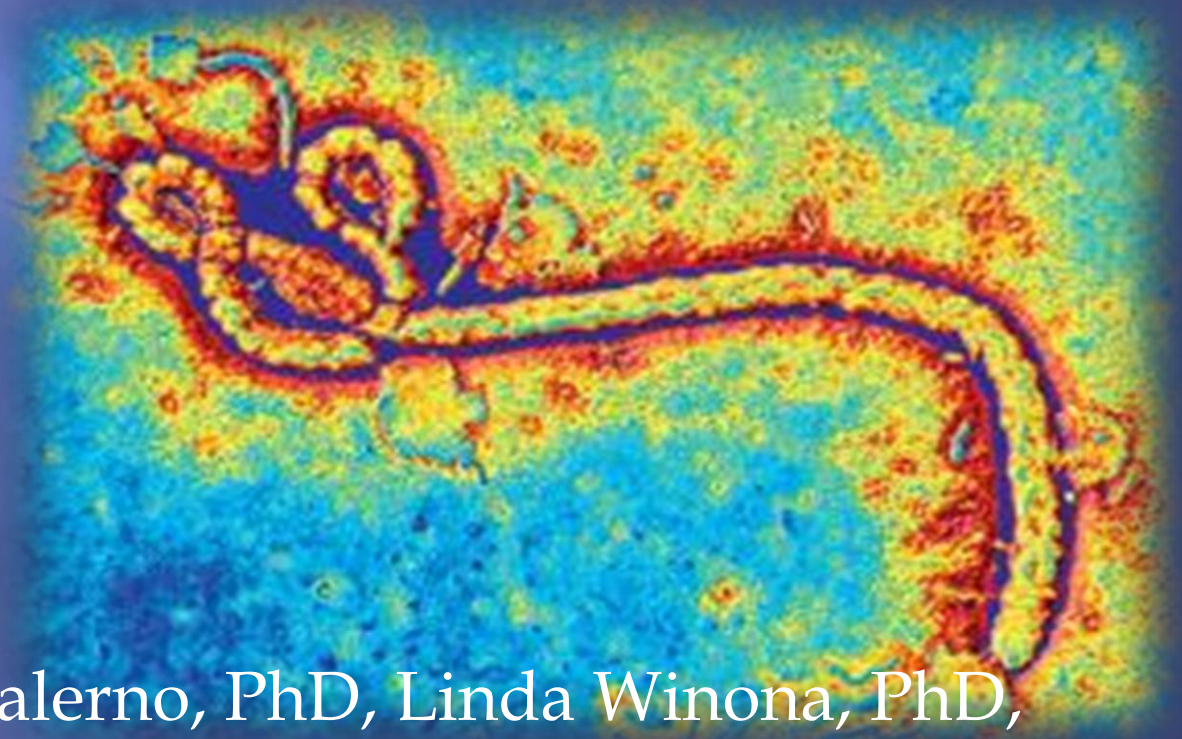


BIORISK MANAGEMENT FOR VACCINE MANUFACTURERS



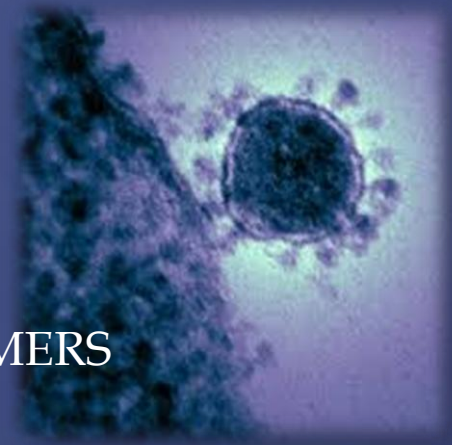
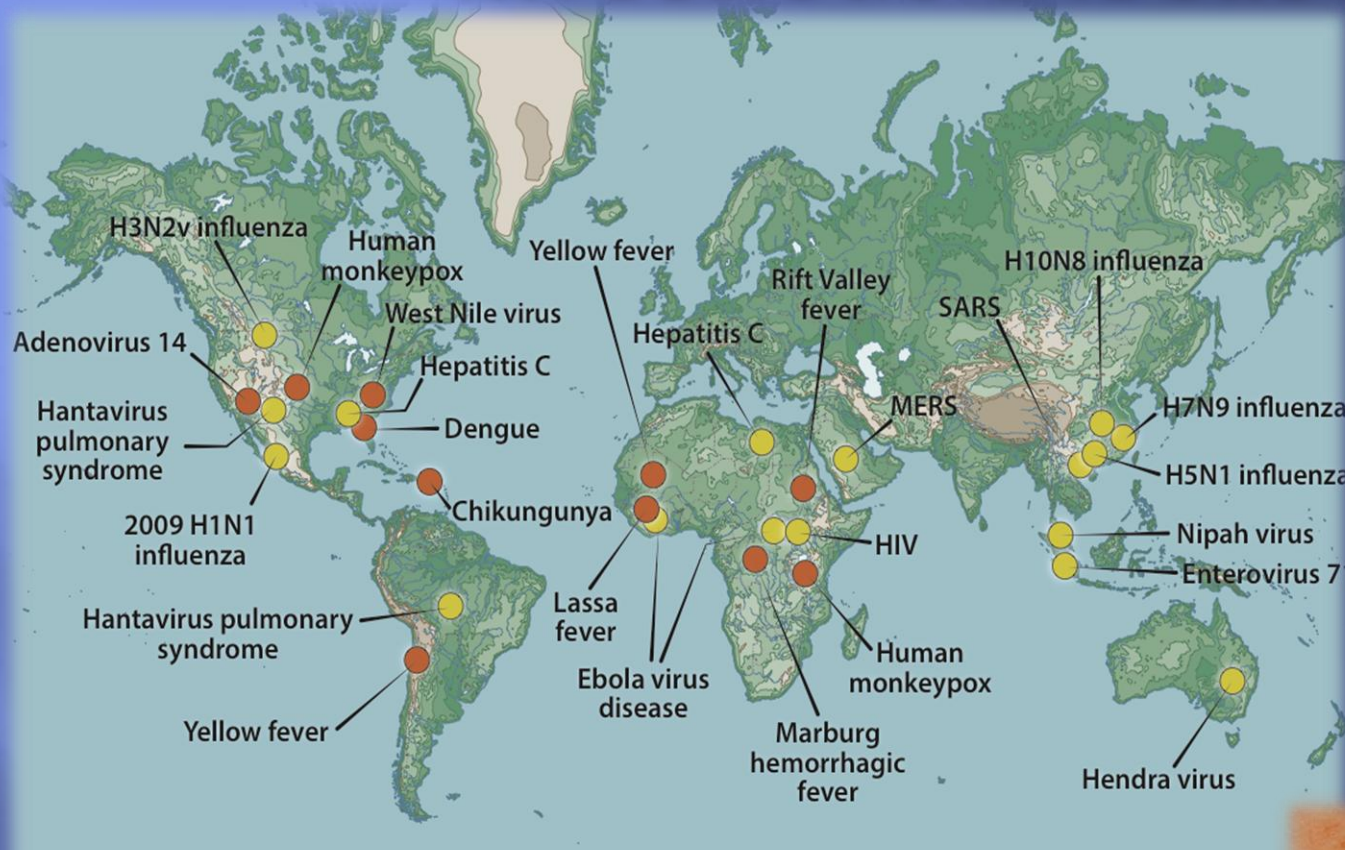
Reynolds M Salerno, PhD, Linda Winona, PhD,
and Vibeke Halkjaer-Knudsen, PhD

Sandia National Laboratories

Albuquerque, NM, USA

October 2014

Emerging and Re-emerging Infectious Diseases



MERS

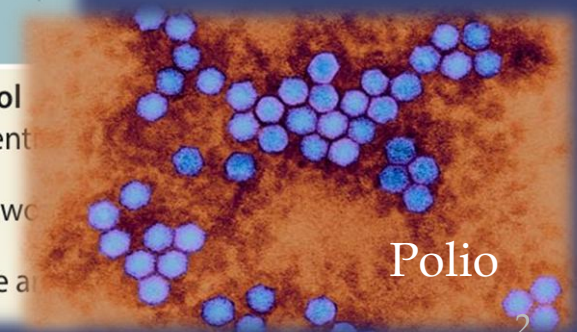
- Newly emerging
- Re-emerging

Developments facilitating spread

- Commercial air travel
- Global trade
- Urbanization
- Unchecked population growth
- Climate change

Advances facilitating control

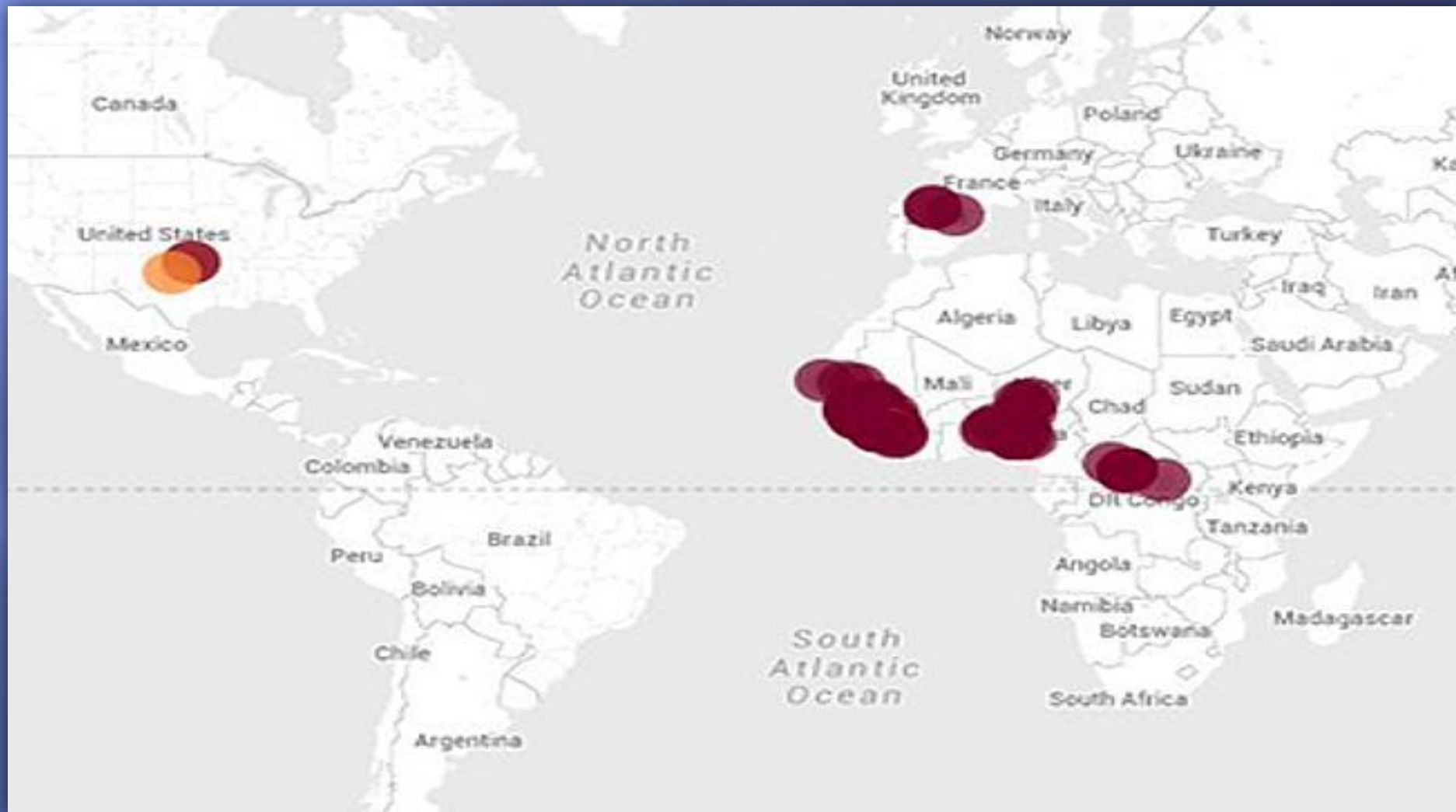
- Genome sequencing to identify emerging viruses
- Global communication networks
- Rapid diagnostics
- New approaches to vaccine and therapeutic design



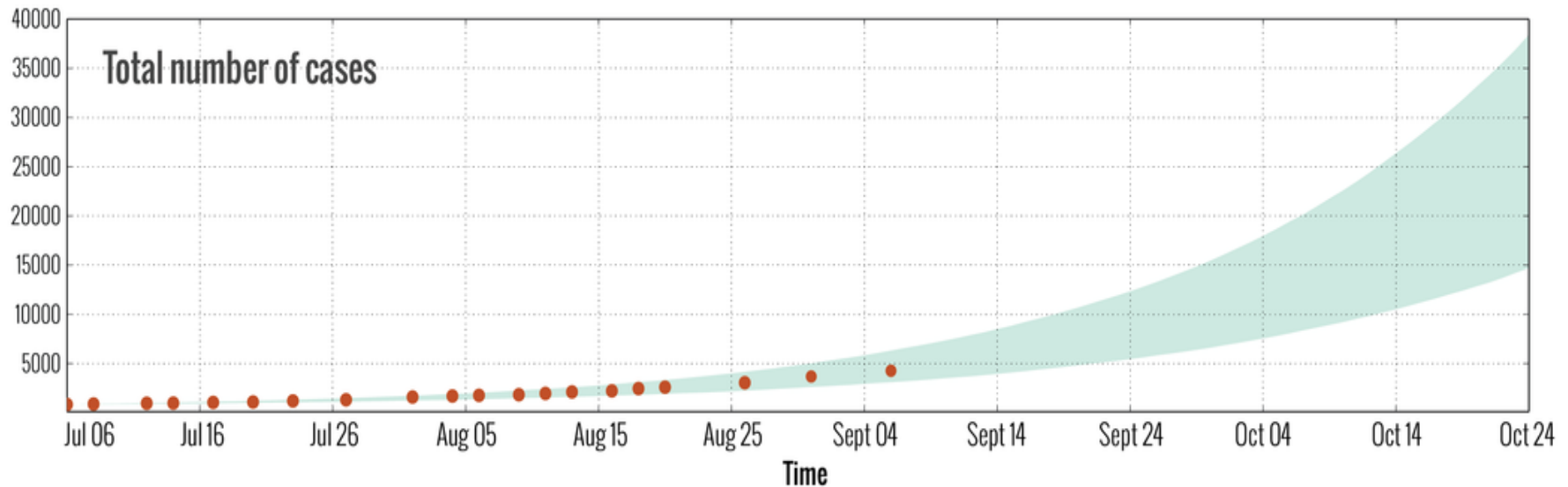
Polio

**Emerging and re-emerging
infectious diseases bring new
opportunities and risks to the
vaccine manufacturing
community**

Current Ebola Outbreak



Ebola Case Projections



Date	Total Number of Cases
Sept 14 2014	[4000 - 8500]
Sept 24 2014	[5500 - 12300]
Oct 04 2014	[7500 - 17900]
Oct 14 2014	[10500 - 26300]
Oct 24 2014	[14800 - 38500]

Projections for the number of cases in Guinea, Liberia, and Sierra Leone.

The shaded areas correspond to the fluctuations cone provided by the stochastic microsimulations of the models selected by the calibration to data. WHO official data are reported as red circles. The projected values consider that the epidemic continues to follow the current growth rate, thus assuming a worst-case scenario in which containment measures are not successful at curtailing the outbreak.

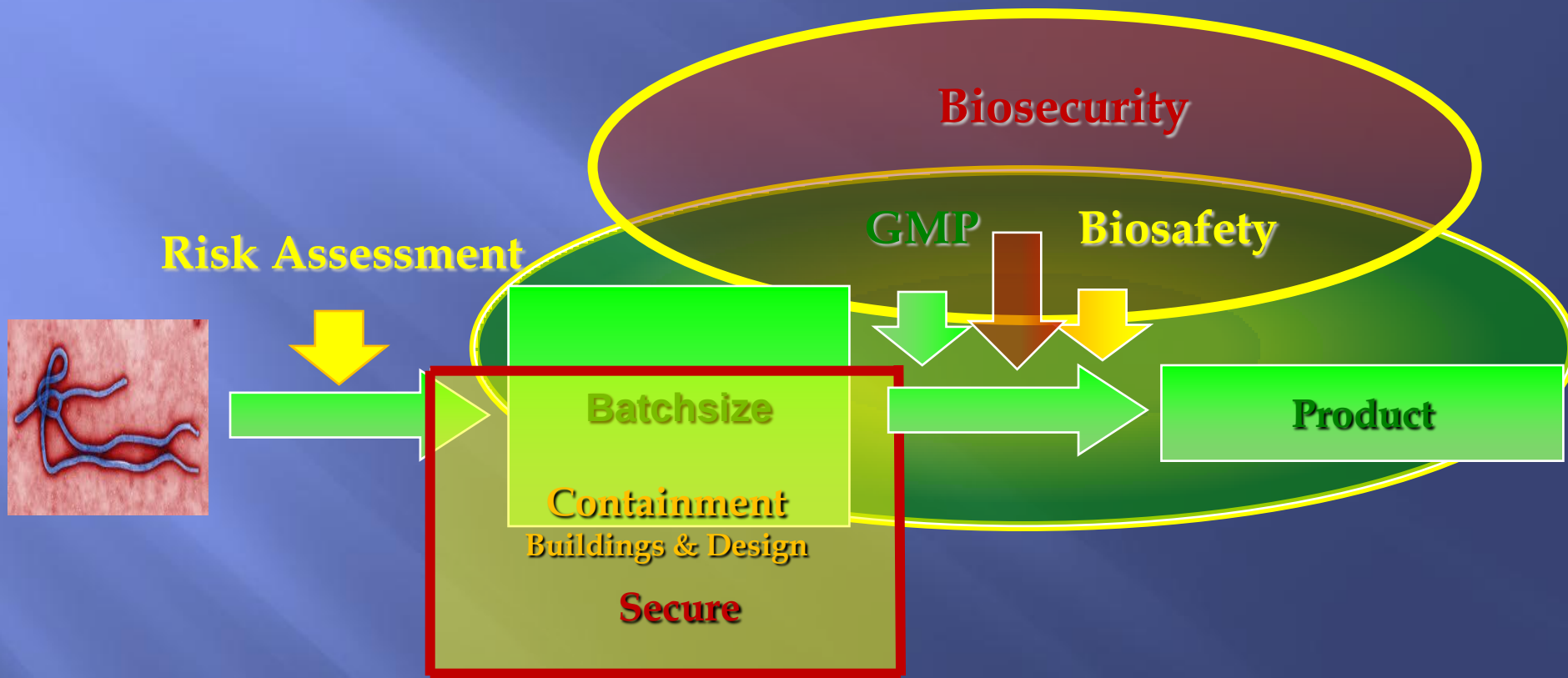
How do we manage the risks of producing and manufacturing vaccines for emerging and re-emerging infectious diseases?

Goals for Biorisk Management



- Protect **vaccine users** from unsafe products
- Protect **employees and the environment** from harmful agents
- Protect **dangerous materials and proprietary information** from someone with malicious intent

Production of Biologicals



GMP – Produce safe product for the end user – no impurities in the product

Biosafety – Protect workers from contagious agent – keep the agent inside

Biosecurity – Protect agent from evil humans – keep it locked away



Traditional Controls for Biosafety and Product Safety



Elimination/
Substitution

Engineering
Controls

Administrative
Controls

Best Work
Practices

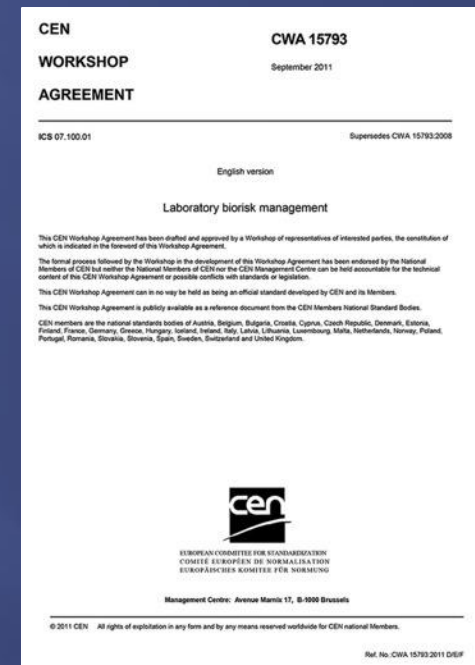
PPE

“Oh No!”



Laboratory Biorisk Management

- CEN Workshop Agreement 15793:2011
- Internationally developed and accepted
- Not based on pre-determined biosafety levels; Performance- and risk-based
- Consistent with other international standards, such as ISO 9001, 14001, and others



Biorisk Management Principles

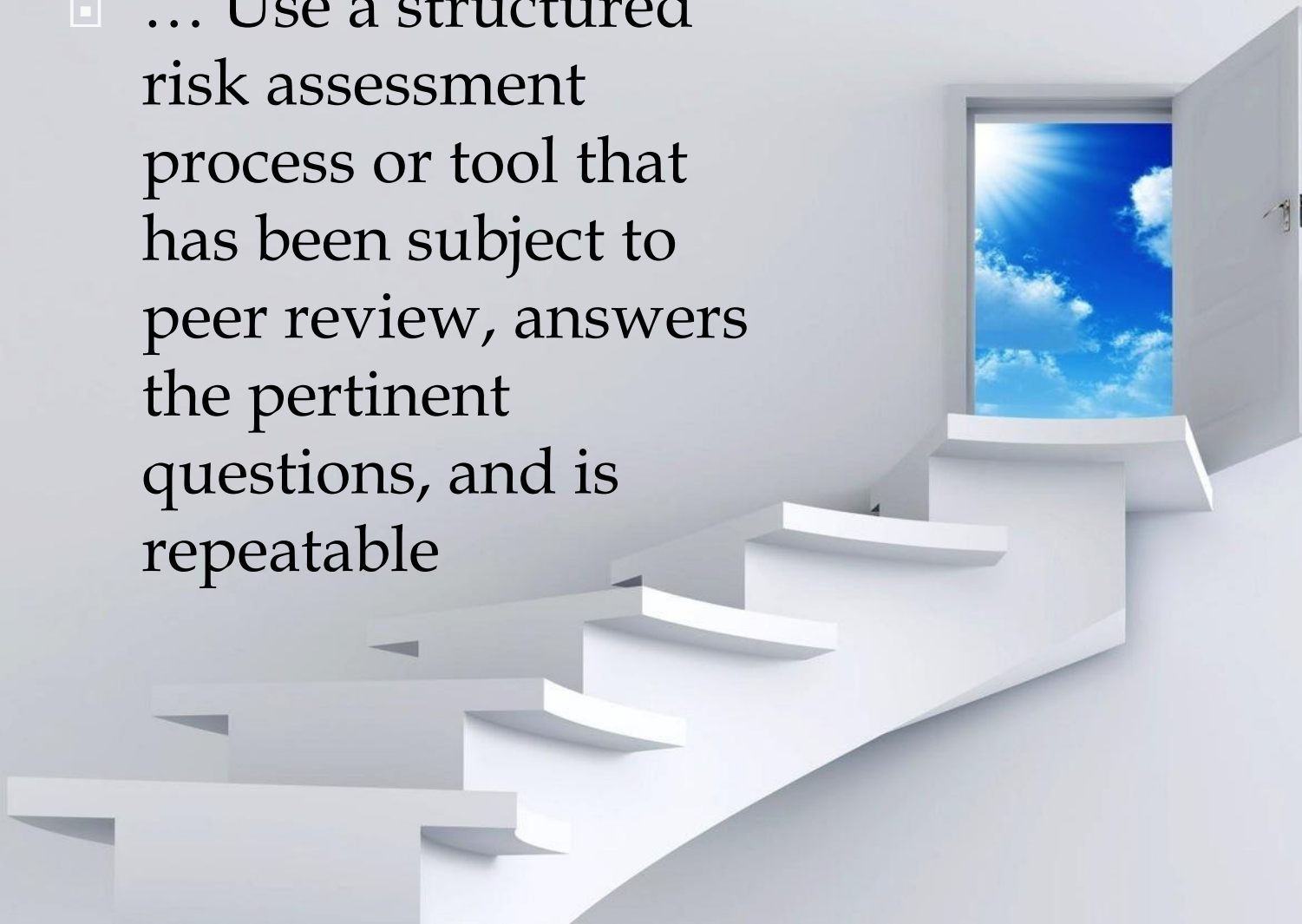
- The AMP model
 - Assessment
 - Mitigation
 - Performance
- Executive management commitment and investment
- Clearly defined roles and responsibilities
- Mitigation measures directly tied to the risk assessment
- Constant monitoring and evaluation for continual improvement





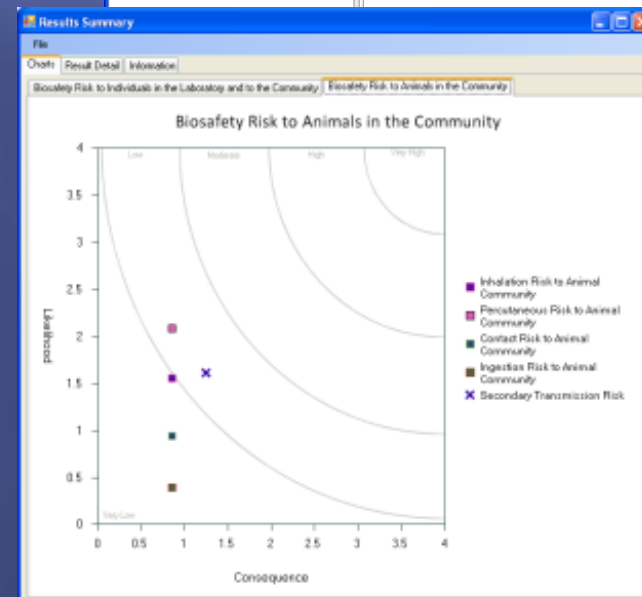
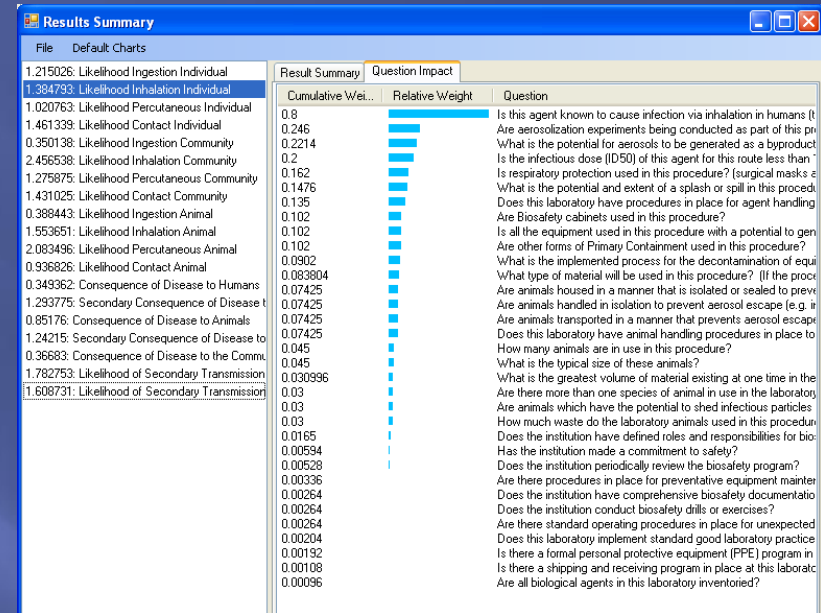
Where do we start?

- ▣ ... Use a structured risk assessment process or tool that has been subject to peer review, answers the pertinent questions, and is repeatable



A tool for decision makers

- Clearly define those criteria that contribute most to the risk (“risk drivers”)
- Allow decision makers to make informed decisions about project planning, mitigation measures, and communication



A tool for rapid response

- Should include documentation of the biological agents, the production processes, and the mitigation measures in place
- Should allow for rapid characterization in the event of unforeseen situations



**What risks are there in
vaccine production
facilities?**

Production Facilities Handle Large Volumes



And a Lot of Waste



Where are the Risks?



Inoculation/
Cell Culture
fermentation



Purification



Inactivation

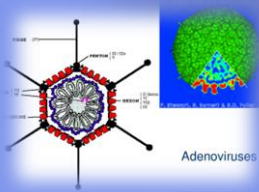


Vial filling
equipment

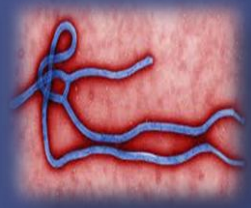
When can the Risks Occur?

- ▣ Normal production conditions
- ▣ Planned/unplanned start up, shut down
- ▣ Fire and power failures
- ▣ CIP/SIP

- ▣ For all above scenarios, evaluate the following conditions:
 - Temperature (high/low)
 - Pressure (high/low)
 - Flow (fast, slow, reverse)
 - Volume level (high/low)
 - Mixing & surface tension/bubbles
 - pH, redox, density
 - Leakage, breaking
 - Tanks, pumps, tubes, pipe valves
 - Computer, alarm, communication
 - Etc



Manufacturing an Ebola Vaccine



- ❑ Live attenuated virus vaccine and recombinant protein virus vaccine tested successfully, but safety a concern
- ❑ Gene based vaccines much safer, but human trials are extremely important to demonstrate efficacy and safety
- ❑ Current Ebola vaccine development by GSK-Belgium
 - ❑ Vaccine has two glycoprotein genes (Ebola Sudan and Ebola Zaire) inserted within Chimpanzee Adenovirus serotype 3
 - ❑ Able to stimulate the immune system to produce antibodies to Ebola
 - ❑ Currently being fast-tracked to human trials
 - ❑ Phase I: NIH, Oxford, Mali -- expected results by end of the year
 - ❑ Phase II: will involve vaccinations of thousands of frontline healthcare workers in West Africa
 - ❑ If it provides protection without significant side effects, GSK may initiate large-scale production of the vaccine

Summary

- ▣ Biorisk Management Systems:
 - Provide for the health and safety of laboratory workers and environment
 - Ensure the containment of hazardous infectious substances in laboratory/facilities
 - Maintain citizens' confidence in the activities of the vaccine manufacturing community
 - Increase transparency to investors in the biomedical and biotechnology industries
 - Protect valuable research and commercial assets
 - Reduce the risks of crime and terrorism
 - Strengthen overall performance (profits!)

Thank You!!!

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SAND No 2014-19028C

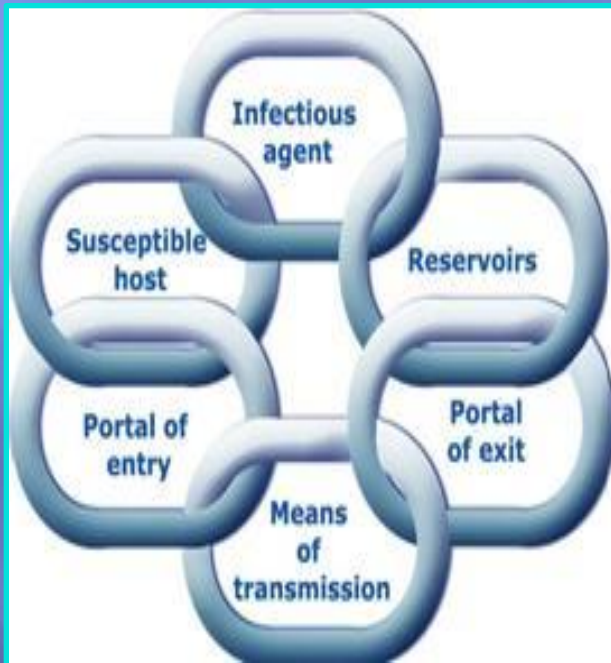
Sandia is a multiprogram laboratory operated by Sandia Corporation,
a Lockheed Martin Company, for the United States Department of Energy's
National Nuclear Security Administration
under contract DE-AC04-94AL85000



BRM Supplements Traditional Controls

Risk Mitigation Measures:	Addresses the Area of:		
	GMP	Biosecurity	Biosafety
Restricted access	x	x	x
Segregation of production areas	x	x	x
HEPA filtration system in the facility ~ 20 ACH	x		x
Validate process, systems, equipment & facilities	x	x	x
Equipment must be inspected periodically	x	x	x
Easy cleaning/decon	x		x
Liquid/Solid waste disposal		x	x
Mandatory PPE (face shields, gloves, Tyvek suits etc...)	x		x
Mandatory trainings, periodical health check-ups, physicals and vaccination	x	x	x
Documentation, double signatures, etc	x	x	x
Written policies and procedures	x	x	x
Job Certifications, work areas, security level of access	x	x	x
Annual performance checks of policies and procedures	x	x	x

Chain of Infection for all Microorganisms



- Reservoirs/Storage of Pathogens
 - Buildings/procedures
- Portal of Exit/Escape
 - Equipment
 - Procedures & administrative controls
- Means of Transmission/Source
 - Personal Protective Equipment (PPE)
- Portal of Entry/Method & Infectious Dose
 - Decontamination
- Susceptible Host
 - Immunizations
- Infectious Agent/Incubation Period
 - Surveillance
 - Quarantine

Ebola re-emerged in 2014 – Deadliest, Largest, and Most Complex Outbreak

- As of Oct 15, WHO reported 9,000 suspected cases and 4,493 deaths
- Healthmap models predict that the cases could double in a month
- Secondary spread to the United States and Spain



Air traffic connections from West Africa countries to the rest of the world