

AETAP 2018 Helsinki

Novel Threats at the Convergence of Biosecurity and Cybersecurity

Ryan N. Burnette, Ph.D.

Director, Biosafety and Biosecurity Programs



www.merrick.com



Thank You





What I Want You To Know

- Biosecurity is a unique subset of the security discipline with global implications
- Information gap is closing rapidly = Threats are evolving rapidly
- Negligent researchers, malicious insiders, and curious do-gooders are equal threats
- Cyberbiosecurity is indeed a thing

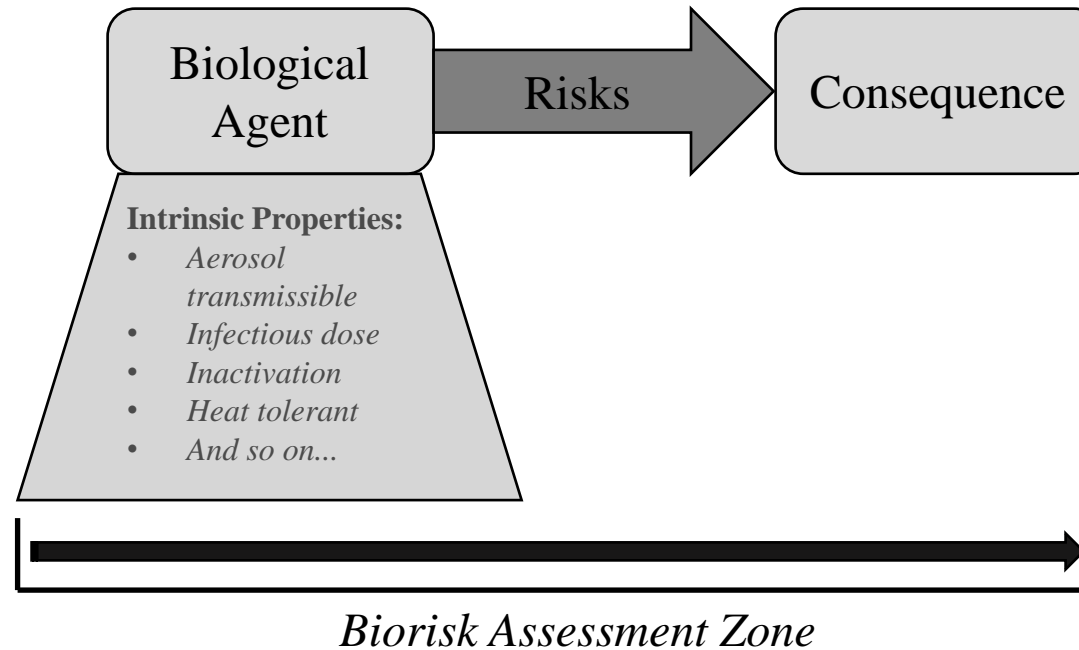
Biosecurity Is a Unique Subset of Security with Global Implications

PART I



Risk Assessment
is the Foundation
of Biosafety

BIORISK ASSESSMENT

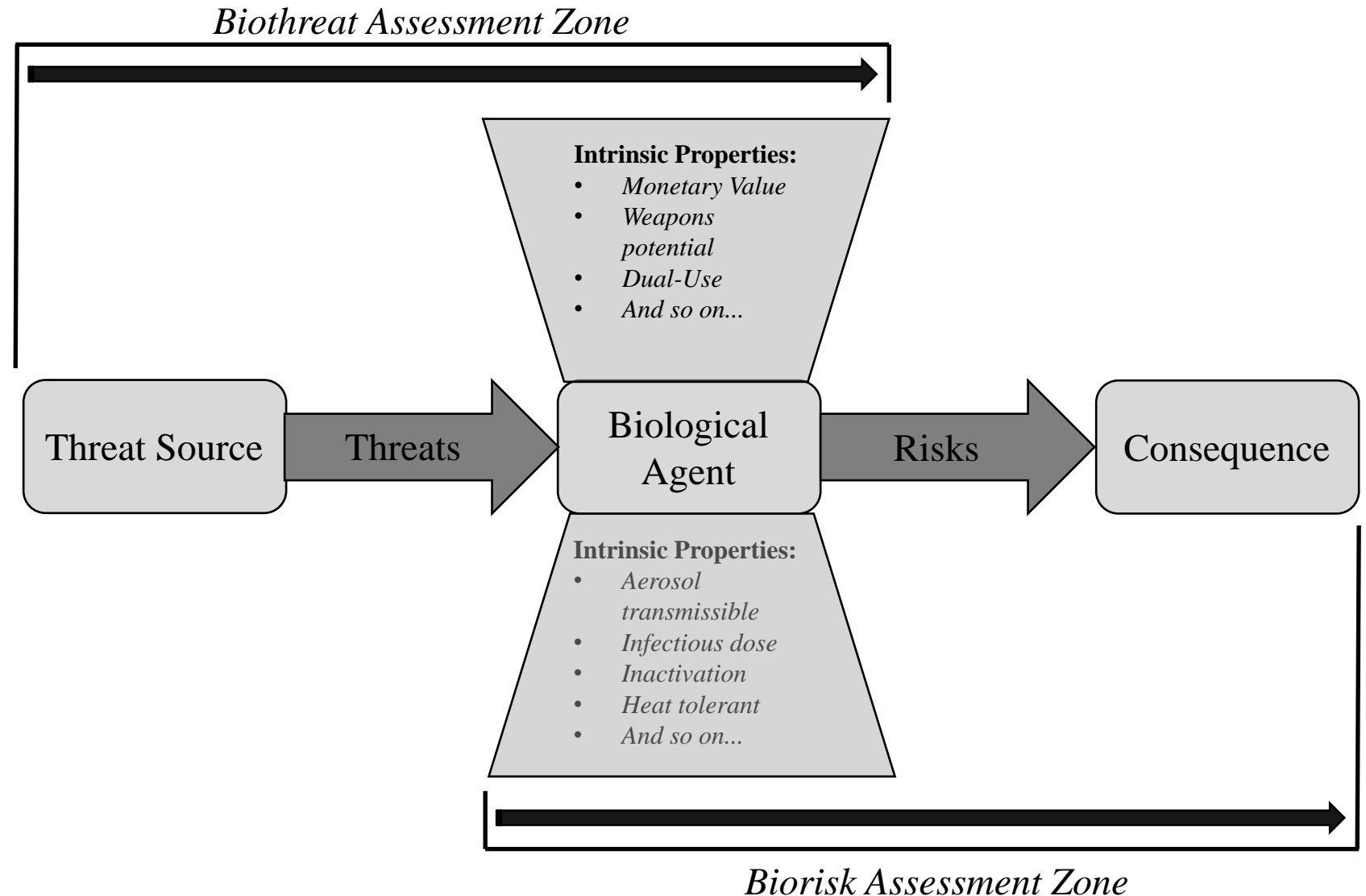


Taken from "Biosecurity in Global Health, Defense, and Developing Technologies," 2018, R. Burnette, in process



Threat
Assessment is
the Foundation
of Biosafety

BIOTHREAT ASSESSMENT

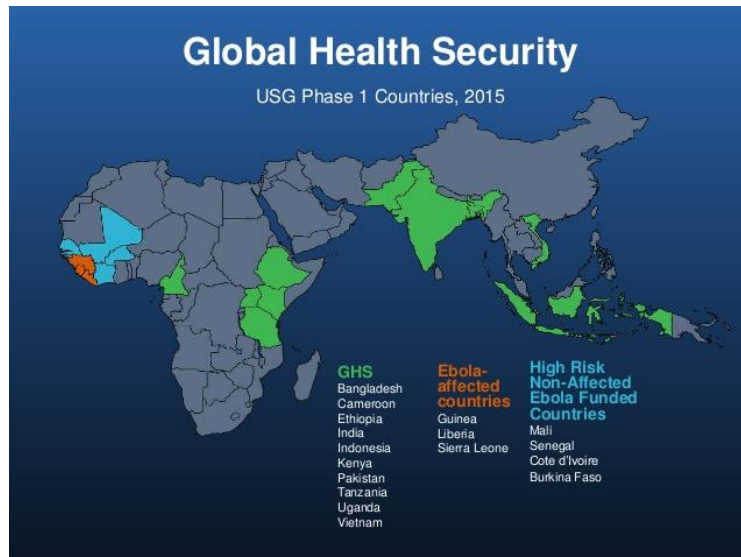


Biosecurity Has Global Implications

GHSA

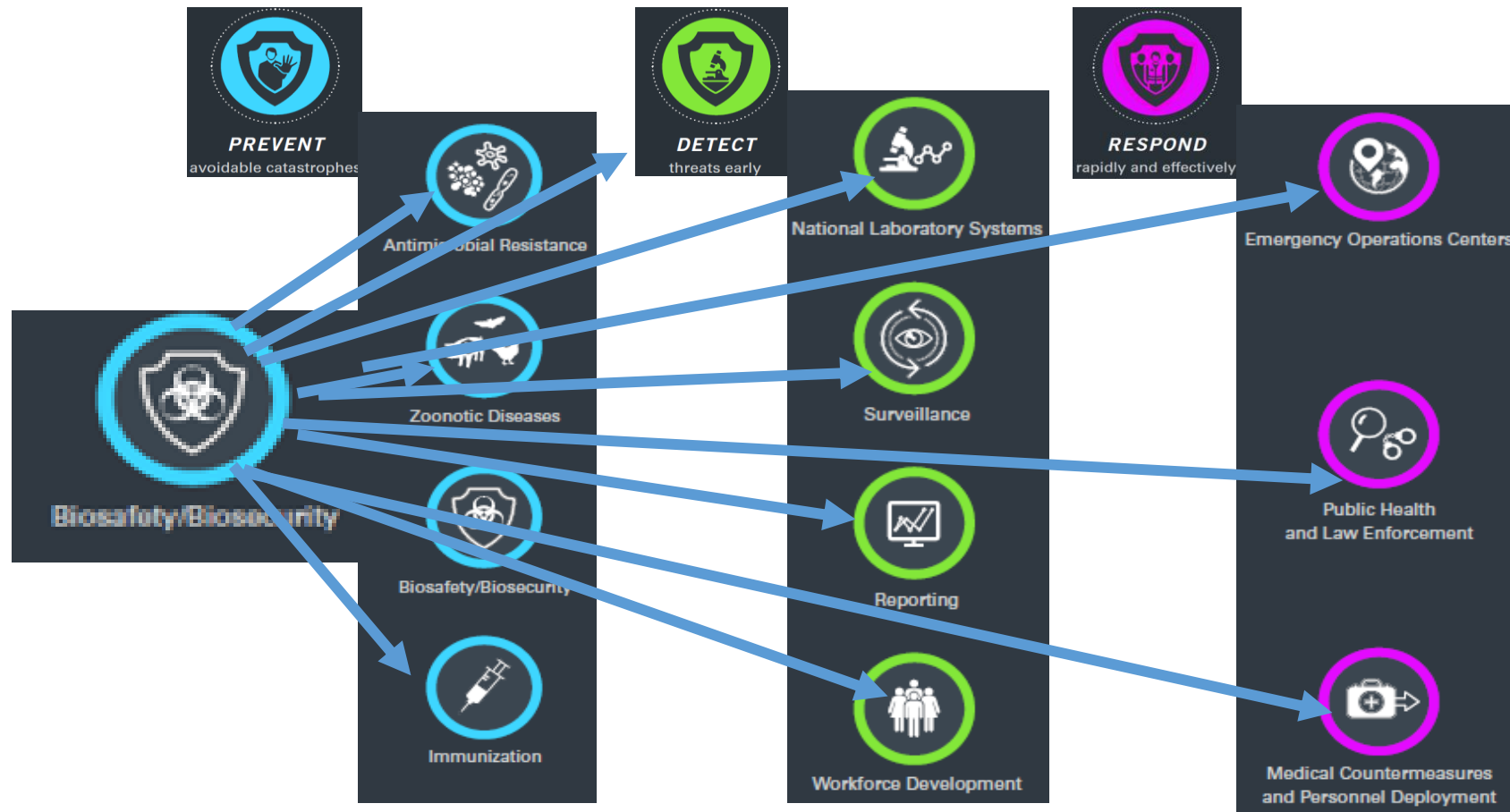
...We must come together to prevent, and detect and fight every kind of biological danger – whether it's a pandemic, the H1N1, a terrorist attack, or a treatable disease."

President Barack Obama, 2011



Biosecurity Has Global Implications

GHSA



Biosecurity Has Global Implications

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Wainstein
Panel Member



Biosecurity Has Global Implications

Gene Editing a WMD Threat?

- *“Given the broad distribution, low cost, and accelerated pace of development of this **dual-use** technology, its deliberate or unintentional misuse might lead to far-reaching economic and national security implications.”* James R. Clapper, Dir. Of National Intelligence



<https://www.technologyreview.com/s/600774/top-us-intelligence-official-calls-gene-editing-a-wmd-threat/>

U.S. Policy

Dual Use Research of Concern

- 15 Agents and Toxins
- 7 Categories of Experiments
 - Enhances the harmful consequences of the agent...
 - Disrupts immunity...
 - Confers therapeutic resistance...
 - Increases the stability, transmissibility, or the ability to disseminate the agent or toxin
 - Alters the host range... of the agent or toxin
 - Enhances the susceptibility of a host population to the agent or toxin
 - Generates or reconstitutes an eradicated or extinct agent or toxin

http://osp.od.nih.gov/sites/default/files/resources/United_States_Government_Policy_for_Oversight_of_DURC_FINAL_version_032812_1.pdf

Applies to engineering pathogens with genome editing tools or any other methods

Does not apply to any other uses of genome editing tools

The Information Gap is Closing Rapidly (but still a way to go...)

PART II



Community Labs, Biohackers and DIYBio OH MY!

- “... biology should be accessible, affordable, and open to everyone.”
- Positive momentum between community labs and biosafety associations – future discipline for biosafety professionals?
- Greater emphasis on responsible science

Membership

Join Our Community of Biohackers

Monthly membership unlocks:

BSL1 lab, co-working space and shared equipment

Class and event discounts

Storage space in lab fridge, chemical cabinet and freezer

Free safety training & orientation

Office space with appointment

[LEARN MORE](#)



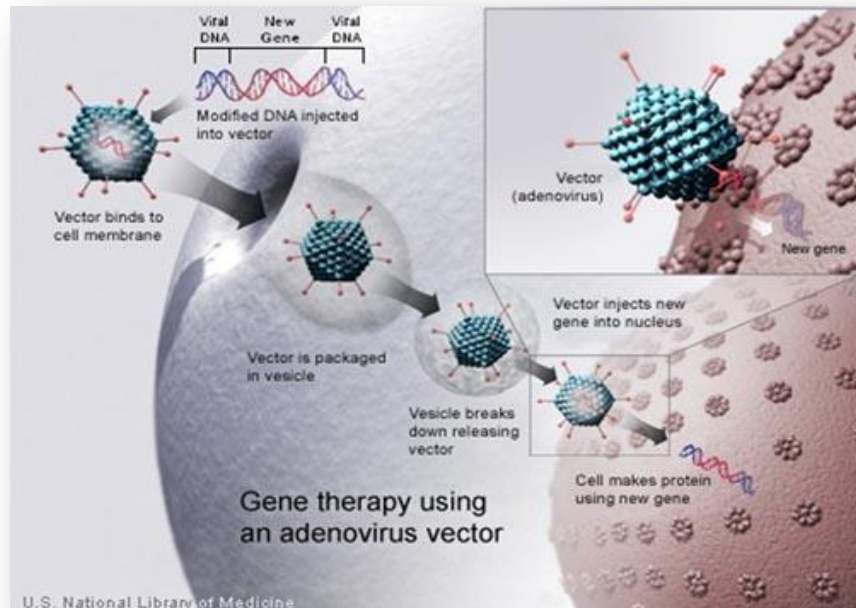
What are they doing in there?

Gene Editing

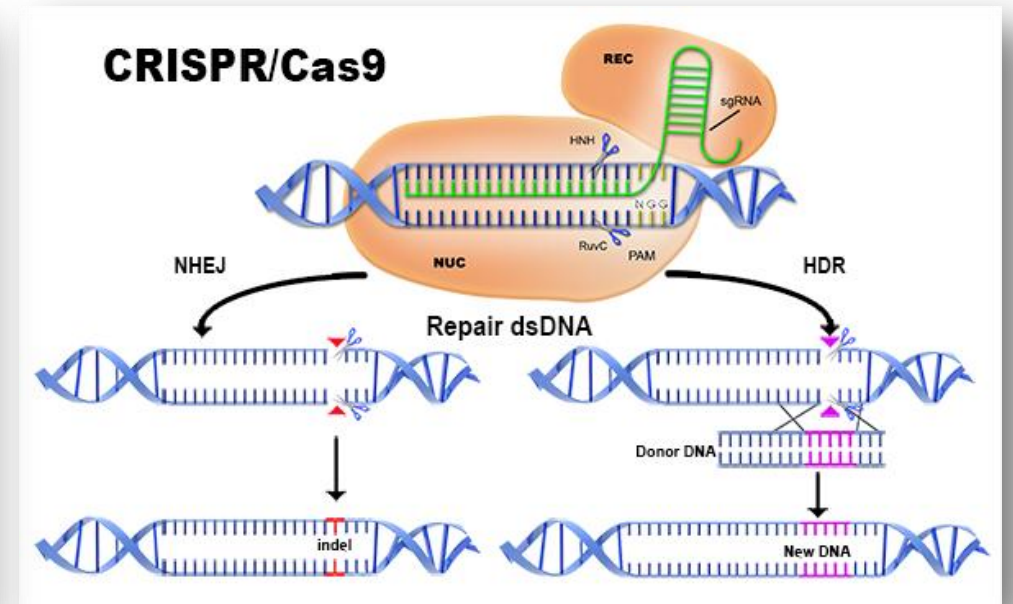
- Recombinant DNA Technology goes back decades
- New molecular tools (CRISPR/Cas9) allows strategic modification of genetic sequences
- Potential tool to treat genetic diseases (gene therapy)
- Also, in vivo and ex vivo human gene therapies (HGT)



<https://www.technologynetworks.com>



http://web.alsa.org/site/PageServer?pagename=ALSA_Gene_Therapy

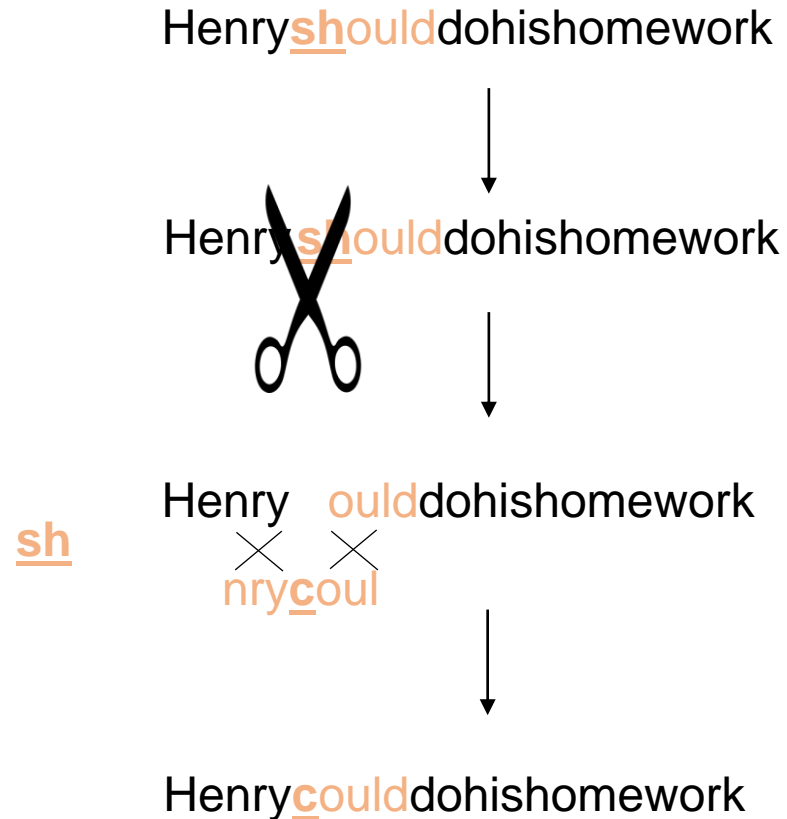


<https://www.aati-us.com/instruments/fragment-analyzer/crispr/>

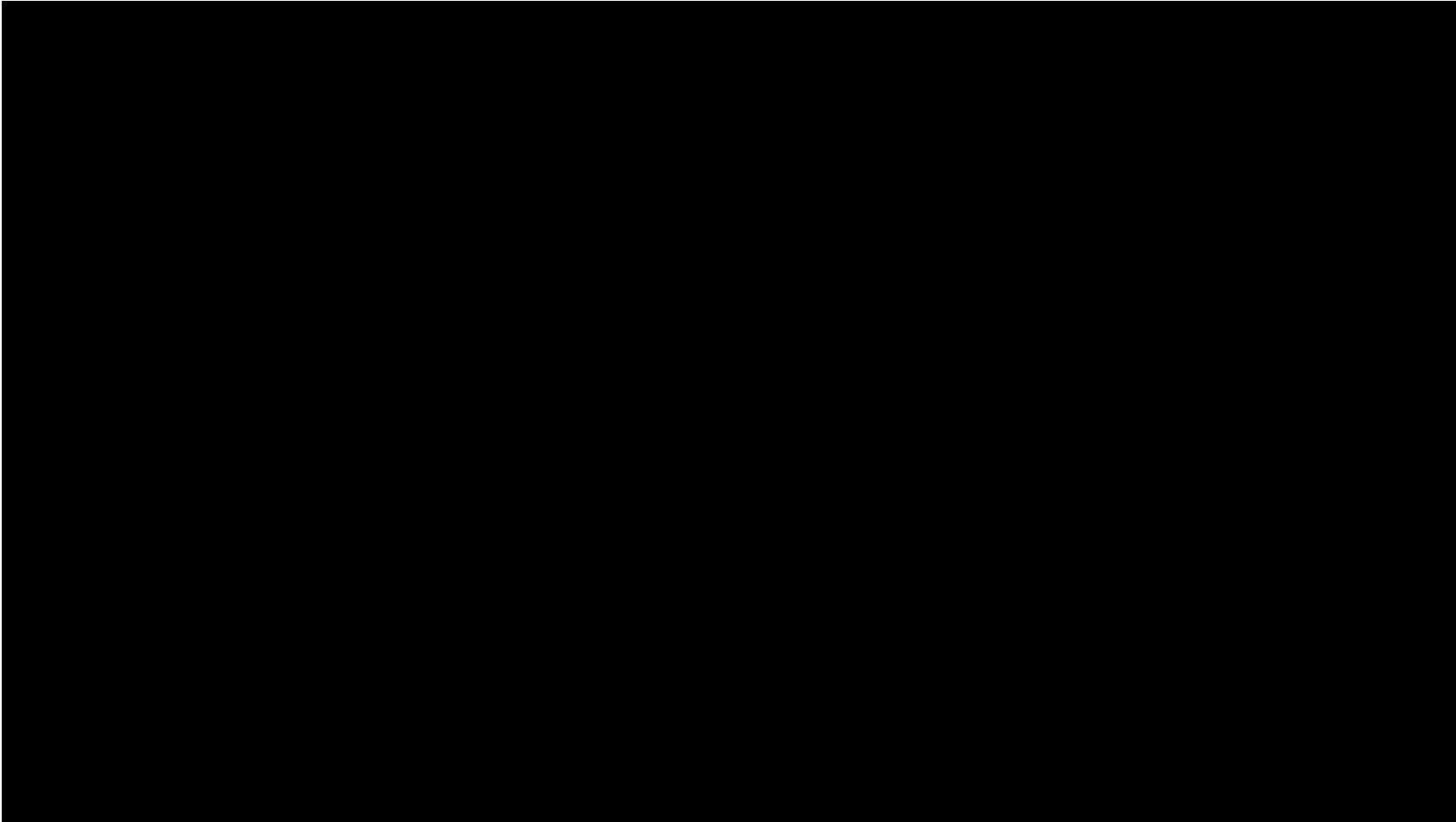
Gene Editing

How Does It Work?

Change the should to could.



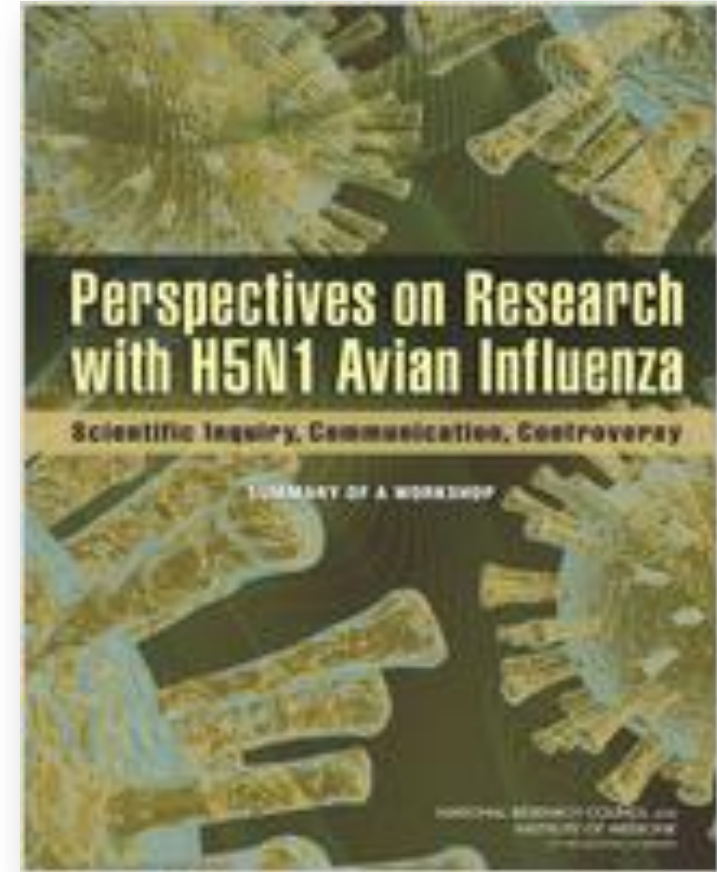
Gene Editing
CRISPR-Cas9



Gene Editing

Great Possibility. Great Risk.

- (2012) Genetic modification technology was used to “augment” H5N1 avian influenza:
 - Ease of transmission
 - Severity of infection
- Why? Predicting flu virus mutations can help vaccine development
- Publication of two separate studies in *Nature* and *Science*, respectively, hotly debated
- Why? Materials and Methods required for scientific peer review to validate approach and conclusions
 - Basically, a “recipe” for how to do this



Gene Editing

Can We Edit Anything? In Theory.

- Smallpox (Variola)
- Eradicated in 1977
- Routine vaccinations ceased in 1980
- Related pox viruses pose as a “template”?



Image courtesy of the Public Health Image Library of the Centers for Disease Control and Prevention.

Nucleotide sequence of 21·8 kbp of variola major virus strain Harvey and comparison with vaccinia virus

Begoña Aguado,[†] Ian P. Selmes and Geoffrey L. Smith*

Sir William Dunn School of Pathology, University of Oxford, South Parks Road, Oxford OX1 3RE, U.K.

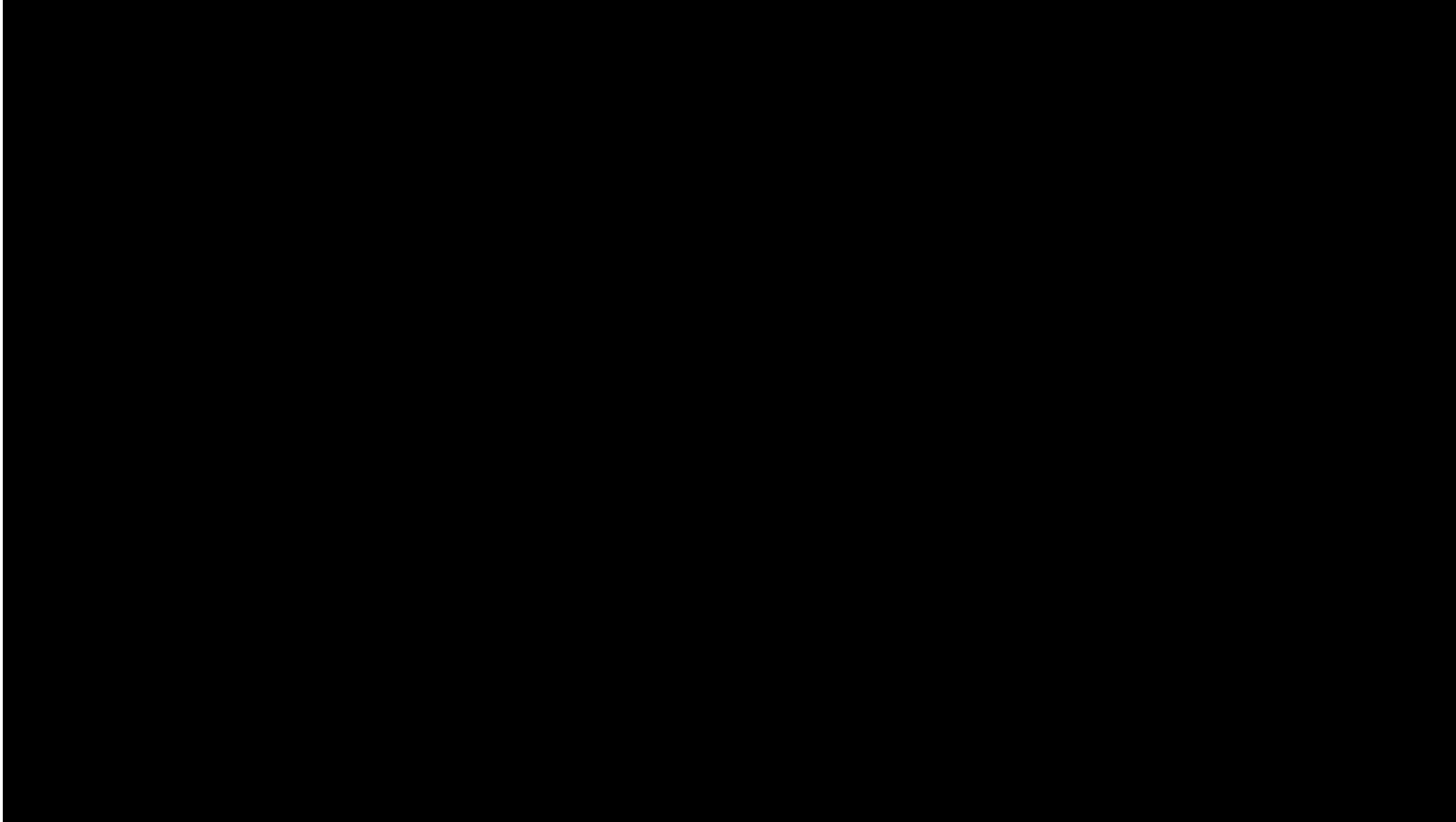
A 21·8 kbp region of the genome of variola major virus (strain Harvey), a virus that caused haemorrhagic-type smallpox, has been sequenced and shown to possess 96% nucleotide identity to the corresponding region of vaccinia virus, the smallpox vaccine. Overall the gene arrangement in the two viruses is highly similar and individual open reading frames (ORFs) display a high degree of amino acid identity, for instance 26 of the 32 variola virus ORFs have $\geq 90\%$ identity with their vaccinia virus counterparts. A remarkable difference is the disruption of seven vaccinia virus ORFs into small fragments in variola virus. These include the variola virus homologue of vaccinia virus SalF2R, which encodes a protein related to C-type animal lectins, and SalF7L, which encodes an active 3β -hydroxysteroid dehydrogenase enzyme that contributes to vaccinia virus virulence. Upstream of the variola virus haemagg-

lutinin gene there is a deletion of 1910 bp so that the equivalent of vaccinia virus gene SalF17R is truncated, and SalF16R, which shows amino acid similarity to the tumour necrosis factor receptor, is absent. The region sequenced includes the genes for thymidylate kinase and DNA ligase both of which are active in vaccinia virus and are highly conserved in variola virus. Other conserved ORFs with interesting homologies are those encoding profilin, superoxide dismutase and part of guanylate kinase. Two vaccinia virus genes encoding glycoproteins of the outer envelope of extracellular enveloped virus are also conserved in variola virus and this homology is likely to have contributed to the immunological protection which vaccinia virus evoked against smallpox. Lastly, there are multiple instances in which short oligonucleotide direct repeats flank a region absent from either variola or vaccinia virus.



“Biohacker” Injects Self with Untested Herpes Gene Therapy

Wow...



Genome Editing

The Business and Market

- Global Market in 2015 was \$400 Million
- Forecasted compounded annual market growth rates exceed 14% per year
 - Some economic estimates are as high as 39% per year
- Estimated total market size in 2021 will be \$2-\$6 Billion
- Growth rate forecasts of the genome editing market are equivalent to the forecasts of the mobile app market



<https://elearningindustry.com/aligning-learning-to-business>

Community Labs Provide Opportunities

- Entrepreneurship
- Novel projects
- Under-addressed issues in biology
- ***But also...***
 - Open access to training and tools
 - Less stringent personnel reliability programs
- ***Progress...***
 - FBI engagement
 - Developing ABSA International relationship



Biocurious.org

Considerations

Risk Assessment Gaps

- Detailed understanding about the functions of specific sequences limited and frequently irreproducible.
- The effects of specific changes in different genetic backgrounds not well known.
- Designing and conducting experiments using genome editing tools is fraught with uncertainty because of limited information, human variability, and error.
- Ecological consequences of modification are not well-known.
- Operational utility and feasibility depends on the organism being edited, the availability of gene delivery approaches, and the efficiency, accuracy, and predictability of repair.



The Nexus of Biology and Cybersecurity

Cyberbiosecurity

“The cyber–physical nature of biotechnology raises unprecedented security concerns. Computers can be compromised by encoding malware in DNA sequences, and biological threats can be synthesized using publicly available data. Trust within the biotechnology community creates vulnerabilities at the interface between cyberspace and biology. Awareness is a prerequisite to managing these risks.” J. Peccoud, J.

Gallegos, R. Murch, W. Buchholz, and S. Raman. Trends in Biotechnology, January 2018, Vol. 36, No. 1



<https://www.peccoud.org/synthetic-biology-informatics/cyberbiosecurity-biological-security/>

- Biomanufacturing (cell types, therapeutics, etc.) IT-rich processes.
- DNA sequence has been used as a computer virus (no, really)
- DNA sequences can also encode “blueprints” for novel biological threats
- Lab equipment becomes more automated, linked to Laboratory Information Management Systems (LIMS)



Cyberbiosecurity Vulnerabilities At the Laboratory Level

- Unwanted Access to and Theft of Intellectual Property?
- Corruption of Laboratory Experimental Data or Data Analytics?
- Unwanted Monitoring or Hacking of Electronic Communications?
- Undetected Manipulation or Corruption of Critical Stored Data and Metadata?
- Unwanted Access to and Manipulation of Cyber – Physical Interfaces (e.g., Networked or Remotely Accessed Instrumentation)?
- Monitoring of Procurement Actions Which Could Lead to Compromise of Integrity of Supply Chain?
- Degradation of Facility Access Security Systems?
- Others (e.g., Environmental Monitoring and Control Systems)?



<http://www.bugssonline.org/>

October 4-5, 2017, Virginia Tech

First Cyberbiosecurity Workshop

- **Objectives:**

- Initiate a standing “Securing the Bioeconomy” Community of Interest
- Formally introduce Cyberbiosecurity as a new discipline, which is emerging at the interface of biosecurity and cybersecurity;
- Develop a national (and perhaps international) agenda to raise awareness and sustainable engagement
- Identify opportunities and priorities for Community of Interest development, policy research, standards of practice development and implementation, and technology research, development and transition to advance Cyberbiosecurity.

- **Attendees Representing:**

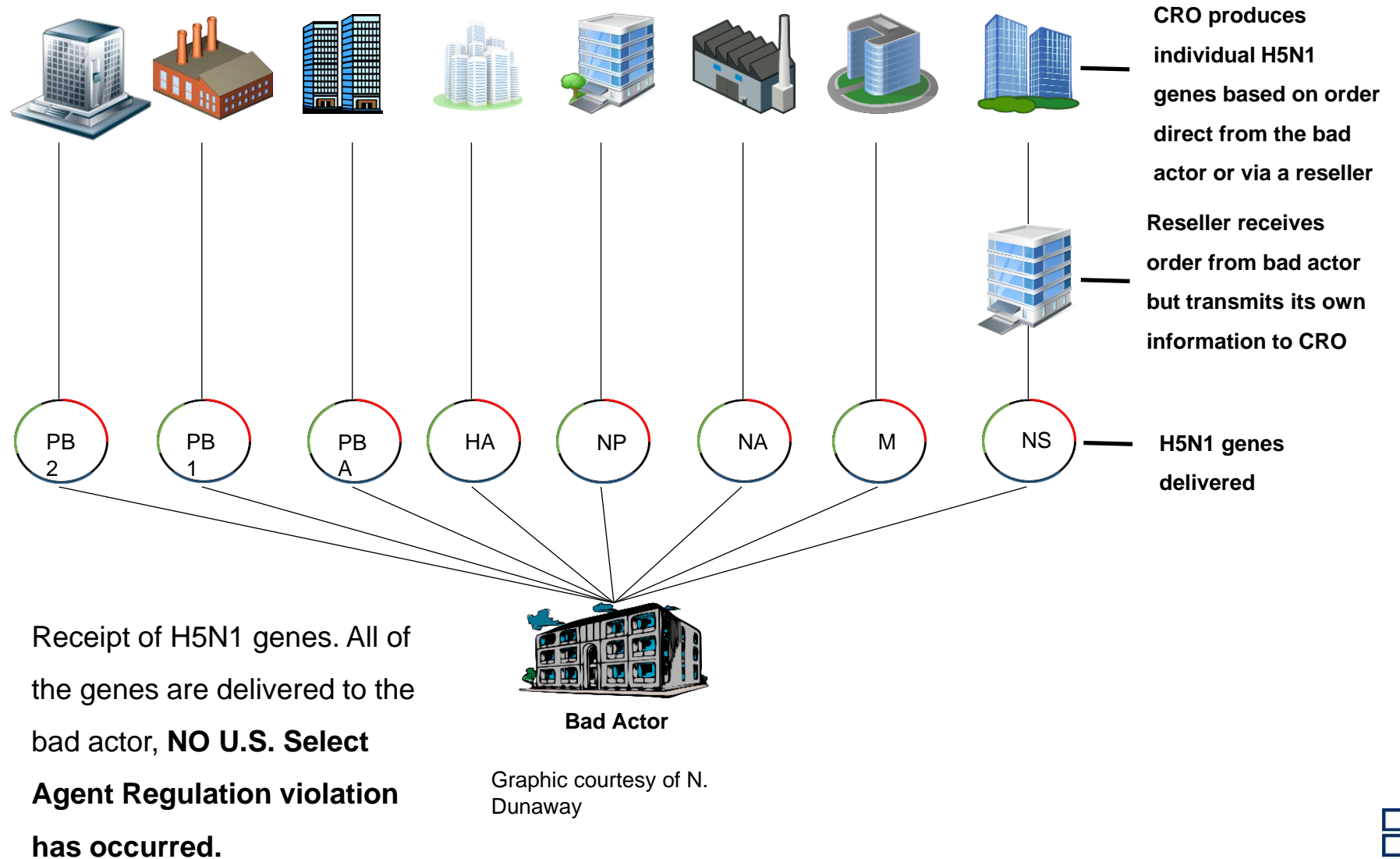
- 8 US Federal Government agencies
- 10 academic institutions
- Two pertinent non-profit organizations
- Four companies (including two which were sponsors of the event)

- **Next Steps:**

- Federal agencies represented and others which are expected to have interest to meet and determine priorities and next steps
- Publish a series of papers to introduce and formally define and map Cyberbiosecurity as a discipline
- Engage popular media to determine interest in articles on this topic,
- Initiate planning for the next Cyberbiosecurity Workshop projected to be held during Summer 2018
- Create a standardized Cyberbiosecurity presentation for awareness and education purposes
- Identify an initial set of “pilot efforts” and acquire support

Cyberbiosecurity

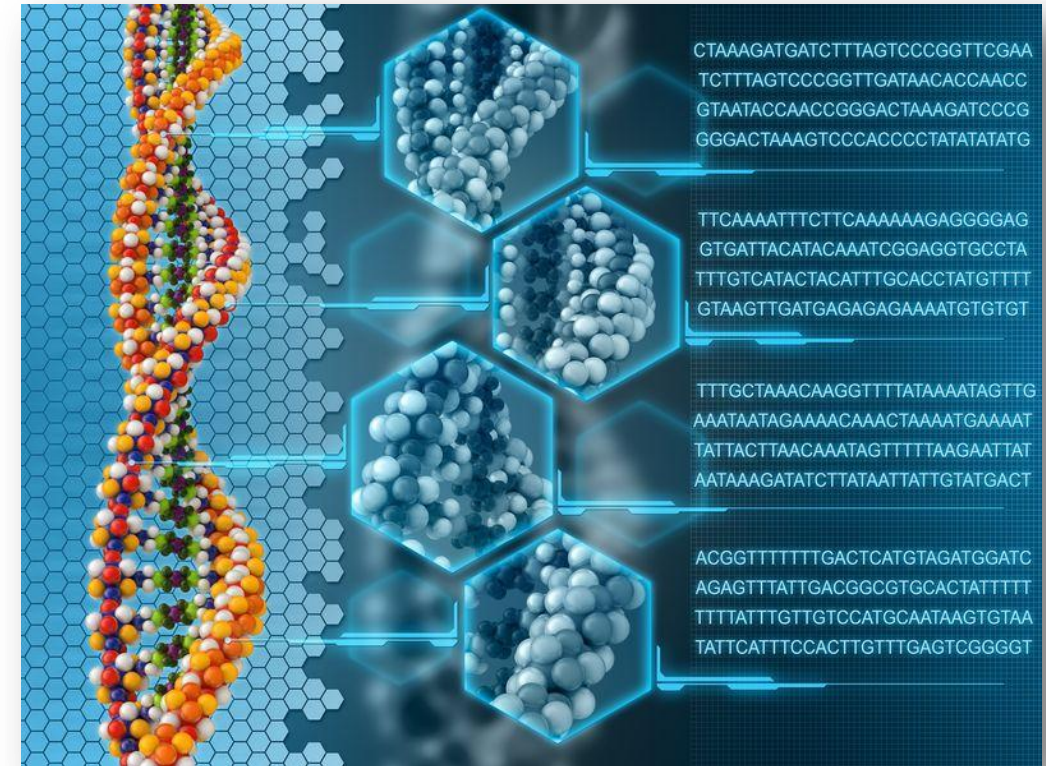
Gene Synthesis



Advancing Technology and Biosecurity

What is Boils Down To

- Limited policy or technology currently supporting these “gaps”
- Synthetic bio “community” generally in favor of “rules”
- “Bad actors” don’t care about the policies anyway...
- Vulnerability identification and mitigation can actually REVEAL gaps
- Dual, Dual-Use Conundrum (DDUC)[™]



<https://www.biotechnika.org/2016/04/apply-for-research-assistant-in-bioinformatics-institute-of-bioinformatics-bangalore/>

Sony BMG Music

Dual, Dual-Use, Conundrum

- Sony CDs carried spyware being installed on users' computers
- Discovered by Princeton student, but student did not report issue- why?
 - Afraid of legal consequences from Digital Millennium Copyright Act (DCMA)
- Meanwhile, spyware kept getting installed... Opening doors for additional viruses
- DCMA intended to be a solution, but also introduced vulnerabilities



DDUC

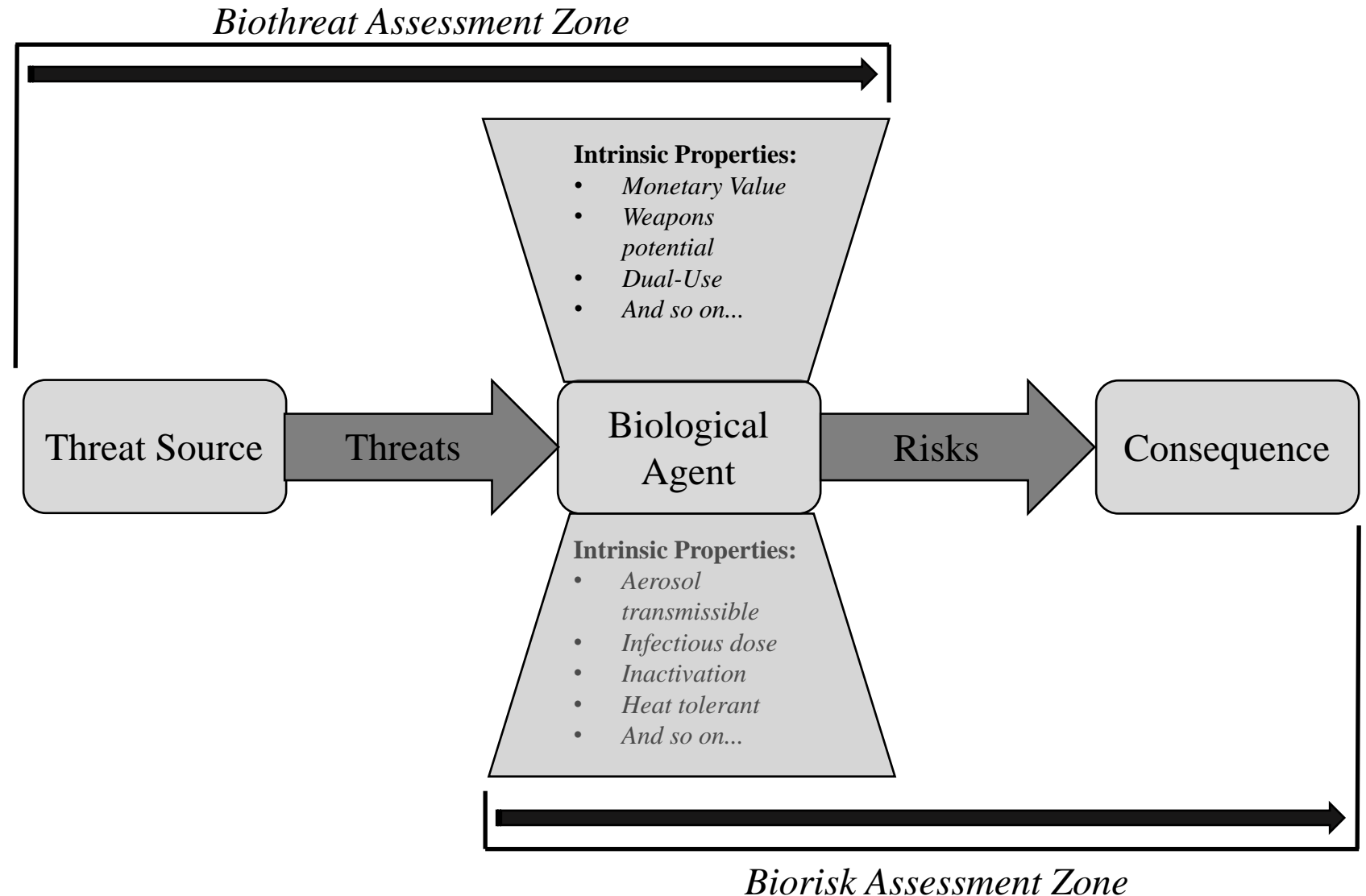
Smart Corrective Action

- In the context of Biosecurity...
- We're not writing code and pushing buttons to correct cyber vulnerabilities
- Timeline for "patching" bio vulnerabilities much longer
- Ergo, thought needs to be given on the best way to ID vulnerabilities without exposing them to "bad actors"
 - 2011 H5N1 papers...
- However, introduces regulatory anchor points at both the agent level and the experiment level



Threat
Assessment is
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BIOTHREAT ASSESSMENT



Biosecurity

Changing the Paradigm?

“laboratory biosecurity...[as the] institutional and personal security measures designed to prevent the loss, theft, misuse, diversion, or intentional release of pathogens and toxins.”

World Health Organization. Laboratory Biosafety Manual, 3rd Ed.



DIYBio

Gene Editing

Gene
Synthesis

Cyberbio

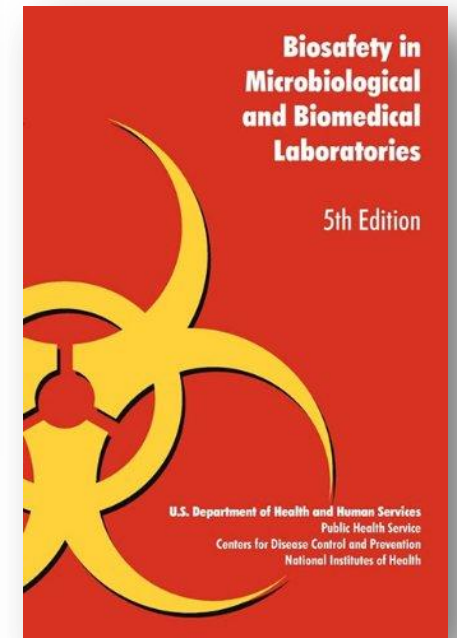
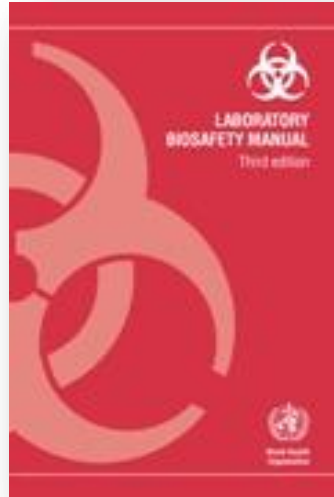


Integration of Biosecurity is Critical to Secure Research and Production

PART III



Path Forward **Accountability & Integration**

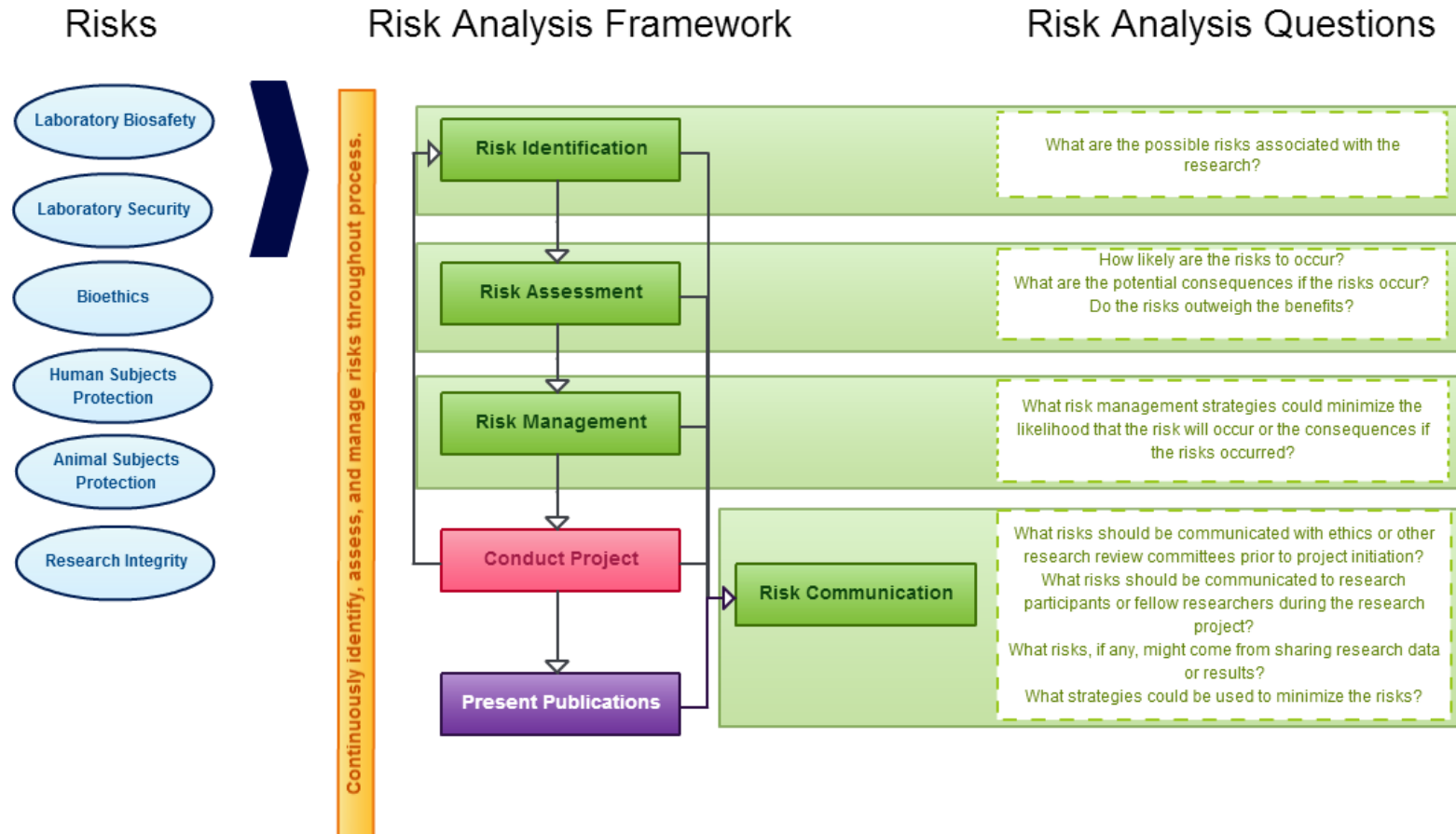


Assessing **Biorisks**

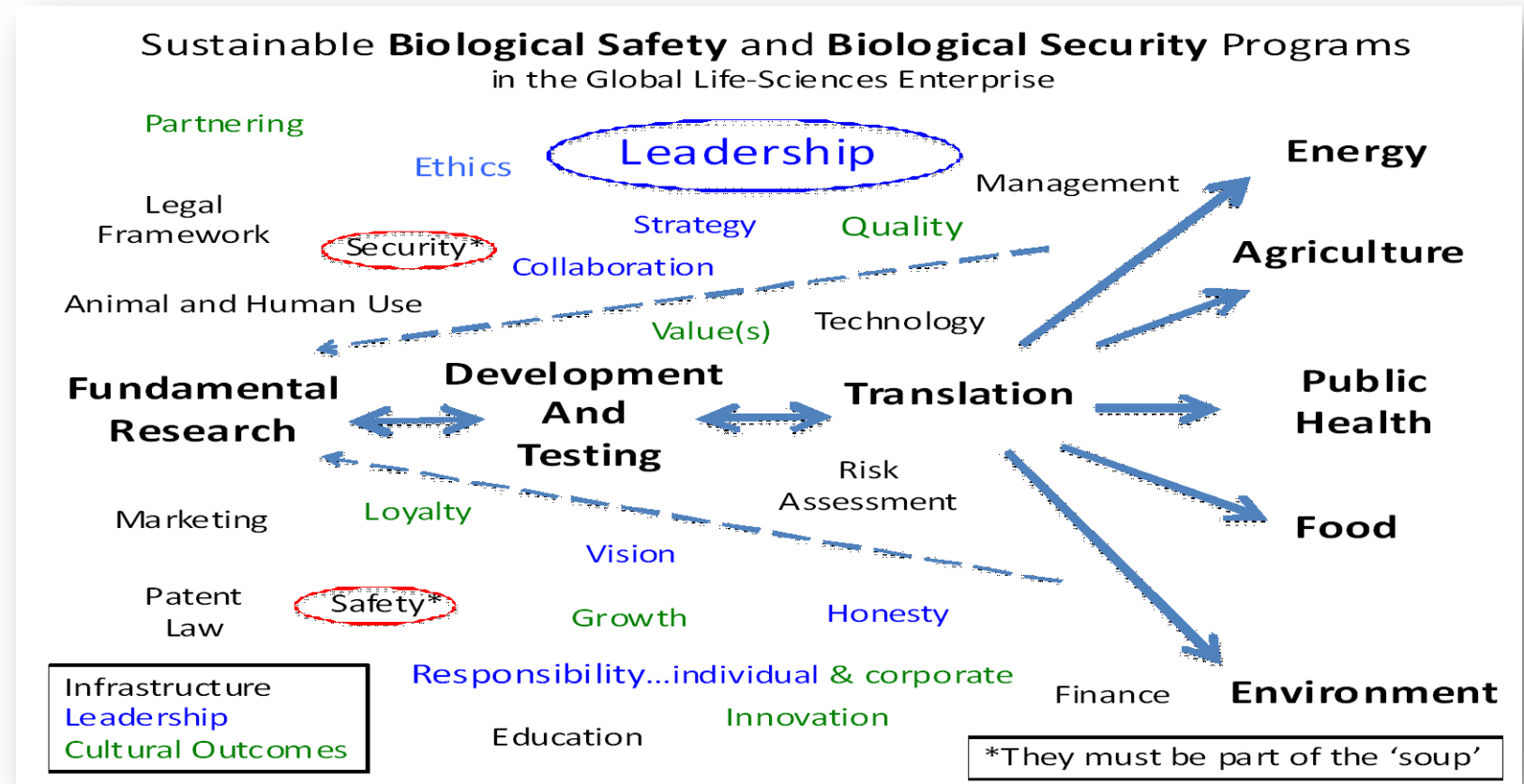
Spectrum of Biological Risk and Responsible Science



A Practical Framework for Analyzing Risk



Biorisk Management Programs



Courtesy of: David Franz

ABSA
International

Biosecurity Credentialing Taskforce



- What would a credential look like?
- What are the credentialing criteria?
 - What are the necessary resources?
- Is there a market for a biosecurity credential?



Thank You

Ryan N. Burnette,
Ph.D.

Director,
Biosafety &
Biosecurity
Programs

Merrick & Co.

Ryan.Burnette@
Merrick.com

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ABSA International

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