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



Commercial air travel

Unchecked population growth

Global trade

Urbanization

Climate change

Re-emerging

- Genome sequencing to ident
 emerging viruses
- Global communication netwo
- Rapid diagnostics
- New approaches to vaccine a 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 offical 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.

🍰 MOBS LAB

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



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





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



anagement Centre: Avenue Mamix 17, B-1000 Brussels

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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







Risk Assessment



Check

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

🛃 Results Summary

17

File Derault Charts	
1.215026: Likelihood Ingestion Individual	Result Summary Question Impact
1.384793: Likelihood Inhalation Individual	Cumulative Wei Relative Weight
1.020763: Likelihood Percutaneous Individual	0.8
1.461339: Likelihood Contact Individual	0.246
0.350138: Likelihood Ingestion Community	0.2214
2.456538: Likelihood Inhalation Community	0.2
1.275875: Likelihood Percutaneous Community	0.162
1.431025: Likelihood Contact Community	0.126
0.388443: Likelihood Ingestion Animal	0.135
1.553651: Likelihood Inhalation Animal	0.102
2,083496: Likelihood Percutaneous Animal	0.102
0.936826: Likelihood Contact Animal	0.0902
0.349362: Consequence of Disease to Humans	0.083804
1 293775: Secondary Consequence of Disease t	0.07425
0.85176: Consequence of Disease to Animals	0.07425
1 24215: Secondary Consequence of Disease to	0.07425
D 36683: Consequence of Disease to the Commu	0.045
1 782753: Likelihood of Secondary Transmission	0.045
1 600721: Likelihood of Secondary Transmission	0.030996
1.000731. Elkelihood of Secondary Haltshission	0.03
	0.03
	0.0165
	0.00594
	0.00528
	0.00336
	0.00264
	0.00264
	0.00204
	0.00204
	0.00108
	0.00000

Are aerosolization experiments being conducted as part of this pri
What is the potential for aerosols to be generated as a byproduct
Is the infectious dose (ID50) of this agent for this route less than
Is respiratory protection used in this procedure? (surgical masks a
What is the potential and extent of a splash or spill in this procedu
Does this laboratory have procedures in place for agent handling
Are Biosafety cabinets used in this procedure?
Is all the equipment used in this procedure with a potential to gen
Are other forms of Primary Containment used in this procedure?
What is the implemented process for the decontamination of equi
What type of material will be used in this procedure? (If the proce
Are animals housed in a manner that is isolated or sealed to preve
Are animals handled in isolation to prevent aerosol escape (e.g. in
Are animals transported in a manner that prevents aerosol escape
Does this laboratory have animal handling procedures in place to
How many animals are in use in this procedure?
What is the typical size of these animals?
What is the greatest volume of material existing at one time in the
Are there more than one species of animal in use in the laboratory
Are animals which have the potential to shed infectious particles
How much waste do the laboratory animals used in this procedure
Does the institution have defined roles and responsibilities for bio
Has the institution made a commitment to safety?
Does the institution periodically review the biosafety program?
Are there procedures in place for preventative equipment mainter
Does the institution have comprehensive biosafety documentatio
Does the institution conduct biosafety drills or exercises?
Are there standard operating procedures in place for unexpected
Does this laboratory implement standard good laboratory practice
Is there a formal personal protective equipment (PPE) program in
Is there a shipping and receiving program in place at this laborate
Are all biological agents in this laboratory inventoried?

Is this agent known to cause infection via inhalation in humans

Question



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







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!!!

Reynolds M Salerno, PhD Sandia National Laboratories Albuquerque, NM, USA

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BRM Supplements Traditional Controls

Risk Mitigation Measures:		Addresses the Area of:		
	GMP	Biosecurity	Biosafety	
Restricted access	x	х	x	
Segregation of production areas	x	х	х	
HEPA filtration system in the facility ~ 20 ACH	x		x	
Validate process, systems, equipment & facilities	x	х	x	
Equipment must be inspected periodically	x	х	x	
Easy cleaning/decon	x		x	
Liquid/Solid waste disposal		х	x	
Mandatory PPE (face shields, gloves, Tyvek suits etc)	x		x	
Mandatory trainings, periodical health check-ups, physicals and vaccination		х	х	
Documentation, double signatures, etc	х	Х	х	
Written policies and procedures	х	Х	х	
Job Certifications, work areas, security level of access	x	Х	x	
Annual performance checks of policies and procedures		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 28