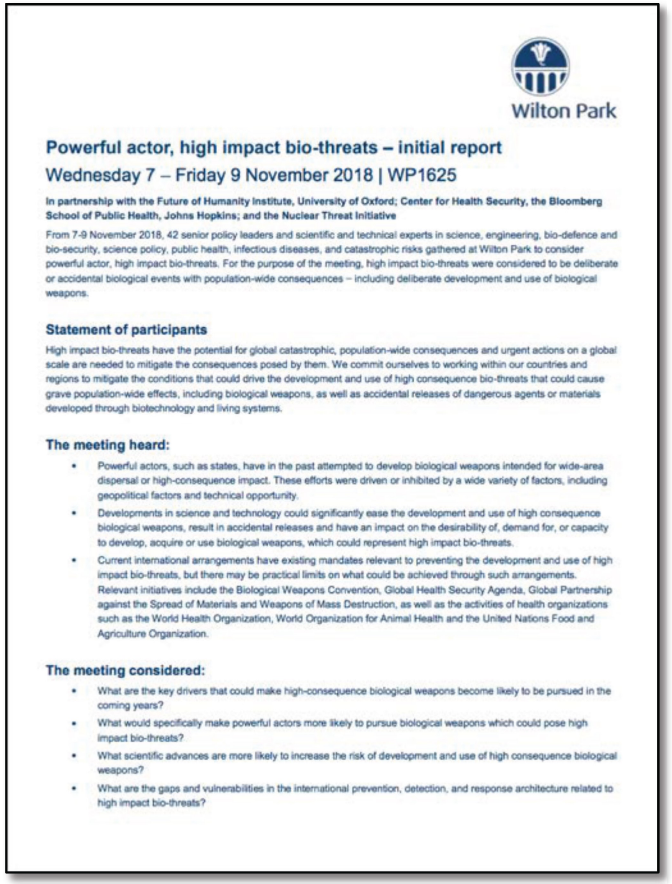
https://royalsociety.org/topics-policy/projects/biological-toxin-weapons-convention/

FHI

Future of Humanity Institute
UNIVERSITY OF OXFORD

UNIVERSITY OF OXFORD

FHI - Process



Wilton Park

Powerful actor, high impact bio-threats – initial report

Wednesday 7 – Friday 9 November 2018 | WP1625

In partnership with the Future of Humanity Institute, University of Oxford; Center for Health Security, the Bloomberg School of Public Health, Johns Hopkins; and the Nuclear Threat Initiative

From 7-9 November 2018, 42 senior policy leaders and scientific and technical experts in science, engineering, bio-defence and bio-security, science policy, public health, infectious diseases, and catastrophic risks gathered at Wilton Park to consider powerful actor, high impact bio-threats. For the purpose of the meeting, high impact bio-threats were considered to be deliberate or accidental biological events with population-wide consequences – including deliberate development and use of biological weapons.

Statement of participants

High impact bio-threats have the potential for global catastrophic, population-wide consequences and urgent actions on a global scale are needed to mitigate the consequences posed by them. We commit ourselves to working within our countries and regions to mitigate the conditions that could drive the development and use of high consequence bio-threats that could cause grave population-wide effects, including biological weapons, as well as accidental releases of dangerous agents or materials developed through biotechnology and living systems.

The meeting heard:

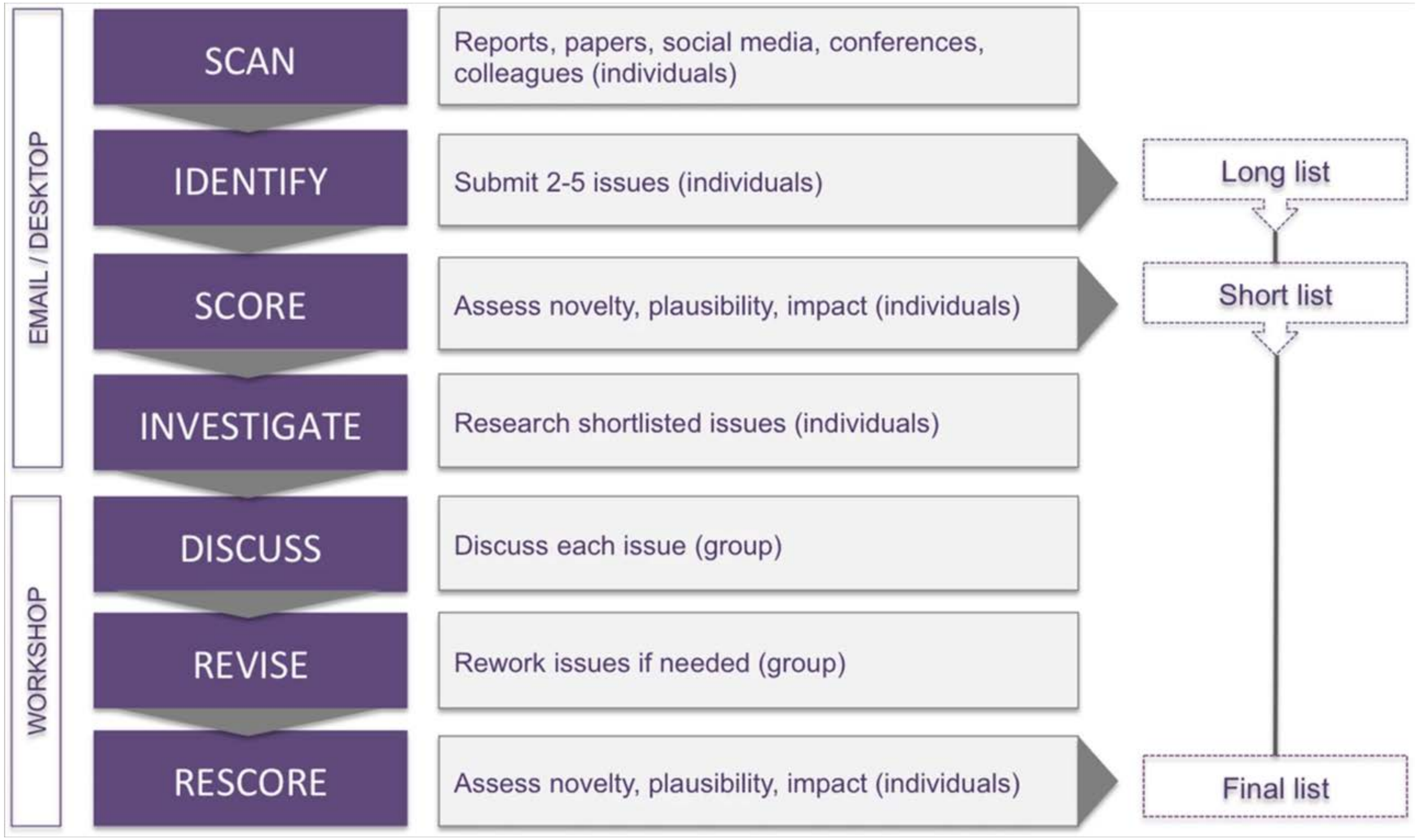
- Powerful actors, such as states, have in the past attempted to develop biological weapons intended for wide-area dispersal or high-consequence impact. These efforts were driven or inhibited by a wide variety of factors, including geopolitical factors and technical opportunity.
- Developments in science and technology could significantly ease the development and use of high consequence biological weapons, result in accidental releases and have an impact on the desirability of, demand for, or capacity to develop, acquire or use biological weapons, which could represent high impact bio-threats.
- Current international arrangements have existing mandates relevant to preventing the development and use of high impact bio-threats, but there may be practical limits on what could be achieved through such arrangements. Relevant initiatives include the Biological Weapons Convention, Global Health Security Agenda, Global Partnership against the Spread of Materials and Weapons of Mass Destruction, as well as the activities of health organizations such as the World Health Organization, World Organization for Animal Health and the United Nations Food and Agriculture Organization.

The meeting considered:

- What are the key drivers that could make high-consequence biological weapons become likely to be pursued in the coming years?
- What would specifically make powerful actors more likely to pursue biological weapons which could pose high impact bio-threats?
- What scientific advances are more likely to increase the risk of development and use of high consequence biological weapons?
- What are the gaps and vulnerabilities in the international prevention, detection, and response architecture related to high impact bio-threats?

https://www.wiltonpark.org.uk/event/wp1625/

FHI – Horizon scanning



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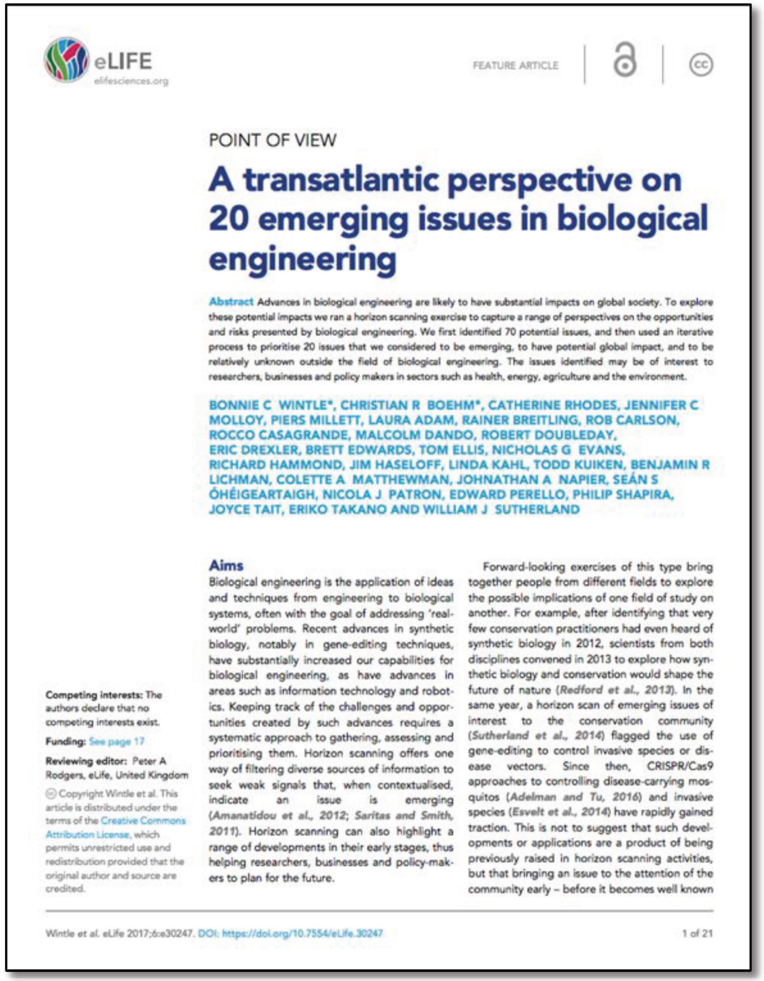
FHI – Key challenge



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FEATURE ARTICLE

POINT OF VIEW

A transatlantic perspective on 20 emerging issues in biological engineering

Abstract Advances in biological engineering are likely to have substantial impacts on global society. To explore these potential impacts we ran a horizon scanning exercise to capture a range of perspectives on the opportunities and risks presented by biological engineering. We first identified 70 potential issues, and then used an iterative process to prioritise 20 issues that we considered to be emerging, to have potential global impact, and to be relatively unknown outside the field of biological engineering. The issues identified may be of interest to researchers, businesses and policy makers in sectors such as health, energy, agriculture and the environment.

BONNIE C WINTLE*, CHRISTIAN R BOEHM*, CATHERINE RHODES, JENNIFER C MOLLOY, PIERS MILLETT, LAURA ADAM, RAINER BREITLING, ROB CARLSON, ROCCO CASAGRANDE, MALCOLM DANDO, ROBERT DOUBLEDAY, ERIC DREXLER, BRETT EDWARDS, TOM ELLIS, NICHOLAS G EVANS, RICHARD HAMMOND, JIM HASELOFF, LINDA KAHL, TODD KUIKEN, BENJAMIN R LICHMAN, COLETTE A MATTHEWMAN, JOHNATHAN A NAPIER, SEÁN S ÓHÉIGEARTAIGH, NICOLA J PATRON, EDWARD PERELLO, PHILIP SHAPIRA, JOYCE TAIT, ERIKO TAKANO AND WILLIAM J SUTHERLAND

Aims

Biological engineering is the application of ideas and techniques from engineering to biological systems, often with the goal of addressing 'real-world' problems. Recent advances in synthetic biology, notably in gene-editing techniques, have substantially increased our capabilities for biological engineering, as have advances in areas such as information technology and robotics. Keeping track of the challenges and opportunities created by such advances requires a systematic approach to gathering, assessing and prioritising them. Horizon scanning offers one way of filtering diverse sources of information to seek weak signals that, when contextualised, indicate an issue is emerging (*Amanatidou et al., 2012; Saritas and Smith, 2011*). Horizon scanning can also highlight a range of developments in their early stages, thus helping researchers, businesses and policy-makers to plan for the future.

Forward-looking exercises of this type bring together people from different fields to explore the possible implications of one field of study on another. For example, after identifying that very few conservation practitioners had even heard of synthetic biology in 2012, scientists from both disciplines convened in 2013 to explore how synthetic biology and conservation would shape the future of nature (*Redford et al., 2013*). In the same year, a horizon scan of emerging issues of interest to the conservation community (*Sutherland et al., 2014*) flagged the use of gene-editing to control invasive species or disease vectors. Since then, CRISPR/Cas9 approaches to controlling disease-carrying mosquitos (*Adelman and Tu, 2016*) and invasive species (*Esvelt et al., 2014*) have rapidly gained traction. This is not to suggest that such developments or applications are a product of being previously raised in horizon scanning activities, but that bringing an issue to the attention of the community early – before it becomes well known

Competing interests: The authors declare that no competing interests exist.

Funding: See page 17

Reviewing editor: Peter A Rodgers, eLife, United Kingdom

Value of a methodology

https://elifesciences.org/articles/30247

iGEM

iGEM - Process

iGEM – Horizon scanning

Introduction

In iGEM, we have clear expectations for teams when it comes to safety and security, including for **Project Design**, **Laboratory Work**, and **Transfer Practices**.

WHAT IS SAFETY & SECURITY

2018 iGEM safety and security insights

This document provides an overview of important safety and security issues that came to light during the 2018 iGEM competition. It is not intended as an exhaustive record. Risks discussed in this document were identified and managed by the Safety and Security Committee (SSC) which is made up of safety and security experts, regulators, leading scientists and After iGEMmers from around the world. The issues discussed are representative of those occurring globally in many of the facilities making use of advanced biotechnologies. iGEM is compiling this document as part of its Safety and Security Program to share our experiences and lessons learned. We hope that making this information more widely available will assist technical experts, policy makers and technical communities in keeping biological engineering safe and secure.

General trends

Our efforts remain important in keeping iGEM safe and secure. In 2018, 39 of the 317 (12%) teams participating in the Giant Jamboree were referred to the SSC, indicating a need for more substantive consideration of safety and security issues. There were comparable referral rates in recent years (42 of 312 teams, or 13% in 2017, and 26 of 299 teams, or 9% in 2016). As the competition continues to grow, there will be a need for better tools and more sustainable and scalable approaches to enable teams to appropriately assess and manage risks associated with their work.

Seven teams approached the SSC seeking permission to use particularly hazardous agents or materials. In all cases relevant projects were carefully reviewed by the SSC and appropriate risk management implemented. Three teams wanted to use short fragments of from dangerous pathogens, including Chikungunya Virus, Dengue Virus, MERS Virus, and Zika Virus. They were to be used in lieu of pathogens to demonstrate the effectiveness of diagnostic projects. Some teams, including one project involving the causative organism of Cholera, worked with live pathogens. In general, work was conducted in facilities used to working with the pathogen and by specialists, with team members observing. In a few cases, such as a project involving rattlesnake venom to test an antitoxin they had developed, team members carried out the work but under the direct supervision of subject matter experts and in full compliance with local and national laws, rules and regulations. In several cases, teams opted to replace potentially hazardous materials. One team replaced an active form of Botulinum Toxin C with an atoxic alternative. Another team replaced a scorpion toxin which could harm humans and animals with one that only affects insects.

Teams sought to use higher containment levels in 2018. For example, in their initial safety and security forms, two teams declared access to high containment (BSL3) laboratories. They were reminded that in iGEM they are not permitted to use such spaces (or undertake work that would require them). Both teams decided they did not need such high containment levels and would be working in spaces appropriate for their projects. Equally, by the end of June iGEM became aware that 13 of the 31 registered high school teams had declared access to BSL2 laboratories. To understand why, iGEM carried out a survey. Over half the teams indicated they were borrowing laboratory space from a university and a BSL2 lab had been allocated. Most of the others had either miscommunicated or had access but would be working in BSL1 spaces. Only two teams suggested their projects would require elevated containment. Both teams work were reviewed by the SSC.

2018 demonstrated the challenges of parts-based biotechnology within current regulatory frameworks. For example, one team wanted to work with a gene from Chikungunya Virus. Given the current Australia Group rules, this would have required two export licenses – one covering the export from the synthesis company to the team, and another for the team to ship its subsequent part back to iGEM HQ. The team opted not to use a whole gene and eventually worked with a much shorter fragment. Another team identified an implementation challenge in national and international export control rules. They wanted to use known pathogenicity islands from a pathogen not on common control lists. The genes were to come from a close relative of a bacteria which does appear on these lists. The function of the genes is identical and the sequence homology very close. Ultimately, the team sourced functionally equivalent genes from another organism – one not on any of the lists and which could be obtained without crossing international trade borders. There was also one example of a team working with a part with a known function (estimated by sequence homology and confirmed experimentally) without a known specific donor organism, as it was derived via metagenomic sequencing. It is unclear how such a part would be covered by current approaches to biosafety and biosecurity.

Keep it in the lab

iGEM teams should not release any genetically modified organisms or their products outside the lab (or put them in people). See the **Do Not Release** policy for more information on complying with laws, being responsible and what constitutes a release.

DO NOT RELEASE

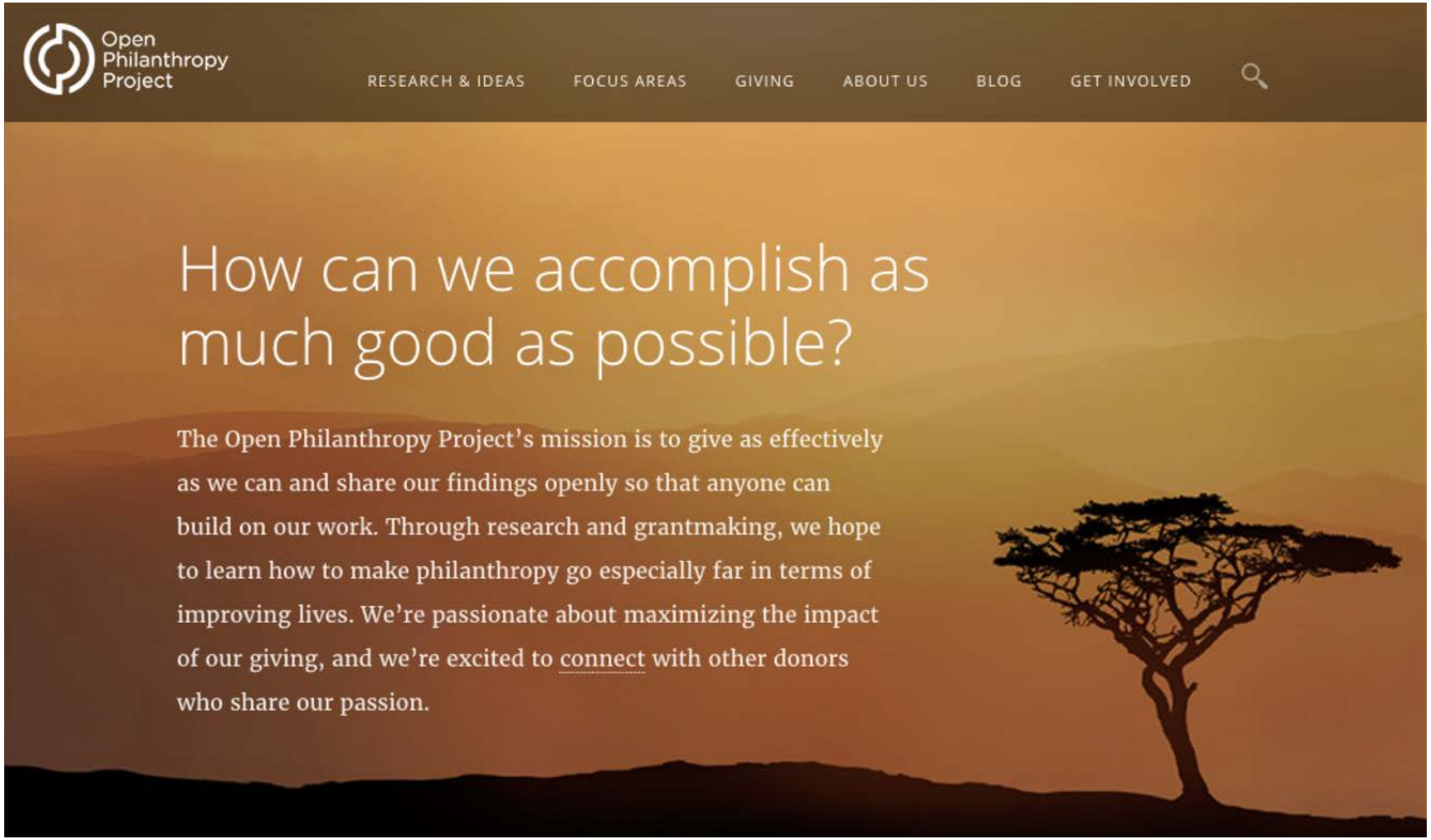
http://2018.igem.org/Safety

iGEM – Key challenge

Key challenges

- Trends not individual advances
- Audience must understand output
- Focus on most relevant developments
- Strong science advice process
- Structured methodologies
- Global action to address global challenges

Thanks to our funder



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