



**Biosecurity:  
A Multi-Dimensional Challenge of  
Escalating Complexity and Urgency**

**Dr. George Poste, DVM, PhD**

Chief Scientist, Complex Adaptive Systems Initiative  
and Regents Professor of Health Innovation

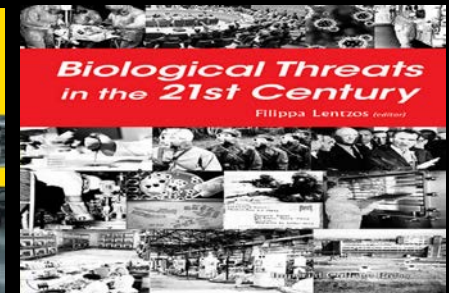
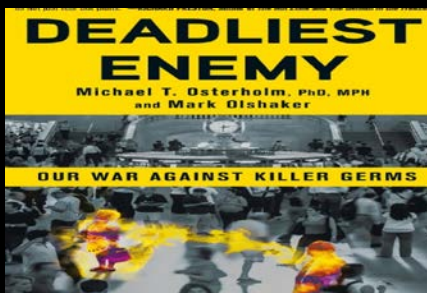
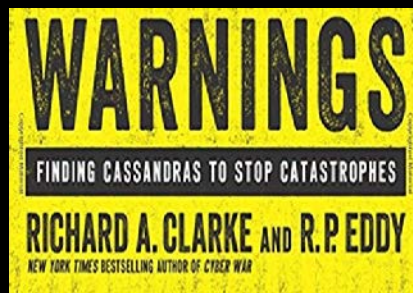
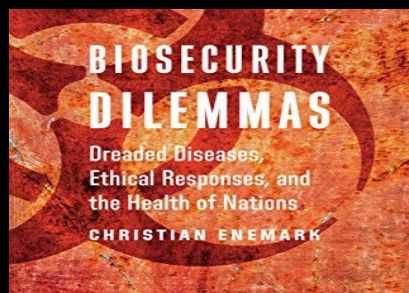
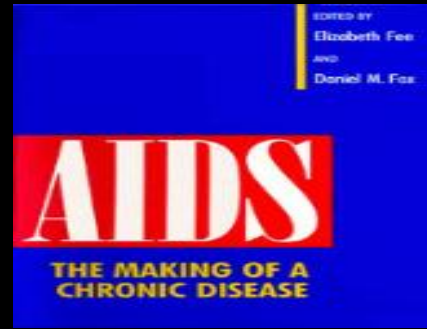
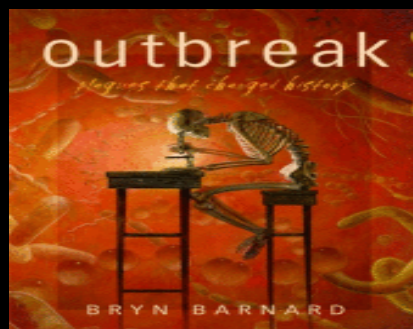
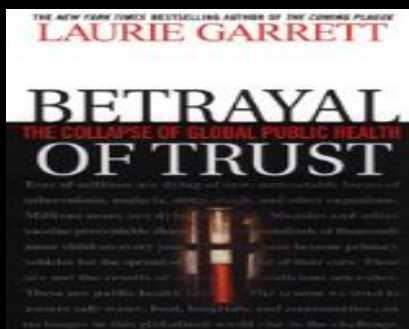
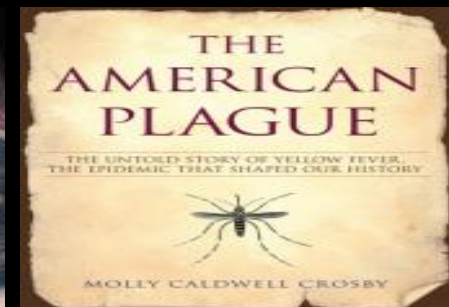
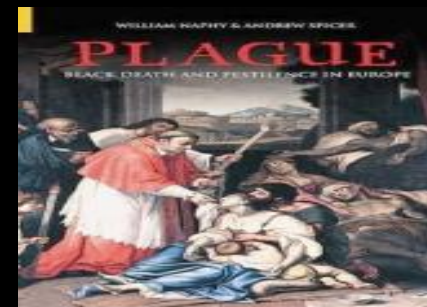
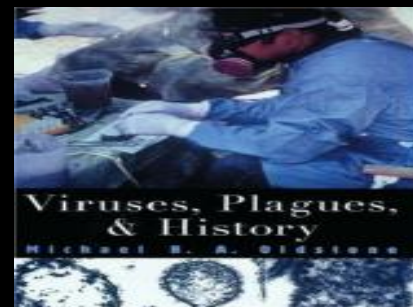
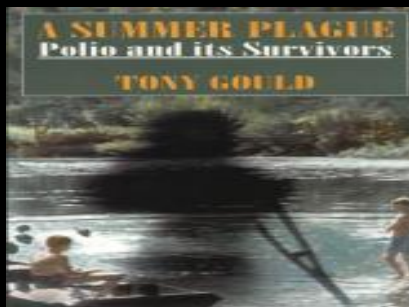
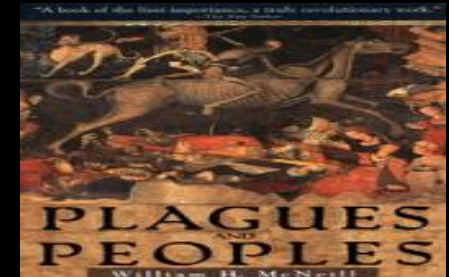
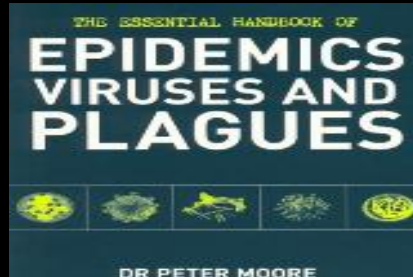
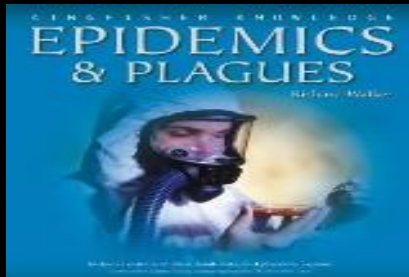
Arizona State University

[george.poste@asu.edu](mailto:george.poste@asu.edu)

[www.casi.asu.edu](http://www.casi.asu.edu)

**Biosecurity and Bioterrorism Response  
BIOE 122, EMED 122/222, PUBLPOL 122/222  
Stanford University School of Medicine  
23 January 2019**

# Infectious Diseases: A Powerful Force in Human Evolution

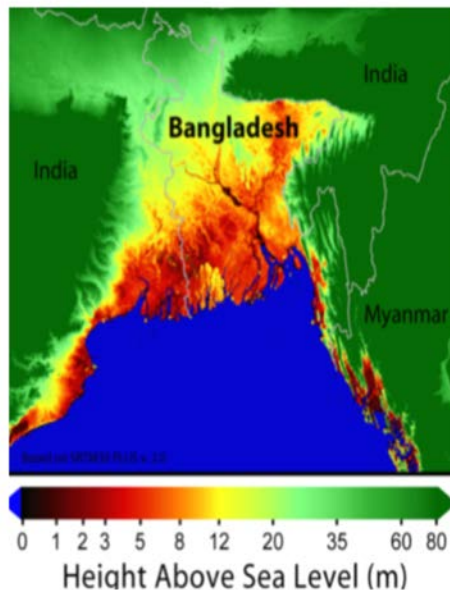
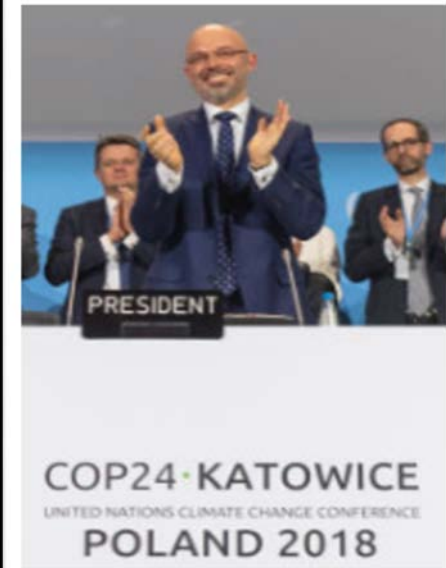
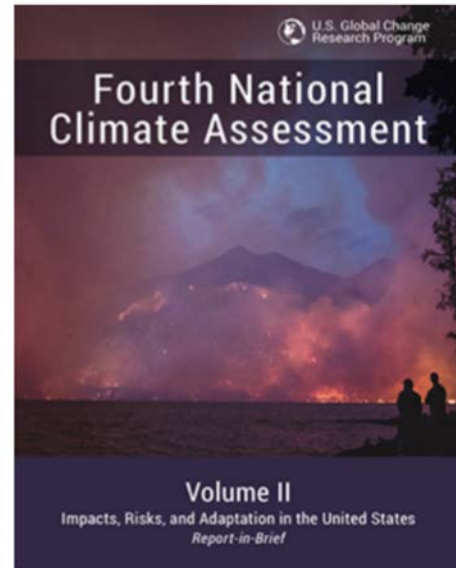




# Climate Change, Ecosystem Disruption and Implications for Human Health

WORLD ECONOMIC FORUM  
COMMITTED TO IMPROVING THE STATE OF THE WORLD  
Insight Report

## The Global Risks Report 2018 13th Edition





# Anthropogenic Effects on Ecosystem Stability and Altered Patterns of Infectious Diseases

**famine**



**contaminated water**



**no water and desertification**



**depletion of natural resources**



**climate change and  
new vector ranges**



**new vulnerabilities**



# Increased Refugee Migration and Humanitarian Disasters Created by Conflict





**JANUARY 10, 2019**



The NEW ENGLAND JOURNAL of MEDICINE

## Disease and Famine as Weapons of War in Yemen

Amir M. Mohareb, M.D., and Louise C. Ivers, M.D., M.P.H., D.T.M.&H.

# 1,000,000

# SUSPECTED CHOLERA CASES IN WAR-TORN YEMEN

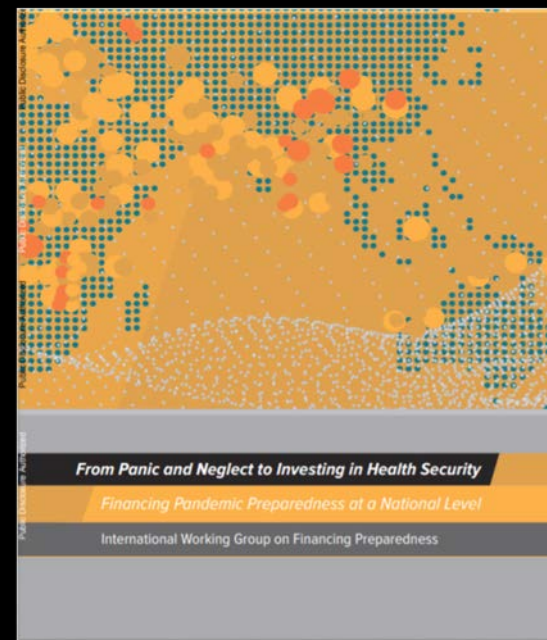
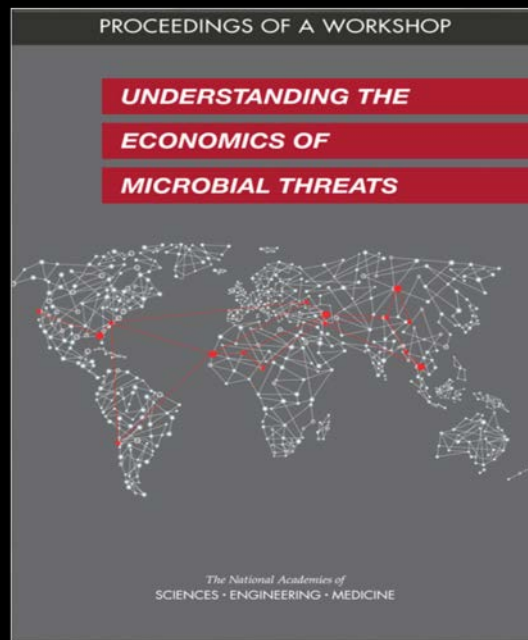
**80%** of Yemenis lack access to:



more than  
**2,200**  
are estimated  
to have died  
since late  
September

**21** out of **22**  
governorates and  
**90%**   
of Yemen's districts  
have been affected





- SARS \$ 30 billion
- Ebola W. Africa \$ 53 billion
- Ebola U.S. \$ 2.4 billion
- Amerithrax decontamination \$320 million
- Projected cost of 1918 influenza – type pandemic
  - \$683 billion US economy
  - \$ 4 trillion global economy and 5% drop in GDP

# The Relentless Changing Dynamics of Infectious Diseases

**old foes resurgent:  
Rx – resistance**



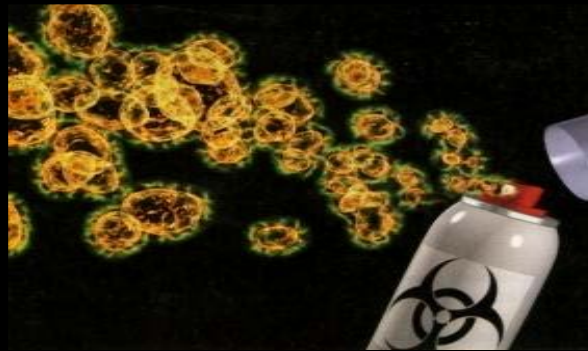
**omnipresent  
pandemic threats**



**new foes:  
emerging infectious diseases**



**global connectivities**



**bioterrorism and bioweapons**



**expansion of dual-use  
technological risk**



# **Biosecurity**

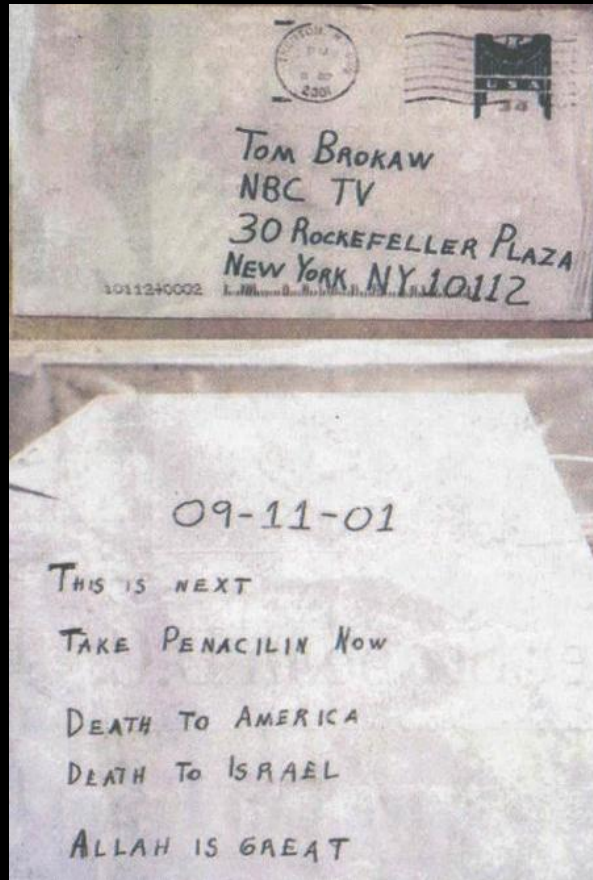
## **Shared Feature of Natural and Nefarious Threats**

- **surprise, stealth, spread and speed**
- **‘all hazards’ and ‘resilience’ the foundations of response preparedness and planning**
- **cross-agency coordination (within government)**
- **cross-sector inter-dependencies (public, private, NGOs)**
- **local events can quickly become global**
- **global coordination (public health, diplomacy, media, law enforcement, intelligence communities, military, industry supply chains)**

# **“Amerithrax” October 2001**

***“I will show you fear in a handful of dust”***

**-T. S. Elliot**

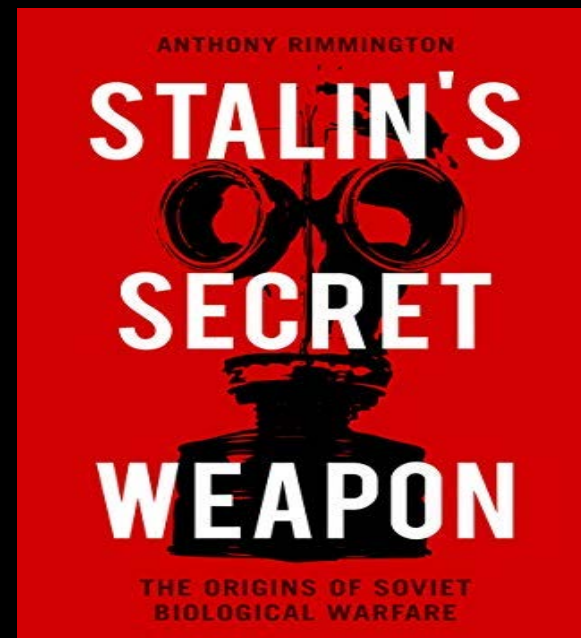
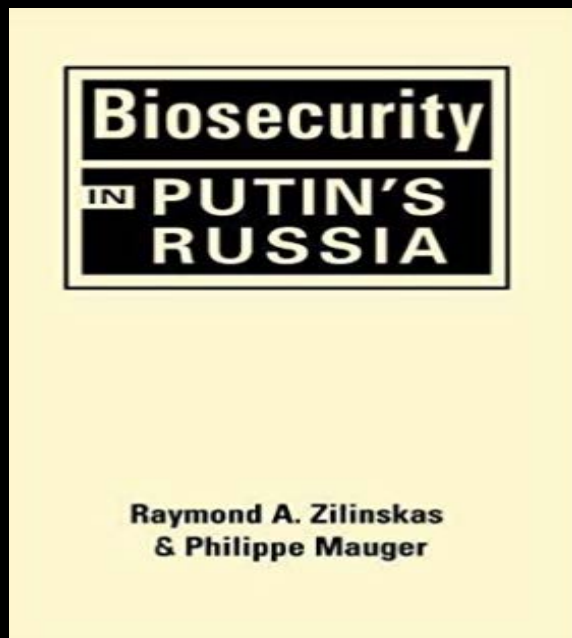
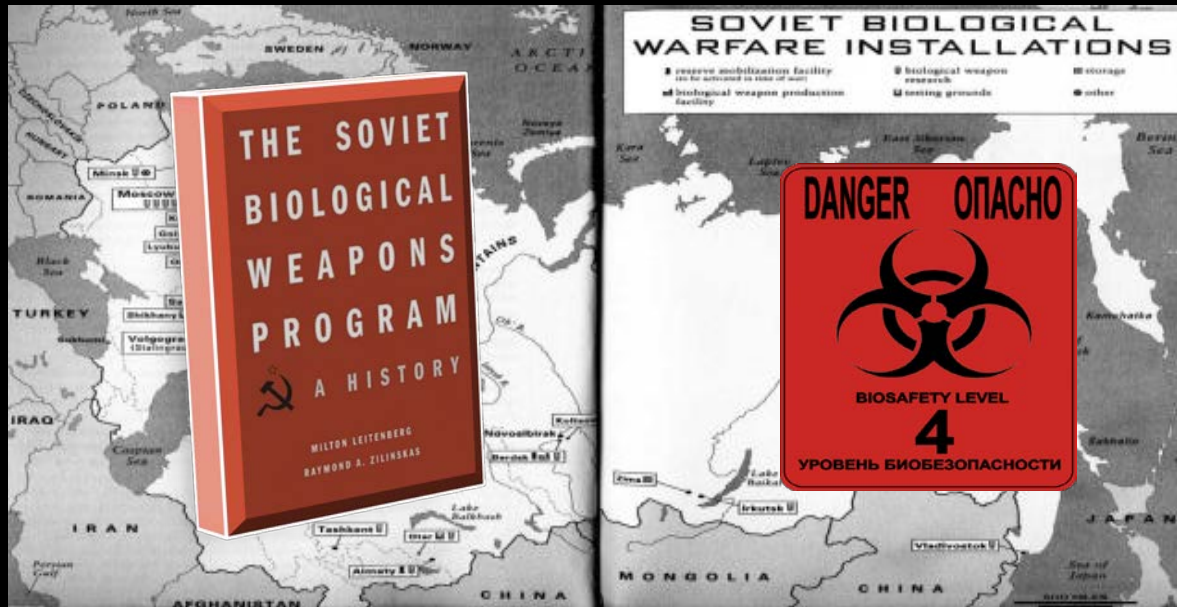




# **Strategic and Operational Objectives of Purposeful Bioattacks**

- **civilian and military targets**
- **confuse diagnosis**
- **frustrate treatment**
- **circumvent immunization protections**
- **overload healthcare and other incident response capacities**
- **economic disruption of supply chains of essential goods**
- **spread public panic and erode trust in authorities**
- **deception to hide attribution**
- **use of combinations of agents**

# The FSU Covert Biopreparat Program: Violation of 1972 BWC







**“Armies of the future will need weapons based on new physical principles, including genetic and psychophysical science.”**

**President Vladimir Putin  
essay, Rossiyskaya Gazeta, 2012**





## Pyongyang Bio-Technical Institute June 25, 2015



PROJECT ON MANAGING THE MICROBE

# North Korea's Biological Weapons Program

The Known and Unknown

Hyun-Kyung Kim  
Elizabeth Philipp  
Hattie Chung

 HARVARD Kennedy School  
**BELFER CENTER**  
for Science and International Affairs

REPORT  
OCTOBER 2017

## The Challenge of North Korean Biological Weapons



Bruce W. Bennett

RAND Office of External Affairs

CT-401

October 2013

Testimony presented before the House Armed Services Subcommittee on Intelligence, Emerging Threats and Capabilities on  
October 11, 2013

# The Appeal of CBW for Asymmetric Warfare and Terrorism



松本智津夫(63)  
(麻原彰晃)



早川紀代秀(68)



土谷正実(53)



遠藤誠一(58)



新実智光(54)



井上嘉浩(48)



中川智正(55)

سنجعلكم تخافون من الهواء الذي تتنفسونه  
WE WILL MAKE YOU FEAR THE AIR YOU BREATHE



Provided by  
MEMRI JTMM



الارهاب البيولوجي  
BIO TERROR





# Domestic Activists, Lone Wolf and Biohackers

"Win McCormack has put a penetrating spotlight on Indian guru Bhagwan Rajneesh and his bizarre and very dangerous cult. An utterly fascinating work."

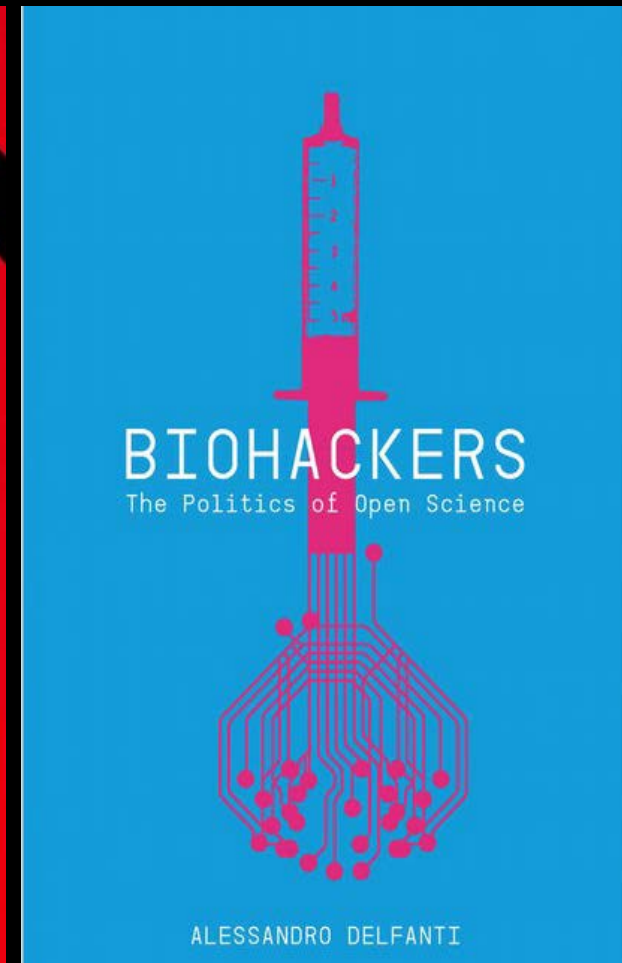
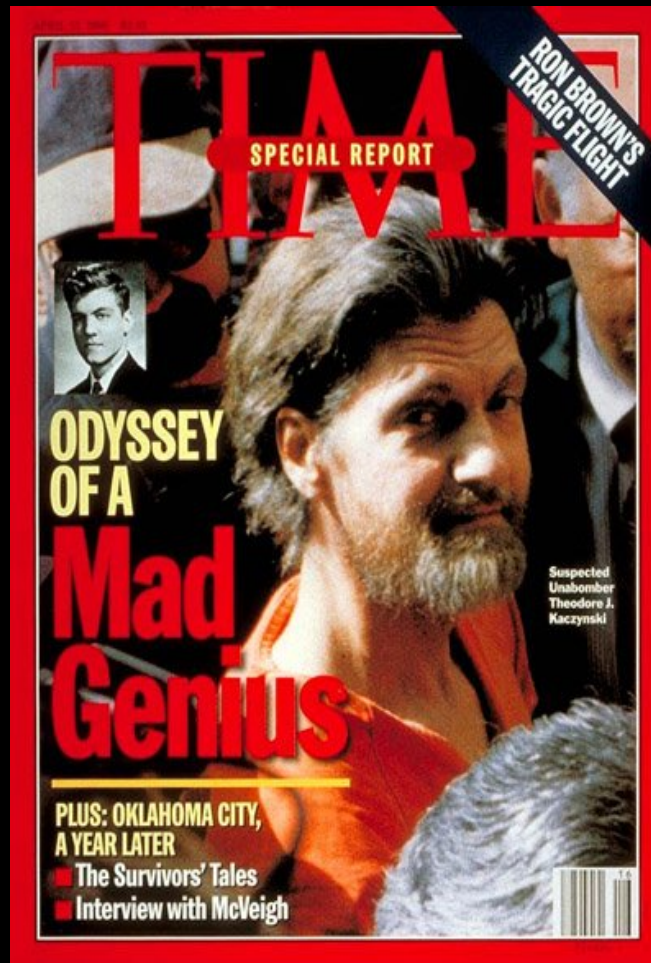
—VINCENT BUGLIOSI, author of *Helter Skelter*



## THE RAJNEESH CHRONICLES

The True Story of  
the Cult That Unleashed the First  
Act of Bioterrorism on U.S. Soil

WIN MCCORMACK



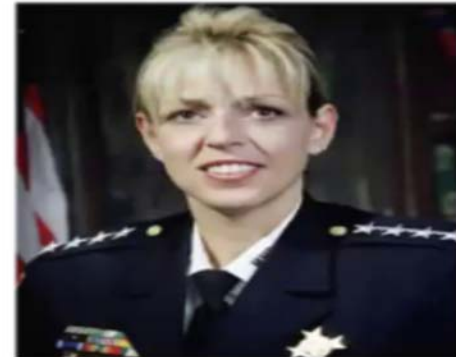






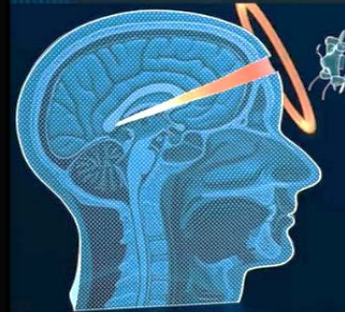
**A dramatic increase in the number of threats, incidents, and incursions by drones at NFL stadiums. We are all very fortunate that the drone over Levi's Stadium dropped only leaflets.**

**CATHY LANIER**  
Senior VP of Security, NFL





# Drone Swarms with Ordinance or CBW Payloads and Facial Recognition Homing





# Use of Drones in Remote and Low Resource Regions for Delivery of Specimens, Blood, Drugs and Vaccines

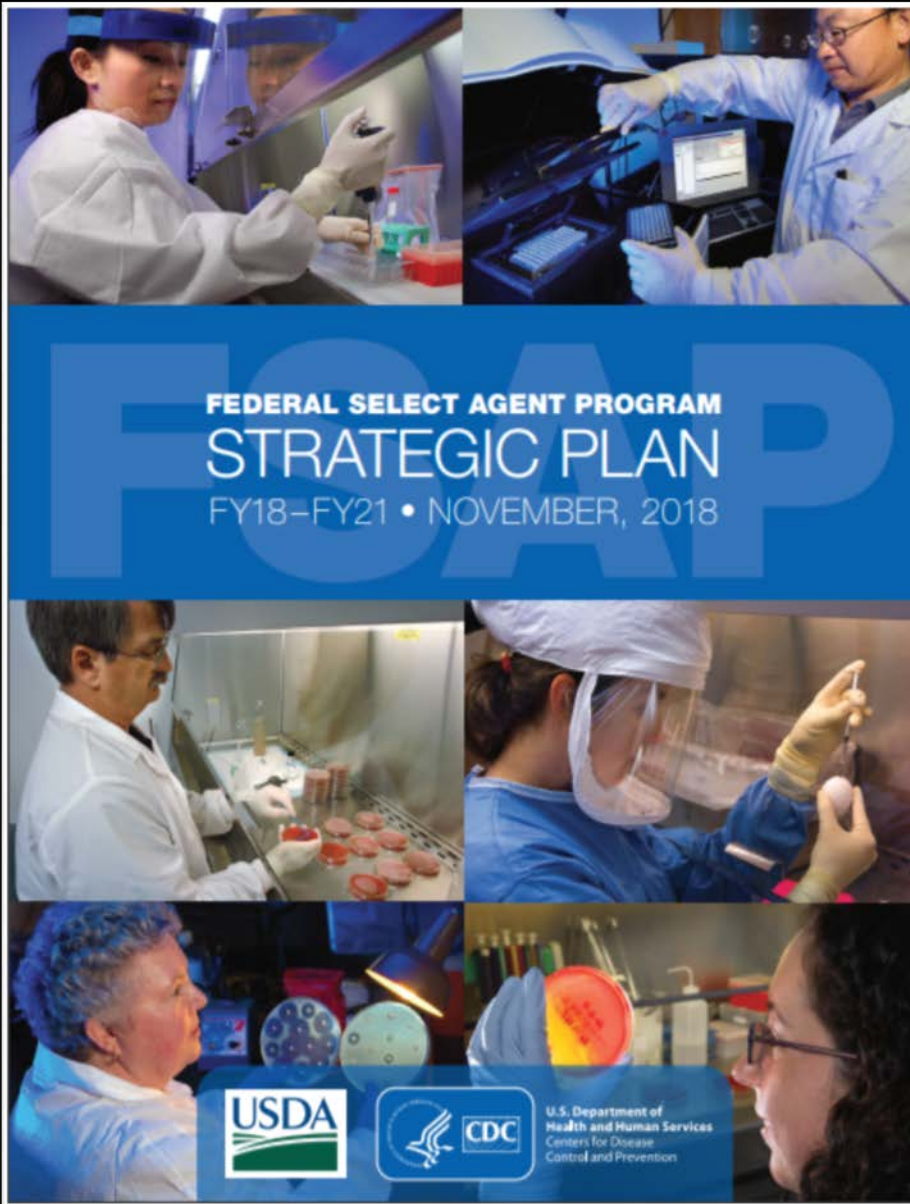


# The Biosecurity Threat Spectrum

Time	Low Probability: High Consequence	High Probability: High Consequence
<b>today</b>		
• bioterrorism	X	
• natural infectious diseases(pandemic)		X
<b>2029 (?)</b>		
• bioterrorism		?
• natural infectious diseases (pandemic)		?
• convergent technologies		?
- synthetic biology		
- artificial intelligence		
- robotics/autonomous systems		
- error/accident		



# Beyond Select Agents: The Expanded Threat Spectrum



## AGENT X

- exotic natural EID/zoonose ?
- deliberately engineered agent?
- extended chronic morbidity and overwhelm healthcare resources ?

# U.S. National Security Policy

## NATIONAL SECURITY STRATEGY

*of the United States of America*

DECEMBER 2017



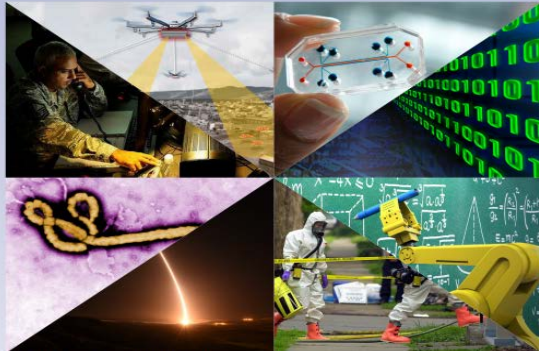
DECEMBER 2018

## NATIONAL STRATEGY for COUNTERING WEAPONS of MASS DESTRUCTION TERRORISM



## NATIONAL BIODEFENSE STRATEGY

2018



Report to Congressional Committees

### NATIONAL SECURITY

Long-Range Emerging Threats Facing the United States  
As Identified by Federal Agencies

December 2018

## The Neglected Dimension of Global Security

A Framework to Counter  
Infectious Disease Crises



## United States Health Security National Action Plan:

Strengthening Implementation of the International Health Regulations  
based on the 2016 Joint External Evaluation

October 2018



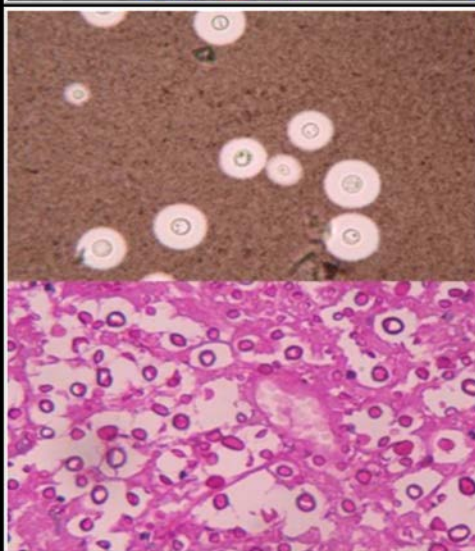
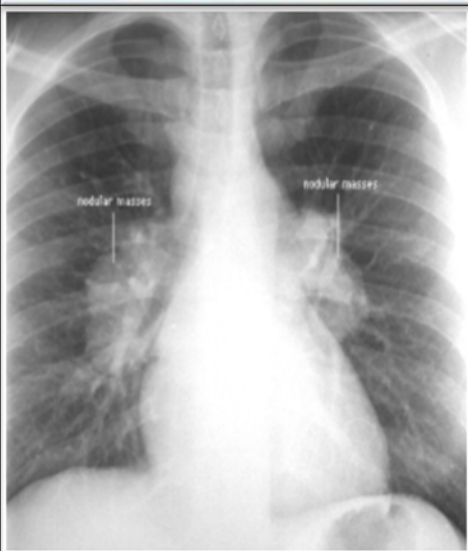
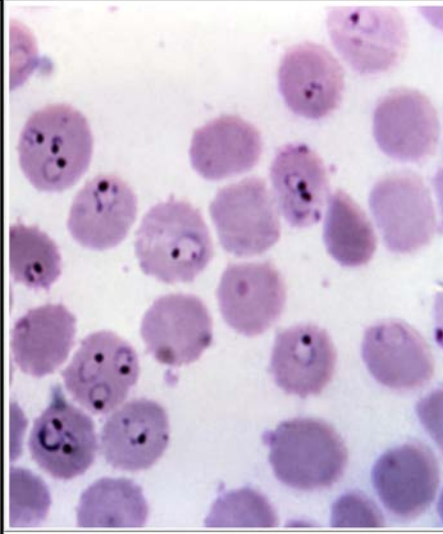
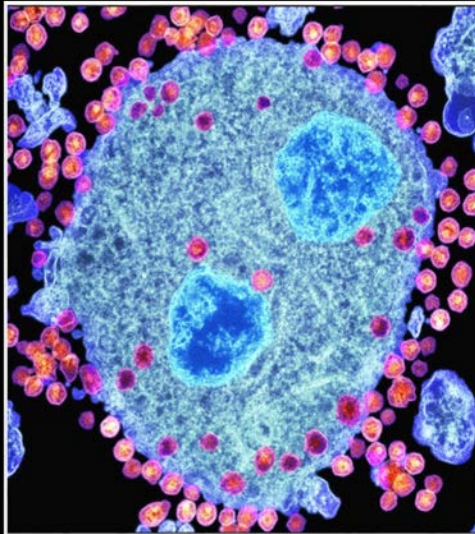
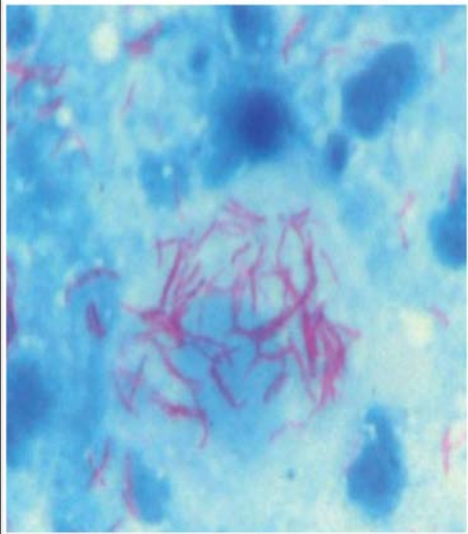
# “The Big Four”

**TB**

**HIV**

**Malaria**

**Rx Resistance**





# A Decade of New and Resurgent Viral Threats

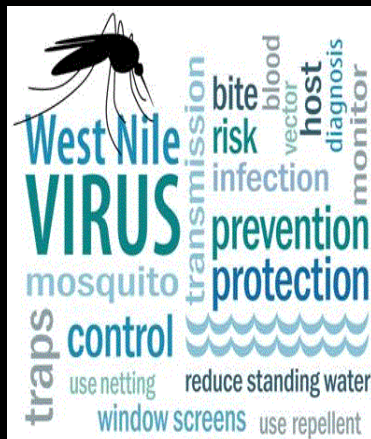
## SARS-CoV



## MERS-CoV



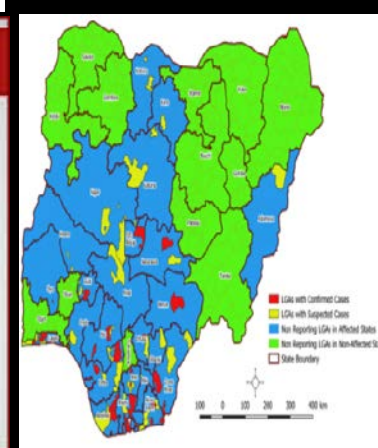
## West Nile



## Yellow Fever



## Dengue



## Chikungunya

## Ebola

## Zika

## Monkeypox

## Acute Flaccid Myelitis (AFM)



# Urbanization and Mega-Cities in Developing Countries and the Increased Threat of Exotic Zoonotic Diseases

**High Population Density With Inadequate Biosurveillance**



**Expanded Eco-niches and New Zoonotic Exposures/Risks**



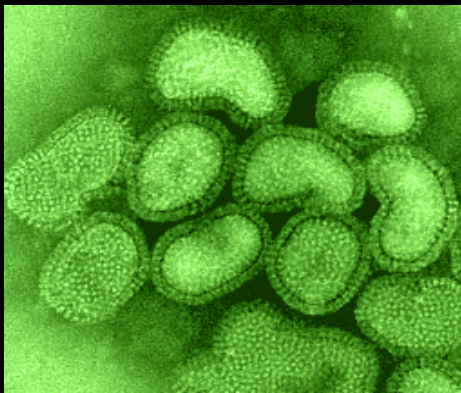
**Major Gaps in Health Infrastructure and Disease Reporting**



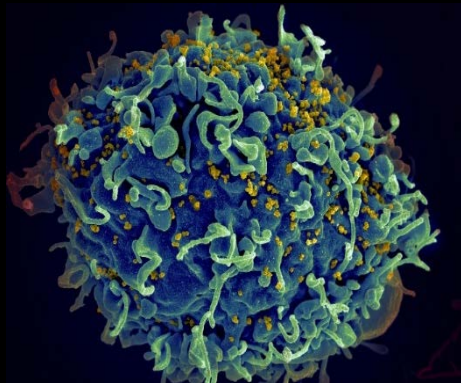
# One Health:

## Recognition of the Importance of Zoonotic Diseases as Human Health Threats

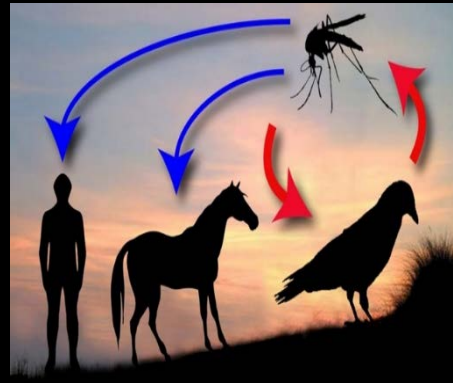
**pandemic (avian)  
influenza**



**HIV**



**West Nile  
virus**



**MERS- CoV**



**Ebola  
virus**



**bush meat  
food chain**



**Zika  
virus**

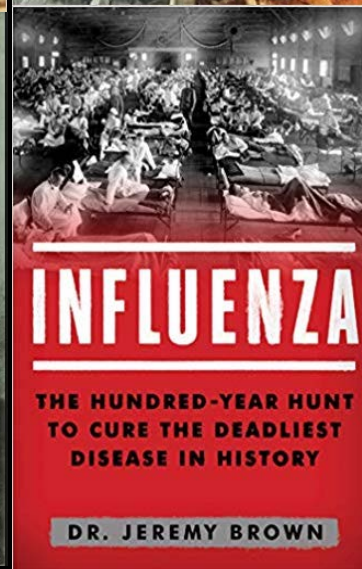
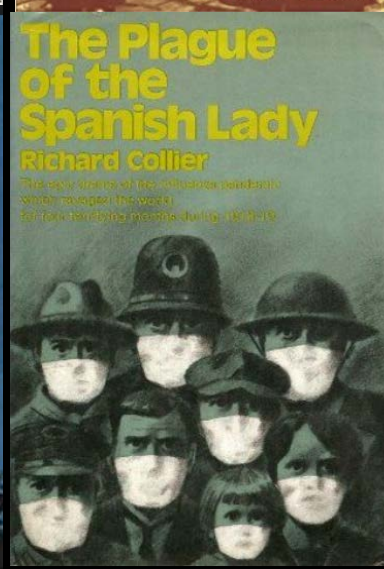
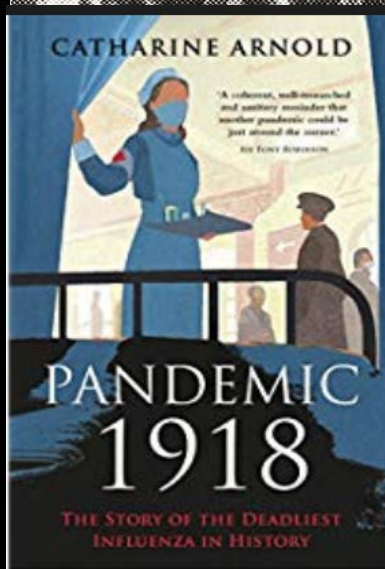
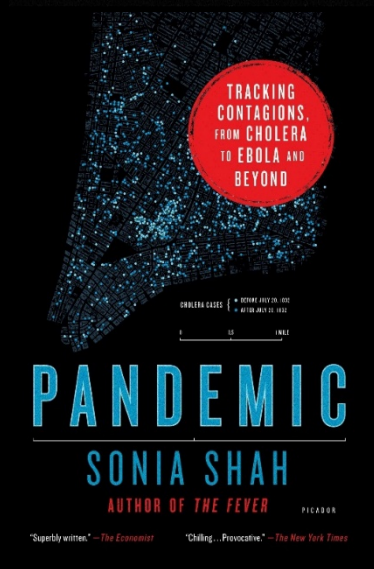
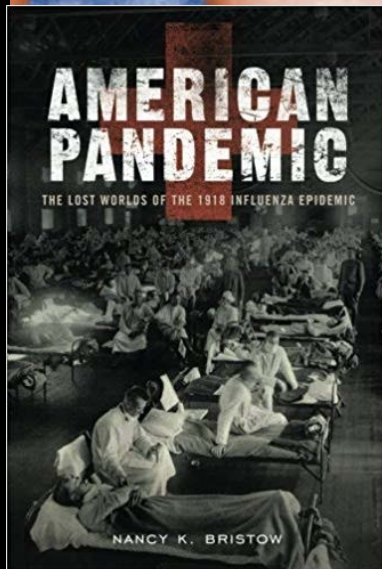
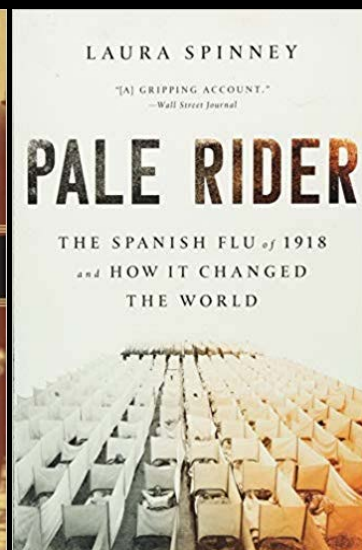
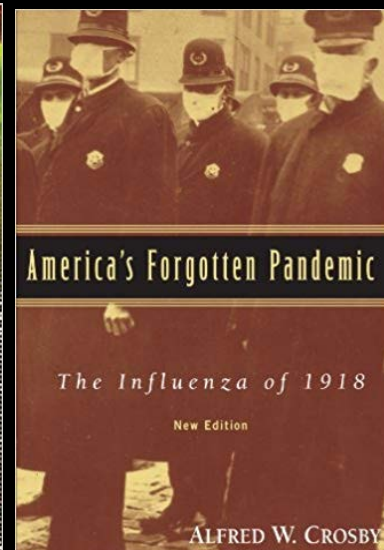
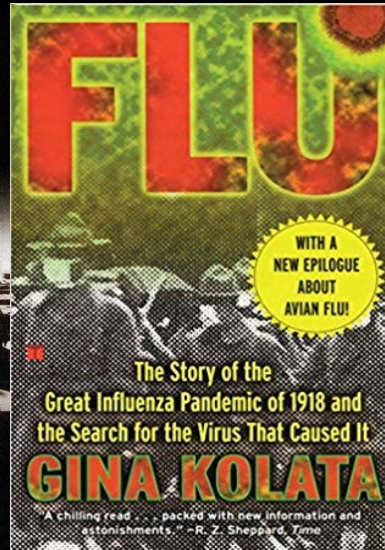
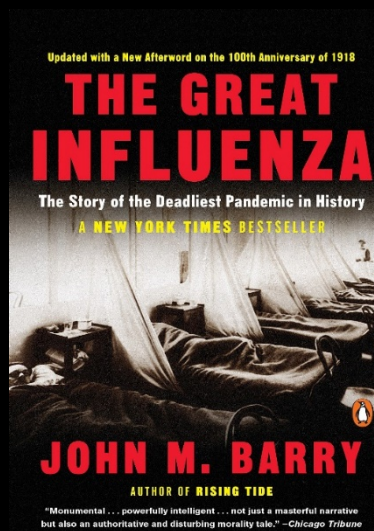
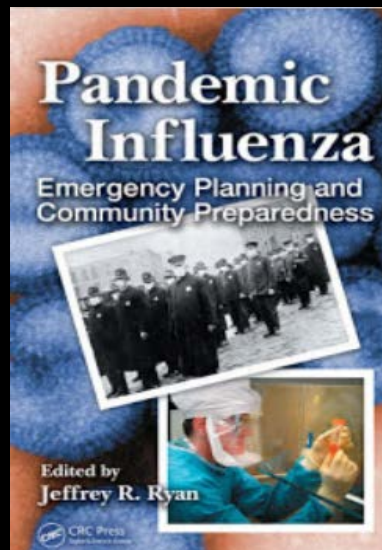


**what's  
out there?**



# The #1 Global Pandemic Threat?

## The Omnipresent Risk of Pandemic Influenza





# The Evolution of Pandemic Influenza Strains: The Bird → Pig → Human Transmission Chain

## Avian Reservoirs and Global Flyways



## Sporadic Transmission to Mammalian Hosts



## Episodic Zoonotic Human Infections





# Intensive Agriculture and Juxtaposition of Poultry and Pigs as a Potential Zoonotic Pathway for Pandemic Influenza



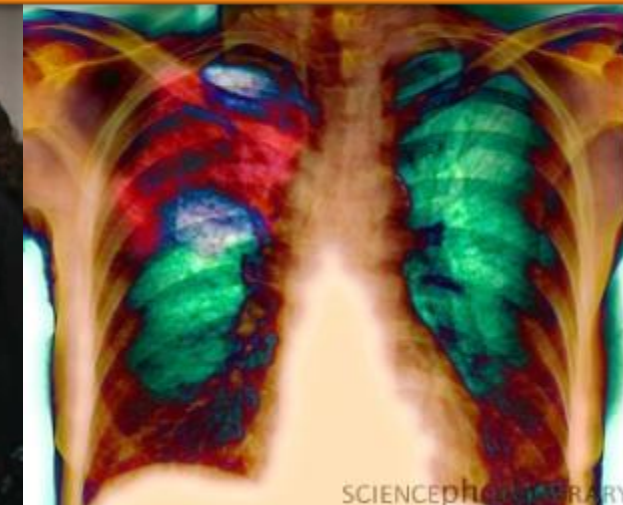


# Detection of Infectious Disease Threats:

## Not A Hazmat Incident



## Emergency Rooms and Farms Will be the Front Line





# The Core Domains of Preparedness

**threat spectrum  
and awareness**

**adaptive,  
resilient response**

**counter-measures  
and mitigation**

**global  
biosurveillance**

**prevention  
and  
incident  
management**

**protection,  
response  
and  
recovery**

**resource  
prioritization  
and  
distribution  
logistics**

**managing the  
'worried well',  
proficient  
communication, and  
critical services**

**integrated  
real time data and  
rapid, robust  
decisions**

**surge  
management**

**sustained  
community resilience**

**situational  
awareness**

# **Biosurveillance and Threat Awareness**

**What's Out There?**

**Early Diagnosis Saves Lives!**

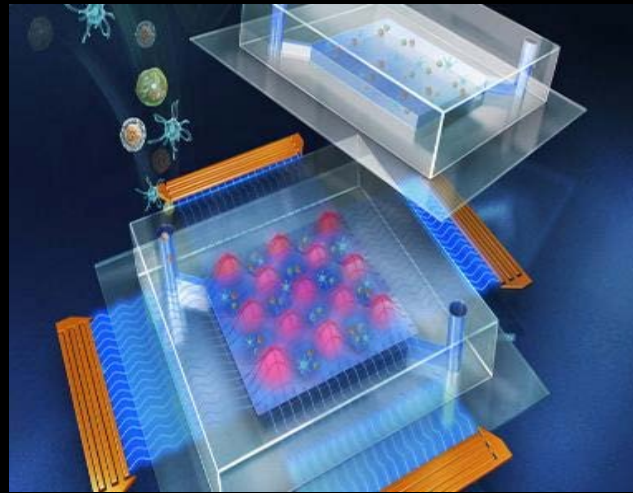


# Faster Diagnosis Saves Lives: The Primacy of Diagnostics in Biosurveillance and Preparedness Mobilization

**Profile:**  
signatures of infectious agents



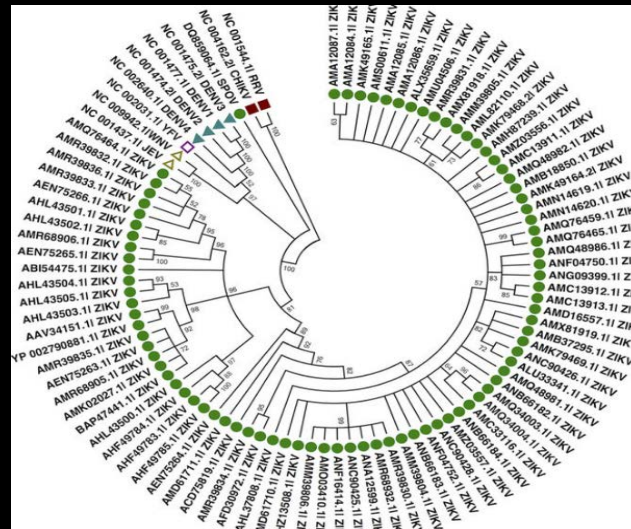
**Detect:**  
rapid automated PON/POC diagnostics



**Act:**  
real-time situation awareness, decisions



**surveillance  
sans frontières**



**pathogen evolution**



**dual-use research and  
engineered biothreats**

# **Ebola in West Africa 2013-15: Underinvestment and Bureaucratic Sclerosis of International Public Health Responses to New Threats**



**26 December 2013**

- index case zero
- Emile Ouamouno (Meliandou, Guinea)

**21 March 2014**

- first report by WHO-AFRO region

**8 August 2014**

- WHO declaration of Public Health  
Emergency of International Concern





# **Ebola in West Africa 2013-15: Underinvestment and Bureaucratic Sclerosis of International Public Health Responses to New Threats**



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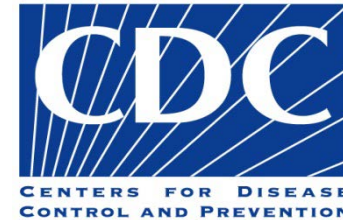
**Over 11,000 Deaths**



# Global Disease Surveillance

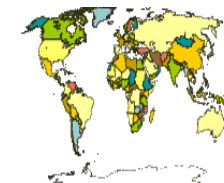


**EMERGENCY ID NET**



**biocaster**

**U.S. Influenza Sentinel Provider Surveillance Network**



**GeoSentinel**

The Global Surveillance Network of the ISTM and CDC  
a worldwide communications & data collection network of travel/tropical medicine clinics

**Quarantine Activity Reporting System (QARS).**



**Public Health Department's Surveillance**

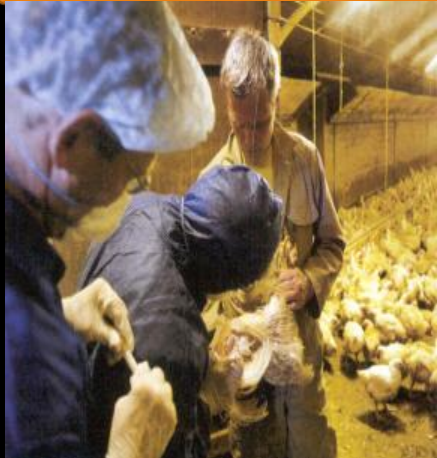
google.org





# Ground Zero Biosurveillance Data

## Comprehensive Front Line Sampling of Sentinel Species



## Real-time Intelligence and Faster Preparedness

# 'One Health' Biosurveillance

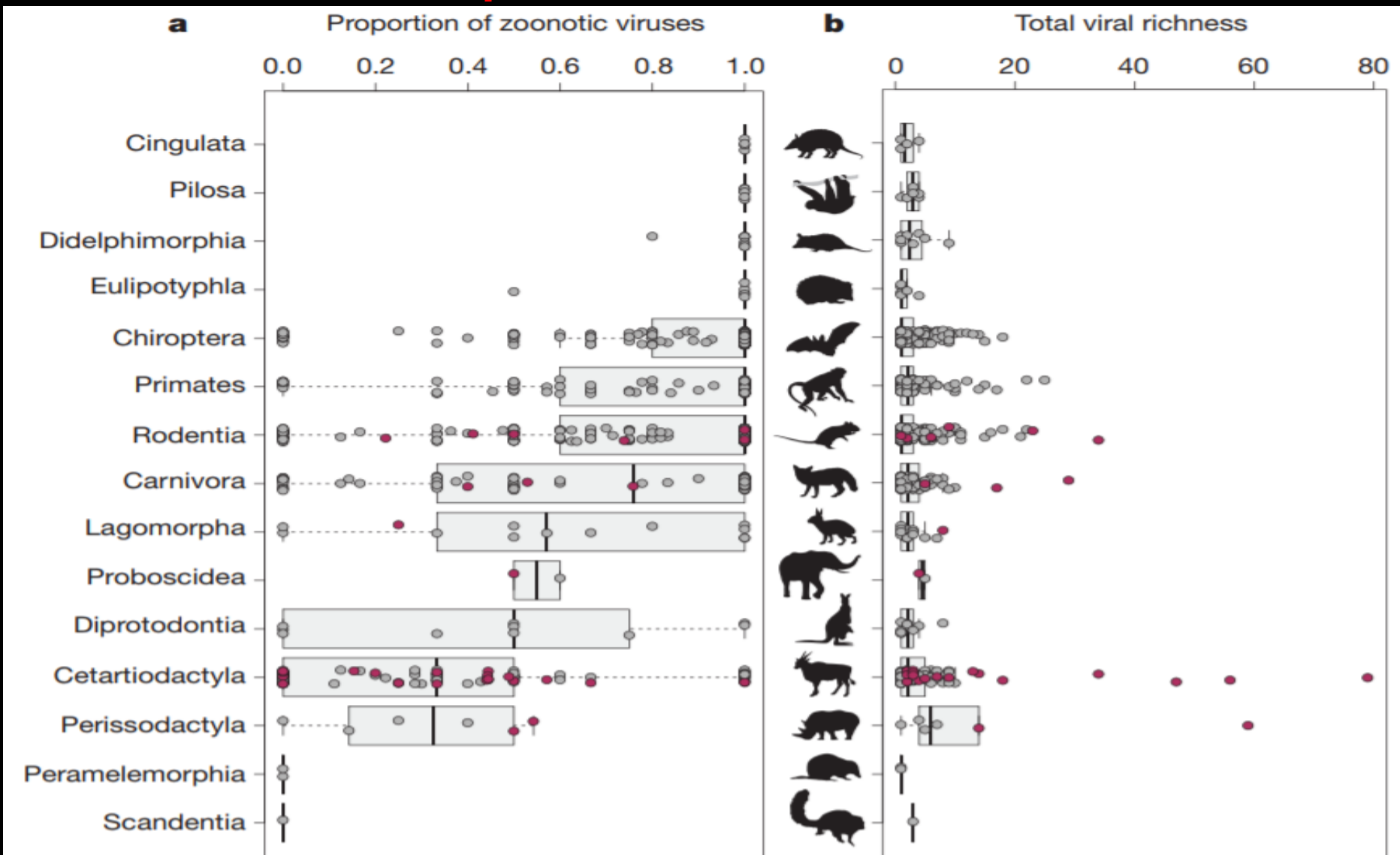


- range and physical contact
- environmental factors

- demographics
- cultural, political and economic factors
- health system capacity to detect/respond



# The Global Virome: Analysis of 2805 Mammalian Host-Virus Associations and Proportion of Zoonotic Viruses



From: K. J. Olival et al. (2017) Nature 546, 646

## “Going to Waste”



- **metagenomics analysis of vital species in sewage**
- **identification of 900 unknown viruses in EPA-NSSR samples**
- **virome 200:1 ratio of unknown to knowns**



# **POC-PON Testing for Infectious Diseases**

- **rapid (< 1hr), actionable information**
- **point-of-care (POC)**
  - **use in healthcare settings**
- **point-of-need (PON):**
  - **portable, field deployable units**
  - **in-home; austere, rugged and remote environments; low resource settings**
  - **high automation and use with minimum technical expertise**
- **move to multiplex, profiling capabilities**
- **integration with mobile technology and telemedicine for real-time biosurveillance and incident situational awareness**

# Integrated Consortium of Laboratory Networks (ICLN): 450 Laboratories





# The Shift in Diagnostic Technologies

## Historical Plating and Culture



- 24-96 hours
- potential overgrowth of slower growing species
- slow detection of resistance and other engineered features
- limited phylogenetic tracing

## Rapid Genome Sequencing and Metagenomics



- 30 mins. to 4 hr.
- profiling of all organisms
- rapid ID of resistance markers and other atypical features
- molecular fingerprints for phylogenetic epidemiology

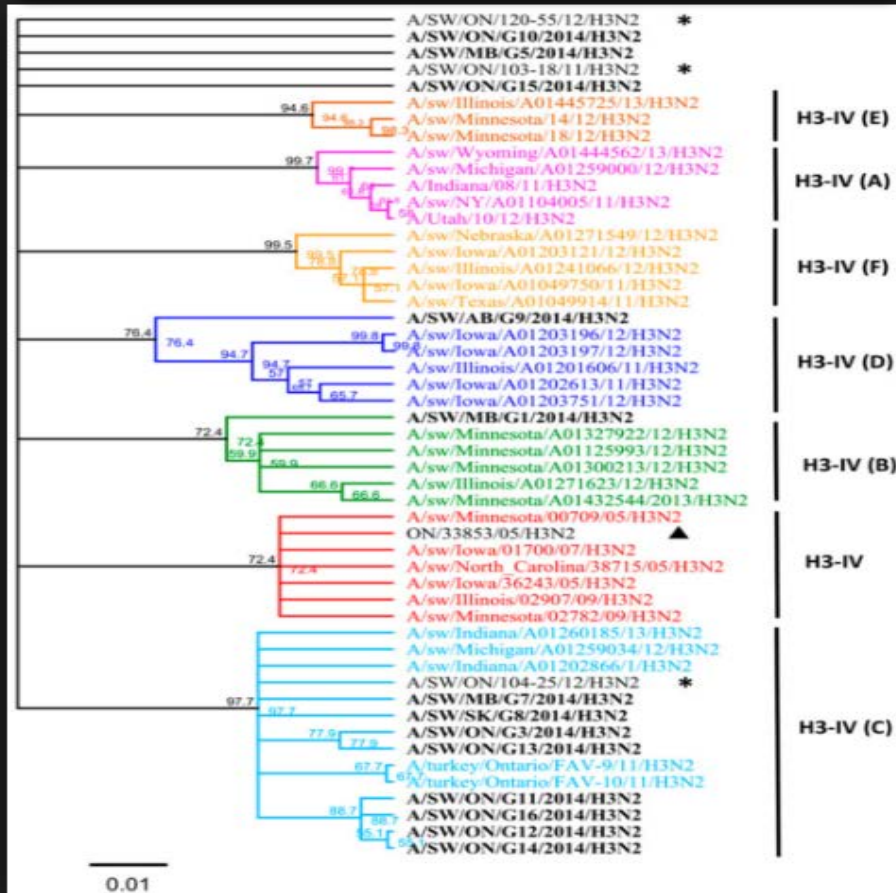


The logic  
of the  
(Ebola) elbow  
greeting

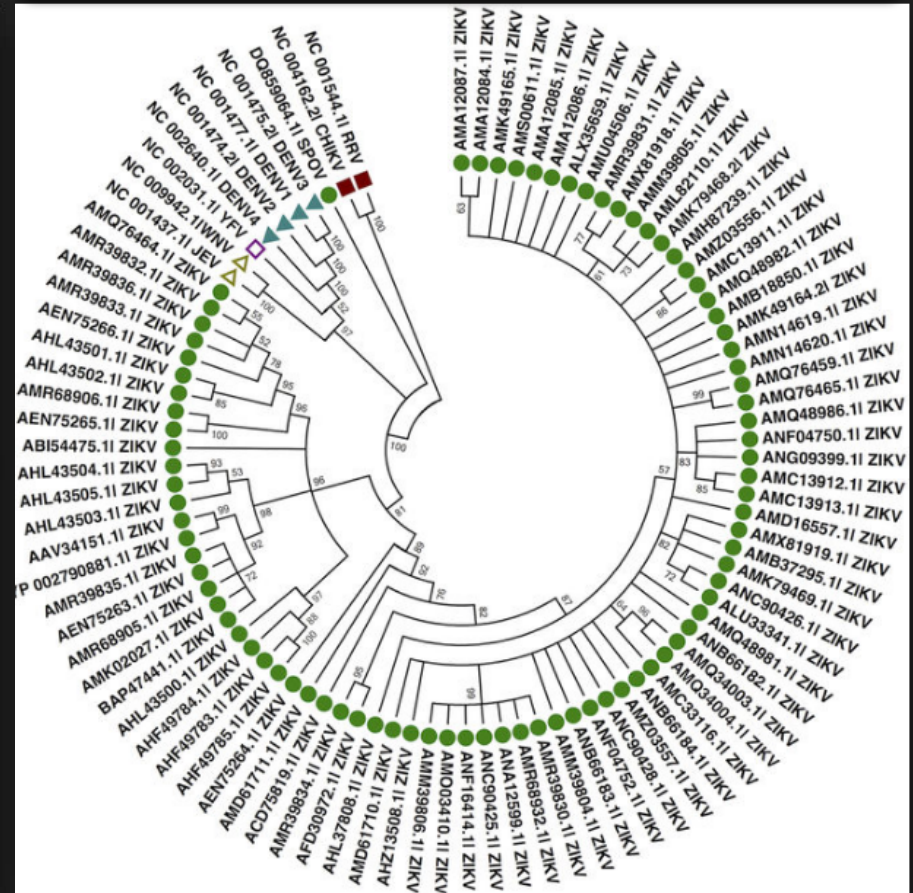


# Metagenomic Profiling of Pathogens and Their Evolution

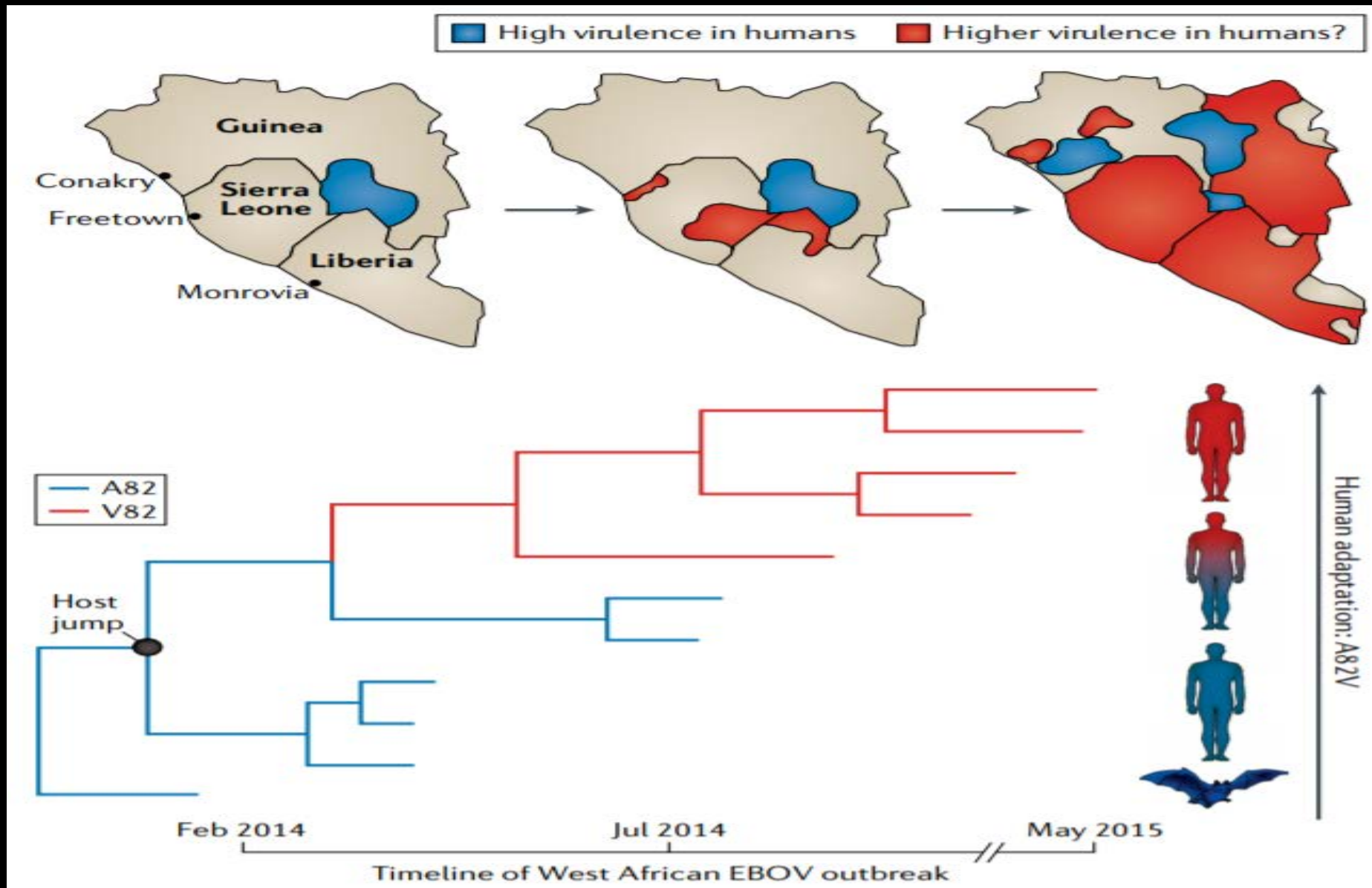
## Influenza Virus



## Zika Virus



# Evolution of a Single Amino Acid Substitution (Glycoprotein A82V) and Increased Ebola Binding to NPC1 Receptor and Reduced Infectivity in Bat Reservoir



From: J.L. Geoghegan and E. C. Holmes (2018) Nature Rev. Genetics 19, 766



# Mobile Devices, Disease Tracking, Contact-Tracing and Education



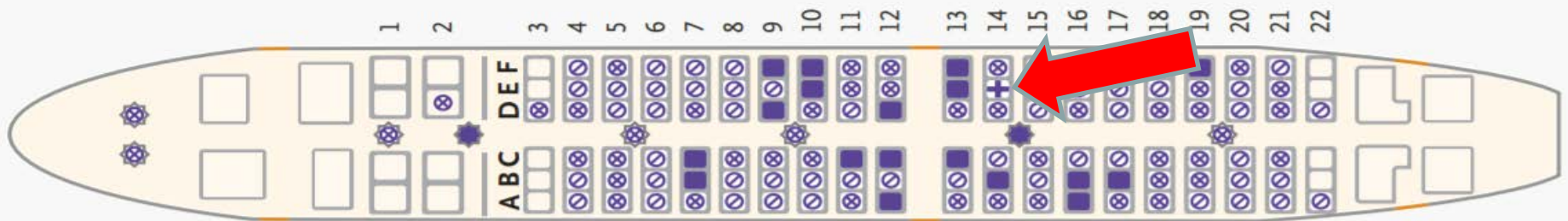


# Faster Detection of Prodromal Infection Saves Lives





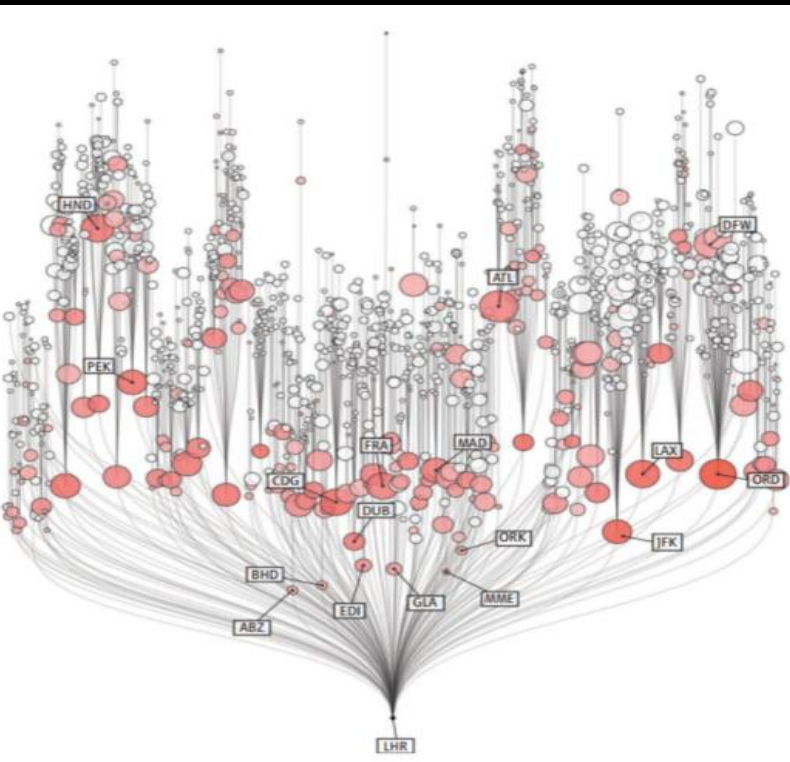
# Coming to an Airport Near You!



- ⊗ No illness (person interviewed)
- ⊗ No illness (person not interviewed)
- Probable case of SARS
- + Index patient
- ★ Crew member
- Empty seat

From: S. J. Olsen et al. (2003) N Engl J Med 349:2416-2422

## Modeling Airport Connectivities, Traffic and Distance Relationships and Implications for Epidemic Spread via the Global Aviation Network



From: A. R. McLean (2013) Science 342, 1330



# Biowatch

## SENSOR SYSTEMS FOR BIOLOGICAL AGENT ATTACKS

PROTECTING  
BUILDINGS  
AND  
MILITARY  
BASES

NATIONAL RESEARCH COUNCIL  
OF THE NATIONAL ACADEMIES





# Monitoring System for Environmental Aerosol Detection of Select Agent Pathogens in US Cities: 'Detect to Protect'



- introduced in response to Amerithrax 2001
- launched 2003 for air sampling in 30+ US cities and high profile events (S. Bowl)
- low statistical probability of detection of focal release away from detectors
- up to 36 hours from sampling to BAR decision (Biologically Actionable Release)
- continued investment despite multiple negative assessments of performance/utility



DECEMBER 13, 2018

# The Government's Bioterror-Response Website May Be Leaking Sensitive Data



U.S. » Crime + Justice | Energy + Environment | Extreme Weather | Space + Science

Live TV • U.S. Edition +

## Super Bowl anti-terrorism documents left on plane

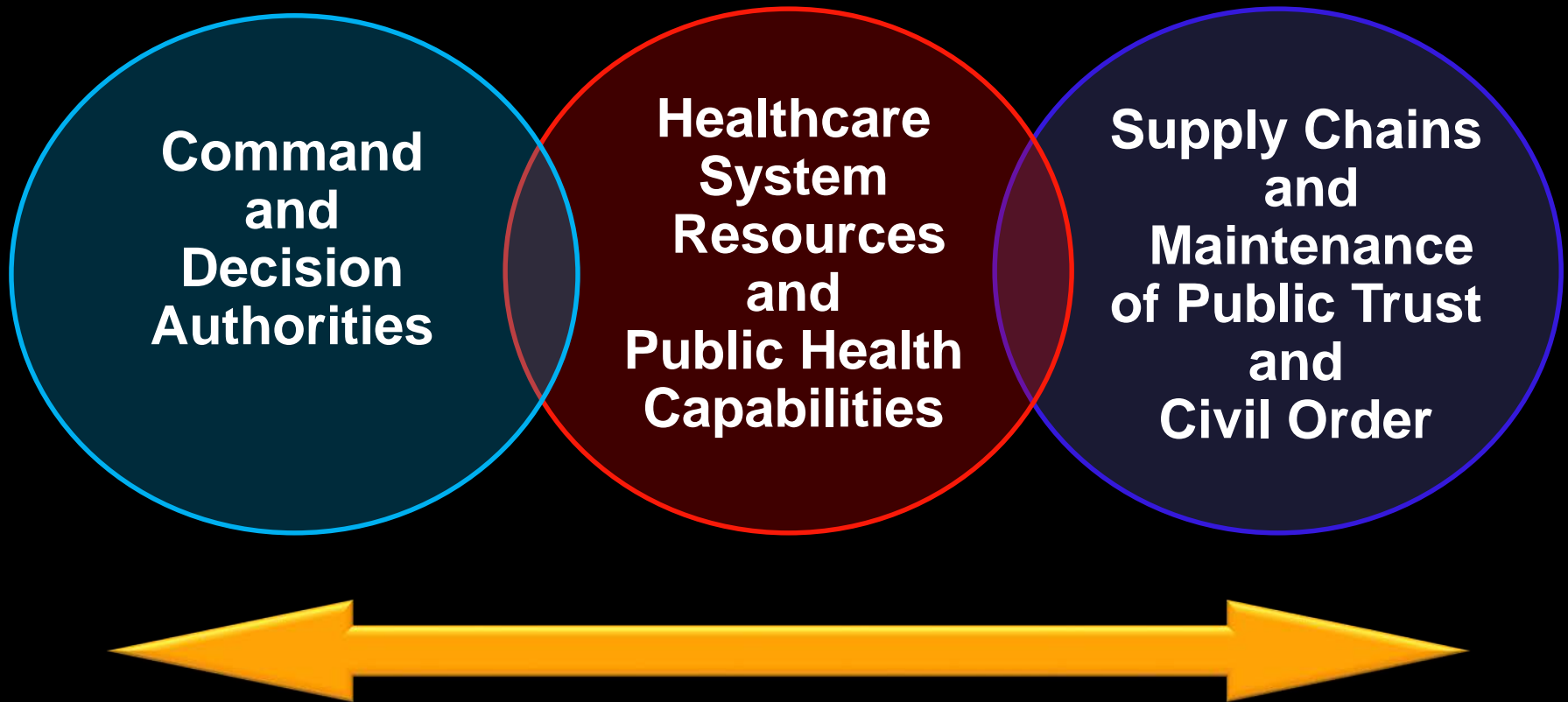
By [Scott Glover](#) and [Drew Griffin](#), CNN Investigates

Updated 1:24 PM ET, Mon February 5, 2018



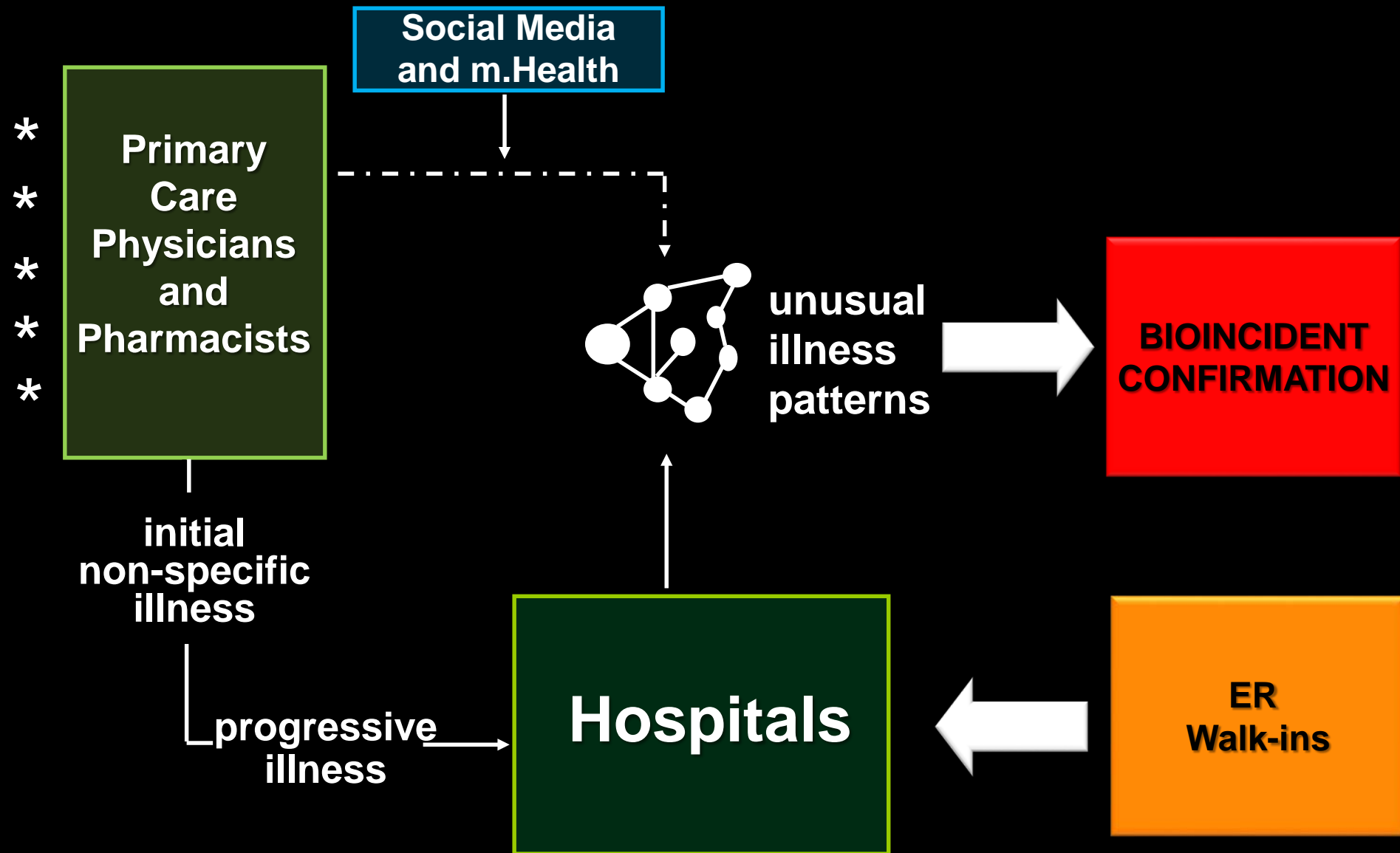


# The Three Core Components of Bioincident Management



- **robust inter-operable communication networks for real-time situational awareness and rapid actions**
- **managing the media and the 'worried well'**
- **transparency, credibility and public trust**

# The Lag Phase in Bioincident Detection

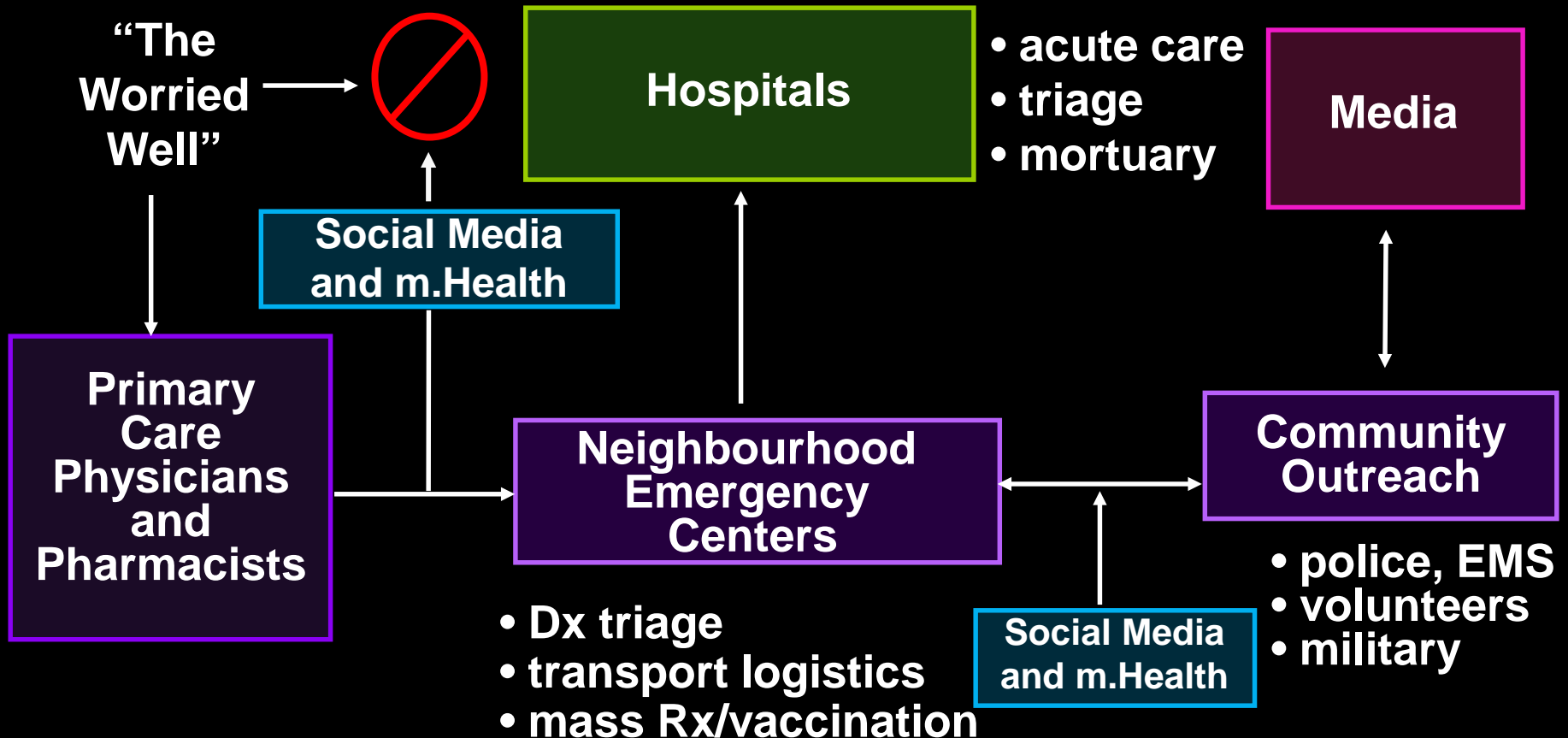




# Consequence and Crisis Control in a Bioincident

## Command Center

- public health
- logistics
- communications
- medical
- law enforcement
- coordination
- local
- national
- international
- regional



# **The Critical Role of Communication and Gaining Public Trust in a Major Bioincident**

**Managing the “Worried Well”**

**Timely, Authoritative and Accurate Information**

**Gaining and Sustaining Public Trust**



# Political Media Sensationalism, Public Fear and Irrational Decisions by Political Leadership



# **Informing the Public: A Critical and Unenviable Challenge**

- **media sensationalism and public panic**
- **pressure on governments to make illogical but politically expedient decisions**
- **in a severe outbreak the shock factor from any major level of fatalities will be unprecedented in modern peace times with unpredictable consequences for public responses**
- **unpredictable unilateral decisions by other governments, restricting trade, travel and shipment of goods**
- **extended supply chains might break down completely**



# **Data Sharing and Inter-Operable Databases**

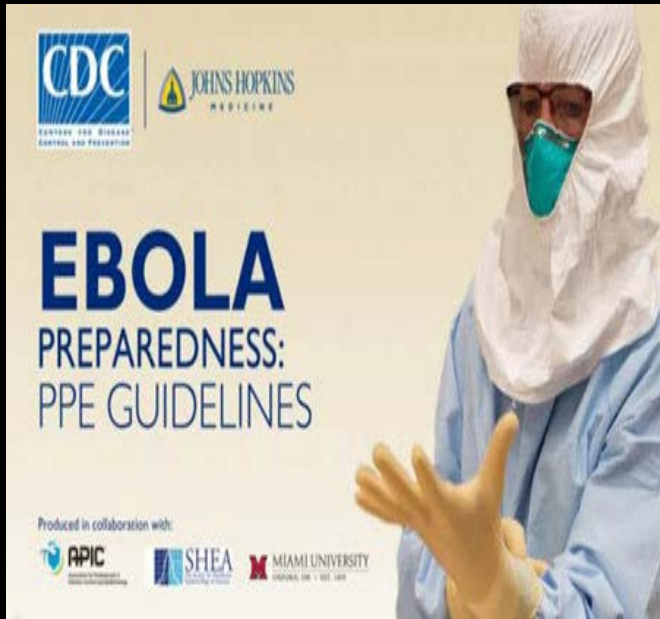
- **despite the obvious theoretical appeal of real time sharing of critical public health data significant obstacles remain**
- **data siloing in multiple databases with no inter-operability**
  - **variable data quality and lack of standardization of data formats**
- **concerns over reuse by third parties**
  - **privacy, commercialization**
- **cybersecurity**
- **gray zone threats**



CALIFORNIA REPUBLIC

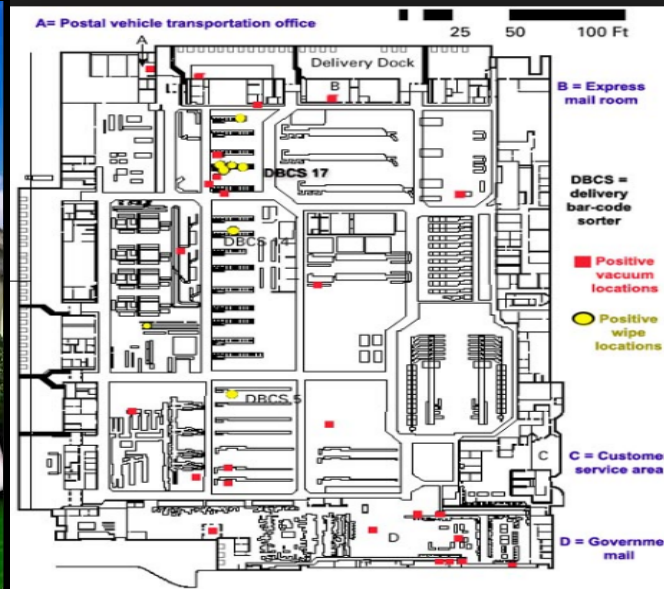


# Biocontainment Protocols and HCP Training





# Large Scale Decontamination and Disposal



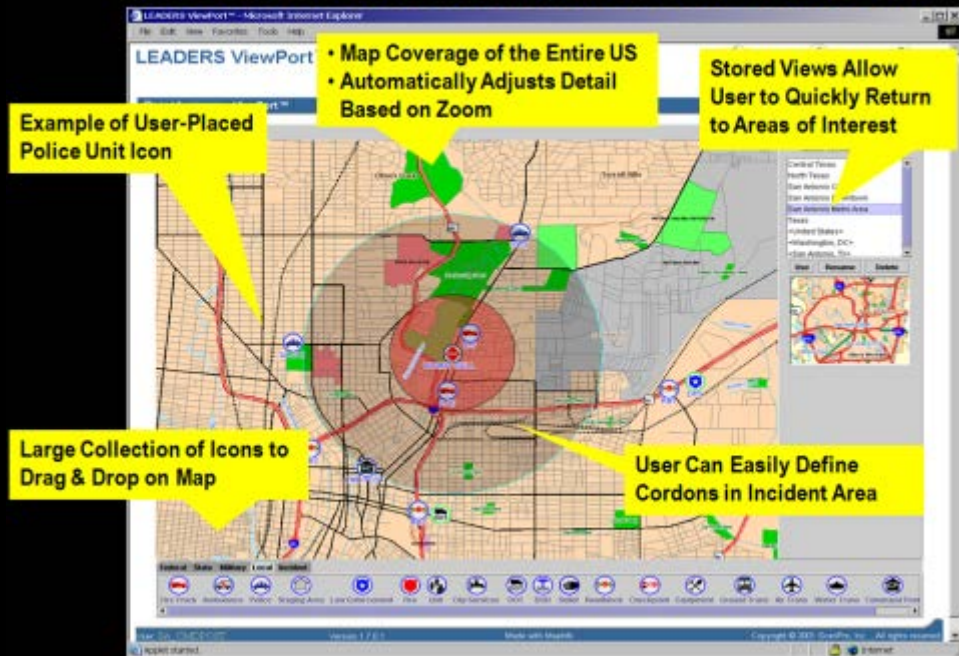


- **pre-positioning for known threats: The Strategic National Stockpile (select agents only)**
- **rapid movement by commercial carriers**
- **managing political/public/media responses for bioincidents caused by pathogens with limited or no  $R_x$ /vaccine options**

# Use of GIS for Management of Population Movement, Healthcare Facilities and Supply Chains for Optimum Bioincident Control



## Resource/Situation Awareness - ViewPort™





# **Vulnerability of Global, National and Local Supply Chains in a Major Epidemic/Pandemic**

## **Medicines**

- **“just-in-time” supply networks**
  - **major hospitals 2 or 3 deliveries per day**
- **out-patient prescription drugs**
  - **insurance company limits on prescription volume (USA)**
- **majority of drug intermediates, excipients and final products sourced off-shore**
- **95% generic drugs used in US (80% of total Rx) are made off-shore, primarily in PRC and India**
- **no national stockpile for routine prescriptions**

# Medical Countermeasures (MCMs) for Special Populations: Emergency Use Authorization

**Children**



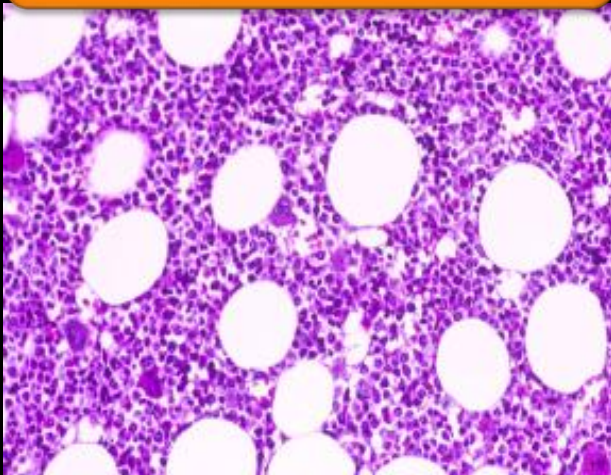
**Pregnant**



**Aged**



**Immunosuppressed**



**Impaired Major  
Organ Function**



**ICU  
Critical Care**





# Sustaining Critical Systems and Infrastructure



# Control of Population Movement and Supply Chain Networks





# Supply Chain Logistics in Disaster Management



Home to some 50 pharmaceutical manufacturing sites, Puerto Rico is a key component of the global pharmaceutical manufacturing chain.



**1 Juncos:** Amgen's Juncos site is the largest in its manufacturing network, with roughly 2,700 people working across its five plants to produce 13 of the company's drugs.

**2 Las Piedras:** Merck & Co., which employs roughly 600 people on the island, shipped over a 1,500-kW generator from its West Point, Pa., site to support operations in Las Piedras.

**3 Jayuya:** Many employees living near Abbvie's site in Jayuya were still without power 11 months after the hurricane.

**4 Barceloneta:** Abbvie's Barceloneta site benefited from a cogeneration plant, which allowed it to power another company and the local bakery after the storm.

**5 Vega Baja** Pfizer's Vega Baja site, one of three that collectively employ about 1,900 people plus contractors, packed its first batch of medicines on Nov. 2nd, about six weeks after the storm.

**6 Guaynabo** J&J's Guaynabo site, home to corporate and commercial functions, is part of a broad network on the island, with some 3,700 employees working across six manufacturing sites.

**7 Carolina** Eli Lilly & Co. is one of six companies to manufacture biologic products, like the insulin made at its Carolina site.



# Stockpiling Ventilators for Influenza Pandemics: Estimated Deaths and Hospitalization



## Ethical Considerations for Decision Making Regarding Allocation of Mechanical Ventilators during a Severe Influenza Pandemic or Other Public Health Emergency



*Prepared by the Ventilator Document Workgroup,  
Ethics Subcommittee of the Advisory Committee to the Director,  
Centers for Disease Control and Prevention*

July 1, 2011

**1918**

- **estimated 675,000 US deaths, 50 million globally**

**moderate pandemic: 1957, 1968**

- **865,000 ILI hospitalizations**

**severe pandemic similar to 1918**

- **projected 9.9 million hospitalizations**

# Constraining Capabilities for Effective Mechanical Ventilation for Large Scale Public Health Emergency

Components	Number of Additional Patients that can be Ventilated at Capacity Level
beds	177,300
staff/physicians	229,500
respiratory therapists	135,000
critical care nurses	75,000 - 301,900

Adapted from: A. Ajao et al. (2015) Disaster Med Public Health Prep 9, 634



# The 'Fog of Disaster': Crisis Standards of Care and Proliferation of Unanticipated Events and Consequences





# Breakdown of Civil Order and Incident Management

## Constrained Mobility



## Constrained Access



# Resource Asymmetries in Management of Global Bioincidents



# **Ebola: West Africa 2014-15**

**A Glimpse of the On-Ground Challenge of Managing Epidemic Disease In Locations With Inadequate Infrastructure and Frightened Populations**

**Still a Small Scale and Relatively Easily Contained Epidemic Versus the Challenge of a Global Pandemic Incident(s)**



# Ebola in West Africa (2014-15)



# Fear and Distrust: Proliferation of Myth and Misinformation



- deliberate spread by Governments
  - delay elections
  - genocidal assault on Kissi tribe
- treatment centers as organ harvesting operations for western countries
- deliberate spread by healthcare workers (HCW)
- attacks on HCW and contact tracers



# Ebola West Africa: 2014-15

## The Logistics (and Risks) of Waste Disposal



## Burial Practices





# Ebola (DRC: 2018-19)

## Scientists seek hidden sources of Ebola

*Two-thirds of new infections in the Democratic Republic of the Congo cannot be linked to known cases.*



An Ebola health worker carries a child at a hospital in the Democratic Republic of the Congo.

- epicenter in Butembo
- concern over shift to more dangerous N. Kivu province
- assaults on HCW by armed militia
- large number of unregistered clinics that offer traditional medicine
  - no infection control and high exposure rate
- greater challenge in contact tracing versus Ebola in W. Africa



# **Containing Epidemics Without Effective Drugs or Vaccines**

# Notice the Resemblance?

## Hygiene and Quarantine as the Only Effective Containment Absent Drugs or Vaccines

Bubonic Plague  
Physician 15th Century



Ebola, Liberia  
21<sup>st</sup> Century



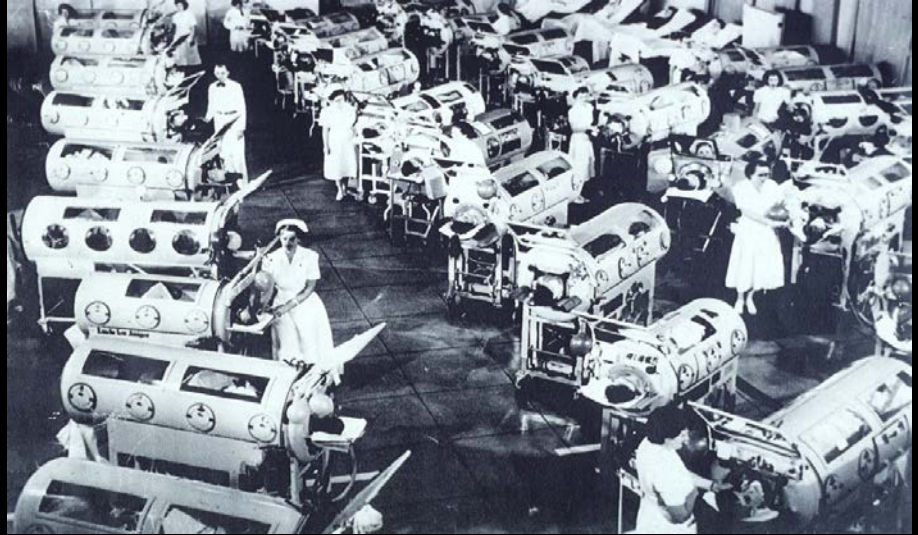
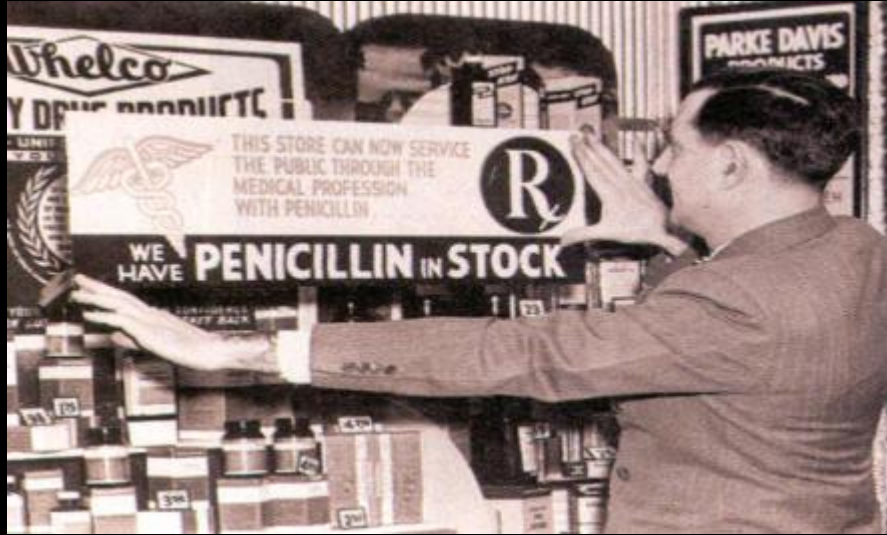


**Out of Sight: Out of Mind!**

**The Cocoon of Protection: How Quickly We  
Forget Past Epidemics and Their Toll**

**Reduced Investment in Public Health and Biosecurity:  
Myopic and Flawed Policy**

# Comfort and Complacency: The Enemies of Vigilance and Preparedness





## Who Pays for Preparedness?



## The Obligate Role of Private-Public Partnerships in Biosecurity Policy

PROCEEDINGS OF A WORKSHOP

Engaging the  
**Private-Sector Health  
Care System** in Building  
Capacity to Respond to  
Threats to the **Public's  
Health and National  
Security**

*The National Academies of*  
SCIENCES • ENGINEERING • MEDICINE

# NO ESKAPE!: Resistant Bugs and Few New Drugs

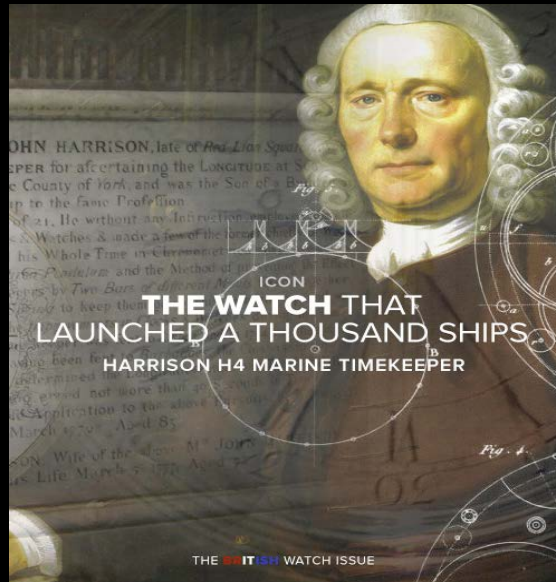


- increasing resistance in G<sup>+</sup> and G<sup>-</sup> pathogens in hospital and community settings
- the **ESKAPE** pathogens
  - Enterococcus faecium*
  - Staphylococcus aureus*
  - Klebsiella pneumoniae*
  - Acinetobacter baumannii*
  - Pseudomonas aeruginosa*
  - Enterobacter species*





# New Incentives to Accelerate Investment in Drugs and Vaccines for Public Health



## Material Threat Medical Countermeasure Priority Review Vouchers

Guidance for Industry

### DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to <https://www.regulations.gov>. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact the Office of Counterterrorism and Emerging Threats (OCET) at 301-796-8510 or [AskMCM@fda.hhs.gov](mailto:AskMCM@fda.hhs.gov).

U.S. Department of Health and Human Services  
Food and Drug Administration  
Office of the Commissioner  
Office of the Chief Scientist  
Office of Counterterrorism and Emerging Threats

January 2018

Procedural

January 17, 2018

**Pre-clinical  
development**  
Pre-IND

**CARB-X**

**Push incentive**

Direct investment via  
accelerators into  
pre-clinical development

Est. 2016

**Clinical  
development**  
Phase I-III



**Push incentive**

Clinical stage  
Public: Private partnerships

Est. 2010

# Alma-Ata (1978) to Astana (2018)



**Global Health  
Security Agenda**

- **prevent, detect and respond to infectious disease**
- **safeguard economies**
- **end the cycle of panic and neglect**
- **need for sustained investment commitment**
- **essential public health capacities represent recurring cost**



## **The Joint External Evaluation Exercise (JEE): January 2016\***

- **major deficits in 89% of the 55 countries evaluated to date**
- **surveillance for highly antibiotic resistant pathogens and antimicrobial stewardship**
- **biosecurity and surveillance for zoonotic diseases, food poisoning and water-borne illness**
- **insufficient personnel and training**
- **investment levels**
- **major risks to cross-border disease spread**

# *China Has Withheld Samples of a Dangerous Flu Virus*

Despite an international agreement, U.S. health authorities still have not received H7N9 avian flu specimens from their Chinese counterparts.

Aug 27, 2018



Health workers attending to an H7N9 avian flu patient in Wuhan, China, in 2017.

Agence France-Presse -- Getty Images



# Sharing of Specimens and Data is Crucial for Global Biosurveillance and Real Time Situational Awareness

- **PRC**
  - obfuscation about SARS
  - current H7N9 influenza strains in human
  - highly pathogenic avian influenza (HPAI) strains
  - African Swine Fever virus isolates
- **Indonesia**
  - H5N1 influenza
- **Saudi Arabia**
  - MERS-CoV

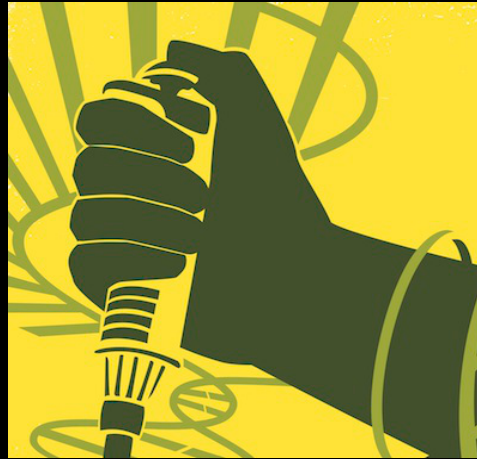
# Dual-Use Applications of Synthetic Biology and the Expanded Spectrum



Statement for the Record  
Worldwide Threat Assessment  
of the  
US Intelligence Community  
Senate Select Committee on Intelligence



James R. Clapper  
Director of National Intelligence  
February 9, 2016



**Technology Diffusion,  
Automation,  
Simplification and Cost  
Reduction**

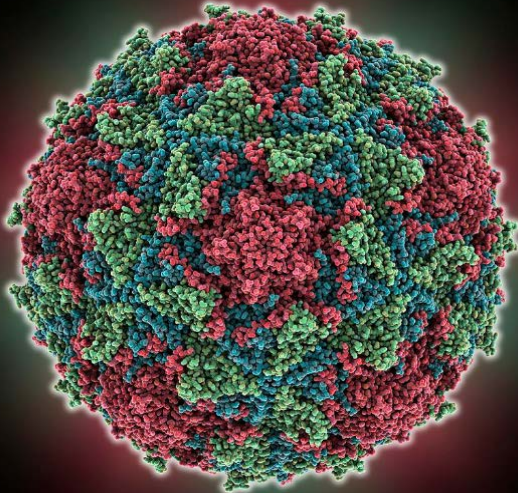


**New Oversight  
Mechanisms and  
International  
Harmonization**

- **beneficent and maleficent applications of same knowledge**
- **potential to cause profound societal disruptions based on misuse, error or accident**



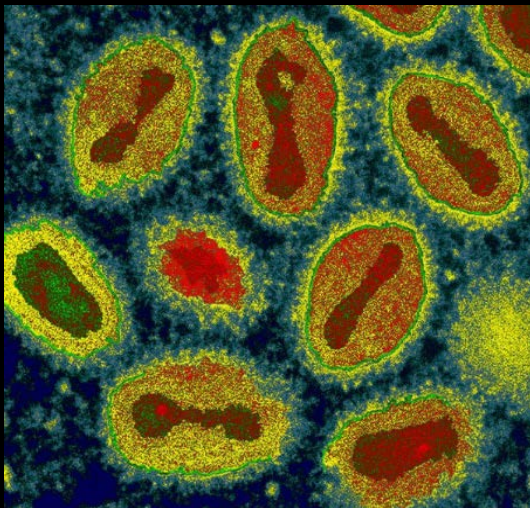
# De Novo Synthesis of Pathogens



Science (2002) 297, 1016

## Chemical Synthesis of Poliovirus cDNA: Generation of Infectious Virus in the Absence of Natural Template

Jeronimo Cello, Aniko V. Paul, Eckard Wimmer\*



PLOS ONE <https://doi.org/10.1371/journal.pone.0188453> January 19, 2018

## Construction of an infectious horsepox virus vaccine from chemically synthesized DNA fragments

Ryan S. Noyce<sup>1</sup>, Seth Lederman<sup>2</sup>, David H. Evans<sup>1</sup>\*

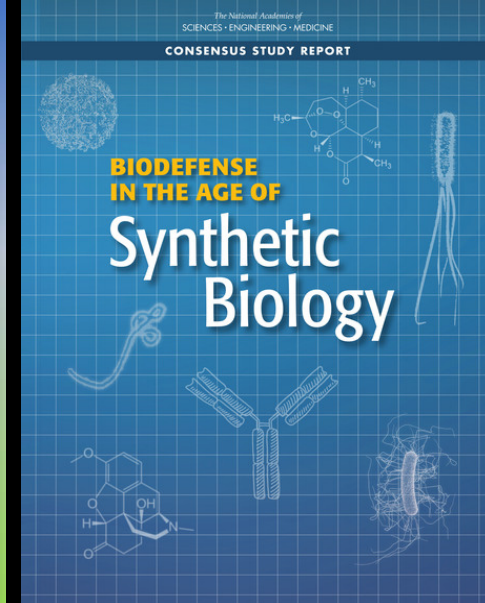
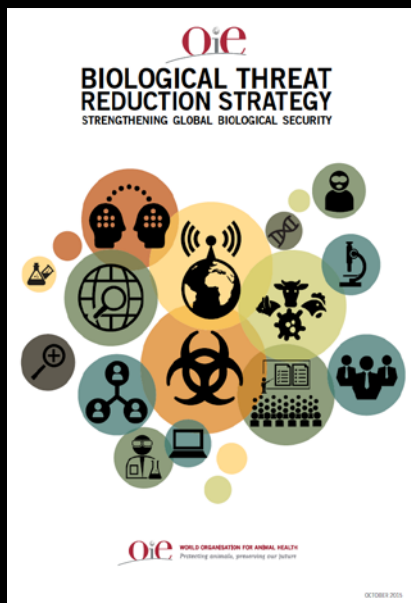
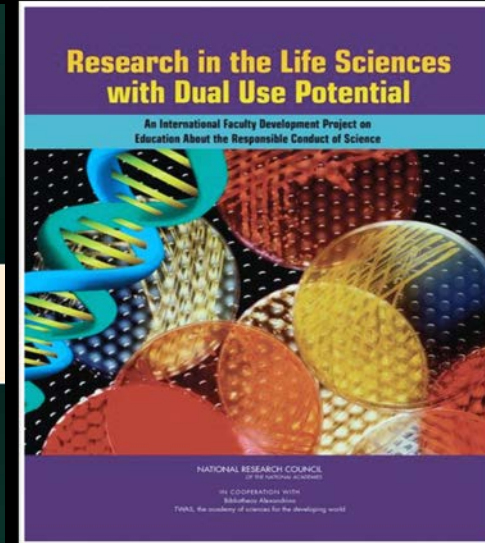
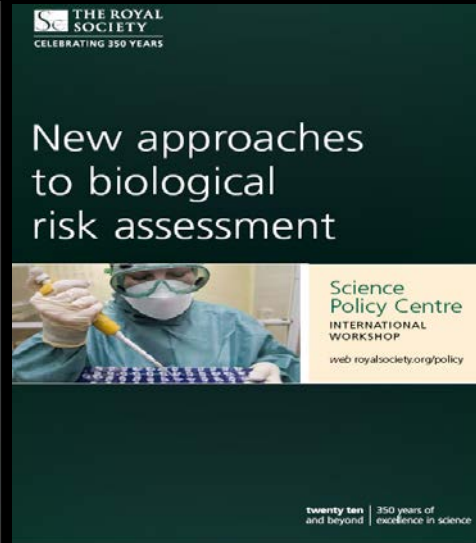
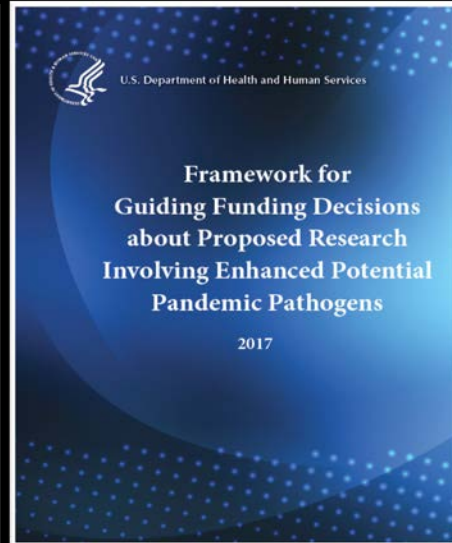
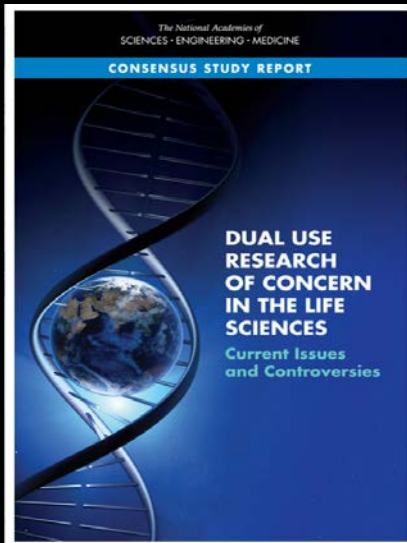
<sup>1</sup> Department of Medical Microbiology & Immunology and Li Ka Shing Institute of Virology, University of Alberta, Edmonton, Alberta, Canada, <sup>2</sup> Tonix Pharmaceuticals, Inc., New York, New York, United States of America

# Digital Biology

- **biology at internet speed**
- **transmission of digital instruction code to any location**
- **geographic uncoupling of design (code) from manufacture (synthesis and assembly)**



# Policy Frameworks for Dual-Use Research of Concern (DURC): Primary Focus on Pathogenic Microorganisms



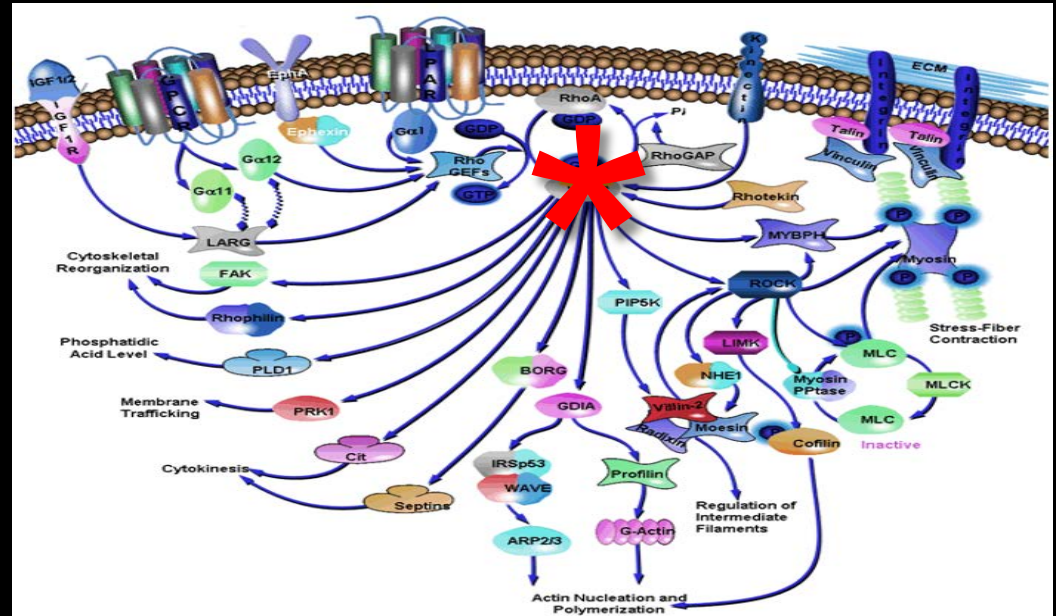
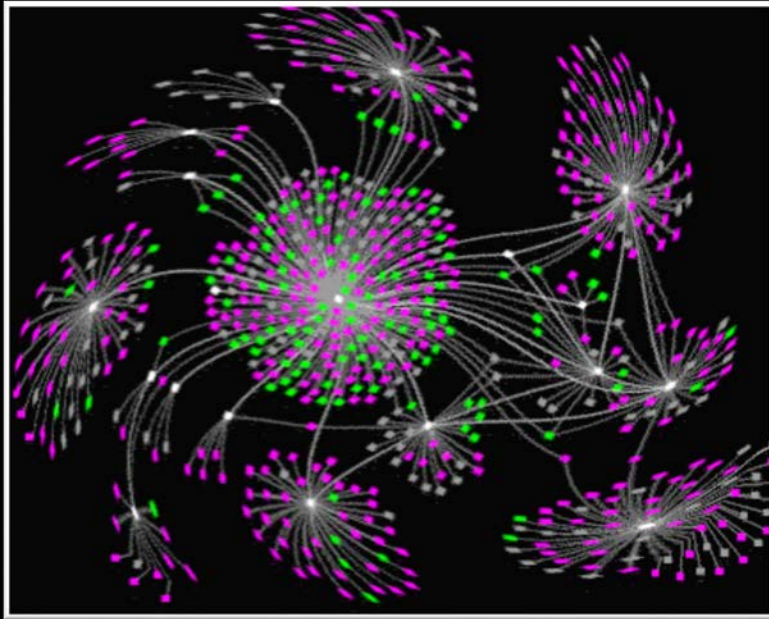
# Editing the Human Germ Line: No Longer An Abstract Question



- **editing humanity: moral and legal constraints or hubris and irresistible inevitability?**
- **long standing science fiction scenarios and philosophical, religious, ethical, legal debates on the societal implications**
- **no longer a theoretical debate**



# Synthetic Biology and DURC: Thinking “Beyond Bugs”



- **precision medicine**
  - mapping the molecular networks (circuit diagrams) of every cell type in the body and disruptions in disease
- **roadmap for next-generation chemical warfare agents to target specific molecular circuits and body functions**

# Dual-Use Implications of Advances in Brain Science

## Mapping Sensory, Motor and Cognitive Functions



BRAIN RESEARCH THROUGH ADVANCING  
INNOVATIVE NEUROTECHNOLOGIES

# BRAIN INITIATIVE

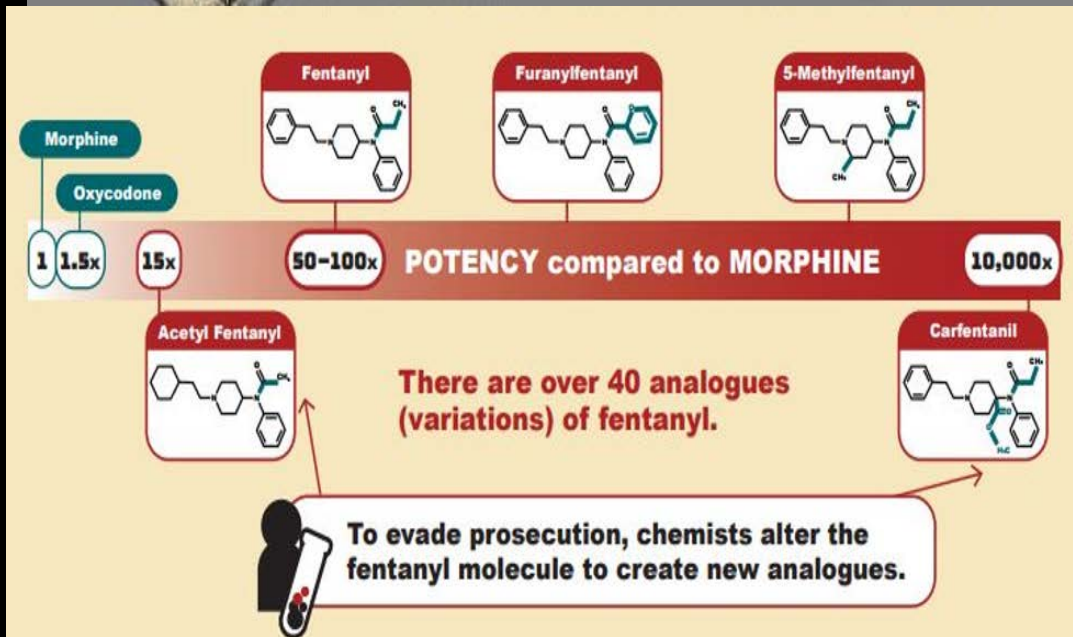


## Chemical or Electronic Modulation of Specific Neural Circuitry: New Warfare Capabilities and Societal Vulnerabilities

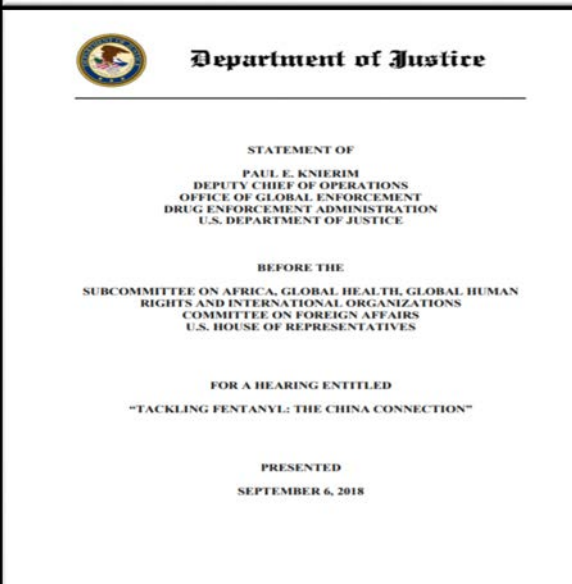
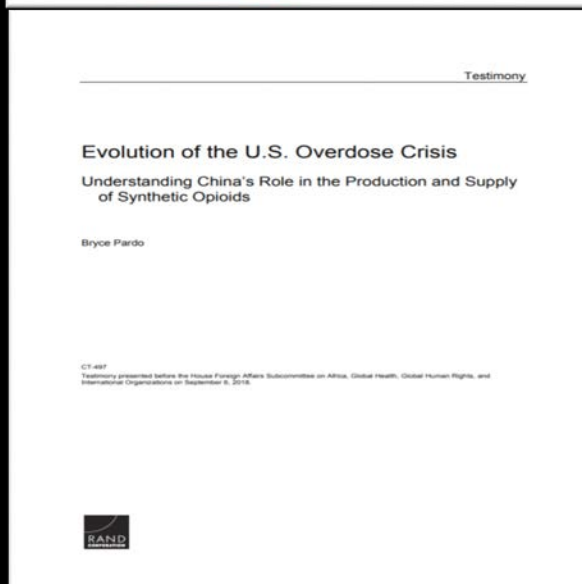
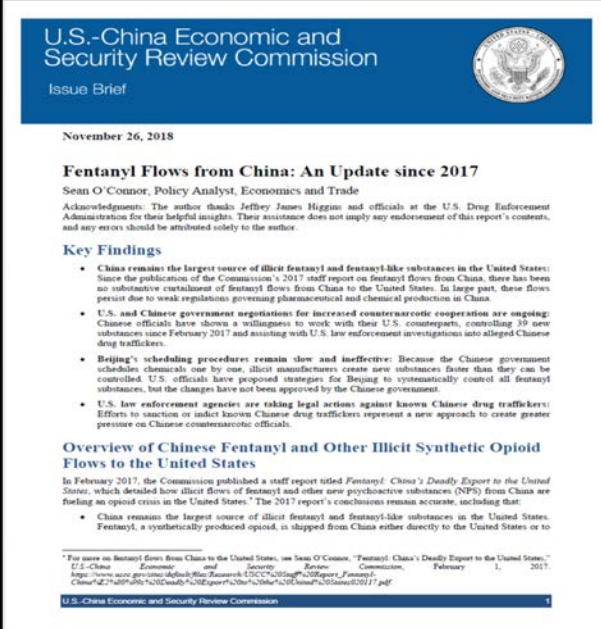
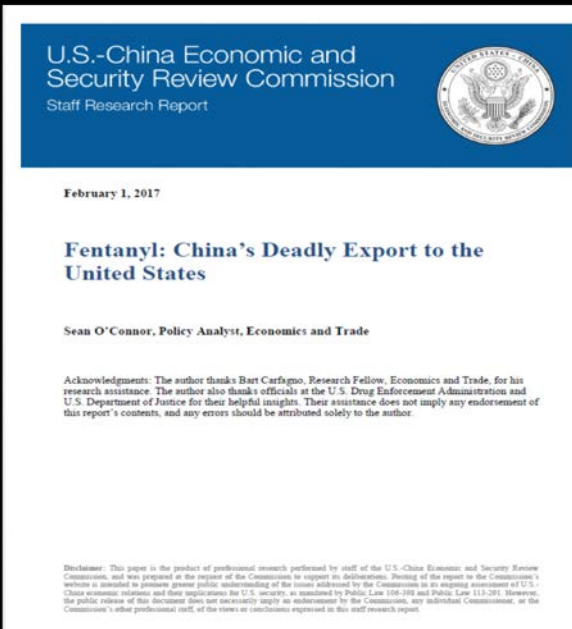
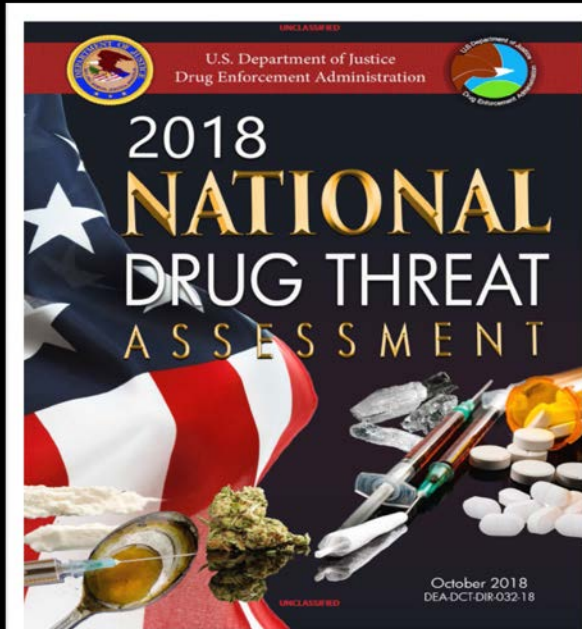
- fear, depression, suicidal ideation
  - aggression
- disruption of sleep patterns
  - memory modulation
- lethargy      ● addiction



# Purposeful Societal and Economic Disruptions Via Synthesis of Ever-Changing Pipeline of Addiction Drugs by Synthetic Biology



# China's Export of Fentanyl and Derivatives: A New Biosecurity Threat





# **Gray Zone Threats**

## **The Emerging Dimension of Hybrid Warfare**

### **New Risks in the Gray Zone Between Peace and Major Conflict**

### **Implications for Biosecurity**

# **Darker Shades of Gray: The Emerging Dimension of Hybrid Warfare**

- weaponized narratives
- deception, disinformation and propaganda
- lawfare; exploiting loopholes and seeding ambiguity
- plausible deniability
- exploit Western public reluctance for formal military deployments





# Hybrid Warfare: The Putin-Gerasimov Military Doctrine



# **Gray Zone Tweets and Biosecurity: Russian Trolls and Twitter Bots**

- **weaponized health communications**
  - **anti-vaxxer campaigns**
  - **anti-GMO movements**
- **compromise health care computer systems and or other critical computing capabilities in bioincidents**
- **Novochok chemical attack UK 2018**
  - **Salisbury UK hospital computers**
  - **thwarted hack of Organization for Prohibition of Chemical Weapons (The Hague) conducting forensic analysis**



# Gray Zone Threats

- **between peace (zero) and major military conflicts (five)**
- **are we already facing level one/two – level escalation ?**



# **BIOLOGICAL WEAPONS CONVENTION**



# Export Controls on Technologies for WMD Threats and CBW Weaponization



## The U.S. Export Control System and the Export Control Reform Initiative

Ian F. Fergusson  
Specialist in International Trade and Finance

Paul K. Kerr  
Specialist in Nonproliferation

August 9, 2018

Congressional Research Service  
7-5700  
www.crs.gov  
R44916

CRS REPORT  
Prepared for Members and  
Committees of Congress



## Dual-Use Technologies and Export Control in the Post-Cold War Era

Documents from a Joint Program of the  
National Academy of Sciences and the  
Russian Academy of Sciences

National Research Council



## DETECTING SUSPICIOUS PROCUREMENT ATTEMPTS

Regrettably, not all buyers approach Australian industries with a legitimate commercial purpose. The following information is designed to assist industry identify activities that may indicate an attempt to illegally acquire conventional arms or procure goods, services and technologies for weapon of mass destruction (WMD) programs.

Illicit WMD programs and proliferation of conventional arms pose significant threats to the safety of all Australians, and to regional and global security. It is in Australia's interest to ensure would-be proliferators are denied access to conventional weapons and items that may contribute to WMD activities are appropriately controlled.

The Defence Export Control Office works closely with other government agencies to prevent the proliferation of WMD and conventional weapons and, in turn, protect Australia's reputation as a responsible member of the global exporting community.

To this end, industry should ensure that all exports are compliant with all statutory and regulatory requirements. Applications to export regulated defence and dual-use goods, and goods and services that could contribute to a WMD program, must be lodged with DECO.

Australian industry can help prevent the proliferation of WMD and conventional weapons by reporting all suspicious approaches to DECO.

## IDENTIFYING SUSPICIOUS APPROACHES

There are certain 'red flags' that can indicate an attempt to proliferate. These include:

- Approaches from persons or entities on the Department of Foreign Affairs and Trade's Consolidated List
- Approaches from countries subject to sanctions, or with a WMD program
- Unusual or inappropriate requests for goods to be manufactured to military, or unusually high, specifications
- Unusually favourable, or non-standard payment terms
- Unusual requests regarding the shipment route, or labelling of the goods

If you have encountered any of these red flags, you may have had a suspicious approach. More red flags can be found over the page.

## WHAT NOW?

Members of industry who have information that could identify a suspicious enquiry or purchase are encouraged to contact DECO via:

Phone - 1800 66 10 66

Online - access our 'Reporting A Suspicious Approach' form at [www.defence.gov.au/strategy/deco](http://www.defence.gov.au/strategy/deco)

Mail - mark all letters 'In Confidence'

and post to:

Defence Export Control Office  
Department of Defence  
R11-AUS, Russell Offices  
CANBERRA ACT 2600

For further information on DECO's Privacy Policy click on the link to the 'Reporting A Suspicious Approach' form above.

## Australia Group Common Control List Handbook

Volume I: Chemical Weapons-Related Common Control Lists



## Australia Group Common Control List Handbook

Volume II: Biological Weapons-Related Common Control Lists



The Voice for  
Australia's exporters



## Intergovernmental Agreement on Biosecurity Review

July 2016

Submission by the Export Council of Australia

# Screening of

# Gene Sequences of Concern



- screening orders to synthesize potentially dangerous sequences
  - focus on select agents
- likely increasing irrelevance as a biosafety/surveillance tool
  - lower cost of synthesis machines
  - digital genome computer codes bypass screening and surveillance tools
  - new gene editing tools makes any gene a target

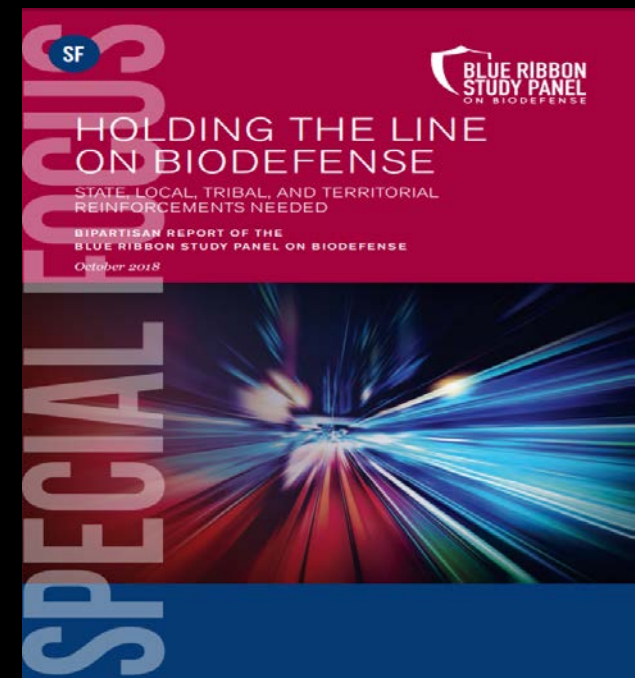
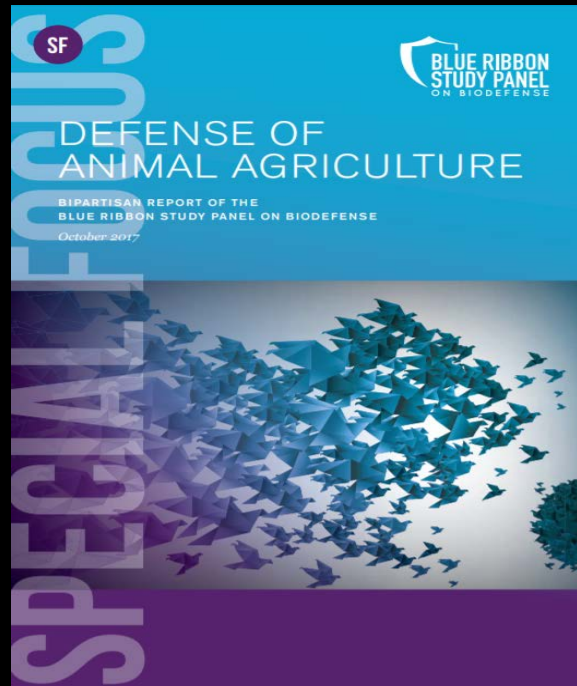
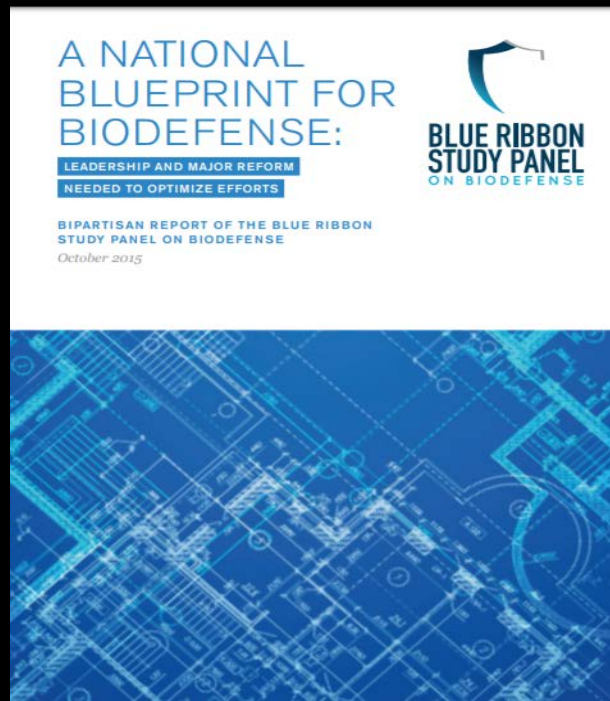


# Biosecurity



# “Fits and starts: Reactionary Biodefense”

October 2018







**PROCRASTINATE  
NOW  
AND  
PANIC  
LATER**

# **The Biosecurity Challenge**

- **complex, multi-dimensional problems cannot be solved by uni-dimensional approaches**
- **danger of episodic investment and/or uni-dimensional interventions versus sustained systems-based investment to develop and sustain resilient systems**
- **strong preparedness and attribution capabilities are a deterrent to adversaries**



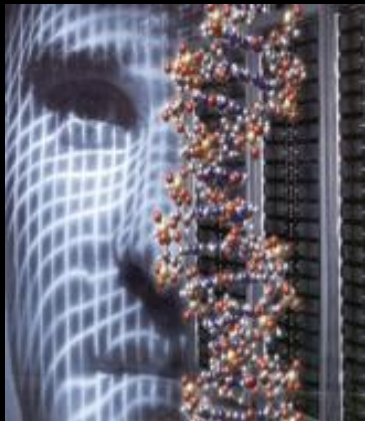
# **The Changing Biosecurity Landscape**

## **COMPLACENCY!!**

- **need for higher priority of biosecurity in national security strategy and international engagement**
- **development of more sophisticated threat assessment capabilities**
- **strengthen surveillance, analysis deterrence capabilities in national security, IC, law enforcement**
- **greater investment in robust and agile threat mitigation capabilities**
  - **obligate private sector engagement**
  - **logistics and operational integration (and training) for complex bioincident management**
- **more relevant oversight mechanisms and international harmonization**

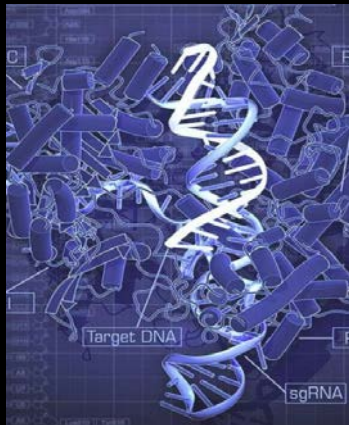
# Escalating Complexities in Biosecurity

**All Hazards  
Analysis**



**“Threat  
Space”**

**Synthetic  
Biology,  
Digital Biology**



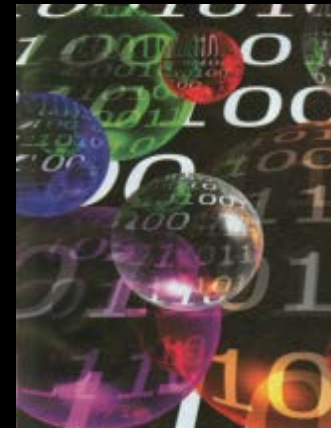
**“Design  
Space”**

**Biosurveillance  
and  
Diagnostics**



**“Detection  
Space”**

**Meta-Data,  
Advanced  
Computing,  
AI**



**“Analysis  
Space”**

**Agent X and  
Proliferation  
of Dual-Use  
Risks**



**“Preparedness  
Space”**



**“Politics is the art of the possible,  
the calculated science of survival”**

**Prince Otto von Bismarck**



**“Survival owes little to the art of politics,  
but everything to the calculated application  
of science”.**

**Professor Rudolph Virchow  
(in reply)**



**Slides Available**  
**@ <http://casi.asu.edu/>**

