National Emerging Infectious Diseases Laboratories (NEIDL) Risk Assessment

Boston Public Meeting

October 5, 2010

Presentation Outline

- Risk Assessment Overview
- NEIDL Risk Assessment
- Methodology and preliminary results
  - Centrifuge Release Example
  - Earthquake Event Example
- Site Differences
- Summary

What is Risk Assessment?

- Risk is “the chance of harmful effects occurring to human health or to ecological systems”
- Risk Assessment is the process used “to characterize the nature and magnitude of health risks to humans and to ecological systems”

Purpose of NEIDL Risk Assessment

- Estimate the human health risks of a potential loss of biological containment
- Determine if the risks would be different if the facility were sited in an area with a lower population density

NEIDL Risk Assessment

- Questions
  - What could go wrong?
  - What are the probabilities?
  - What would be the consequences?
- Approach
  - Review facility design and protocols
  - Review high-containment lab experience
  - Event-based risk assessment

Facility Design Features

- Steel-reinforced concrete building
- Buffer zone between building and street
- Redundancy in power supply and ventilation blowers
- Vent air from low to high potential contamination

	BSL-3	BSL-4
Construction	Building design	Box within a box concept
Space (Total 192,000 sq ft)	24,960 (13%)	30,720 (16%)
HEPA-filtered discharge	Single	Double

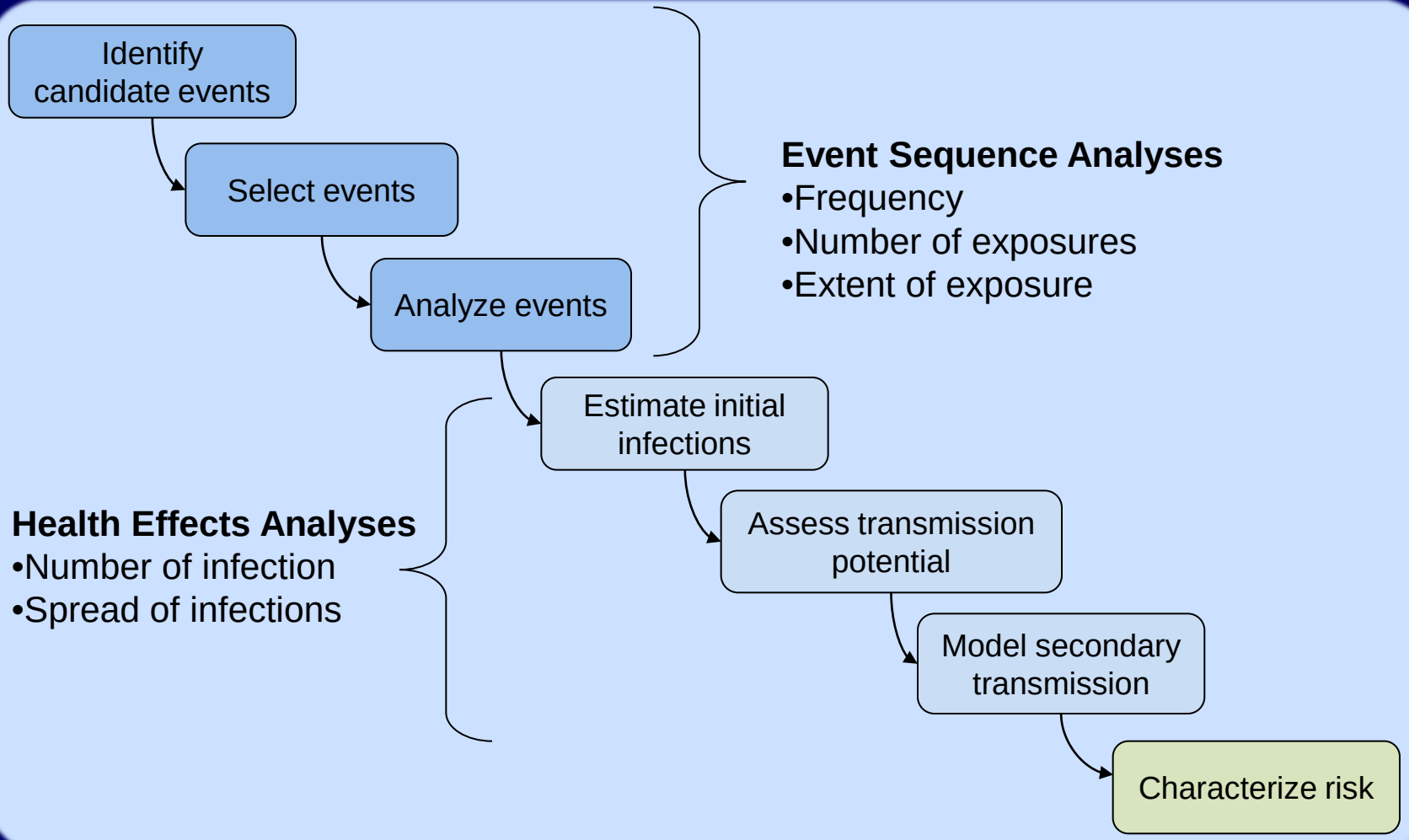
Safety Equipment and Protocols

- Safety equipment
  - Break-resistant lab-ware
  - Bio-safety cabinets
  - Personal protective equipment
- Laboratory practices and techniques
  - Worker training and oversight
  - Operating procedures

High-Containment Lab Experience

- Sources of data
  - Extensive literature review
  - Data from NIH
  - Johnson bio-safety report
- Updated Johnson report findings
  - BSL-3 labs: 2,788,500 worker hours
    - 5 infections in lab workers: one with symptoms
    - No spread to public
  - BSL-4 labs: 692,378 worker hours
    - 0 infections

Event-Based NEIDL Risk Assessment



Routes of Exposure

- Direct
  - Contact
  - Ingestion
  - Sharps/punctures
  - **Inhalation**
- Via animals or arthropods

List of 13 Pathogens

- BSL-3
  - 1918 pandemic influenza virus
  - *Yersinia pestis*
  - *Francisella tularensis*
  - *Bacillus anthracis*
  - **SARS-associated coronavirus**
  - **Rift Valley fever virus**
- BSL-3 or 4
  - Andes hantavirus
- BSL-4
  - Junin haemorrhagic fever virus
  - Tick-borne encephalitis complex (Russian spring-summer encephalitis) virus
  - Lassa fever virus
  - Marburg virus
  - Ebola virus
  - Nipah virus

Example for today: SARS-CoV

- Highly transmissible virus
- High fatality rates
- Real world experience
  - Outbreaks occurred around the world
  - Data available from outbreaks
  - Control strategies known to be effective

What could go wrong? List of potential events

Operational events – inhalation ■ **Centrifuge release** ■ Dropped container ■ Aerosol chamber leak	**Operational events – puncture** ■ **Needle-stick** ■ Broken equipment ■ Scalpel
Natural phenomena ■ **Earthquake** ■ Hurricane ■ Tornado	**Animal-related** ■ **Escaped animal** ■ Bite ■ Airborne release
Other NEIDL areas ■ **Loading dock** ■ Other labs	**Transportation** ■ **Truck delivery from CDC** ■ Truck delivery from airport

Example for today: Centrifuge Related Events

- Selection criteria
  - Common occurrence
  - Relevant for all organisms
  - Potential
    - High level of airborne release
    - To be undetected or unreported
    - For infection in lab workers to spread to public (dependent on event and organism)

NEIDL Procedures Require

BSL-3 respiratory protection

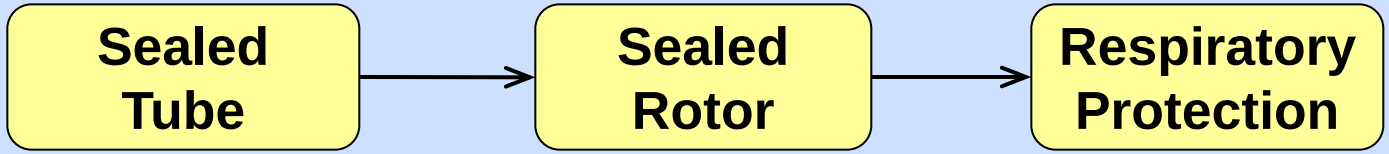
Break-resistant tubes

Sealed centrifuge rotors

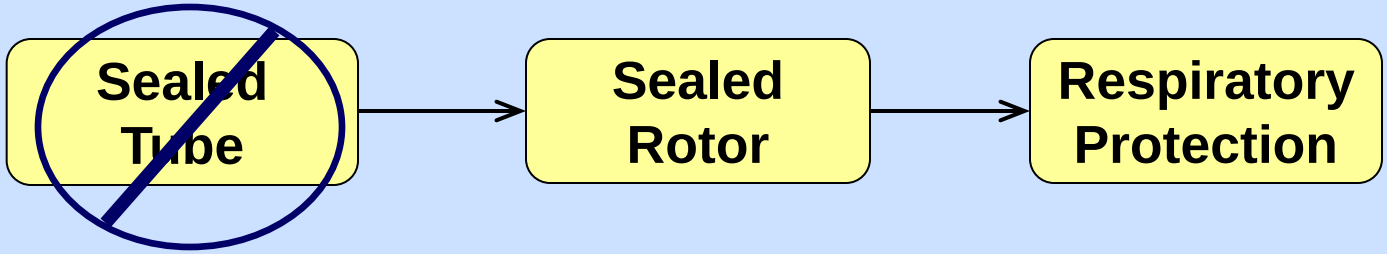
BSL-4 respiratory protection

Centrifuge Operations With No Release

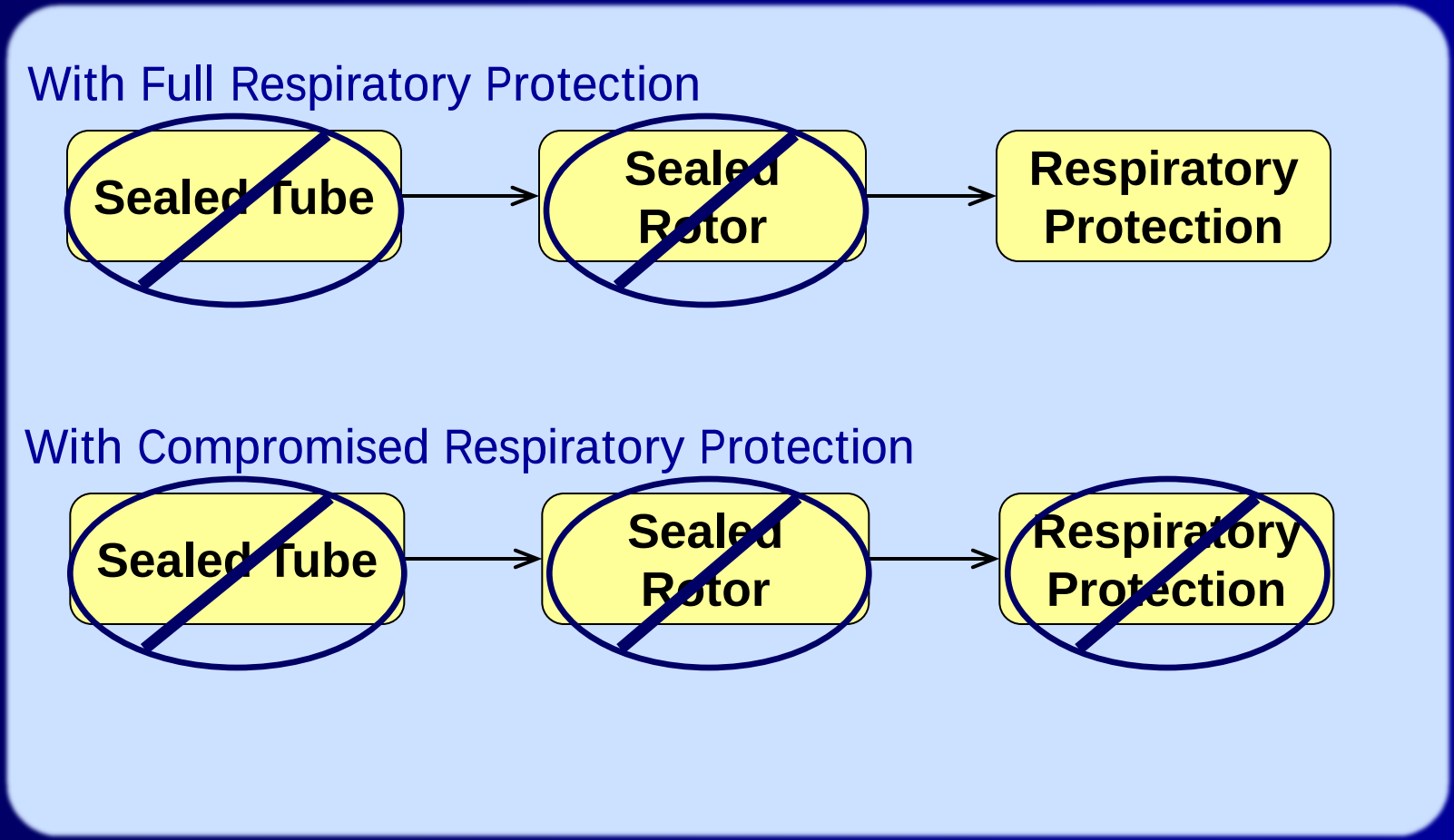
Normal Operations



Tube Leak With No Release

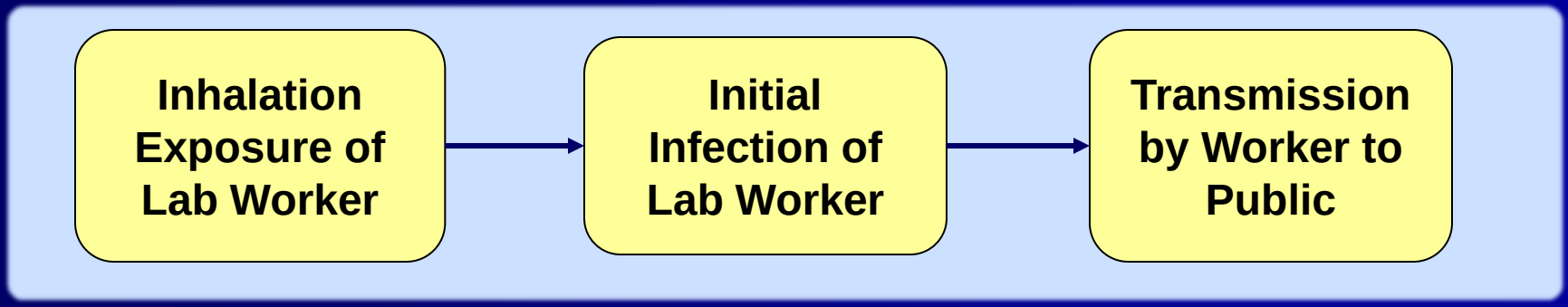


Centrifuge Operations With Release



Centrifuge Release Event / SARS-CoV: Risk to the Public

- Exposure: Contact with an organism
- Infection: Establishment of an organism on or within a person
- Transmission: Spread of infection directly from one person to another



Centrifuge Release Event/SARS-CoV: Potential Exposure to Lab Workers

Respiratory Protection	Frequency Category	Lab Workers Potentially Exposed	Predicted Exposure to SARS-CoV
Full	High (1 to 100 years)	2 to 4	None
Compromised	Moderate (100 to 10,000 years)	1	0-10 organisms

Preliminary results

Estimating Initial Infection Rates

- Not every exposure leads to infection
- Primary factors involved
  - Number of people exposed
  - Amount of exposure per person (more makes infection more likely)
  - Condition of exposed person
  - Infectiousness of the organism

Estimating Initial Infections

- Key question: what is the probability of an exposure causing infection?
- Obtained expert opinion to supplement data
- Used modified Delphi method
  - A reliable, formal, commonly used approach
  - 8 experts in bio-defense and microbiology participated
  - All reviewed the scientific literature
  - All provided their best estimates

Addressing Uncertainty

- Uncertainty always exists about values needed to predict infections
- Use mathematical procedures to include impact of uncertainty on our estimates
- Procedures look at ranges in considering variation in all combinations of values
- Results show how confident one is of an estimate

Centrifuge Release/SARS-CoV: Risk Category for Lab Worker Infection

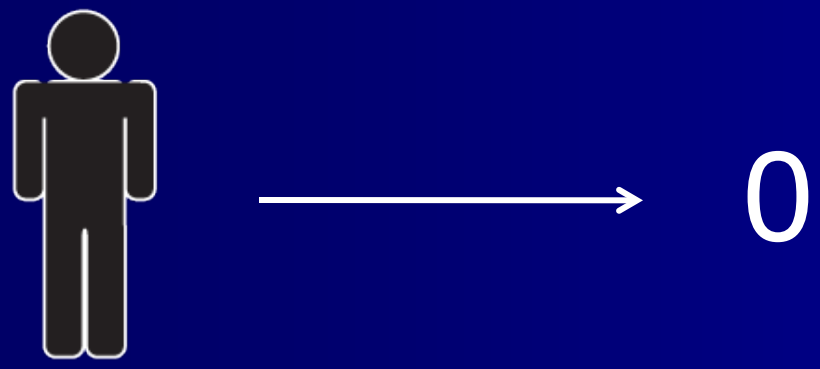
	# of Lab Workers Infected	**High** (1 to 100 yrs)	**Moderate** (100 to 10,000 yrs)	**Low** (10,000 to 1,000, 000 yrs)	**Beyond Reasonably Foreseeable** (>1 million yrs)
Centrifuge release with full respiratory protection	1 or more	-	-	-	**100%**
Centrifuge release with compromised respiratory protection	1 or more	-	-	23%	**77%**
	2 or more	-	-	-	**100%**

Preliminary results

Modeling Transmission in the Public

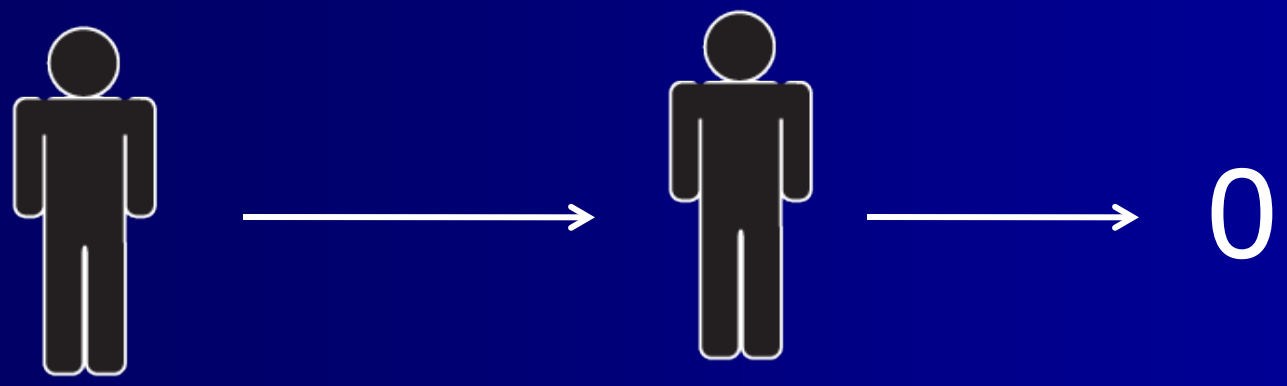
- Occurs when a person with an initial infection spreads it to others
- Use Branching Process Modeling
  - Well developed literature in epidemiology
  - Considers the average number of times a typical person transmits infection
  - Accounts for individual differences in transmission rates
  - Performs large number of trial runs (simulations) to capture variability in outcomes

Branching Process Modeling



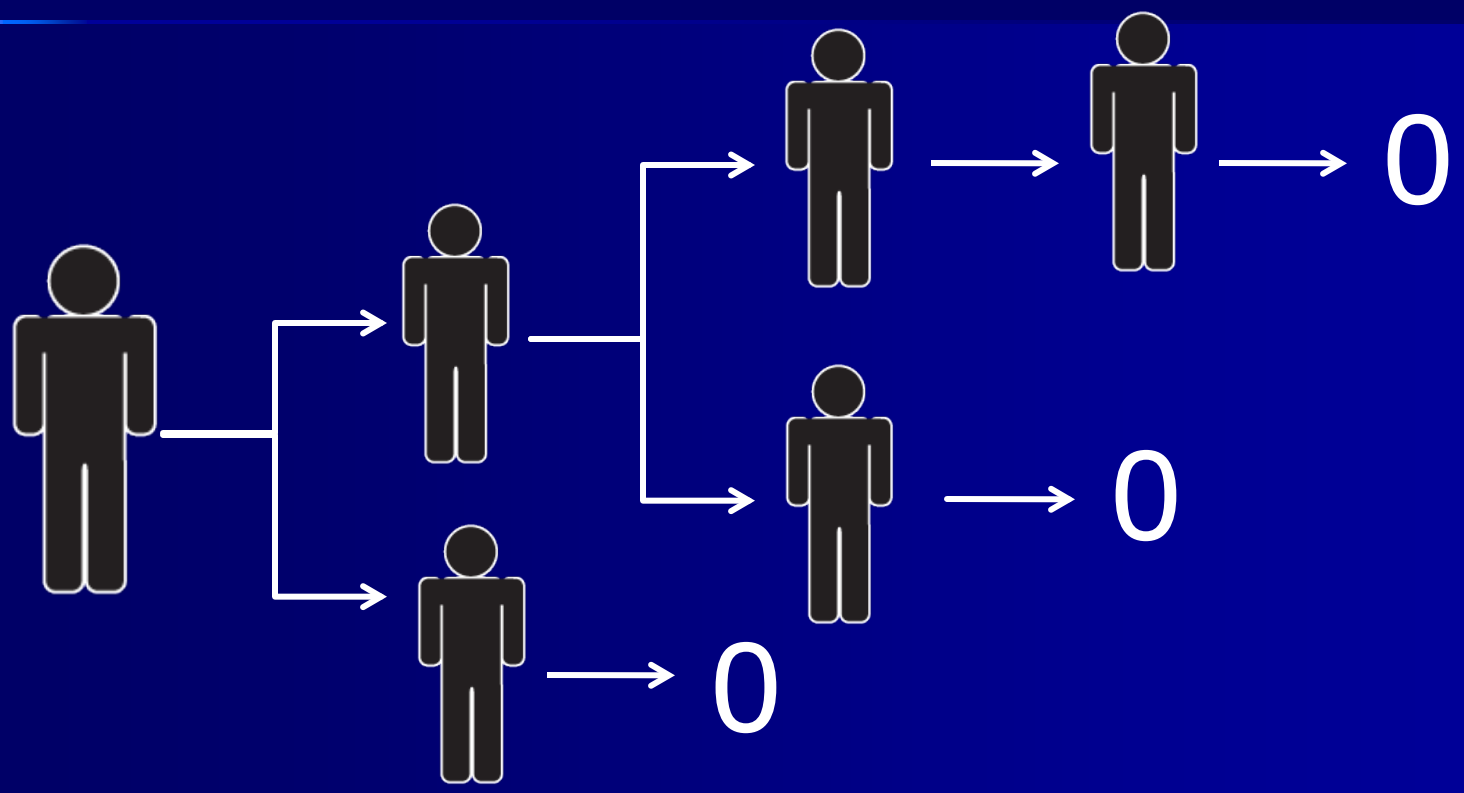
Many simulations result in no transmissions to others

Branching Process Modeling
Single Transmission



Some simulations result in one secondary transmission

Branching Process Modeling
Multiple Transmissions



Some simulations result in multiple secondary transmissions

Centrifuge Release/SARS-CoV: Risk Category for Public Infection

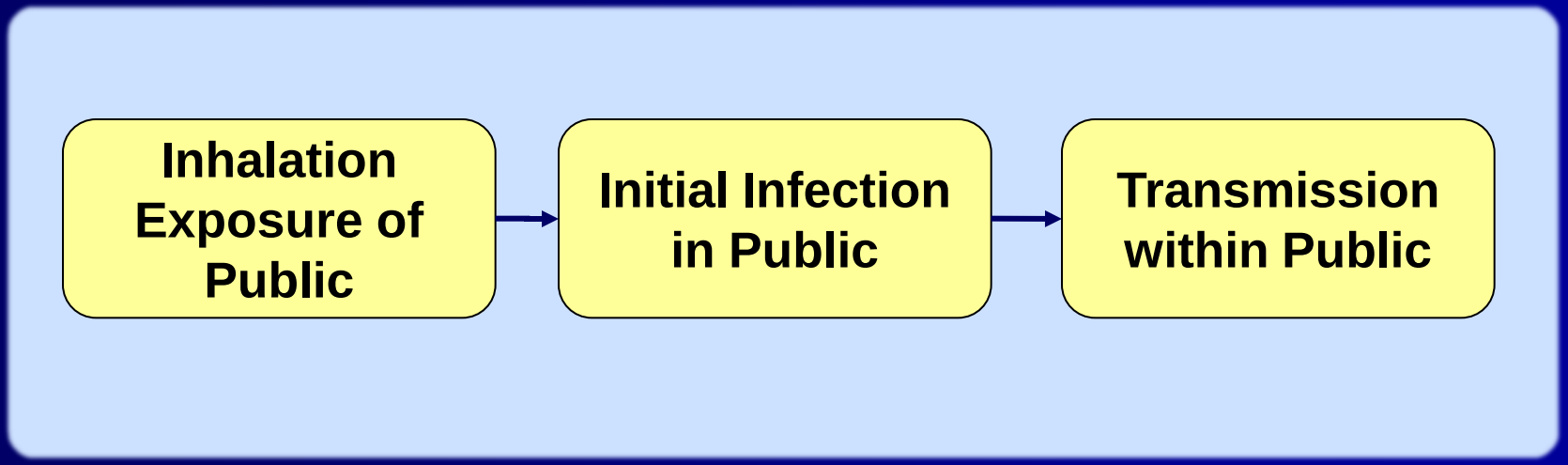
	# of public Infections	High (1 to 100 yrs)	Moderate (100 to 10,000 yrs)	Low (10,000 to 1 million yrs)	Beyond Reasonably Foreseeable (>1 million yrs)
Centrifuge release with full respiratory protection	1 or more	-	-	-	**100%**
Centrifuge release with compromised respiratory protection	1 or more	-	-	10%	**90%**
	5 or more	-	-	5%	**95%**

Preliminary results

Earthquake: Maximum Release Event

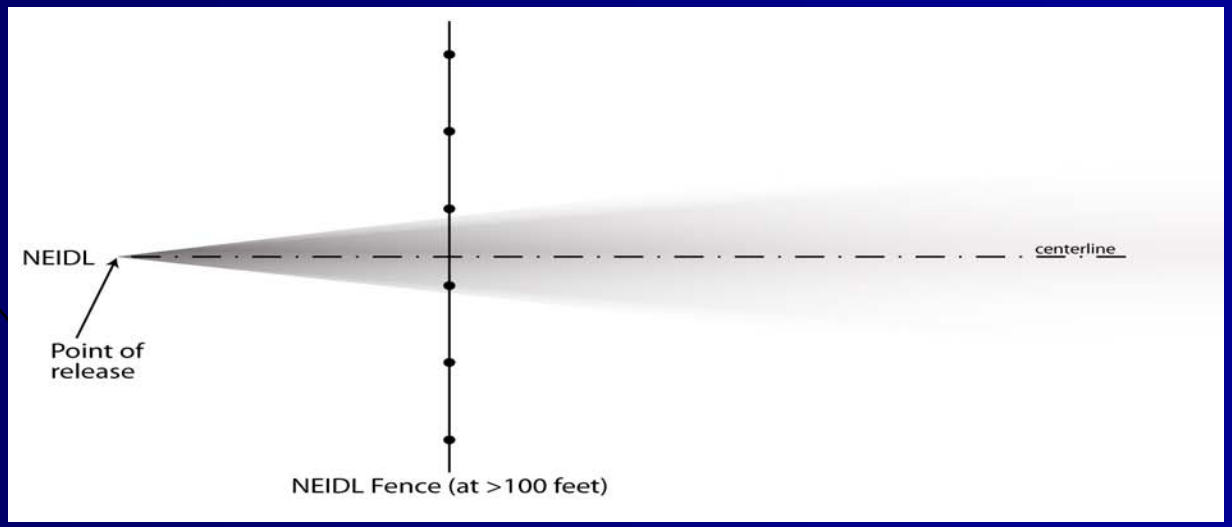
- Consider events occurring more than once in 1 million years
- Considered natural phenomena
  - Earthquake, hurricane and tornado
- Earthquake determined to be highest impact
- Catastrophic failure of the structure
  - Low frequency: once in 10,000 to 1 million yrs

Earthquake Event / SARS-CoV: Risk to the Public



Exposure After Earthquake

- Organisms are spread by wind (plume)
- Dose calculated
  - Based on ground-level release
  - At plume centerline



Earthquake Event/SARS-CoV: Potential Exposure to the Public

	Urban Boston/NEIDL (daytime)	Urban Boston/NEIDL (residents)	Suburban Tyngsborough, MA (residents)	Rural Peterborough, NH (residents)
Population within 500m (estimate)	25,000	3,000	250	15
Average # of people inhaling 1 organism of SARS-CoV	<1	<1	<1	<1

Preliminary results

Earthquake Event/SARS-CoV: Risk Category for Public Infection

- Risk category is for both initial and transmitted infections
- Results are similar for all sites

	# of public Infections from SARS-CoV	**High** (1 to 100 yrs)	**Moderate** (100 to 10,000 yrs)	**Low** (10,000 to 1 million yrs)	**Beyond Reasonably Foreseeable** (>1 million yrs)
Earthquake Event	1 or more	**-**	**-**	**-**	**100%**

Preliminary results

Earthquake Event/RVFV: Potential Exposure to the Public

- Rift Valley fever virus (RVFV) used in higher concentration than other viruses so has highest exposure potential for public

	Boston/ NEIDL Urban (daytime)	Boston/ NEIDL Urban (residents)	Suburban Tyngsborough, MA (residents)	Rural Peterborough, NH (residents)
Population within 500m (estimate)	25,000	3,000	250	15
Average # of people inhaling 1 organism of RVFV	16	2	<1	<1

Preliminary results

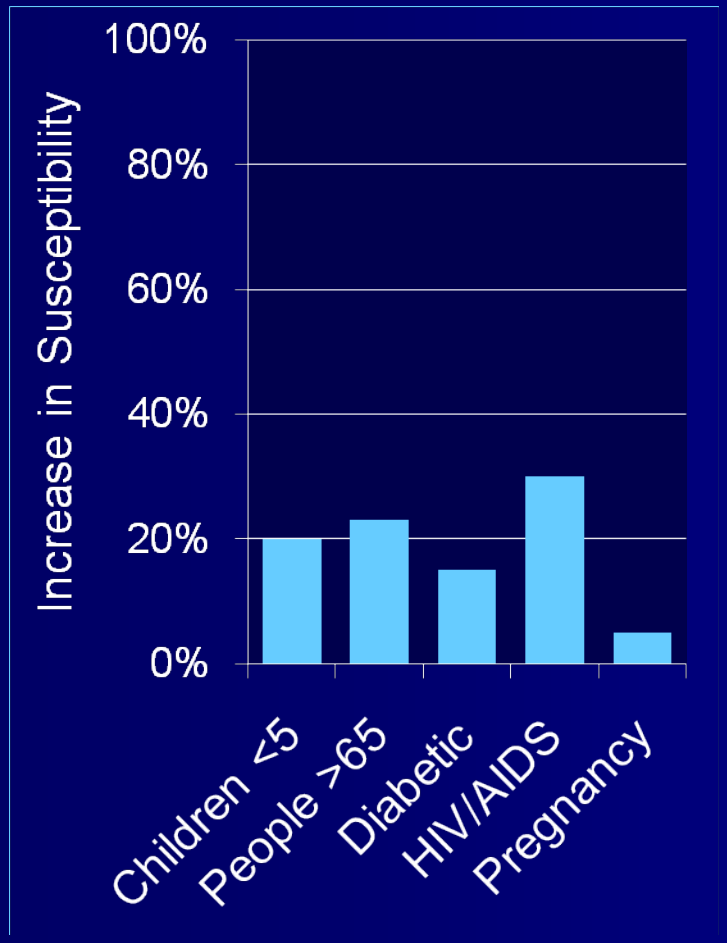
Earthquake Event/RVFV: Risk Category for Public Infection

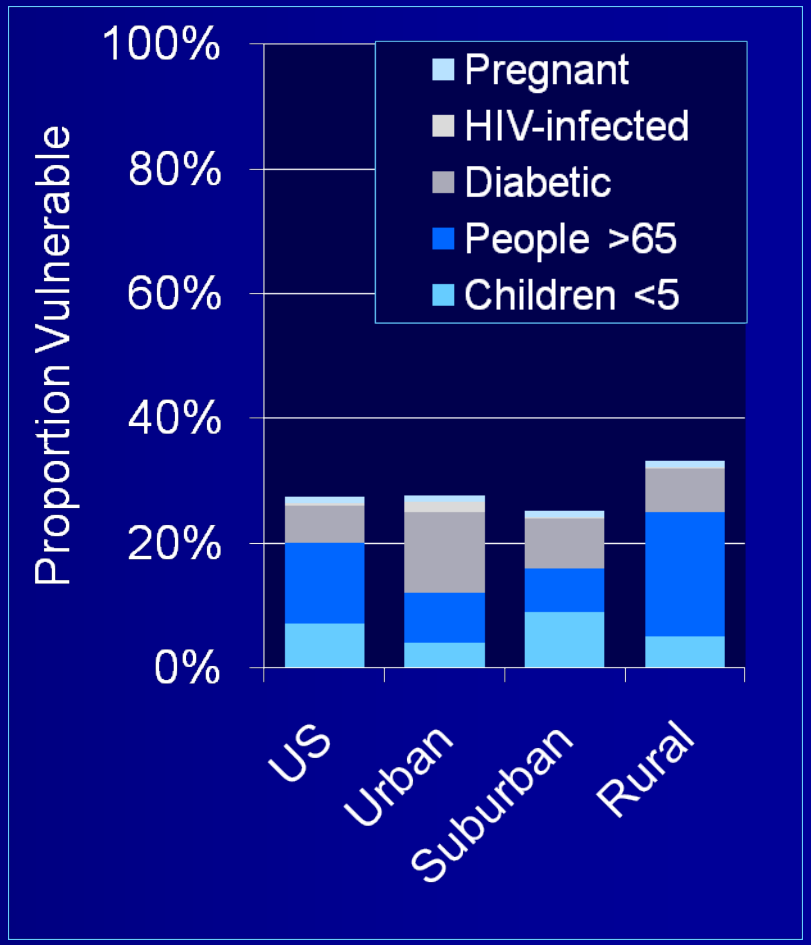
- Risk category is for both initial and transmitted infections
- Results are similar for all sites

	# of public Infections from RVFV	**High** (1 to 100 yrs)	**Moderate** (100 to 10,000 yrs)	**Low** (10,000 to 1 million yrs)	**Beyond Reasonably Foreseeable** (>1 million yrs)
Earthquake Event	1 or more	**-**	**-**	3%	**97%**

Preliminary results

Medically Vulnerable Populations





Medically Vulnerable Populations: Average Susceptibility

- Some subgroups are more susceptible to infection
  - Amount estimated from literature and expert opinion
- Site differences in proportions of persons in vulnerable groups nearly balance out
- Overall differences in average susceptibility are <1.4%
- Differences of this size will have very little effect on overall infection and spread in the community

Summary: Risk Reduction Features at NEIDL

- Biocontainment features limiting risk
  - Facility design and construction that protects facility workers and the public from exposure
  - Laboratory practices and techniques that minimize risk of release and exposure
  - Safety equipment that protects workers from exposure and infection
  - Small organism inventories that are containerized and not readily releasable

Summary:
Risk of Any Public Infections

- BSL-3 centrifuge event with SARS-CoV when respiratory protection is
  - Full = 100% BRF
  - Compromised = 90% BRF (10% Low)
- Earthquake event (urban daytime)
  - SARS-CoV = 100% BRF
  - RVFV = 97% BRF (3% Low)

BRF = Beyond Reasonably Foreseeable

Summary: Potential Site Differences

- Operational events
  - No difference in risk of lab worker infections
- Earthquake
  - Potential differences in exposures due to meteorology and population density
  - Public infections are estimated to be Beyond Reasonably Foreseeable (≥97%) for all sites
- Average susceptibility to infection
  - Overall no significant site differences expected

Ongoing Analyses

- Other events that would lead to exposure
- Remaining organisms
- Further analyses of site differences

TETRA TECH