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National Emerging Infectious Diseases Laboratories Risk Assessment

TETRA TECH

Introduction

- Frank Gallegos – Tetra Tech Project Manager
- Deputy Director Security Protective Services Group

The Tetra Tech Team

- Event Sequence Team
  - Event sequence up to exposure
- Human Health and Ecology Team
  - Pathogen biology, disease characteristics, and biocontainment
- Modeling Team
  - Initial infections and secondary transmission
- Threat Assessment Team
  - Malevolent acts

NRC Letter Report: March 19, 2010

- In general, the NRC found the proposed approaches for conducting the risk assessment suitable and well planned
- Selected Agents
  - Appropriate and comprehensive,
  - Qualitative assessment for all 13 pathogens, and
  - Quantitative analyses for five of the pathogens

NRC Letter Report: March 19, 2010 (continued)

- Modeling
  - Branching process and compartmental modeling is appropriate (include sensitivity and uncertainty analyses)
  - Use available data, well-documented judgment from experts and case studies
  - Should not attempt to push modeling further than data for the agents allow

NRC Letter Report: March 19, 2010 (continued)

- Risk Assessment Development
  - Additional personnel and subject matter experts from a variety of specialties should be used
  - Focus on vulnerable populations where transmissibility and/or susceptibility may be higher
  - Deliver a clear, accessible, and transparent Risk Assessment Report

Court and Public Concerns

- Court and Public Concerns
  - Assess the potential risk to the surrounding community from operational events
  - Assess the potential risk to the surrounding community from a “worst-case” (maximum reasonably foreseeable) scenario
  - Determine if the risks would be different in a less densely populated area

Key Questions to be Addressed by RA

1. What could go wrong?
2. What are the probabilities?
3. What would be the consequences?

Presentation Outline

- Event Sequence
  - Methodology Overview
  - Operational Event Example
  - Maximum Reasonably Foreseeable Event Example
  - Site Differences
    - Boston/NEIDL = Urban
    - Tyngsborough, MA = Suburban
    - Peterborough, NH = Rural

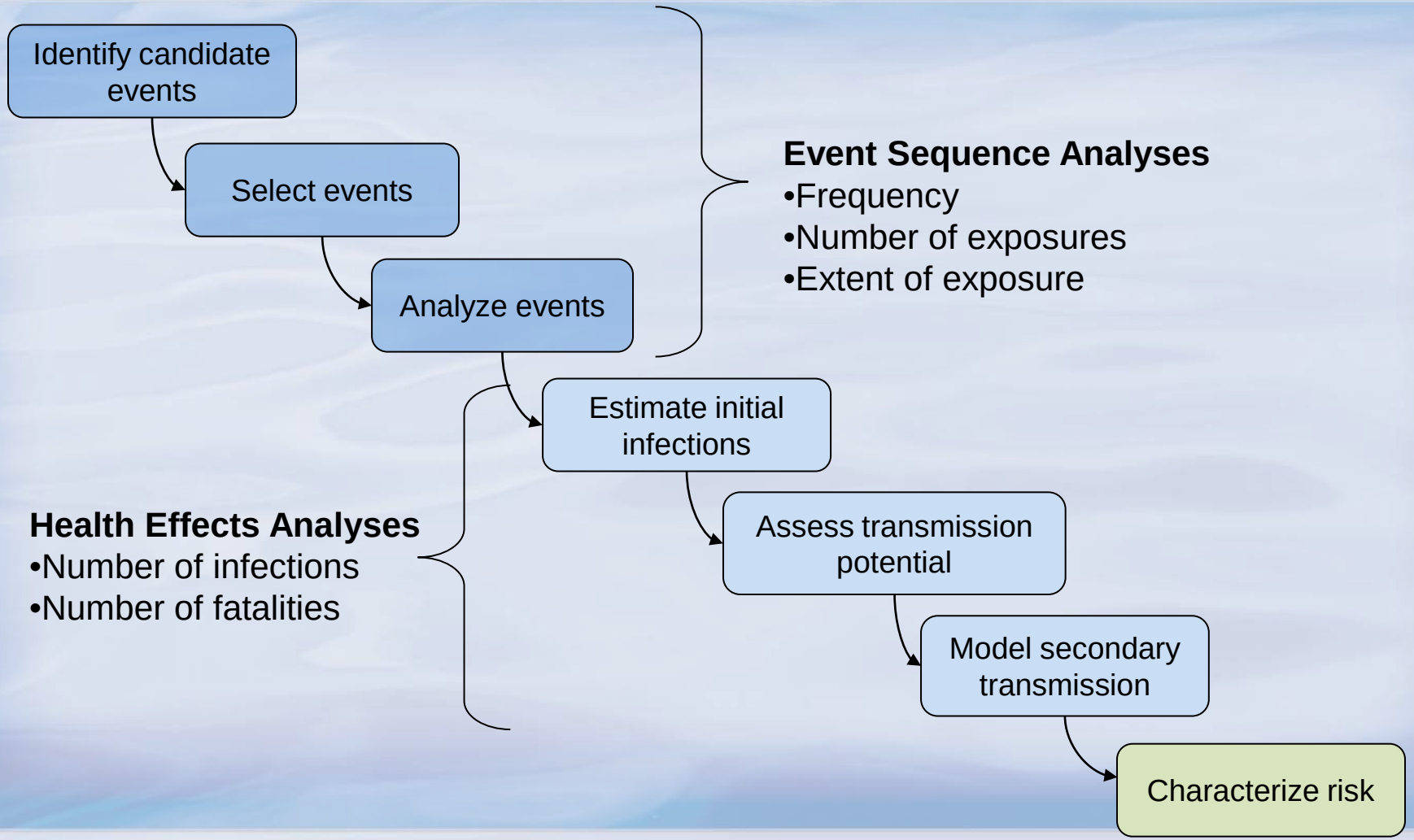
Presentation Outline (continued)

- Health Effects
  - Initial Infection
    - Rift Valley fever virus (RVFV)
    - SARS-associated coronavirus (SARS-CoV)
  - Secondary Transmission
    - SARS-CoV

Presentation Outline (continued)

- Risk Characterization
  - Presentation of frequency and Consequences for
    - Operational Events
    - Maximum Reasonably Foreseeable Event(s)
    - Site Differences

Process Overview



Event Sequence Analysis

- Ken Bulmahn, P.E.
- Event Sequence Team Lead

Event Sequence

- Approach Overview
- Operational Events
  - Addresses 1st objective: *Assess the potential risk to the surrounding community from operational events*
- Maximum Reasonably Foreseeable Event(s)
  - Addresses 2nd objective: *Assess the potential risk to the surrounding community from a maximum reasonably foreseeable scenario*

Event Sequence (continued)

- Site Differences
  - Addresses 3rd objective: *Determine if the potential risks would be different in a less densely populated area*
- Summary

Approach Overview

- Scope of Event Sequence Analyses
- Criteria for Methodology
- Guidance for Reasonably Foreseeable Event(s)
- Event Categories
- Selecting Event-Pathogen Pairs

Scope of Event Sequence Analyses

- Included initiating and subsequent events
- Concluded at the point of exposure (≥1 pathogen particle)
  - Does not include initial infections
  - Does not include secondary transmission
- Provided frequency of occurrence, number of exposures, and extent of exposure
- Input for determining the number of initial infections

Criteria for Methodology

- Uses EPA and DOE NEPA and risk assessment guidance
- Transparent and data-driven
- Accounts for data and scenario uncertainty
- Addresses probability and consequences
- Presents results in probabilistic statements
- Includes both
  - Operational events (variety of plausible scenarios)
  - Highly unlikely but credible high-consequence event(s) – maximum reasonably foreseeable

Guidance for Reasonably Foreseeable Event(s)

- Consider events predicted to occur once per one million years
- Rarely necessary to consider events that may occur less than once per ten million years

(DOE NEPA Guidance)

Note: The consequences typically reach a plateau so looking at less frequent events does not add insight.

Event Categories

- Relevant locations
  - BSL-3
  - BSL-4
  - Other internal areas
  - External areas
- Exposed groups
  - Laboratory worker
  - Facility worker
  - General public
  - Animal reservoirs and vectors
- Initial routes of exposure
  - Direct contact
  - Ingestion
  - Inhalation
  - Sharps/punctures
  - Animal and arthropod related

Frequency Categories

Category	Definition	Frequency (per facility lifetime[a])	Return Period (once per)
Routine	Expected annually	$\geq$50	$\leq$1 yr
High	Each event may occur one or more times during facility life	<50 to $\geq$0.5	>1 to $\leq$100 yrs
Moderate	An event in this category may occur once during facility life	<0.5 to $\geq 5 \times 10^{-3}$	>100 to $\leq$10,000 yrs
Low	Not expected, but possible	$< 5 \times 10^{-3}$ to $\geq 5 \times 10^{-5}$	>10,000 to $\leq$1,000,000 yrs
Beyond reasonably foreseeable	Unrealistic events	$< 5 \times 10^{-5}$	>1,000,000 yrs

[a] Major facility renovations are expected within the next 50 years, rendering a longer facility lifetime unreasonable.

Categories for Number of Workers Exposed

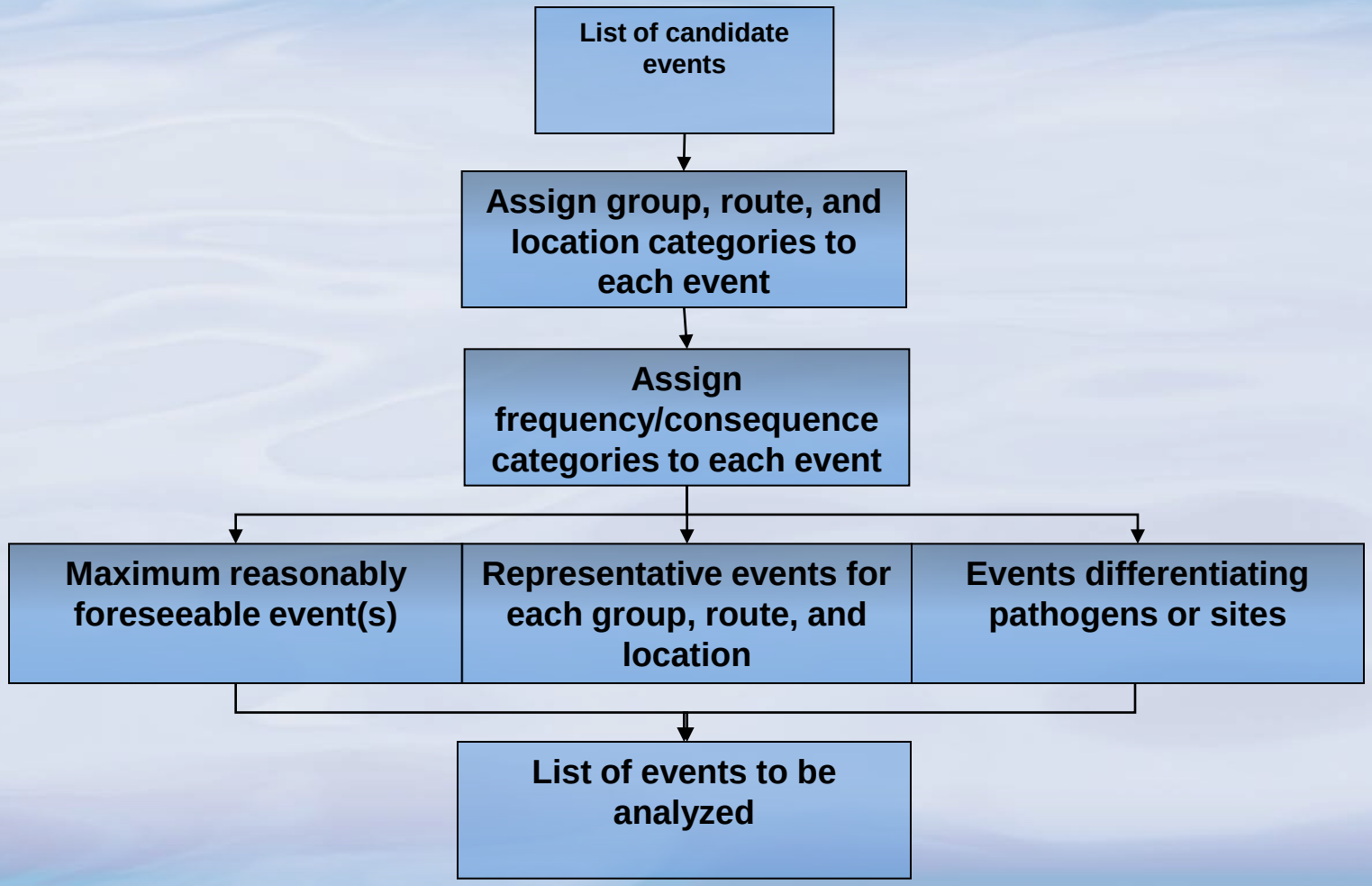
Category	Laboratory Worker (number of workers)	Facility Worker (number of workers)
None	0	0
Low	One person (1)	A few individuals on same floor (<10)
Moderate	Most individuals (2 - 4)	Most individuals on floor (≤90 BSL-3, ≤30 for BSL-4)
High	Large number (>4)	Most individuals in building (<300)

Categories for Public Exposure

- Based on radial distances from the facility to account for differences among site populations
- Nearest public access is 30 m

Category	Public (radius)
None	≤30 m
Low	>30 to ≤300 m
Moderate	>300 to ≤3,000 m
High	>3 km

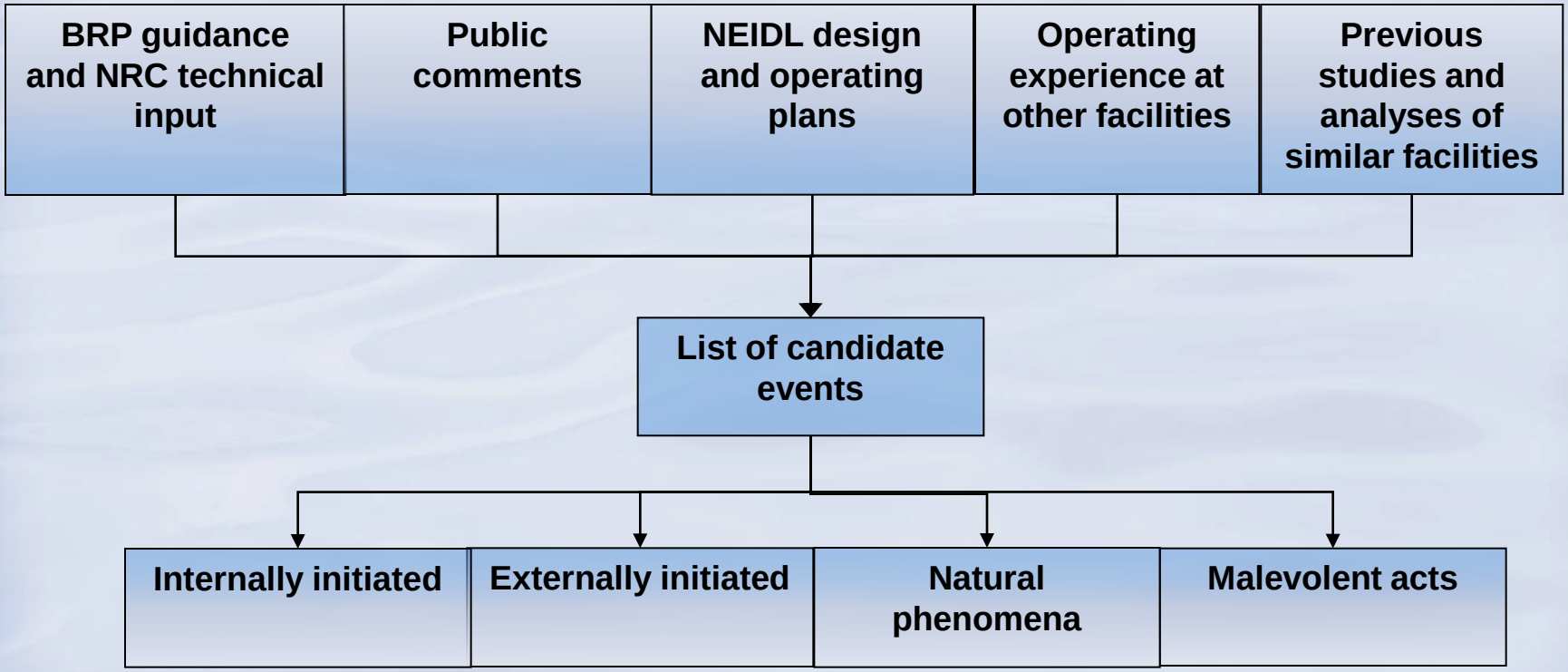
Selecting Event-Pathogen Pairs



Operational Event Example

- Identification and selection of events
- BSL-3 centrifuge incident examples
- Event description
- Analysis of event
- Results

Identification of Candidate Events



Event Selection Process

- Consolidate similar events
- Select events based on the following
  - Largest number of people exposed
  - Likelihood of being undetected or unreported
  - Precedent and interest
  - At least one for each exposed group for each route of exposure
  - Address site and pathogen differences
- Document basis for selection or dismissal

Basis for Selecting Centrifuge Aerosol Release

- Relatively high frequency
- High level of airborne release
- Potential for multiple routes of exposure
- Potential to affect all workers in the room
- Potential to be undetected or unreported
- Frequently analyzed in Environmental Impact Statements (EISs)
- Relevant for all pathogens

BSL-3 Centrifuge Incident Examples

No.	Date	Cause	Detected	Reported	People	Outcome
1	2007	Container leaked	Yes	Yes	4	No treatment or infection
2	2006	Container lid broke	Yes	Yes	1	Treatment, no infection
3	2005	Container broke	Yes	Yes	1	Evaluation, no infection
4	1994	Container leaked	Yes	No	1	Infection, successfully treated

Initiating Event – Suspension Leak

- Leak from container may be caused by
  - Human error
    - Under or over tightened container cap
  - Equipment failure
    - Faulty container cap or seal
    - Leaking container
    - Container cracks during centrifugation

Note: Use of unbreakable, aerosol-tight containers is required at NEIDL.

Contributing Event – Rotor Seal Leak

- Rotor seal leak may be caused by
  - Human error
    - Under or over tightened rotor lid
  - Equipment failure
    - Faulty lid
    - Faulty seal

Note: Rotors must have aerosol-tight seals and rotors are only opened in a biosafety cabinet (BSC) at NEIDL.

Centrifuge Aerosol Release Experiment

- Performed for both fixed angle rotor and swinging buckets
  - Fixed angle rotor produced the higher concentration
- Fixed angle centrifuge conditions
  - 10 ml of suspension pipetted into rotor
  - O-ring removed from rotor lid
  - Operated at 4,000 rpm
  - Centrifuge was stopped and door opened promptly
- Room air concentration was measured

(Bennett and Parks, Journal of Applied Microbiology, 2006)

Room Air Concentration

- Projected NEIDL room air concentration is based on the Bennett and Parks experimental results
- Differences between experiment conditions and NEIDL

	Experiment	NEIDL
Room airflow	No flow	8 air replacements/hour
Centrifuge speed	4,000 rpm	10,000 rpm

- To account for differences, maximum air concentration was increased by factor of 10

Laboratory Worker Exposure

- 2 to 4 workers in the room
- Exposure depends upon location relative to the release
- 10 minute exposure at peak concentration (average room air replacement time is ≤7.5 minutes) (NIH Design Requirements Manual)
- Based on standard breathing rate (DOE)
- Assigned protection factor (APF) of 1,000 for NEIDL PAPR (29 CFR 1910.134)

Note: BSL-3 lab workers are required to wear PAPR at NEIDL.

Frequency Category

- Event sequence consists of
  - 10 ml leak from container into rotor, but only a small fraction is aerosolized
  - Rotor seal leaks
  - Undetected or unreported release
- HIGH frequency category (frequency of 0.5 to 50 events in the facility lifetime) because
  - Event considered possible once in the facility lifetime

Results with Full PAPR Protection

Frequency Category	Exposed Group Category	Route of Exposure	Pathogen	Minimum Exposure (particles inhaled)	Maximum Exposure (particles inhaled)
HIGH (0.5 to 50 per facility lifetime)	Laboratory workers: MODERATE (2 to 4)	Inhalation	SARS-CoV	0	<1
			RVFV	0	10
	Facility worker: NONE (0)	n.a.	n.a.	n.a.	n.a.
	Public: NONE (0)	n.a.	n.a.	n.a.	n.a.

n.a. = not applicable.

Results with Degraded PAPR Protection (APF of 10)

Frequency Category	Exposed Group Category	Route of Exposure	Pathogen	Minimum Exposure (particles inhaled)	Maximum Exposure (particles inhaled)
MODERATE (0.005 to 0.5 per facility lifetime)	Laboratory workers: LOW (1)	Inhalation	SARS-CoV	0	10
			RVFV	0	1,000
	Facility worker: NONE (0)	n.a.	n.a.	n.a.	n.a.
	Public: NONE (0)	n.a.	n.a.	n.a.	n.a.

n.a. = not applicable.

Maximum Reasonably Foreseeable Event Example

- Identification and selection of events
- Guidance for earthquake analysis
- Analyses of event
- Results

Identify Candidates and Select Events

- Considered
  - Natural phenomena (earthquake, hurricane, tornado)
  - External causes (aircraft crash)
- Focused on events that can concurrently
  - Produce an aerosol release and
  - Compromise the building confinement barrier

Candidate Event Selection

- Earthquake was selected because of its potential to
  - Affect the entire facility inventory
  - Compromise all biocontainment features
  - Result in fire or no fire
  - Occur under any meteorological conditions
- Earthquake typically “bounds” other natural phenomena events (DOE-HDBK-3010)

Guidance for Accident Analyses

- NEPA Guidance (DOE)
  - Use bounding approaches
    - Streamlines analyses where uncertainties are large
    - More defensible
    - Less likely to underestimate risks
  - Use typical meteorology

Guidance for Earthquake Analyses

- Guidance for earthquake analysis (ANSI/ANS-2.26)
  - No protection provided by systems, structures, or components
  - Release is only limited by inventory quantity, concentration, and form
  - Uses mean release factors

Airborne Release Phenomena

- Considered range of release phenomena
- Spill phenomenon was selected because
  - Most likely to occur
  - Release fractions are comparable to or greater than for other phenomena
  - Fire are anticipated to inactivate most pathogens

Airborne Release Fractions

- Release fraction is based on
  - 3 m spill to account for forces involved
  - Median release factors for aqueous solution
  - Debris results in 90% reduction in release

(DOE-HDBK-3010)

Airborne Dispersion Model

- Modeled as a ground level release
  - Actual elevation would be several stories above ground
  - Concentrations from a ground-level release are greater than from an elevated release
  - This is a conservative assumption

Airborne Dispersion Calculation

- Dispersion was calculated
  - Using code approved and widely used for such purposes (MACCS2)
  - Based on 1 year of hourly data for each site
  - Adverse wind conditions were selected independent of direction

Exposure Calculations

- Based on standard breathing rate (DOE)
- Based on plume centerline (point of highest concentration)
- Assumes exposure for duration of plume transit
- Does not include biological inactivation or decay
- Maximally exposed individual (MEI) exposure
  - 100 m downwind
- Population exposure
  - People in a 22.5^{o} sector

Frequency

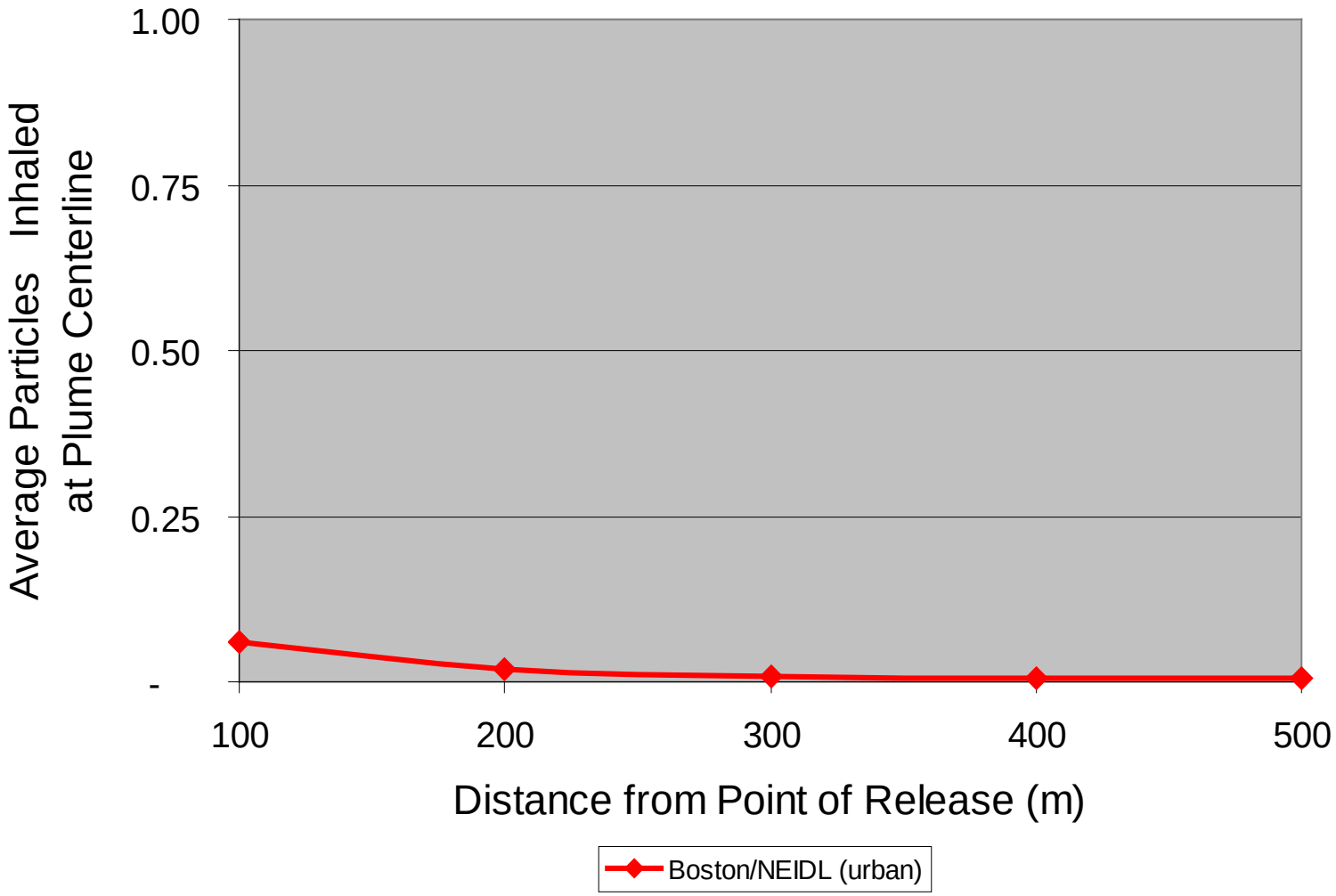
- All sites are in a relatively low earthquake hazard area (USGS)
- Mean seismic failure rate for buildings designed to International Building Code (IBC) is $<1x10^{-3}$/yr (ANSI/ANS-2.26)
- Safety factors incorporated into the design that minimize the potential for catastrophic failure
- Catastrophic failure event assigned to the LOW frequency category (return period of 10,000 to 1,000,000 years)

Note: NEIDL design meets or exceeds applicable Massachusetts design criteria.

MEI Exposure Results

Frequency Category	Exposed Group Category	Route of Exposure	Pathogen	Average Exposure (particles inhaled)
LOW (return period of 10,000 to 1,000,000 years)	LOW (≤300 m)	Inhalation	SARS-CoV	<1
			RVFV	<1

Exposure in Boston/NEIDL for Earthquake-Initiated RVFV Release



Consideration of Results

- This is a bounding analysis with considerable conservatism (i.e., overestimate of risk)
- Expected to result in less than 1 inhaled particle for the MEI for all pathogens
- Public risk resulting from damage to other buildings in the area may far exceed the risk due to the potential release of pathogens from NEIDL

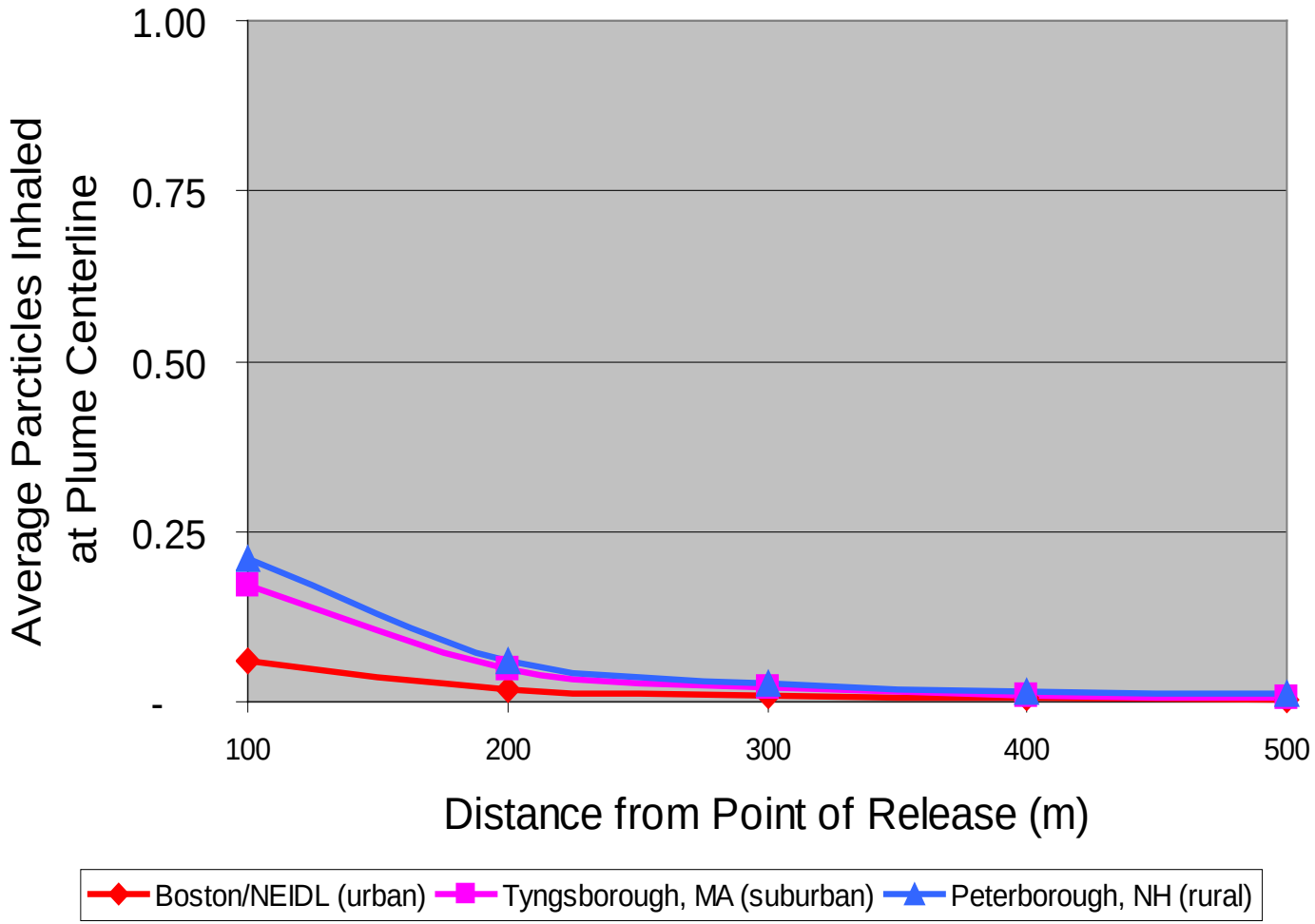
Site Differences

- Meteorology
- Population
- Number of anticipated exposures

Meteorology

- Used 1 year of hourly site-specific data
- Airborne concentrations at the suburban and rural sites are about 2 to 4 times greater than the concentrations at the urban site
- Lower concentration at the urban site results from additional air-mixing due to buildings

Exposure at 3 Sites for Earthquake-Initiated RVFV Release



Population Exposure

- Determined resident population for all 3 sites based on most recent U.S. census data
- Because of large influx, also determined daytime population for the urban site

	Urban (daytime population)	Urban (residents)	Suburban (residents)	Rural (residents)
People within 0.5 km	25,333	2,904	225	12
People inhaling 1 particle (RVFV)	16	2	<1	<1

Summary – Operational Events

- BSL-3 centrifuge aerosol release event with PAPR
  - Exposure is in the HIGH frequency category (0.5 to 50 per facility lifetime)
  - Laboratory worker exposure is predicted to be
    - <1 particle for SARS-CoV
    - 0 to 10 particles for RVFV
  - No facility worker or public exposures expected

Summary – Operational Events (continued)

- BSL-3 centrifuge aerosol release event with degraded PAPR
  - Exposure is in the MODERATE frequency category (0.005 to 0.5 per facility lifetime)
  - Laboratory worker exposure is predicted to be
    - 0 to 10 particles for SARS-CoV
    - 0 to 1,000 particle for RVFV
  - No facility worker or public exposures expected

Summary – Maximum Reasonably Foreseeable Event

- Earthquake is considered the highest impact event
- Catastrophic failure of the structure is in the LOW frequency category (once in 10,000 to 1,000,000 years)
- Based on a conservative analysis, the average MEI exposure is <1 particle for all pathogens

Summary – Site Differences

- Airborne pathogen concentrations would be approximately 2 to 4 times greater at the suburban and rural sites than at the urban site
- Roughly an order of magnitude decrease in population density between
  - Urban daytime
  - Urban resident
  - Suburban resident
  - Rural resident

Summary – Site Differences (continued)

- Number of people exposed to 1 particle of RVFV

Urban daytime	16
Urban resident	2
Suburban resident	<1
Rural resident	<1

- There are differences among the sites but the exposures are low at all sites