

# Pathogens, Synthetic Biology, and Implications for the Future

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## Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction (1975)

Key provisions of the Treaty include obligations on States parties:

- ▶ to never under any circumstances acquire or retain biological weapons (Article I);
- ▶ to destroy or divert to peaceful purposes biological weapons and associated resources (Article II);
- ▶ to not transfer, or in any way assist, encourage or induce anyone else to acquire or retain biological weapons (Article III);
- ▶ to take any national measures necessary to implement the provisions of the BWC domestically (Article IV);
- ▶ to consult bilaterally and multilaterally to solve any problems with the implementation of the BWC (Article V);
- ▶ to request the UN Security Council to investigate alleged breaches of the BWC and to comply with its subsequent decisions (Article VI);
- ▶ to assist States parties which have been exposed to danger as a result of a violation of the BWC (Article VII);
- ▶ to do all of the above in a way that protects and encourages the peaceful uses of biological science and technology (Article X).

# U.S. BALLISTIC MISSILE WITH BOMBLETS

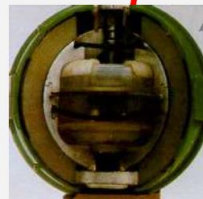


**MGM-29  
Sergeant Missile  
(135 km range)**



**M210  
Biological Warhead**

**720 M143  
Bomblets:  
cover 131 km<sup>2</sup>**



Source: Wikipedia

**M143 Bomblet:**

- 212ml tularemia
- 0.2% dissemination efficiency

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## FEDERAL SELECT AGENT PROGRAM



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[Federal Select Agent Program > Select Agents and Toxins > List](#)

### SELECT AGENTS AND TOXINS LIST

The following biological agents and toxins have been determined to have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. An attenuated strain of a select agent or an inactive form of a select toxin may be excluded from the requirements of the Select Agent Regulations. Here is a list of [excluded agents and toxins](#).

**HHS and USDA Select Agents and Toxins**  
7CFR Part 331, 9 CFR Part 121, and 42 CFR Part 73

**HHS SELECT AGENTS AND TOXINS**

- Abrin
- Bacillus cereus* biovar *anthracis*\*
- Botulinum neurotoxins\*
- Botulinum neurotoxin producing species of *Clostridium*\*
- Conotoxins (Short, paralytic alpha conotoxins containing the following amino acid sequence X<sub>1</sub>CCX<sub>2</sub>PACGX<sub>3</sub>X<sub>4</sub>X<sub>5</sub>X<sub>6</sub>CKX<sub>7</sub>)<sup>1</sup>
- Coxiella burnetii*
- Crimean-Congo haemorrhagic fever virus
- Diacetoxyscirpenol
- Eastern Equine Encephalitis virus<sup>3</sup>
- Ebola virus\*
- Francisella tularensis*\*

**OVERLAP SELECT AGENTS AND TOXINS**

- Bacillus anthracis*\*
- Bacillus anthracis* Pasteur strain
- Brucella abortus*
- Brucella melitensis*
- Brucella suis*
- Burkholderia mallei*\*
- Burkholderia pseudomallei*\*
- Hendra virus
- Nipah virus
- Rift Valley fever virus
- Venezuelan equine encephalitis virus<sup>3</sup>

**USDA SELECT AGENTS AND TOXINS**

- African horse sickness virus
- Blattella germanica* *Blattella germanica*

#### Key Points:

- This is the primary means for US biosecurity regulation
- Requires individual clearance from DOJ, institutional approval
- Should not be considered the only law enforcement tool for biological agents.
- Challenged by synthetic biology and also nature.

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## Synthetic biology

- The design and construction of new biological parts, devices, and systems and the re-design of existing, natural biological systems for useful purposes. (syntheticbiology.org)
- “Collectively refers to concepts, approaches, and tools that enable the modification or creation of biological organisms...” NAS 2018.
- Convergence of engineering, biology, chemistry, computational power.
- Term applies tools (such as CRISPR) as well as the field.
- Ushering in a new era for biology.

**Aims to make biology easier to engineer**

## Industrialization of biology

- Industrialization = formation of industries in a country or region, on a wide scale. *e.g.*, the Industrial Revolution of the 18<sup>th</sup> and 19<sup>th</sup> century.
- Replacing chemical engineering processes, or resource- intense harvesting from nature. *e.g.* medicine, tires, adhesives, flavorings (including vanilla and saffron), detergents, cosmetics, and mining.



## Personalization of biology

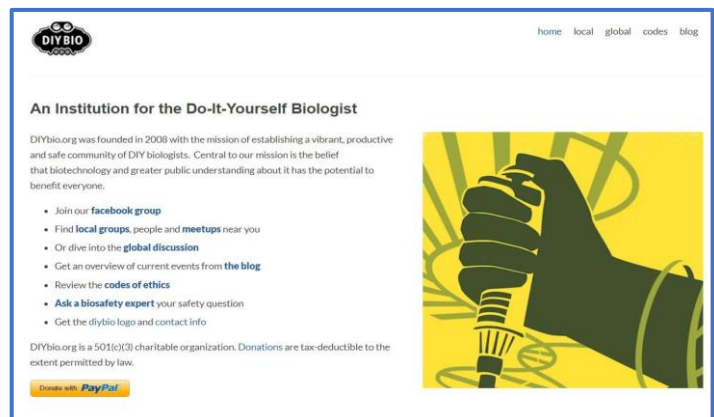
- Personalized medicine e.g. CAR-T
- Tools are accessible, powerful
  - CRISPR
  - Gene synthesis and gene sequencing
- Ancestry.com, 23andme, PatientsLikeMe
- Applications may be personally and immediately relevant
  - What is in your food?
  - Which dog owner isn't picking up after their pet? Or, personalized pets.



**People can use biology to answer their own questions.**

## Amateur biology/citizen science

- iGEM: International Genetically Engineered Machine competition.
- DIY Bio
- Community laboratories: 44 across the US and Canada, 31 in Europe, 17 in Asia, South America, and Oceania



## Bioweapons concerns

- There are many biosecurity vulnerabilities with “ordinary” microbiology-- synthetic biology and other emerging biotechnology *add* to them.
- However:
  - More people who have access to these technologies than ever before;
  - Misuse may not require pathogen access (and biosecurity regulatory system is largely built on access control).

## Norms against illegal weapons

## Dual use research

- Dual use: advances that lower the barriers to misuse
- Dual use research of concern: “Life sciences research that, based on current understanding, can be reasonably anticipated to provide knowledge, information, products, or technologies that could be directly misapplied to pose a significant threat with broad potential consequences to public health and safety, agricultural crops and other plants, animals, the environment, materiel, or national security.”
- Conundrum: Legitimate scientific inquiry, often with medical benefits, and not everyone sees the risks and benefits in the same way.

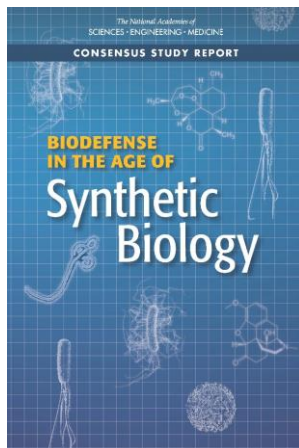




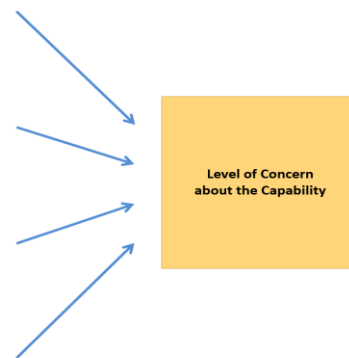
# There is strong interest in managing DURC

- Yet: Misuse by **whom** and to what degree?
- Dual use research of concern can be identified, but can the risks and benefits be truly quantified?
  - More likely they will be experiment-dependent, context-dependent, and time-dependent
  - Not all nations will balance the risks and benefits the same way
  - **Consensus will remain difficult, particularly as experts view the threat differently**
- Who decides?

## Framework for Assessing Relative Concern



Usability of the Technology
<ul style="list-style-type: none"> <li>• Ease of use</li> <li>• Rate of development</li> <li>• Barriers to use</li> <li>• Synergy with other technologies</li> </ul>
Usability as a Weapon
<ul style="list-style-type: none"> <li>• Production and delivery</li> <li>• Scope of casualty</li> <li>• Predictability of results</li> </ul>
Requirements of Actors
<ul style="list-style-type: none"> <li>• Access to expertise</li> <li>• Access to resources</li> <li>• Organizational footprint requirements</li> </ul>
Potential for Mitigation
<ul style="list-style-type: none"> <li>• Deterrence and prevention capabilities</li> <li>• Capability to recognize an attack</li> <li>• Attribution capabilities</li> <li>• Consequence management capabilities</li> </ul>



# Analysis of the Complete Genome of Smallpox Variola Major Virus Strain Bangladesh-1975

ROBERT F. MASSUNG,\* LI-ING LIU,†‡ JIN QI,\* JANICE C. KNIGHT,\* THOMAS E. YURAN,\*  
ANTHONY R. KERLAVAGE,†‡ JOSEPH M. PARSONS,\* J. CRAIG VENTER,†‡  
AND JOSEPH J. ESPOSITO\*<sup>1</sup>

*\*Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia 30333; †National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland 20892; and ‡The Institute for Genomic Research, Gaithersburg, Maryland 20878*

*Received December 6, 1993; accepted February 17, 1994*

- “nobody anticipated that... advances in genome sequencing and genome synthesis would render substantial portions of [variola] accessible to anyone with an internet connection and access to a DNA synthesizer.”
- – World Health Organization (2010)

## Synthetic biology and safety

- Not associated with any accidents to date
- Categories for concern:
  - “outside the laboratory” applications
  - Experience of practitioners
  - General concern that biosciences could lead to bioerrors
- Need for more data



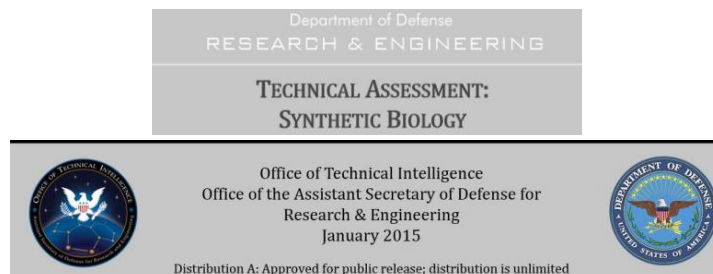
## US National Competitiveness

- Synthetic biology born in the US, but other nations are investing heavily.
- NIH: “erosion of the competitive position of the US life sciences industry over the past decade.”
  - China will overtake US in R&D spending by 2020

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## Department of Defense

“There are few highly-experienced program managers in the Department, few leading scientists, and even fewer individuals in uniform with deep knowledge of the [synthetic biology] field. The lack of uniformed expertise is particularly troubling.”



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# Boosting and Safeguarding the Bioeconomy



## NEWS

### DoD Announces Request for Information for a New Manufacturing Innovation Institute Dedicated to Synthetic Biology



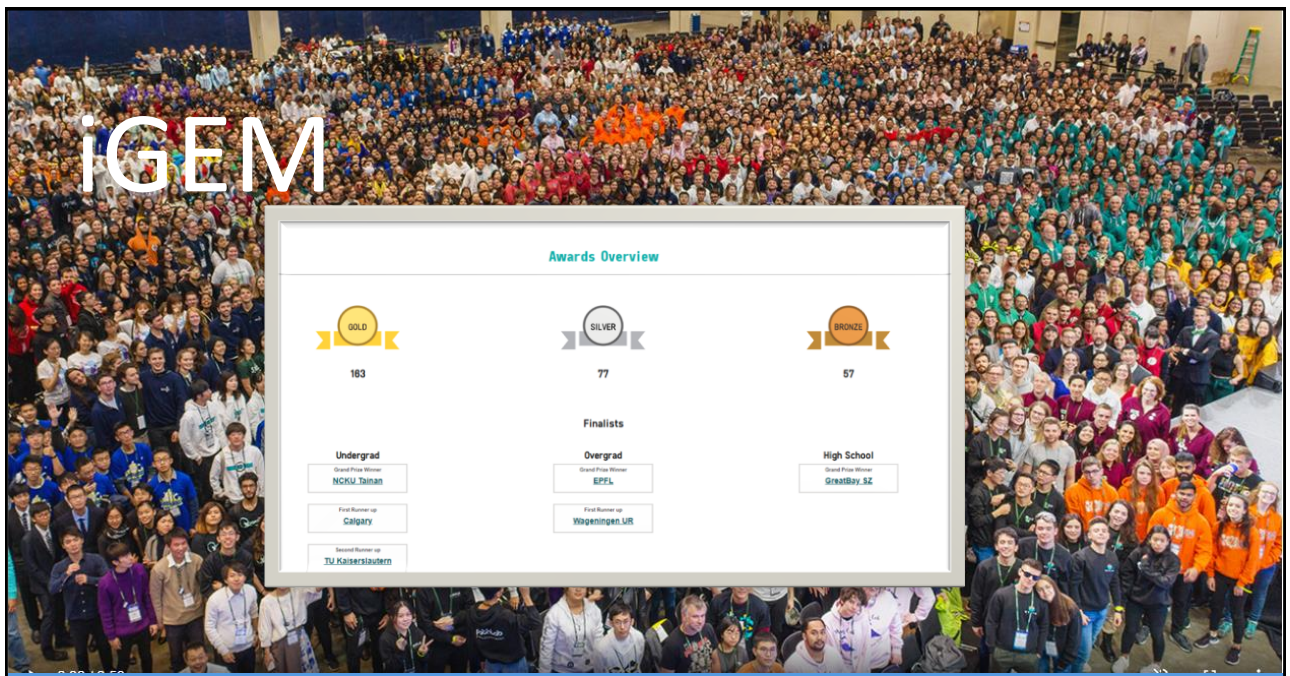
September 30, 2019 | Department of Defense | [Automation, Biomanufacturing, Composites, Design, Economy, Education, Energy, IIOT, Impact, Innovation, Materials, Network, Photonics, Process, Security, Sustainability, Workforce](#)

The Department of Defense is announcing a request for information (RFI) to identify partnership opportunities for a new Manufacturing Innovation Institute dedicated to synthetic biology, or SynBio, for non-biomedical applications. The SynBio institute aims to deliver new capabilities by "scaling-up" critical bio-manufacturing processes and related biotechnologies in partnership with industry and academia. Responses to the RFI will gauge interest and scope technology focus areas to provide commercial- and defense-relevant products and applications through the institute. The RFI signals DoD's continued commitment toward public-private partnerships that facilitate collaboration, leverage existing resources and encourage co-investment in manufacturing technologies with broad commercial and defense applications.

# Why does it matter?

- For the economy
- For our nation's security:
  - NSS 2015: "A strong economy, combined with a prominent US presence in the global financial system, creates opportunities to advance our security."
  - DoD applications
- Lost opportunities in early governance and direction of synthetic biology applications; scientists at the leading edge are setting norms and expectations
  - Germline edits– "designer babies"
  - Gene drives– to eradicate mosquitoes
  - De-extinction
  - What will be next?

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# Are you using synthetic biology products?



## Vegan dairy group Perfect Day valued at \$440m in funding round

Group raised \$140m in round led by Singapore's Temasek



© Perfect Day

## Ready For Meat Grown From Animal Cells? A Startup Plans A Pilot Facility

January 22, 2020 · 3:56 PM ET

ALLISON AUBREY



This chicken from Memphis Meats was produced with cells taken from an animal and grown into meat in a "cultivator." The process is analogous to how yeast is grown in breweries to produce beer.

Allison Aubrey/UPM



## How This Startup Is Using Bacteria to Grow Bricks From Scratch

North Carolina-based startup BioMason has found a way to create masonry without heat or clay.

in f t



By Kevin J. Ryan, Staff writer, [HKS](#) [@whereasKJ](#)



Far right: BioMason co-founder and CEO Ginger Krieg Dosier. COURTESY COMPANY



## Genomatica makes nylon precursor from sugar

Milestone for renewable intermediate marks waypoint for commercial scale up

by Melody M. Bunge

JANUARY 29, 2020 | APPEARED IN VOLUME 98, ISSUE 5



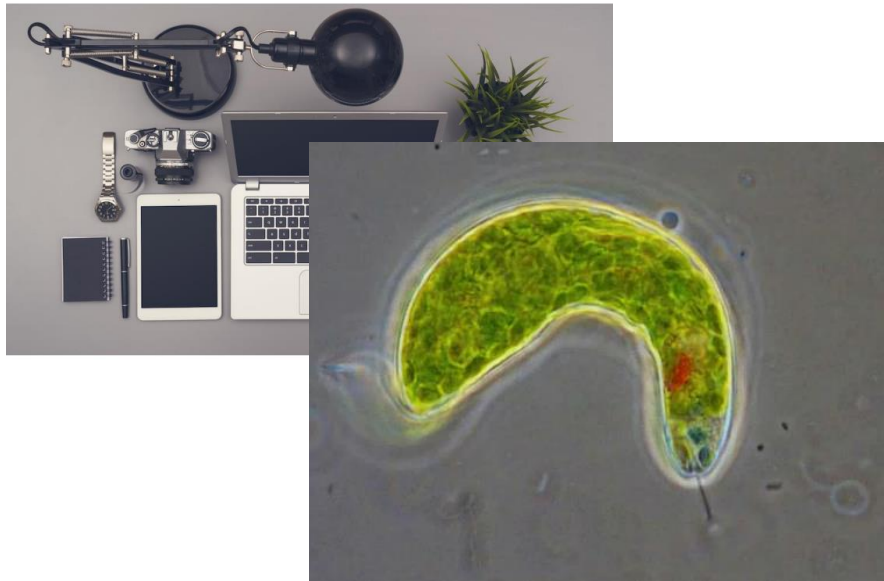
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From Jason Kelly, CEO of Ginkgo Bioworks

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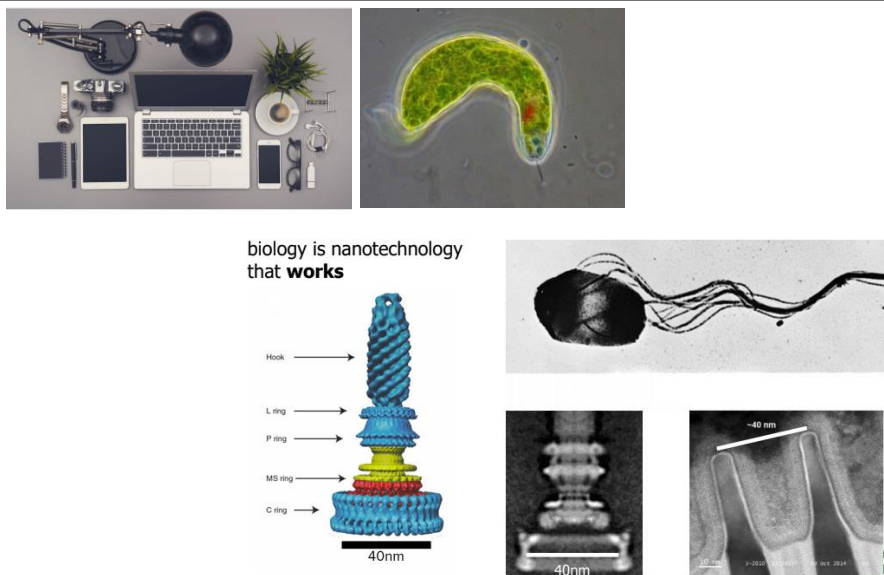
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From Jason Kelly, CEO of Ginkgo Bioworks

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From Jason Kelly, CEO of Ginkgo Bioworks

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## What can we do?

The US should pursue maintain competitiveness in S&T, including in synthetic biology.

- Fund basic research with minimal fluctuations from year to year;
- Fund STEM educational initiatives;
- Institute financial incentives to discourage synthetic biology companies and other biotechnology companies from locating offshore;
- Develop the workforce through training programs;
- Ensure that women are targeted for advancement in STEM fields; and
- Encourage foreign students who receive their PhDs in the US in technical areas to stay in the US, by receiving green cards enabling them to work here.
- Consider the holistic cost of products for procuring US government contracts and making technology investments, which would demonstrate savings for biotechnological approaches
- Consider the security benefits of distributed manufacturing.

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## What must we prepare for?

- In 2012, when listing tasks to be accomplished during his administration, Russian President Vladimir Putin included “the development of weapons based on new physical principles: radiation, geophysical wave, genetic, psychophysical, etc.”
- In 2017, Putin spoke of the dangers associated with the creation of “genetically-modified superhuman soldiers” that will be “worse than a nuclear bomb.”
- In 2020, Putin said, “As one energy specialist used to say, the Stone Age ended not because people ran out of stones but because new technologies came along. The same applies to defense, probably, at some point nuclear arms will not be the most effective weapon or will become obsolete.”

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