Risk and benefit analysis: high-risk research and its implications for the BWC

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Our Mission

The Center for Health Security works to protect people’s health from the epidemics and disasters and to ensure that communities are resilient to major challenges.
Activities of our Center

Conduct non-partisan research and analysis on major domestic and international health security issues.

Engage with researchers, the policymaking community, and the private sector to make progress in the field.

Educate a rising generation of scholars, practitioners, and policymakers.

Majority of our funding comes from philanthropy and minority from government grants or contracts.

Priority Activity Areas:

- Global Health Security
- Deliberate Biological Threats
- Opportunities & Risks in the Life Sciences
- Medical and Public Health Preparedness & Response
Global catastrophic risks

- catastrophic forms of climate change, nuclear war, natural or engineered pandemics, volcanic eruptions, economic collapse, worldwide tyranny --

- or catastrophic disruption from unprecedented technologies like artificial intelligence or nanotech --

- global catastrophic risk cascades, or particularly extreme global catastrophic risks pose an existential risk
Global catastrophic biological risk (GCBR)

• “Those events in which biological agents—whether naturally emerging or reemerging, deliberately created and released, or laboratory engineered and escaped—could lead to sudden, extraordinary, widespread disaster beyond the collective capability of national and international governments and the private sector to control.

• If unchecked, GCBRs would lead to great suffering, loss of life, and sustained damage to national governments, international relationships, economies, societal stability, or global security.”

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Biotechnology advances as possible causes of catastrophic events
### Key SynBio approaches in use

<table>
<thead>
<tr>
<th>Approach</th>
<th>Beneficial application</th>
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<tbody>
<tr>
<td>Re-creating known bacteria, viruses, algae</td>
<td>Vaccine design, other MCMs</td>
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<tr>
<td>Making existing pathogens more dangerous</td>
<td>Pathogenesis studies</td>
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<tr>
<td>Creating new bacteria or viruses</td>
<td>Biofuel production or cleanup</td>
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<tr>
<td>Manufacturing chemicals using metabolic pathways</td>
<td>Pharmaceuticals, biofuels</td>
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<tr>
<td>Modifying the human microbiome</td>
<td>Reprogramming the gut</td>
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<tr>
<td>Modifying the human immune system</td>
<td>Immunotherapeutics</td>
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<td>Modifying the human genome</td>
<td>Somatic vs germ line</td>
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Synbio Framework

From

“Biodefense in the Age of Synthetic Biology” (NASEM 2018)
Framework

Usability of the Technology
- Ease of use
- Rate of development
- Barriers to use
- Synergy with other technologies

Usability as a Weapon
- Production and delivery
- Scope of casualty
- Predictability of results

Requirements of Actors
- Access to expertise
- Access to resources
- Organizational footprint requirements

Potential for Mitigation
- Deterrence and prevention capabilities
- Capability to recognize an attack
- Attribution capabilities
- Consequence management capabilities

Level of Concern about the Capability
Introduction to Framework (Tucker)

Begin to monitor dual use technology

Assess **Risk of Misuse** using four parameters
1. accessibility
2. ease of misuse
3. magnitude of potential harm
4. imminence of potential misuse

Determine Risk of Misuse by averaging the values (high, medium low) yielded by the 4 parameters

Assess **Governability** using five parameters
1. embodiment
2. maturity
3. convergence
4. rate of advance
5. international diffusion

Determine **Governability** by averaging the values (high, medium low) yielded by the 5 parameters

Changes Detected?

Yes

- Continue monitoring

No

Is the risk of misuse high or medium?

Yes

- Continue monitoring

No

Changes Detected?

- Continue monitoring
Case examples

Applied the frameworks to two case examples:

- Change in transmissibility of an emerging viral pathogen “Gain of Function”

- Engineering and controlling commensal bacteria for targeted “live” therapeutics – “Microbiome Engineering”
Framework for benefits assessment?

• Gets everyone on the same page
• Is a tool everyone can see themselves in
• Helps standardize terminology to make sure everyone is talking about the same thing
• Makes different assessments comparable since they have the same categories
• Helps communicate complex thinking in a relatively compact format – inside and outside the community of experts
TECHNOLOGIES TO ADDRESS
Global Catastrophic Biological Risks
Global Catastrophic Biological Risks (GCBRs)

• Global Catastrophic Risks are a class of risks – naturally or technologically driven – that have potential to inflict serious damage to human wellbeing on a global scale

• GCBRs might include:
  • Naturally occurring severe pandemics
  • Deliberately created and released pathogens
  • Laboratory engineered and escaped pathogens
Opportunities for Intervention in Severe Pandemics

Prevent Spread from Animals to Humans or Detect First Human Case
- INDEX CASE

Identify First Cluster and Prevent an Epidemic
- INDEX CLUSTER

Prevent National and International Spread
- LOCALIZED EPIDEMIC

Limit Spread and Introduction to Major Urban Environments
- INTERNATIONAL EPIDEMIC

Reduce Morbidity and Mortality
- GLOBAL PANDEMIC

Prevent Existential Risk to Humanity
- GCBR
Categories of Applicable Technologies

Environmental Monitoring
- Recognition and Characterization of an Emerging Biological Event to Prevent Spread
  - Public Health Surveillance

Infectious Disease Diagnostics
- Drugs, Vaccines, and Nonpharmaceutical Interventions to Reduce Transmission, Illness, and Death
  - Medical Countermeasure (MCM) Development

MCM Manufacturing
- MCM Distribution, Dispensing, and Administration

Community Medical Care
- Clinical Care

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Project Approach

• Structured exploration of **extant and emerging technologies** with the potential to radically alter the trajectory of severe infectious disease events with catastrophic potential

• **Goals:**
  • ID areas of need for tech solutions to address pandemic and GCBRs;
  • ID technologies that have significant potential to reduce GCBRs; and
  • Provide context for those technologies

• **Uses:** results should be used to guide further detailed analyses
Technology Evaluation Process

• Our Questions:
  • What is the technology?
  • What problem does it solve?
  • How do we do it now?
  • What does success look like?
Ubiquitous Genomic Sequencing and Sensing

• What is the technology?
  • Rapid, accurate, affordable, and fieldable nucleotide sequencing for detection of pathogens in human and environmental samples – nanopore sequencing

• What problem does it solve?
  • Sequencing can be used to detect novel or unexpected pathogens, whereas other molecular diagnostics like PCR only test for known pathogens

• How do we do it now?
  • Prior to nanopore, sequencing was centralized and laboratory-based

• What does success look like?
  • Ubiquitous sequencing will allow for the near real-time characterization of pathogen biology, including determinations of virulence, transmissibility, sensitivity or resistance to medicines or vaccines.
Drone Networks for Environmental Detection

• What is the technology?
  • Drone networks sampling air, water and soil and processing biological samples onboard

• What problem does it solve?
  • Help detect an aerosolized attack or potentially catastrophic change in aquatics ecosystems

• How do we do it now?
  • Environmental surveillance is conducted on a small scale, and is not networked

• What does success look like?
  • A network of land, sea, and air-based drones autonomously conducting environmental surveillance
Cell-Free Diagnostics

• What is the technology?
  • Cell-free diagnostics take bioengineered cellular machinery from lysed cells, freeze dries these components, and uses them for diagnosis

• What problem does it solve?
  • It provides cheap, accurate, and portable diagnostics

• How do we do it now?
  • Diagnostics like polymerase chain reaction (PCR) require laboratories and expensive equipment

• What does success look like?
  • Cell-free diagnostics could be rapidly manufactured and distributed widely
3D Printing of Chemicals and Biologics

• What is the technology?
  • 3D printing (additive manufacturing) of drugs and vaccines

• What problem does it solve?
  • Even when a drug or vaccine is developed in time to respond to a pandemic, getting access to them will be difficult in many parts of the world. 3D printers could be used in doctors’ offices, pharmacies, and even at home

• How do we do it now?
  • Most MCM manufacturing occurs at centralized sites and on dedicated platforms

• What does success look like?
  • 3D printing could allow for greater and earlier access to medical countermeasures developed in response to or identified in a GCB event
Microarray (Microneedle) Patch Vaccines

• What is the technology?
  • Microarray patches can be used in place of needle and syringe for vaccination

• What problem does it solve?
  • With needle and syringe, you need healthcare providers to administer vaccines. MAPs eliminate that need

• How do we do it now?
  • Vaccines can be given only by healthcare providers

• What does success look like?
  • Elimination of needle and syringe, and move toward self-administration for vaccines in a pandemic or GCBR
Synthetic Vaccinology: Self-Amplifying mRNA Vaccines

- What is the technology?
  - SAM vaccines use the genome of a modified RNA virus to introduce an antigen of interest and replicate in the body

- What problem does it solve?
  - Safer and easier to deliver than other nucleic acid vaccines
  - Reduces dose needed, and induces a broader immune response than other vaccines

- How do we do it now?
  - Viral vectors hampered by immune response and have risk of reversion to wild type
  - Large amounts of antigen and sometimes multiple doses and difficulty manufacturing

- What does success look like?
  - Fast, dose-sparing technology could mean a vaccine that is available rapidly and can protect many more people
New technologies and the BWC

Dangers arising from technological advances were understood at the time of the treaty’s negotiation:

“[t]he potential undoubtedly exists for the design and development of infective agents against which no credible defense is possible, through the genetic and chemical manipulation of these agents”.

• Joshua Lederberg, United Nations Conference of the Committee on Disarmament on 5 August 1970.