



*United States Department of*

**Health & Human Services**

Office of the Assistant Secretary for Preparedness and Response



# Host Directed Therapeutics and Immunomodulators

**An alternative to “one bug-one drug?”**

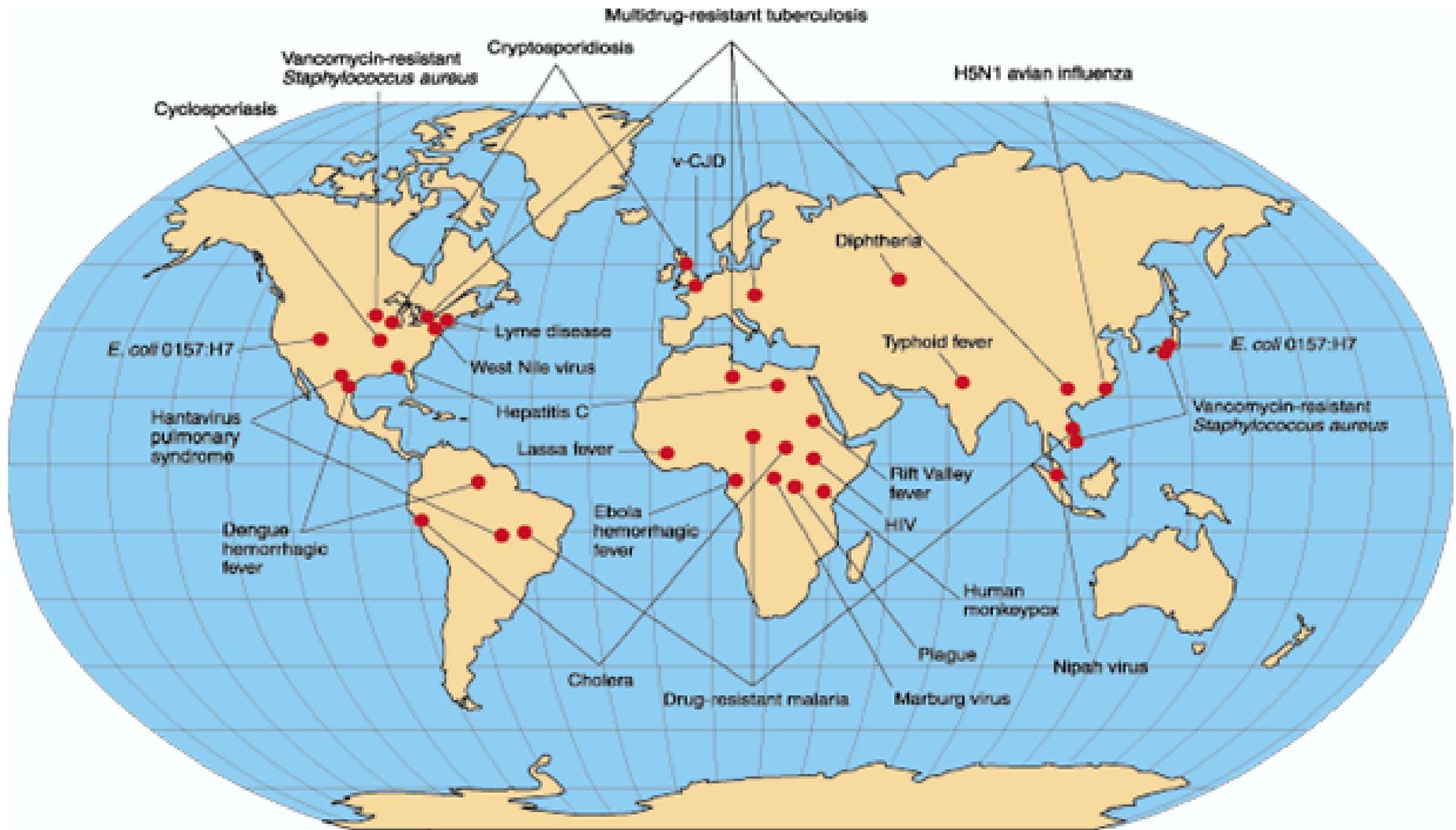


# PHEMCE Vision

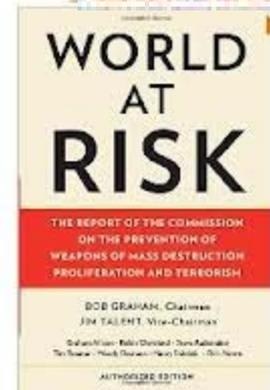
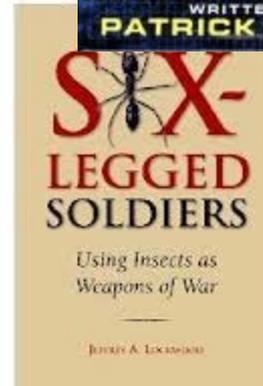
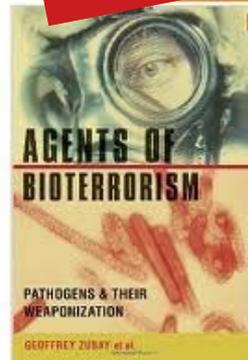
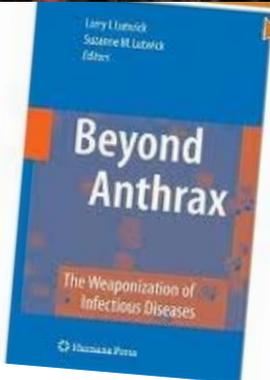
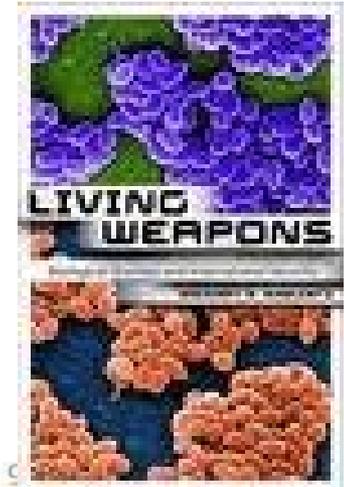
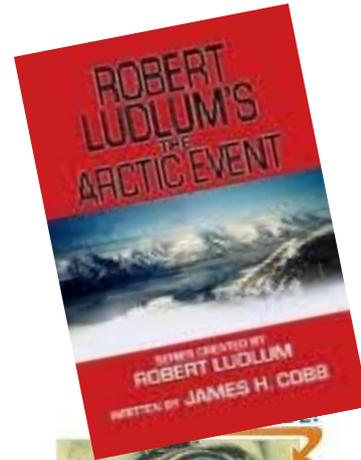
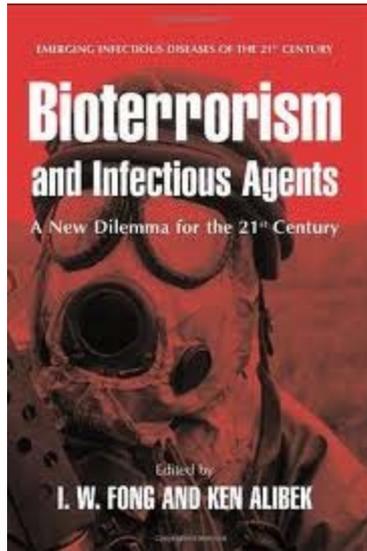


- Our nation must have the nimble, flexible capacity to produce MCMs rapidly in the face of an attack or threat, known or unknown, including a novel, previously unrecognized, naturally occurring emerging infectious disease

# Emerging Infectious Disease



# Weaponized Infectious Disease





# MCM Development Issues



- Naturally occurring or bioengineered pathogens
- Pathogen focus limits breadth and utility
- Reduced Industry R&D spend on Infectious Diseases
- Increased cost of development and reduced probability of success
- Limited shelf-life
- Pathway to licensure



# Strategy



- To succeed, a new strategy is needed. One that
  - Exploits new scientific concepts and the potential for multiple use products (including drug repositioning)
  - Can rapidly procure or produce MCMs in the face of attack or threat
  - Provides prophylactic or therapeutic benefit in the face of an unidentified pathogen
  - Mediates the effects of multiple pathogens
  - Requires decreased resources for stockpiling



# Responses



- Structural:
  - Establishment of Working Group focused on New and Emerging Threats
  - BARDA SST BAA ; Area of Interest “3”
    - *Therapeutics to Treat Novel and Emerging Threats*
      - *Immune modulators, anti-inflammatory agents and regulators of innate immunity*
      - *Therapeutics with broad-spectrum mechanism of action that target a host-response*
- Scientific
  - Focus on Host Immunity



# Aspects of Host-directed Innate Immunity



- Non-specific, rapid response, may reduce likelihood of resistance mutations, interfere with host enablement of infection
- Complement, PMN's initiate pathogenic lysis and opsonophagocytosis, chemotaxis, release of proinflammatory cytokines, activate adaptive immunity and generation of T-cell and B-cell populations
- Concerns
  - Brief duration
  - Overactivity, *i.e.* cytokine cascade
  - Genetic polymorphism (potential lack of specific dose)
  - Gender differences
  - Potential narrow therapeutic window
  - Complexity





# Host-directed Mechanisms/ Classes



- IDR peptides, e.g. Defensins and mimetics
- CTLA-4 / CD28/IDO- T Cell control
- Cell surface modification
- Vaccine adjuvants
- Broad spectrum vaccines
- Toll-Like and other pattern recognition receptors
- Interferons
- Immunomodulators



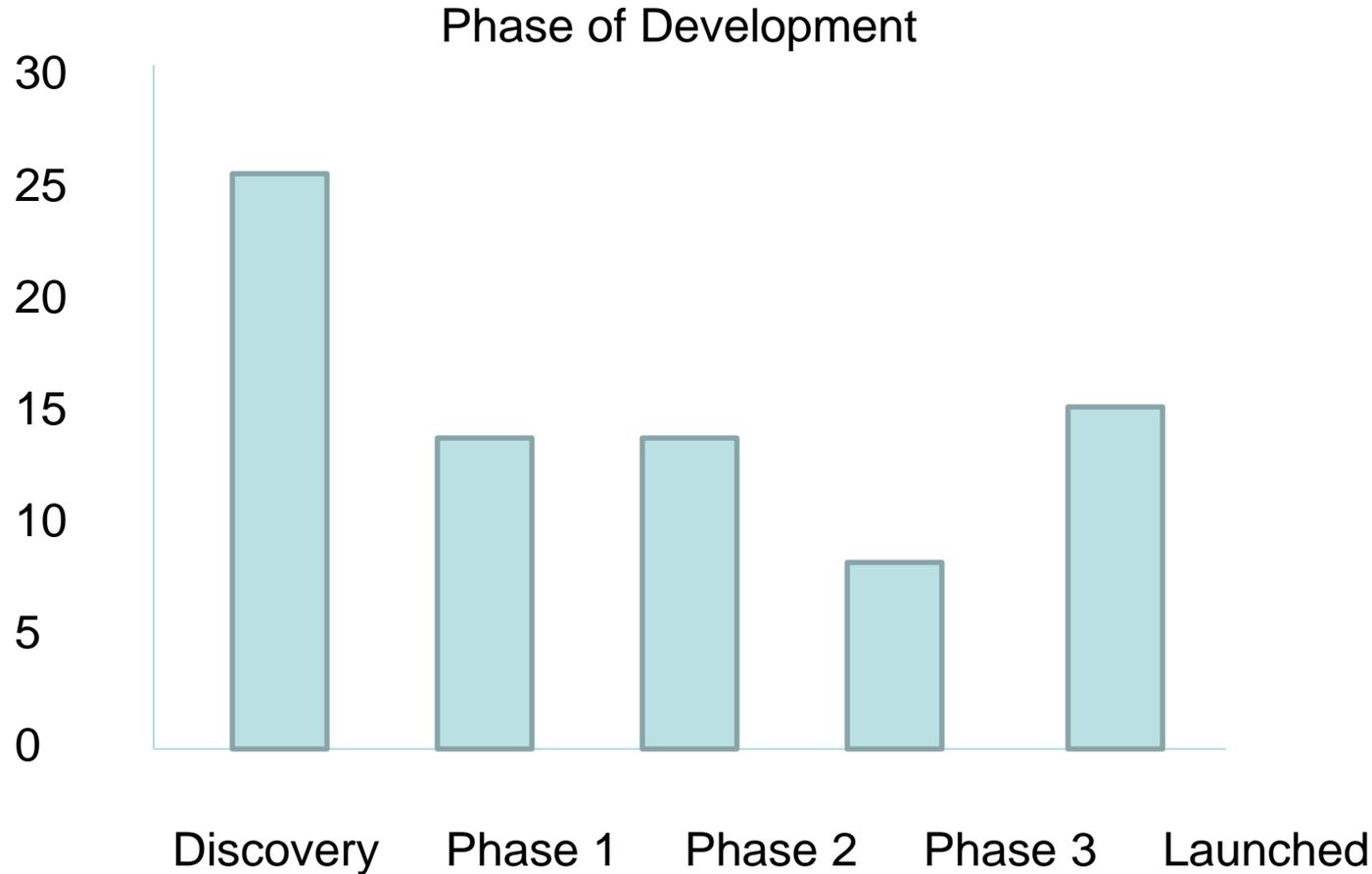
# Immunomodulators



- Inflammation: positive and negative aspects
  - Process required to recruit PMNs, release cytokines
  - May cause morbidity if not controlled
  - Can treatment be tailored to individuals?



# Potential Host-Directed Antimicrobial Drugs





# SUMMARY



- Clear need for new and better treatments that can serve as MCMs
- Reduced “Big Pharma” activity
- Host-Directed innate immunity offers an opportunity
- Consider drug repositioning
- Commercial and MCM use



# Partnerships



- We Want to hear from you!
  - This Meeting
  
  - Medicalcountermeasures.Gov
    - <https://www.medicalcountermeasures.gov/announcements/nowopenbaa.aspx>



# Host-Directed Agents



## Questions