Security Aspects of Synthetic Biology

Meeting Report: 7-8 March 2013, Hong Kong

ICLS

A Special Thanks to the Meeting Sponsors

Foreign & Commonwealth Office

ALFRED P. SLOAN FOUNDATION

IASB

International Association Synthetic Biology

Table of Contents

The Issue

Advances in synthetic biology, genomics, genome design tools and information technology raise the risk that commercial producers of synthetic genomes might be used unwittingly to assist in the production of designer biological weapons.

To address this issue, two associations, the International Association for Synthetic Biology (IASB) and the International Gene Synthesis Consortium (IGSC) created independent codes of conduct based on customer screening, gene sequence screening, record keeping and points of contact with law enforcement. Subsequently, the US Department of Health and Human Services (DHHS) issued customer and sequence screening guidelines for the sale of synthetic genes.[1]

The International Council for the Life Sciences (ICLS) convened a meeting of industry representatives, government officials, academics, NGOs, international agencies, clients of the gene synthesis industry and citizen scientists in Heidelberg, Germany in March 2012. The meeting addressed practical issues of implementing and developing the codes, the feasibility of creating a 'seal of approval' for those implementing the codes, and how to promote wider adoption of the codes. It also addressed how to expand the scope of the codes to others involved in synthetic biology, such as academics, citizen scientists and corporations with in-house synthetic biology capabilities. A document recording the outcomes of the meeting was agreed by participants, together with a plan of action to continue the efforts towards global adoption of the codes (http://iclscharter.org/files/2012/09/ICLS-Syn-Bio-report-web-Mar-2012.pdf).

To raise awareness of, and advance the tenets of the codes, ICLS organized a second, international meeting in Hong Kong 7-8 March 2013. This meeting looked at recent developments in gene synthesis, reviewed implementation of the Codes of Conduct, assessed global developments in synthetic biology, and examined the status, applicability and adequacy of laws and regulations governing biotechnology for ensuring that synthetic biology is exploited safely, securely and responsibly.

1 The DHHS "Screening Framework Guidance for Providers of Synthetic Double-Stranded DNA" is at http://www.phe.gov/Preparedness/legal/guidance/syndna/Documents/syndna-guidance.pdf

Next Steps

After discussion of the technology and market changes expected to impact the field of synthetic biology in the coming years, recorded at **Appendix A**, it was suggested that the following objectives should be pursued:

1. **Codes of Conduct**
    a. Developing end-user approaches which, in addition to the gene foundries, engage clients of the gene synthesis industry the safety and security actions;
    b. Increased emphasis globally on early review and approval of synthetic biology research by institutional biosafety committees and funders to ensure safe, secure and responsible research;
    c. Involving a wider array of synthetic biology practitioners in safety and security discussions and activities;
    d. Examining whether the development of a virulence factor database, which could improve the effectiveness and reduce the cost of implementing the Codes of Conduct, was technically feasible and politically advisable; and
    e. Conducting trial audits by third parties of gene foundries' compliance with the Codes of Conduct in order to assess the effectiveness, burden a value of such auditing.
2. **Spreading Best Safety and Security Practices Globally**: it was agreed to engage biosafety associations in raising awareness of and increasing capabilities related to biological safety and security, especially as these pertain to synthetic biology.
3. **Legal Issues**: it was agreed to conduct a global survey of current national laws and regulations governing biotechnology, prepare a comparative compilation of these laws and regulations to help identify best practice, and to assess where gaps exist.

ICLS will coordinate and work with its international partners to endeavour to progress this agenda.

Conclusion

This meeting continued the process, started at the Heidelberg meeting, of building a global forum for discussing all policy, safety and security aspects of synthetic biology in order to facilitate its rapid, safe and responsible development and to ensure that all players globally are operating to the same high standards. As suggested in the Heidelberg meeting, it sought to garner broader involvement, both geographically and in terms of institutions and sectors, to ensure that progress in synthetic biology can happen in an environment that is conducive to scientific and technological innovation while fully protecting society by ensuring that the science is conducted safely, securely and responsibly.

Acknowledgments

Both the Heidelberg and Hong Kong meetings were made possible by financial support from the UK government's Strategic Programmes Fund, Federal Bureau of Investigation and the Alfred P. Sloan Foundation, as well as the expertise of the participants from academia, governments and the private sector.

Discussions at the meeting in Hong Kong

Appendix A

Synthetic Biology: Globalising Codes of Conduct Outcomes of the Meeting

ICLS organized a meeting in Hong Kong 7-8 March 2013 to further progress consideration of global security issues arising from developments in synthetic biology and to promote the global adoption of and adherence to the Codes of Conduct developed by the International Association for Synthetic Biology (IASB), the International Gene Synthesis Consortium (IGSC) and the US Department of Health and Human Services (DHHS).

The meeting was attended by participants from companies that synthesize genes, governmental and intergovernmental agencies, non-governmental organizations and academia from ten countries and five international organizations. The following represents the sense of the meeting. It is understood that the government officials in attendance have not committed their governments to any of the positions or decisions taken.

Recent Developments in Gene Synthesis

Participants agreed that over the past year there have been changes in both the market and the supply chain for synthetic genes:

- With further technological advances reducing the knowledge and skills required to produce synthetic DNA and making DNA synthesis capabilities more globally distributed, synthesis is no longer the sole, or even principal, choke point in the supply chain.

- The market for synthetic DNA has become more segmented:
  - ⇒ Privacy segment. Clients wishing to protect IP are increasingly using in-house production to ensure that absolute confidentiality is maintained;
  - ⇒ Small lot segment. This segment primarily relates to the research sector, and clients look for speed of service completion and product quality;
  - ⇒ Commodity segment. Price is the primary competitive advantage in this segment and hence some consolidation of suppliers in this segment can be expected;
  - ⇒ Full service segment. Fabrication centres aim to provide both design and production services for synthetic DNA to free up clients' research resources for issues other than DNA synthesis.
  - ⇒ Black market. With export controls and the costs associated with doing due diligence on orders from legitimate entities in certain states effectively excluding such entities from the regular market, there is a real possibility of a black market arising for synthetic DNA products to service these excluded entities and potentially more nefarious clients.

The net effect of these developments in the underlying technology, supply side structure and market is that a more multi-layered security approach will be needed. It will not be possible to rely solely on controlling the supply of synthetic DNA from gene foundries: rather security approaches will have to address fabrication centres, in-house production capabilities, and the general culture of all those involved in the design and production of and trade in synthetic DNA.

Codes of Conduct

It was agreed that the IASB and IGSC Codes of Conduct and the US DHHS Guidelines did not need immediate amendment. It was also noted that iGem would soon be issuing a new code for teams entering the competition, which would include more detailed practical guidance on safety and security issues, be more user friendly and result in better screening for dangerous sequences.

Participants agreed that there would be future challenges to the Codes of Conduct arising from:

- ⇒ Global diffusion of relevant technology and reduction in the scale of the equipment required;
- ⇒ Increased ability to design and engineer novel metabolic pathways in a range of organisms;
- ⇒ Greater efforts to protect intellectual property leading to more in-house synthetic DNA production with a concomitant loss of transparency;
- ⇒ Increased ability to perform meta-genome screening. In this regard, it was mentioned that it might now be time to re-examine the concept of a VIREP (virulence factor) database; and
- ⇒ Resale or recycling of disposed/'obsolete' equipment in secondary markets.

Suggested approaches to addressing some of these issues included:

- ⇒ Developing end-user approaches which put more of the safety and security burden on clients of the gene synthesis industry;
- ⇒ Increased emphasis globally on early review and approval of synthetic biology research by institutional biosafety committees to ensure safe, secure and responsible research;
- ⇒ Involving a wider array of synthetic biology practitioners in safety and security discussions and activities.

Global Developments in Synthetic Biology

A review of current synthetic biology activities indicated that currently there are active synthetic biology programmes in North America, Europe, China, Japan and Brazil. Elsewhere there is only limited access to synthetic DNA. Participants felt that in due course there would need to be better access globally to the technology and products of synthetic biology and that risk mitigation should be achieved through education and the transfer of safety technology.

In this context, participants agreed that there was a need in much of the world to improve upon biosecurity standards and practice. It was agreed that existing national, regional and international biosafety associations would be good partners in achieving heightened awareness of and capabilities with regards to security issues.

Legislative and Regulatory Issues

Participants reviewed the international treaty landscape as it affects synthetic biology, including the Biological and Toxin Weapons Convention, the Chemical Weapons Convention, the Cartegena Protocol and UN Security Council Resolution 1540 (2004). Participants did not consider that any additional international treaties would be required to address the security issues arising from synthetic biology, as any misuse of this technology would be captured by the prohibitions already present in the listed conventions. Conversely, participants agreed that security measures developed to ensure the safe and responsible application of synthetic biology would reinforce the goals of each of the listed international instruments.

On the issue of how to regulate the release of the products of synthetic biology, there was a sense that, in countries with more advanced biotechnology industries, existing legislation should suffice. However, it was also felt that many countries do not currently have adequate regulatory frameworks to test the new products of synthetic biology and authorize their general market release and consequently that action would be required to address regulatory gaps.

Meeting Participants in Hong Kong

Appendix B

U.S. Federal Bureau of Investigation Synthetic Biology Tripwire Initiative

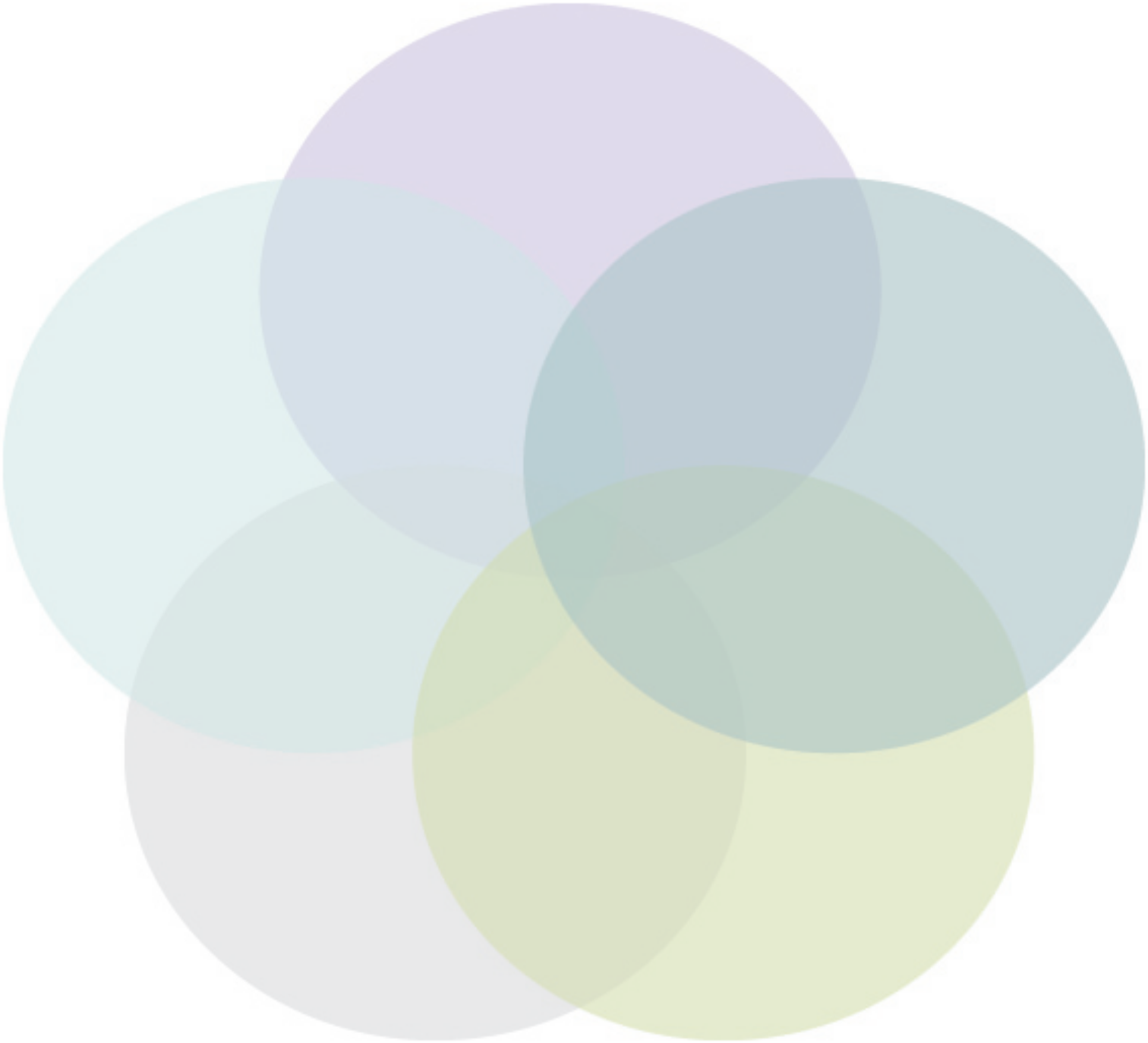
The FBI is the lead U.S. law enforcement agency responsible for investigation of weapons of mass destruction (WMD) threats and preventing attempts to obtain or use WMD materials, technology, and expertise. The FBI Weapons of Mass Destruction Directorate (WMDD) has developed and refined capabilities in the areas of investigations, operations, countermeasures, intelligence analysis, training, and oversight of its WMD Coordinators (FBI Special Agents that manage WMD-related matters in each of the FBI's 56 field offices). The FBI WMD Coordinator is the local point of contact regarding WMD threats and events and acts as the local FBI representative conducting outreach with local biological companies, state and local laboratories, and academia. Additionally, the WMDD maintains details at the International Criminal Police Organization (INTERPOL), the Republic of Georgia, and Singapore for international coordination.

Recently, the capabilities of synthetic biology technologies have dramatically advanced with a concomitant drop in associated costs. While these technologies, particularly gene synthesis, offer amazing promise, they also remain inherently dual-use - just as applicable for nefarious use as reputable use. To that end, the FBI established the synthetic biology/emergent biotechnology initiative, which is a proactive approach to mitigate current and over-the-horizon risks posed by the exploitation of advancements in research and development of scientific fields such as synthetic biology and nanobiotechnology. The synthetic biology initiative has FBI partnered with U.S. synthetic gene providers to render resources and federal reach-back capabilities to evaluate uncertainties in customer and/or sequence orders. Upon encountering suspicious orders, industry members can contact their local FBI WMD Coordinator to report the incident. By leveraging the FBI's expertise supplemented as needed by other federal experts (i.e. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, U.S. Department of Commerce, U.S. Department of Homeland Security and others), the FBI can act as a resource for industry members to address potential security issues without negatively impacting their business practices.

Glossary

Synthetic biology	There are varying definitions of synthetic biology. A useful operational definition is: a. the design, engineering and construction of new biological parts, devices and systems; and, b. the redesign of existing biological systems for useful purposes.
Genomics	The study of the genomes of organisms. The field includes efforts to determine the entire DNA sequence of organisms and fine-scale genetic mapping. The field also includes studies of intragenomic phenomena such as heterosis, epistasis, pleiotropy and other interactions between loci and alleles within the genome. In contrast, the investigation of the roles and functions of single genes is a primary focus of molecular biology or genetics. Research of single genes does not fall into the definition of genomics unless the aim of this genetic, pathway, and functional information analysis is to elucidate its effect on, place in, and response to the entire genome's networks.
Gene foundry	A corporation organization that synthesizes genes and genomes to order.
Fabrication center	Named after the fabrication, or Fab, service laboratories established in the (Fab): early semiconductor industry to make it easier for academic and small industrial labs to design and manufacture small quantities of custom chips. Biological fabrication centers aim to provide industrial and academic partners tools to facilitate and speed up the design, construction, and characterization of engineered genetic systems from standard biological parts in order to 'allow many academic researchers to rapidly prototype, test, and translate their foundational discoveries and ideas into practice'.
Synthetic biology constructs	A plasmid or a sequence of DNA created using the techniques of synthetic biology.
Citizen scientist	Amateur or non-professional scientist who conducts scientific research. Citizen science has been defined as "the systematic collection and analysis of data; development of technology; testing of natural phenomena; and the dissemination of these activities by researchers on a primarily avocational basis".[1]

1 See http://www.openscientist.org/2011/09/finalizing-definition-of-citizen.html



International Council for the Life Sciences
7925 Jones Branch Drive, Suite LL 130
McLean, VA 22102 USA
+1 (202) 659-8058
info@iclscharter.org
www.iclscharter.org