Appendix 12

BUMC/NEIDL RISK ASSESSMENT

SEPTEMBER, 2005

BUMC/NEIDL
Risk Assessment

For the

National Institutes of Health
Division of Occupational Health and Safety
Bethesda, Maryland

Prepared by **CDIC, Inc.**

Consultants in Disease and Injury Control
Atlanta, Georgia USA

September 2005

Table of Contents

Section	Topic	Page No.
1	**Executive Summary**	1
2	**Introduction**	
	2.1 Scope	2
	2.2 Anthrax	3
3	**Methods, Assumptions, Analytical Framework**	
	3.1 Materials Reviewed	5
	3.2 Dispersion of Spores	5
	3.3 Weight of Evidence (WoE)	7
	3.4 Assumptions in Building the Risk Assessment Model	9
	3.5 The Quantitative Risk Assessment Model	12
	3.6 Scenarios	13
4	**Qualitative Risk Assessment**	
	4.1. Overview	18
	4.2 Escape of an Infected Animal	18
	4.3 Release of Biological Material During Shipment	19
	4.4 "Unforeseen" Emergencies	19
5	**Results**	20
6	**Discussion and Conclusions**	
	6.1 Quantitative Outcomes of Risk Scenarios	26
	6.2 Lessons from the MPR Model	30
7	**Bibliography**	32

Tables and Figures

	Title	Page No.
Figure 1	Laboratory Apparatus in the Biological Safety Cabinet.	6
Figure 2	Windspeed and Cone Angle	12
Figure 3	Dispersion of Spores If Released in a Lab Spill	20
Table 1	Comparative Hazard Rankings of *B. anthracis* Preparations	8
Table 2	Relative Hazard Potential Determined in Laboratory Tests for Various *B. subtilis* (anthrax surrogate) Preparations	9
Table 3	Target Exposure Points	21
Table 4	MPR Model Calculation - Number of spores in a release plume at the closest PEDESTRIAN WALKWAY, 300 feet from Release Point	21
Table 5	MPR Model Calculation - Number of spores in a release plume at the closest BUILDING ON E. BROOKLINE ST, 290 feet from Release Point	22
Table 6	MPR Model Calculation - Number of spores in a release plume at the GUARDHOUSE, 300 feet from Release Point	22
Table 7	MPR Model Calculation - Number of spores in a release plume at the FLOWER EXCHANGE BUILDING, 360 feet from Release Point	23
Table 8	MPR Model Calculation - Number of spores in a release plume at the closest BUILDING on E. CANTON ST, 400 feet from Release Point	23
Table 9	Scenarios Spreadsheet, at Closest Target – 290 feet	24

Section

1 Executive Summary

The "maximum possible risk" (MPR) model is used to assess risk of release of pathogens from the proposed biosafety level 4 (BSL-4) bio-containment laboratory at Boston University Medical Center, National Emerging Infectious Diseases Laboratory (BUMC/NEIDL). The MPR model considers reasonably foreseeable errors of behavior, including human performance and mechanical system failure. At each possible risk-defining point through a release event, the worst-case possibility is used for the analysis. The intent is an over-statement of risks, to assure a safety-margin in precautions and strategies for risk control.

Prior work at the National Institutes of Health (NIH) for similar BSL-4 facilities established that the worst-case event within the scope of human error and mechanical failure is the release of anthrax spores to the environment, because unlike most viruses and bacteria, these spores can withstand the conditions of release and survive for long periods outside a laboratory or animal host. Also, these spores are considered the highest classification of bio-terrorism agent (Category A Select Agent) in the U.S. The Centers for Disease Control and Prevention (CDC) has determined that, second to smallpox (which is restricted in its possession and use by international agreements), anthrax poses the greatest real and perceived public health risk if used as a weapon, or through accidental release.

Accordingly, the maximum possible risk model used to evaluate the BUMC/NEIDL is consideration of an aerosol release of anthrax spores in the respirable particle size range.

The risk assessment model ensures a comprehensive analysis while taking into account unique factors of this particular laboratory, including its urban location. Various scenarios illustrating filtration failure, human error, breaches of security, and ambient wind speed and direction are evaluated.

A quantitative dispersion model is applied, which captures the likelihood of human exposure to a potentially pathogenic dose of *Bacillus anthracis* spores at various neighborhood points near the laboratory. Tabular and schematic results of this quantitative analysis are reported herein.

The risk assessment demonstrates that the BUMC/NEIDL design and operations plan will be sufficient to prevent harm to the public from release of infectious agents from the facility under conditions described in the scenarios presented. Anthrax spores were used as the worst-case modeling agent. By extension, since other agents represent lower risk of a biological release/hazardous exposure, building and operating the BSL-4 facility will not cause an appreciable addition of risk of harm to the public health.

Section 2 Introduction

2.1 Scope

A commonly used risk assessment model developed by the U.S. Military is based on a concept of "maximum credible event" or MCE (DOD, 1993). For the BUMC/NEIDL Risk Assessment, a more cautious approach of "maximum possible risk" (MPR) is used. This approach bypasses the issue of what is credible and what is not. The more extreme scenarios modeled here are *not* credible; they are barely conceivable, but "barely conceivable" is consistent with the environment of risk assessment since the attack of 9/11/01 in the U.S.

According to the classical definition of risk, the risk of a potentially harmful event incorporates the probability of the event and how great the impact (loss or cost) of that event would be if it does occur. Mathematically, the risk of a potentially harmful event is the product of probability and impact:

Risk (public health harm) = Probability (harmful spore release) * Impact

The total risk of an action (or inaction) is the sum of the risk of the different potentially harmful events that might follow the action.

For example, not carrying an umbrella on a day with ten percent chance of rain is not considered unreasonably risky because the impact of getting wet is not too severe. Conversely, the general lack of protection against meteorites is justified because the probability of being hit by a meteorite is quite low, even though the impact might be quite severe. For the rain example, the risk is low because he impact is low; for the meteorite, the risk is low because the probability is low.

If one or more potentially-harmful events have probability and impact that are both nonzero, the action is a risky one and it becomes necessary to weigh the level of risk against the benefits expected and the risks and benefits of alternative actions. In choosing between two actions, we must also include the product of the benefits of possible beneficial outcomes times the probability of those beneficial outcomes in the sum, along with the certain financial and other costs of the actions (including risk countermeasures). This presents an additional complication of measuring benefits, financial costs, and possible harm all on a common scale, which makes risk-benefit analysis far more complex than simple risk analysis.

On the other hand, if the action (in this case, building and operating the BUMC/NEIDL) includes sufficient countermeasures to reduce the probability and/or the impact of each potentially harmful event to zero, there is no need to attempt the extremely questionable exercise of

establishing an "acceptable" level of risk -- in effect, the acceptable level can be considered to be zero.

Given the normal operating procedures of the lab, a worst-possible release event for quantitative risk assessment is an aerosol release of biological material through the stack due to a mishap in the laboratory.

The only harmful impact considered in this report is for a pathogenic concentration of anthrax spores reaching the surrounding community. In the absence of such a harmful spore release, there is no public health impact (loss or cost). For the purposes of this report we are relying on the most cautious published evidence, which suggests that the pathogenic level is greater than 500 spores breathed over an 8-hour period (Brachman PS, 1966).

The minimum human infectious dose of anthrax spores is not known, though sources cite between 8,000 to50,000 spores (Albrink 1959, Brachman 1980). Another source suggests that the pathogenic level is achieved from respiration of greater than 500 spores (Brachman 1966). In addition, the identity of the bacterium strain and the influence of host factors on this infectious dose are not completely understood. An MPR approach suggests use of 500 spores as a potentially dangerous level, but clearly this could include a safety margin of as much as two orders of magnitude.

An at-rest respiration rate is about 12 liters/minute for a healthy adult. To put this in perspective, a concentration of 1 spore per liter, breathed for about 40 minutes, would accumulate to 500 spores. The settling time for spores is considerably less than 40 minutes, while additional dispersion would be occurring all the time.

The concentrations presented in the MPR model assume instant saturation to various target points. In reality, there would be further dispersion, and thus further reduction of concentration.

2.2 Anthrax

Bacillus anthracis (anthrax) is a gram-positive, spore-forming bacillus that can cause acute infections in both animals and humans. It is primarily a disease of herbivores, which acquire infection after coming in contact with soil-borne spores. In spore form, the organism can persist in the environment for years; the distribution of anthrax is worldwide.

With regard to laboratory safety, there are four forms of anthrax, each entailing its own level of risk to the laboratory worker and the environment. The four forms are vegetative bacteria, naturally-occurring spores, technical powder (which is simply concentrated natural spores), and enhanced spores which constitute the bio-weapon.

Anthrax bacteria exist primarily as vegetative bacteria, living either within a host or in culture in a laboratory. Cultures are generally either liquid medium in a flask, or agar plates with bacterial colonies. In vegetative form, anthrax bacteria are typically not resistant to standard decontamination methods. The bacteria can easily be killed using chemical disinfectants (bleach, iodine, etc.) or by autoclaving. Since anthrax bacterial cultures are not prone to aerosolization,

the primary safety concerns are spills that create low-level transient aerosols or infectious droplets, or accidental self-inoculation. Liquid droplets from splashes generally do not travel far and, as stated above, can be easily decontaminated.

Under certain conditions, anthrax bacteria form spores. These spores are resistant to desiccation and chemical/heat decontamination. If released, these spores can remain airborne for some time, creating a risk of aerosol exposure. Therefore, anthrax spores are considered to be a much higher safety risk for laboratory workers than vegetative bacterial cultures of the same organism.

Anthrax spores can be "enhanced" for the purposes of biological warfare or terrorism. These spores are also called "weaponized" or "energetic." This process involves taking anthrax spores and treating them with chemical additives. These additives can reduce the effect of static charges on the spores, making them resistant to sticking or clumping. This allows the spores to remain airborne for much longer periods of time. Additives can also reduce the spore's susceptibility to UV light and disinfection. Enhanced spores represent the highest level of laboratory hazard, and the greatest potential for public health risk if released from the laboratory.

However, the BUMC/NEIDL will be doing NO bioweapons research. Accordingly, the spores considered for analysis of public health impacts are the natural spores, or technical powder. Furthermore, the highest concentration of a technical powder of surrogate anthrax spores (*B.subtilis*) that could be achieved by the NIH was 7×10^{11} per gram; thus this is used as a "worst possible case" concentration of anthrax spores for purposes of this risk assessment.

Section 3 Methods, Assumptions, Analytical Framework

3.1 Materials Reviewed

NIH provided the following materials to be reviewed:

- Civil, Landscape, Architectural, and Mechanical drawings for the BUMC/NEIDL, 70% construction documents submittal
- Supplemental Draft Environmental Impact Statement, March 2005
- CDC Emerging Infectious Diseases List
- Report Summary "Public Health Assessment of Biological Terrorism Agents"
- NIAID Bio-defense Research Agenda for CDC Category A Agents
- NIAID Bio-defense Research Agenda for CDC Category B and C Agents

Additional reference materials are listed in the Bibliography.

3.2 Dispersion of Spores

In order to better understand spore dispersion that could occur as a result of a laboratory accident or mechanical failure, NIH conducted a series of experiments designed to determine dispersion potential of *B. subtilis* spores as a surrogate for anthrax spores.

3.2.1. Static Aerosol Chamber:

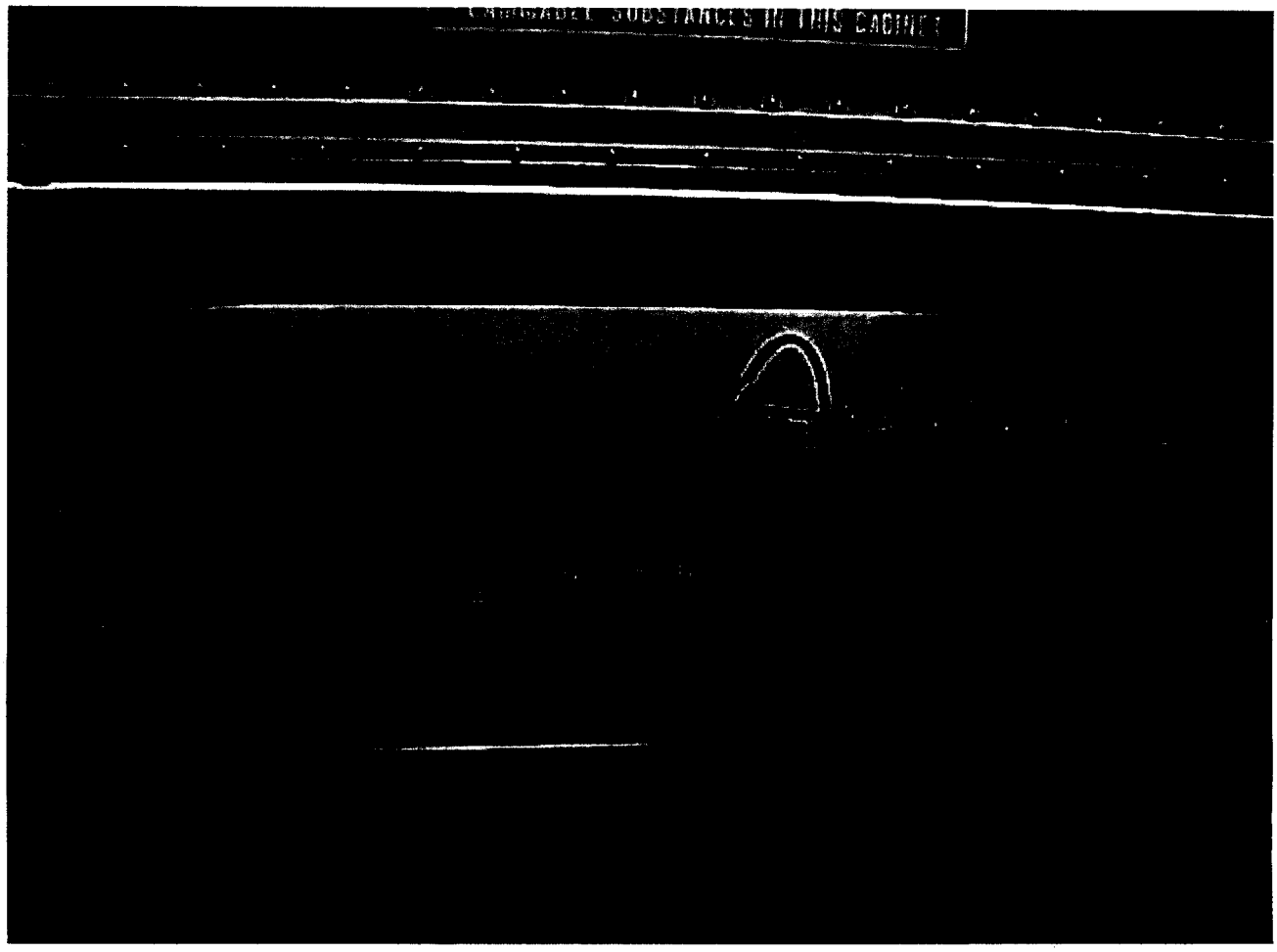
A modified Henderson apparatus (11" x 11.2" x 18") was used to model an accidental laboratory release. The chamber was oriented so that sampling ports and main hatch entry on the surface were parallel to the laboratory bench, the chamber exhaust was attached to house vacuum protected by a HEPA filter. The aerosol generator port and annular ring were sealed and not used in this set of experiments. The pressure relief port on the apparatus was also protected by a HEPA filter, to provide make up air when the chamber was placed under vacuum to clear aerosols from the chamber in between experimental runs and between releases of spore preparations. In between each accidental aerosol release experiment, the chamber was washed, decontaminated with bleach solution, and dried with an alcohol wash. The experiment was repeated 19 times.

3.2.2. Procedure for Release of Aerosols within the Chamber:

Sampling ports on either side of the main chamber hatch were used to insert the sampling probes from 2 particle counters. One counter was calibrated to count and determine the total number of

particles within the respirable range of man (0.3 – 10.0 microns). The other port was fitted with a probe sampling total particles generated. Background measurements were obtained prior to "accidental" release of the spores. A spore preparation contained in a 15 cc conical bottom Falcon tube with the cap loosened and simply sitting on the tube was held parallel to the bench and dropped into the chamber from a height of 15 inches, just at the height of the open hatch. The gasketed hatch was fitted into place as soon as the drop was accomplished. Particle counting was begun prior to the "drop" to establish background, and continued for as long as it took to stabilize at, or close to, zero particle counts after the "drop". The chamber was held static during background and test sampling. A photograph of the laboratory apparatus and set-up is depicted in Figure 1.

Figure 1. Laboratory Apparatus in the Biological Safety Cabinet.



3.2.3. Results:

The lab-based "drop studies" were used to generate data for the fraction of respirable spores which are released when a known quantity of technical powder is spilled. For a fixed-quantity

release of material, a number of trials were made, resulting in different measurements of the respirable spore count from the fixed number of total spores. That is, there was either inherent variance in the fraction of respirable spores present in a given number of total (all size) spores, or there was variance in the measurement technique. Either way, enough trials were made to establish a mean and standard deviation of the observed number of respirable spores.

Nineteen replications of the drop study were performed using technical powder in a 1.2-cubic foot space. For each replication, an upper bound for the total number of respirable spores was calculated as (respirable particles < 0.3 microns minus >10 microns). Since the size of the test chamber was 1.28 cubic feet, the total number of respirable spores was 1.28 x concentration of spores per cubic foot.

The mean upper bound based on 19 replications was 319,703 particles, with standard deviation 155,950 particles. In order to ensure a totally reliable upper bound for the number of respirable particles, six times the standard deviation ("six sigma") was added to the mean, leading to a worst-case release of 1,255,396 of respirable particles from one gram of technical powder.

Applying the MPR modeling strategy to the respirable spore issue suggests application of the quality-based "six-sigma" approach. Six-sigma corresponds to a value which is six standard deviations above the mean value. This means that the actual number of respirable spores will be less than 1,255,396 of the 700 billion total spores, 99.9999999 % of the time. In other words, there is one chance in a billion of getting this many *respirable* spores dispersed from a release of the total number of 700 billion spores; or the probability that 1.255 million respirable spores (or more) would be released is <0.000000001.

Additionally, in these experiments, 90% of respirable spores settled out of the air in the test chamber in 1 minute, and 99% in 2 minutes.

3.3 Weight of Evidence (WoE)

Measurement of probabilities is not realistic for many of the scenarios developed. While it might be possible to use historical lab-safety data to compute the probability of a spill, it is quite impossible to compute the probability of any type of deliberate attack or sabotage. Accordingly, classical loss-function modeling is not applicable.

An integrated Weight-of-Evidence (WoE) approach is used instead, which allows application of data (where these data exist), scientific literature, pathogenesis information, infective dose, and transmissibility, as well as less tangible risk information such as heightened general public awareness and concern. These factors are presented in Table 1.

TABLE 1: COMPARATIVE HAZARD RANKINGS OF *B. anthracis* PREPARATIONS

RANK CRITERIA	*ENHANCED*	*TECHNICAL POWDER*	LIQUID SPORE SUSPENSION	VEGETATIVE BACTERIA
Public Health Hazard				
Disease Morbidity				
Cutaneous	High	Moderate	Low	Low
Respiratory	High	Moderate	Low	Negligible or None
Disease Mortality				
Cutaneous	Low	Low	Low	Negligible or none
Respiratory	Moderate	Low	Low	Negligible or none
		Environmental Hazard		
Dissemination	None*	Moderate	Low	None
Transmissibility	None	None	None	None
		Other Considerations		
Potential for Large Scale Dissemination from Building	None*	None	None	None
Heightened General Public Awareness	High	High	High	Moderate

* Based on the fact that work with "enhanced anthrax spores," a bioweapon, will never be conducted at BUMC/NEIDL.

WoE methodology is a semi-quantitative method. Evidentiary data is collected from both scientific and non-scientific sources such as (a) experimental data, (b) number of experts having a particular view, (c) number of hits on a particular Internet search, (d) number of lines or minutes of news coverage, etc. These inputs are categorized and grouped in a comparable way to produce a Weight-of-Evidence scale, with values such as "++++" for extreme or much, and "++" for moderate or fair. The defining element is that some not-very-precise quantitative observation (evidence) is translated into English-language descriptions of risk which can be ranked. It does *not* mean that four pluses is twice as risky as two pluses, or that "extremely" is twice as risky as "moderately."

Considering the magnitude of aerolized particle concentrations elucidated in this series of experiments, and the time required for "settling" of the particles in the experimental chamber,

qualitative measures of relative hazard potential were assigned to each spore or bacterial preparation. These qualitative values are presented in Table 2.

Table 2. Relative Hazard Potential Determined in Laboratory Tests for Various *B. subtilis* (anthrax surrogate) Preparations

ANTHRAX (SURROGATE) PREPARATION	HAZARD POTENTIAL
Concentrated, enhanced spores	++++
Technical powder	++
Technical powder in suspension	+
Vegetative bacteria on sheep blood agar	+/-

3.4 Assumptions in Building the Risk Assessment Model

In keeping with the concept of "maximum possible risk," simplifying assumptions are made which are more unfavorable than analogous "credible" assumptions. This approach makes calculations in the model easier to understand by eliminating complex turbulence/dispersion estimations or assumptions. The purpose of the model is not accuracy; still less is it to give an "unbiased estimate" because it is virtually impossible to accurately calculate fluid dynamics outside of precisely engineered environments such as airplane wings, internal combustion engines, and oil pipelines. Instead, dispersion patterns are assumed that are certain to deliver more pathogens to a given location than any dispersion pattern that could happen in the real world. This gives extra confidence that the actual risks are less than the risks that are calculated and presented in the risk analysis.

3.4.1 Assumption that Respirable Spores do not Clump or Settle to the Ground.

Reality: NIH simulated laboratory accident release studies in still air indicated that 90% of released spores had settled in 1 minute, and 99% in 2 minutes. Outside the laboratory, wind might re-entrain spores, but grass, foliage, and other surface features would counter this by entrapping spores more efficiently than a smooth surface. Impaction and spore retention in duct work and on building surfaces also reduce the number of respirable spores released from the lab in any scenario.

Net Effect: This assumption will cause the model to overstate the hazard.

3.4.2. Assumption that Particles are Uniformly Distributed Throughout the Dispersion Pattern.

Reality: Particles may be systematically concentrated nearer the release point, leading to lower transient peak concentrations away from the stack. Turbulent eddies will produce small parcels of concentration higher or lower than the model.

When the leading edge of the plume reaches a specified distance from the release point, the concentration of particles is below what it would be under a uniform distribution. Closer to the center of the plume, the concentration reaches a maximum that is higher than what it would be under a uniform distribution.

If the wind speed is low, the region of high concentration will have dispersed to a lower concentration by the time it reaches the specified distance. If the wind speed is high, each breath taken by an exposed person will contain air from various portions of the moving plume so the effective exposure is no more than that implied by a uniform distribution.

Net Effect: This assumption may cause the model to overstate the hazard but will certainty not cause the model to understate the hazard.

3.4.3. Assumption of Cone Dispersion Geometry.

The cone dispersion pattern is a simple model of the dispersion of pathogens into the surrounding environment following a laboratory release. The MPR risk assessment model is based on a series of geometric assumptions. The basic principle is that released spores disperse uniformly inside the specified shape for the given scenario. All shapes assume that spores travel from the dispersion point on, in, or near the building directly toward the perimeter of the campus, spreading into a cone, half-cone, or sphere, before falling to the ground.

In the cone model, there is a wind that confines the pathogens to the "forward" direction. If the release point is high above the ground and there is no turbulence, the pathogens disperse in a conical pattern. At a distance from the release point depending on its height and the cone's opened angle, the pathogens encounter the ground. In a real incident, many of them would remain on the ground and pose no further inhalation threat; however, to be sure of overstating risk, we assume all pathogens are "reflected" from the ground back into the cone, leading to a concentration of pathogens twice that of the simple cone.

In the cone model, the release point is treated as if it were at ground level, the worst possible height given the assumption that no pathogens remain on the ground.

In a very light wind, pathogens would disperse broadly before they were carried far from the release point, leading to a wide opening angle and thus a low concentration of pathogens per cubic meter at a given downwind location. The pathogens would be well confined to this wide cone due to low turbulence.

In a stronger wind, the basic cone would open at a narrower angle. In the absence of turbulence, this would lead to a higher concentration of pathogens at a given downwind location. However, higher wind speed produces greater turbulence, which would blow pathogens outside the basic cone, leading to a wider equivalent opening angle and lower concentrations.

Net Effect: This assumption will cause the model to overstate the hazard.

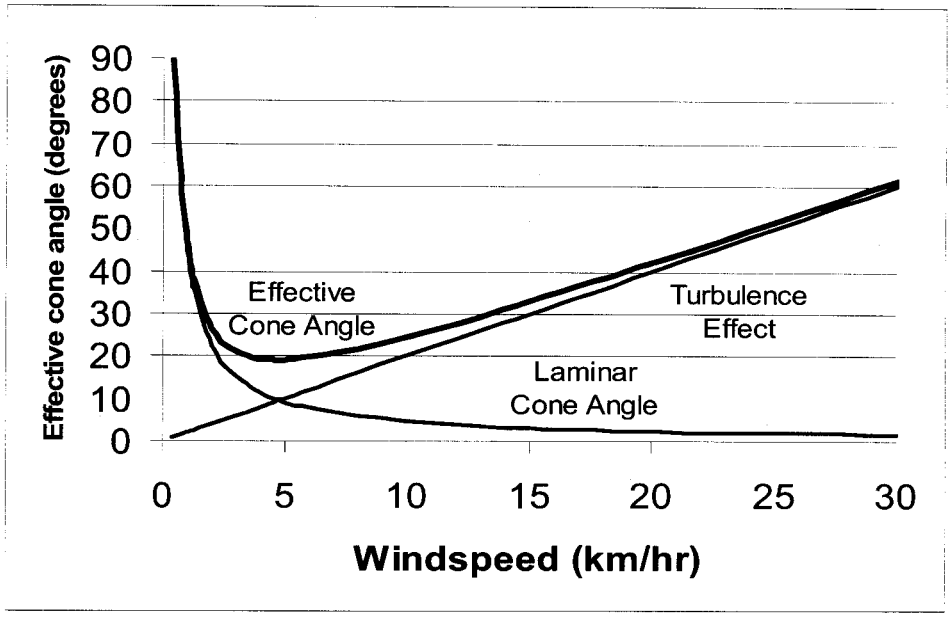
3.4.4. Assumptions of Wind Speed and Direction.

The theoretical worst-case scenario is release of spores to the environment via the normal exhaust stack. There is a matrix of possible outcomes associated with wind speeds and directions. The plume would move in accordance with the prevailing wind and gradually spread; in the absence of turbulence, the spread would be narrower in a strong wind and wider in a light wind.

A full 360-degree range of potential directions was evaluated; the worst-case dispersion spread determined by the wind speed was calculated to be 19 degrees. The worst-case direction would be toward the closest potentially-populated areas such as the parking garage, or less-proximate but more-populated areas such as buildings across Albany Street. Figure 2 shows cone opening angle as a function of wind speed. The lower curve is the turbulence-free cone angle. The effect of turbulence is conservatively estimated as a linear increase in cone angle of three degrees per kilometer per hour. Note that the actual effect of turbulence is strongly nonlinear, the rate increases as wind speed increases. The "extra" degrees of cone angle are shown by the straight line, and the upper curve is the effective cone opening angle as a function of wind speed taking turbulence into account.

A gradual expansion of the spore plume is the net effect of (a) the laminar flow in the direction of the wind and (b) turbulence which would naturally occur around the edges of the dispersion. The tradeoff between straight-line dispersion and spreading-out dispersion creates a mathematical minimum (represented by the low point in the net-effect curve on the plot) at a cone-angle of 19 degrees, which therefore represents the worst-case cone angle in terms of spore concentration in the environment.

Figure 2. Windspeed and Cone Angle



3.5. The Quantitative Risk Assessment Model

3.5.1. MPR Model Calculations

Quantitive inputs to the MPR model include the total number of spores released; number of spores in the respirable fraction (0.3 to 10 microns); the high efficiency particulate air (HEPA) filtration efficiency of 99.97% of the aerosolized particles; angle of cone, and distance to a target exposure point.

For all scenarios, the total spores per vial is 700 billion (7×10^{11}); the number of vials involved in the incident is one; the respirable fraction of spores is 1.255 million of the 700 billion total spores; the exposure "target" is taken from the architectural drawings of the site plan.

3.5.2. <u>The Basic Risk Model for Each Theoretical Scenario</u>:

a. A release point is assumed - For the spills, it is the top of the building exhaust stack. For the criminal releases, it is the drop point, such as the vials thrown off the roof (open already), or the vials dropped and breaking on the sidewalk. For the explosions, it is the center of the lab.

b. A dispersion pattern is chosen that is both simpler and more restrictive than credible, actual dispersion patterns. For all but the explosions it is a cone or half-cone emanating from the release point, as if the worst possible wind pattern is at play. For the high releases, e.g., an exhaust stack, it is a full cone; for the low ones, such as breakage on the sidewalk, it is a half cone. For the explosions, it is a sphere - dispersion in all directions (including downward into the ground).

c. Upper bounds for the total number of spores per vial and the total number of vials involved in the simulated incident are determined and input to the model.

d. The number of filtrations the "cloud" of released spores would undergo in the presented scenario is input into the model.

e. An analysis of the scenarios as they would occur in a BSL-3 laboratory is included to provide reference for the countermeasures (filtrations) employed. The main difference between the BSL-3 and BSL-4 analyses is that there is an additional HEPA filter in BSL-4 building exhaust systems.

3.6 Scenarios

SCENARIOS DEPICTING SPILLS AND WORK DISRUPTION

1. Spill in BSC. A researcher is working within a Class 2 Biological Safety Cabinet (BSC) that is ducted and located within a Biosafety Level 4 (BSL-4) laboratory. He is handling a 15 cc conical tube containing a powder-like preparation of purified anthrax containing 7 x 10^{11} spores. The cap fits loosely. *The researcher accidentally drops the tube on the bare, stainless steel surface of the properly operating BSC.* The cap comes off of the tube upon impact and a visible "cloud" of spores is released within the cabinet.

The cabinet is exhausted through a dedicated HVAC system for the BSL-4 laboratory that contains a properly seated and gasketed high efficiency particulate air (HEPA) filter. The BSC is ducted through a manifold with the other BSCs in the BSL-4 laboratories located in the laboratory building.

What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm.

2. No Filter in HVAC. A researcher is working within a Class 2 Biological Safety Cabinet (BSC) that is ducted and located within a Biosafety Level 4 (BSL-4) laboratory. He is handling a 15 cc conical tube containing a powder-like preparation of purified anthrax containing 7 x 10^{11} spores. The cap fits loosely. *The researcher accidentally drops the tube on the bare, stainless steel surface of the properly operating BSC.* The cap comes off of the tube upon impact and a visible "cloud" of spores is released within the cabinet.

The cabinet is exhausted through a dedicated HVAC system for the BSL-4 laboratory. However, *the HEPA filter was accidentally left out of the filter housing in the building HVAC system.* The BSC is ducted through a manifold with the other BSCs in the BSL-4 laboratories located in the laboratory building.

What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

3. **Spill on Floor; No HVAC Filter.** A researcher is working within a Class 2 Biological Safety Cabinet (BSC) that is ducted and located within a Biosafety Level 4 (BSL-4) laboratory. He is handling a 15 cc conical tube containing a powder-like preparation of purified anthrax containing 7 x 10^{11} spores. The cap fits loosely. *The researcher accidentally drops the tube on the floor of the BSL-4 laboratory.* The cap comes off of the tube upon impact and a visible "cloud" of spores is released within the laboratory room.

The cabinet is exhausted through a dedicated HVAC system for the BSL-4 laboratory. However, *the HEPA filter was accidentally left out of the filter housing.* The BSC is ducted through a manifold with the other BSCs in the BSL-4 laboratories located in the laboratory building.

What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

SCENARIO DEPICTING SAFETY SYSTEM FAILURE

4. Spill on Floor; Power Outage. A researcher is working within a Class 2 Biological Safety Cabinet (BSC) that is ducted and located within a Biosafety Level 4 (BSL-4) laboratory. He is handling a 15 cc conical tube containing a powder-like preparation of purified anthrax containing 7 x 10^{11} spores. The cap fits loosely. *The researcher accidentally drops the tube on the floor of the BSL-4 laboratory.* The cap comes off of the tube upon impact and a visible "cloud" of spores is released within the laboratory room. *At this exact moment, the building is struck by a major electrical outage and the HVAC system fails.*

What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm.

SCENARIOS DEPICTING PHYSICAL REMOVAL OF BIOLOGICAL MATERIAL

5. Accidental; Spill Outside on Sidewalk. *An employee removes a* 15 cc plastic conical *tube of dry anthrax spores* (clean, washed, spores dried and in powder form) from the laboratory in his pants pocket. He leaves the building through the main entrance. When he reaches the outdoors, he removes the tube from his pocket *and accidentally drops it on the sidewalk.* The cap flies off the tube and a plume of spores is released into the air.

What is the probability of public health harm?

6. Criminal Trespass and Occupation of Building. Six radical activists dressed in dark clothing and carrying weapons enter the BUMC Campus late one night by climbing over the perimeter fence. They had read information on a web site that led them to believe that a large amount of anthrax was produced and stored in BUMC/NEIDL. Their plan was to gain control of the anthrax and take hostages until the University agreed to release all the nonhuman primates

housed in its laboratories. If the University did not agree to their demands, they intended to infect the hostages with anthrax and release significant amounts to the environment.

What is the probability that the activists will be successful in entering the building and gaining control of a sufficient amount of anthrax to do harm?

SCENARIOS DEPICTING FIRE

7. Accidental; Fire in Lab. A researcher handling anthrax cultures is hurrying to finish work on a Friday afternoon. Freshly inoculated *B. anthracis* cultures on 5% sheep blood agar plates are placed in the incubator. She places a stock of anthrax spores (7×10^{11} spores in 10 mL of phosphate buffered solution in a 50 cc polypropylene tube) in the secure laboratory refrigerator. In her haste, she does not notice that a heated water bath has been left on and has no water left in it. Sometime late Saturday evening, the water bath overheats and a small fire ignites. Some small cardboard boxes are stored on a shelf above the water bath.

What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

8. Deliberate; Arson in Building. A new employee enters BUMC/NEIDL on a weekend. Unknown to the BUMC, this employee has a psychopathy presenting in remorseless destruction of life and property through fire setting. The arsonist sets a fire in a paper recycling container using a flammable laboratory chemical as a primer. The paper recycling bin is located in an alcove in the main administrative area on the first floor.

What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

SCENARIOS DEPICTING EXPLOSIONS

9. Bomb at Out Wall; Spill on Floor. An employee enters the BUMC/NEIDL carrying a backpack. *The backpack contains explosives* equivalent to DoD applicable explosive wt. II (55 pounds TNT). As he approaches BUMC/NEIDL, he places the backpack *in a trash container against the east wall of the building at the foundation. The backpack explodes.* At the time of the explosion, a technician is handling a tube containing one gram of anthrax spores (7×10^{11} spores) in the BSL-4 laboratory.

What is the effect of the explosion on the BSL-4 lab?
What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

10. Bomb Breaches Lab Wall. An employee enters BUMC/NEIDL carrying a backpack. *The backpack contains explosives* equivalent to DoD applicable explosive wt. II (55 pounds TNT). He *enters the anthrax BSL-4 laboratory through the airlock and places the backpack against the*

wall. The backpack explodes. At the time of the explosion, a technician is handling a tube containing anthrax spores (7×10^{11} spores) in the BSL-4 laboratory.

What is the effect of the explosion on the BSL-4 lab?
What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

11. Bomb on Roof; Spill on Floor. A helicopter drops a *backpack containing explosives* equivalent to DoD applicable explosive wt. II (55 pounds TNT) on the roof of BUMC/NEIDL. *The backpack is remotely detonated and explodes ten minutes later.* At the time of the explosion, a technician is handling a tube containing anthrax spores (7×10^{11} spores) in the BSL-4 laboratory. The technician drops the tube on the floor and a "cloud" of anthrax spores is released into the laboratory.

What is the effect of the explosion on the BSL-4 lab?
What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

12. TOW Missile. A large bed pickup truck with a tarpaulin-covered object is traveling west on Albany Street at 11:00 p.m. As the vehicle approaches the intersection of Brookline Street, men in the back of the truck quickly remove the "tarp" and aim an M-220 tube-launched, optically tracked, wire-guided (TOW) missile launcher at the northeast corner of BUMC/NEIDL. The missile travels at 290 mps and carries 5.4 lbs of explosive filler. The armor penetration of this missile is 700-800 mm. *No one is working in the BSL-4 laboratories at this time of night. Anthrax spores (7×10^{11} spores) in a 15 cc conical plastic tube with the cap tightly in place are stored in a locked cabinet.*

What is the effect of the explosion on the BSL-4 lab?
What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

13. TOW Missile; Spill on Floor. A large bed pickup truck with a tarpaulin-covered object is traveling west on Albany Street at 11:00 p.m. As the vehicle approaches the intersection of Brookline Street, men in the back of the truck quickly remove the "tarp" and aim an M-220 tube-launched, optically tracked, wire-guided (TOW) missile launcher at the northeast corner of BUMC/NEIDL. The missile travels at 290 mps and carries 5.4 lbs of explosive filler. The armor penetration of this missile is 700-800 mm. *A lab technician has just finished harvesting anthrax spores and preparing them in powdered form. The spores are in a 15 cc conical plastic tube. At the sound of the explosion, the technician drops the tube on the floor.*

What is the effect of the explosion on the BSL-4 lab?
What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

14. Arson; Major Fire in Lab. A visiting scientist from a country known to harbor terrorists has been working in the BSL-4 anthrax laboratory for one year. Late one evening, he enters the

mechanical space and disables the air handling units and exhaust fans serving the BSL-4 laboratory. He returns to the lab and lights a Bunsen burner; he then turns on a gas tank secured to the bench in the room. With the intent of disseminating anthrax through the explosion, he leaves and closes the door. Anthrax spores (7×10^{11} spores) are left in a tube on the counter near the Bunsen burner. Over time, the natural gas concentration in the laboratory reaches the lower explosive limit and is ignited by the natural gas flame. The sprinkler system in this zone is inoperable. The resultant fire reaches temperatures of 1300-2000 F.

What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

15. Big Bomb on Roof. A helicopter drops a *backpack containing explosives* equivalent to 300 pounds TNT on the roof of BUMC/NEIDL. *The backpack is remotely detonated and explodes ten minutes later.* At the time of the explosion, a technician is handling a tube containing anthrax spores (7×10^{11} spores) in the BSL-4 laboratory. The technician drops the tube on the floor and a "cloud" of anthrax spores is released into the laboratory.

What is the effect of the explosion on the BSL-4 lab?
What is the potential for release of anthrax spores to the outdoor environment?
What is the probability of public health harm?

Section

4 Qualitative Risk Assessment

4.1 Overview

Unlike the quantitative analysis, there is no "model" for the qualitative analysis. Situation discussed in this section include those for which computations are so wrought with imprecision as to be meaningless. Some of the cases seem plausible at first, but turn out to be beyond even MPR principles due to various circumstances described in the respective situation. Therefore a qualitative approach is used herein to address these situations.

4.2 Escape of an Infected Animal

The likelihood of escape of an infected animal from a containment animal facility is extremely remote. Due to the specialized design and construction of BSL-3 and BSL-4 laboratories, modes of escape are reduced to the maximum extent. Containment husbandry practices further reduce the already miniscule risk. Simultaneous breakdown of multiple levels of physical and procedural countermeasures would need to occur for a live animal to escape from the containment laboratories.

A BSL-4 animal room is an airtight room with positive pressure doors providing an absolute seal when the doors are closed. Access to these areas is through airlocks with interlocking positive pressure doors and a chemical shower, thus adding even more physical barriers. In the event that a small animal escapes from a cage or is dropped during a manipulation, there is no avenue of escape available from the room. In these rodent rooms, baited "live traps" are used as standard practice as an extra precaution so that in the event an animal escapes into the room, the valuable research animal can be recovered alive. All cages and bedding are decontaminated in an autoclave prior to removal from the containment facility. Therefore, should an animal burrow in bedding and not be transferred to a fresh cage prior to removal from the animal room, it would not survive the decontamination process.

The BSL-3 animal rooms are also accessed via air lock through interlocking doors. These doors are fitted with "sweeps" and open inward to preclude animal escapes. Small rodents housed in BSL-3 animal rooms are maintained in micro-isolator cages in ventilated cage racks that serve as a primary barrier preventing escape of the animal. As in the BSL-4 animal room, baited live traps are employed as a secondary measure to prevent escapes and preserve valuable laboratory animals. Daily animal observation is a matter of good husbandry practice and required for accreditation of the BUMC/NEIDL animal care and use program. BSL-3 laboratories are, by design, removed from general access corridors, thus even further reducing the likelihood of an animal reaching an exterior door. As in the BSL-4 case, all cages and bedding are decontaminated in an autoclave prior to removal from the containment facility. Therefore, should an animal burrow in bedding and not be transferred to a fresh cage prior to removal from the animal room, it would not survive the decontamination process.

The probability of any animal escape is so low to defy calculation. The additional conditions that (a) an animal infected with anthrax or other select agent escapes, and (b) it spreads the infection to a human before succumbing to the disease reduce the probabilities to such low levels that the risk to the public from an infected animal is virtually non-existent.

4.3 Release of Biological Material During Shipment

The packaging, labeling, and transport of etiologic agents are regulated 42 CFR 72(Interstate Shipment of Etiologic Agents); 49(CFR 172 and 173 U.S. Dept. of Transportation regulations concerning shipment of hazardous materials); 9 CFR 122 (U.S. Dept. of Agriculture [USDA]-Restricted Animal Pathogens, and International Air Transport Association (IATA) rules. In addition, special rules apply for the transport of materials regulated by the U.S. Food and Drug Administration (21 CFR 312.120, Drugs for Investigational Use in Laboratory Research Animals or in Vitro Tests). Recent legislation-the USA PATRIOT Act, and the Public Health Preparedness and Bioterrorism Response Act of 2001- have further strengthened the regulations controlling transport of certain etiologic agents, referred to as Select Agents, to include controls over possession and use. The BUMC/NEIDL is registered with the Centers for Disease Control and Prevention and the U.S. Dept. of Agriculture for possession, use, and transport of these agents. A Responsible Official is designated at BUMC/NEIDL and approved by the regulating agencies to oversee the shipping, receipt, and usage. Packaging requirements are strictly implemented in accordance with IATA regulations.

There have been no cases of illness attributable to the release of infectious materials during transport, worldwide, although incidents of damage to outer packaging of properly packaged materials have been reported (World Health Organization, 2002; U.S. Department of Transportation, 2001).

The risk to the community surrounding the BUMC/NEIDL from transport of infectious agents or other biologically-derived material is negligible.

"Unforeseen" Emergencies

Only since 9/11/01 has the idea of a truly unforeseen emergency entered the risk arena. Toward that end, the risk of all other hazards and threats, including hurricanes, which are actually foreseeable, must be considered. Still, enumerating inconceivable events and assigning probabilities and specific countermeasures is a fruitless approach. Instead, a general set of procedures, collectively known as an *Emergency Response Plan* is an appropriate and realistic countermeasure. The quality of that plan is paramount.

As a minimum, the Plan should cite the importance of the HEPA filters and the fail-safe systems. It is a training matter that even in an emergency, these systems should not be bypassed or over-ridden.

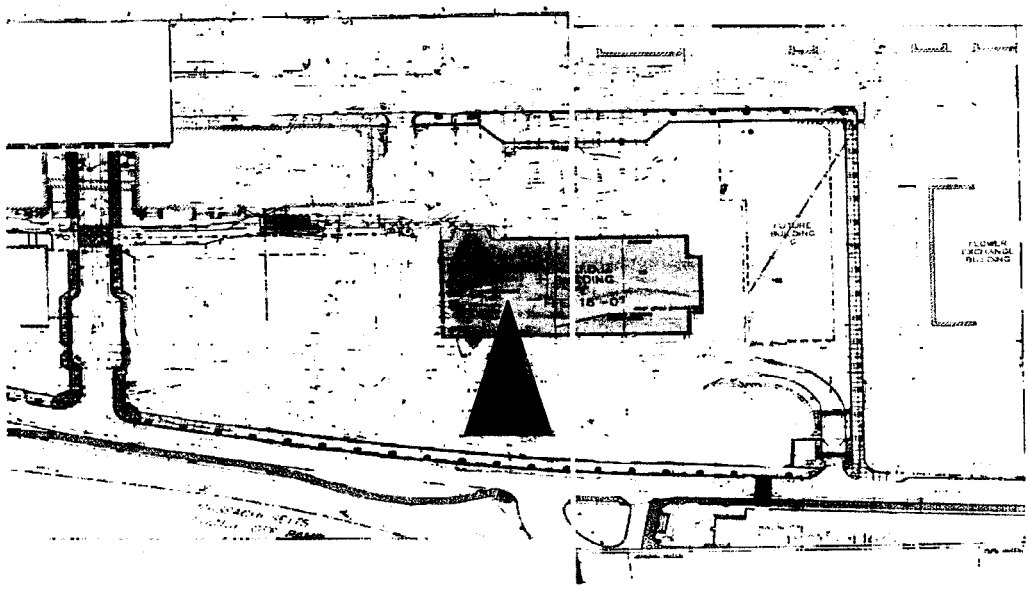
Section

5 Results

Quantitative results are presented for the specified dispersion angle (19°), and for several exposure "targets" away from the lab.

Figure 3 exhibits the campus with overhead view of half-cone plume generated by release of material in a very light wind, which results in a 19-degree spread considering the offsetting effects of laminar flow and turbulence. The length of the half-cone depicted in Figure 3 is 165 feet, because at a breathing rate of 12 lpm, a person at the outer edge of the plume could inhale a potentially pathogenic dose of spores in one hour if the spores persisted without further dispersion.

Fig. 3 Dispersion of Spores If Released in a Lab Spill (Worst-Case, Maximum Possible Risk)



The cone represents the reach of the maximum transient peak concentration of 500 respirable spore/m^3. The "Maximum Possible Risk release" conditions are 700 billion spores that all go up and out the stack with NO filtration, at 19-degree angle half-cone dispersion geometry, in a light uni-directional wind. In order to suffer an exposure of 500 spores, a person would have to breath for 1 hour inside this "dilution/dispersion/settling," which would have to sit static with no dispersion/dilution of spores for the entire 1-hour period.

This report is being done for NIH and BU and is project related; the use of the drawing C1.3 as a reference in the report is acceptable and approved.

Table 3 focuses on five specific "targets" considered in the risk assessment: (1) the pedestrian walkway to the parking garage, (2) E. Brookline Street Building, (3) Guardhouse, (4) Flower Exchange Building, and (5) E. Canton Street Building.

Table 3. Target Exposure Points

	Distance from nearest lab point
Pedestrian Walkway	300 feet
E. Brookline Street Bldg.	290 feet
Guardhouse	300 feet
Flower Exchange Bldg.	360 feet
E. Canton Street Bldg.	400 feet

Table 4. MPR Model Calculations – Number of spores in a release plume at the closest PEDESTRIAN WALKWAY, 300 FEET from Release Point, 19° Cone Dispersal Angle; and the time required to achieve an Exposure of 500 spores breathing at that point

Type of Scenario	Respirable Spores (0.3-10 micron) from Technical Powder Released at Accident or Incident Site	Number of Filtrations (99.97% HEPA Filtration Efficiency) and Total Respirable Spores Potentially Released into the Environment		Hours needed to breathe 500 Spores	
		Filtration	Spores Released		
Light, uni-directional wind, release approximately at ground level (half-cone only)	1,255,396	3	Less than 1		*
	1,255,396	2	Less than 1		*
	1,255,396	1	377		*
	1,255,396	0	1,255,396		6.2

* Since less than 500 total respirable spores are released, it is not possible to breathe the MPR possible pathogenic dose.

Table 5. MPR Model Calculations – Number of spores in a release plume at the closest BUILDING ON E. BROOKLINE STREET, 290 FEET from Release Point, 19° Cone Dispersal Angle; and the time required to achieve an Exposure of 500 spores breathing at that point

Type of Scenario	Respirable Spores (0.3-10 micron) from Technical Powder Released at Accident or Incident Site	Number of Filtrations (99.97% HEPA Filtration Efficiency) and Total Respirable Spores Potentially Released into the Environment		Hours needed to breathe 500 Spores	
		Filtration	Spores Released		
Light, uni-directional wind, release approximately at ground level (half-cone only)	1,255,396	3	Less than 1		*
	1,255,396	2	Less than 1		*
	1,255,396	1	377		*
	1,255,396	0	1,255,396		5.6

* Since less than 500 total respirable spores are released, it is not possible to breathe the MPR possible pathogenic dose.

Table 6. MPR Model Calculations – Number of spores in a release plume at the GUARDHOUSE, 300 FEET from Release Point, 19° Cone Dispersal Angle; and the time required to achieve an Exposure of 500 spores breathing at that point

Type of Scenario	Respirable Spores (0.3-10 micron) from Technical Powder Released at Accident or Incident Site	Number of Filtrations (99.97% HEPA Filtration Efficiency) and Total Respirable Spores Potentially Released into the Environment		Hours needed to breathe 500 Spores	
		Filtration	Spores Released		
Light, uni-directional wind, release approximately at ground level (half-cone only)	1,255,396	3	Less than 1		*
	1,255,396	2	Less than 1		*
	1,255,396	1	377		*
	1,255,396	0	1,255,396		6.2

* Since less than 500 total respirable spores are released, it is not possible to breathe the MPR possible pathogenic dose.

Table 7. MPR Model Calculations – Number of spores in a release plume at the FLOWER EXCHANGE BUILDING, 360 FEET from Release Point, 19° Cone Dispersal Angle; and the time required to achieve an Exposure of 500 spores breathing at that point

Type of Scenario	Respirable Spores (0.3-10 micron) from Technical Powder Released at Accident or Incident Site	Number of Filtrations (99.97% HEPA Filtration Efficiency) and Total Respirable Spores Potentially Released into the Environment		Hours needed to breathe 500 Spores	
		Filtration	Spores Released		
Light, uni-directional wind, release approximately at ground level (half-cone only)	1,255,396	3	Less than 1		*
	1,255,396	2	Less than 1		*
	1,255,396	1	377		*
	1,255,396	0	1,255,396		10.7

* Since less than 500 total respirable spores are released, it is not possible to breathe the MPR possible pathogenic dose.

Table 8. MPR Model Calculations – Number of spores in a release plume at the closest BUILDING ON E. CANTON STREET, 400 FEET from Release Point, 19° Cone Dispersal Angle; and the time required to achieve an Exposure of 500 spores breathing at that point

Type of Scenario	Respirable Spores (0.3-10 micron) from Technical Powder Released at Accident or Incident Site	Number of Filtrations (99.97% HEPA Filtration Efficiency) and Total Respirable Spores Potentially Released into the Environment		Hours needed to breathe 500 Spores	
		Filtration	Spores Released		
Light, uni-directional wind, release approximately at ground level (half-cone only)	1,255,396	3	Less than 1		*
	1,255,396	2	Less than 1		*
	1,255,396	1	377		*
	1,255,396	0	1,255,396		14.7

* Since less than 500 total respirable spores are released, it is not possible to breathe the MPR possible pathogenic dose.

Table 9. Scenarios Spreadsheet (at closest target - 290 feet)

Scenario	Respirable Spores Released	Dispersion Pattern and	BSL-3 Number of Filtrations, and	Total Respirable Spores Released	Hours needed to breathe 500 spores	BSL-4 Number of Filtrations, and	Total Respirable Spores Released	Hours needed to breathe 500 spores
1 Spill in BSC	1,255,396	cone	2	0	<500 spores*	3	0	<500 spores*
2 No filter in HVAC	1,255,396	cone	1	377	<500 spores*	1	377	<500 spores*
3 Spill on floor, no HVAC filter	1,255,396	cone	0	1,255,396	11.2	0	1,255,396	11.2
4 Spill on floor; power outage	-	shutdown	-	-	<500 spores*	-	-	<500 spores*
5 Spill outside on sidewalk	1,255,396	half-cone	0	1,255,396	5.6	0	1,255,396	5.6
6 Takeover of bldg.	1,255,396	cone	0	1,255,396	11.2	0	1,255,396	11.2
7 Fire in a lab	-	none	-	-	<500 spores*	-	-	<500 spores*
8 Arson in the bldg	-	none	-	-	<500 spores*	-	-	<500 spores*
9 Bomb at outer wall, spill on floor	1,255,396	cone	1	377	<500 spores*	2	0	<500 spores*
10 Bomb breaches lab wall	-	shutdown	-	-	<500 spores*	-	-	<500 spores*
11 Bomb on roof; spill on floor	1,255,396	cone	0	1,255,396	11.2	1	377	<500 spores*
12 TOW missile	-	no breach	-	-	<500 spores*	-	-	<500 spores*
13 TOW missile, spill on floor	1,255,396	cone	0	1,255,396	11.2	1	377	<500 spores*
14 Arson major fire in lab	-	none	-	-	<500 spores*	-	-	<500 spores*
15 Big bomb on roof	-	no breach	-	-	<500 spores*	-	-	<500 spores*

*Since less than 500 total respirable spores are released, it is not possible to breathe the MPR possible pathogenic dose.

Section 6 Discussion and Conclusions

6.1 Quantitative Outcomes of Risk Scenarios

SCENARIOS DEPICTING SPILLS AND WORK DISRUPTION

1. Spill in BSC

Outcome: *All* of the spores in the tube are assumed to be released and the aerosolized spores are filtered through the BSC HEPA filter and through the building HVAC HEPA filter. The filtered air, which then contains no spores, is released to the environment via the building's normal exhaust stack.

Q.: What is the potential for release of anthrax spores to the outdoor environment?
A.: There is no potential for release of anthrax spores to the external environment.

Q.: What is the probability of public health harm?
A.: None.

Discussion: This scenario is the most likely to occur and the least likely to cause public harm. BSL-4 countermeasures (HEPA filtrations) are designed for and are effective in containing this potential release.

2. No Filter in HVAC.

Outcome: *All* of the spores in the tube are assumed to be released and the aerosolized spores are filtered through the BSC HEPA filter, but bypass further filtration since the HVAC HEPA filter is assumed to be missing. The once-filtered air is released to the environment via the building's normal exhaust stack.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: A total of approximately 377 respirable spores would be released from the building exhaust stack.

Q: What is the probability of public health harm?
A: None

Discussion: This scenario is contrived to yield some escape of spores from the building since various engineering and procedural controls such as pressure differential monitors and alarms as well as routine testing and certification of all HEPA filter installations by the BUMC/NEIDL

would prevent the scenario from occurring. Even so, it could not be shown that a potentially pathogenic dose could be released from the laboratory facility.

3. Spill on Floor; No HVAC Filter.

Outcome: *All* of the spores in the tube are assumed to be released and the fraction of the spores which are aerosolized are not filtered at all since the spill is outside the BSC and since the HVAC filter is assumed to be missing. The un-filtered air, which then contains approximately 1.79×10^6 respirable spores, is released to the environment via the building's exhaust stack. The plume disperses in a 19 degree cone-shaped pattern emanating from the top of the exhaust stack.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: Assuming no interference caused by static charges or settling in turns of exhaust duct, 1,255,396 spores in the respirable size range would be released.

Q: What is the probability of public health harm?
A: None. A harmful exposure in this scenario could only be achieved by breathing the contaminated air for 11.2 hours under the worst case assumption described at 3.4.4.

Discussion: The engineering controls designed into BUMC/NEIDL would cause a shutdown of laboratory exhaust in the event of the pressure change caused by a HEPA filter not properly operating in the housing. This scenario is contrived to yield some escape of spores from the building since various engineering and procedural controls such as pressure differential monitors and alarms as well as routine testing and certification of all HEPA filters would prevent the scenario from occurring.

SCENARIO DEPICTING SAFETY SYSTEM FAILURE

4. Spill on Floor; Power Outage.

Outcome: The typical BSL-4 HVAC system is designed with safety controls in place. In the event that either the exhaust or supply "shut down," electronic interlocks assure that the laboratory is not pressurized. In the event of a total electrical outage, the laboratory pressure differential drops to "zero" and the room becomes static with regard to airflow. Additionally, positive pressure bubble dampers, installed for decontamination purposes, close and isolate the air in the laboratory.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: None

Q: What is the probability of public health harm?
A: None

SCENARIOS DEPICTING PHYSICAL REMOVAL OF BIOLOGICAL MATERIAL

5. Single Vial Release Just Outside Building; Spill Outside on Sidewalk.

Q: What is the probability of public health harm?
A: None.

Discussion: As a first line of defense, the security precautions including background investigations, FBI clearance and fingerprinting will limit the chances that a compromised employee will have access. The access to Select Agent laboratories is strictly limited.

Nevertheless, this scenario was created to test the theoretical removal of the biological material, and release outside the building. As shown in Table 9, the expected dispersion of the spores would require 5.6 hours of breathing the air at the transient peak concentration. The model overstates (perhaps substantially) the true concentration that would remain after a duration of hours, because the model computes the potential exposure as if, among other unrealistic assumptions, there were no passage of time for settling to occur.

6. Criminal Trespass and Occupation of Building.

Q: What is the probability that the activists will be successful in entering the building and gaining control of a sufficient amount of anthrax to do harm?
A: None

Discussion:
Security design features planned for BUMC/NEIDL include surveillance cameras, building security guards, physical and electronic barriers to unauthorized entrance. Even so, should criminals steal the biological material and disperse it outside the building, the maximum quantities of Select Agents in any labs will not be sufficient to render public health harm.

SCENARIOS DEPICTING FIRE

7. Accidental; Fire in Lab.

Outcome: The spores are secured in a locked refrigerator. All personnel are pre-screened in compliance with the USA Patriot Act. The laboratory mist suppression system will discharge as soon as the cardboard combustibles begin to burn, dousing the fire. In the event that the mist system fails to completely douse the fire, the Fire Department will respond and perform manual discharge of the secondary suppression system. Additionally, the re-enforced walls prevent expansion of the fire beyond this laboratory module.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: None.
Q: What is the probability of public health harm?
A: None.

8. Arson in the Building.

Outcome: The building sprinkler system will discharge as soon as the cardboard and paper combustibles begin to burn, dousing the fire. In the event that the sprinkler fails to completely douse the fire, the Fire Department responds within minutes. Additionally, fire rated walls in all laboratories will prevent the fire from impacting laboratory operations.
Employee screening, background checks, fingerprinting and other personnel-reliability programs used for workers in the BUMC/NEIDL further reduce the probability of this occurrence.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A. None.

Q: What is the probability of public health harm?
A: None.

SCENARIOS DEPICTING EXPLOSIONS

9. Bomb at Outer Wall; Spill on Floor.

Q: What is the effect of the explosion on the BSL-4 lab?
A: The explosion at the outer wall of the building has no appreciable structural effect on the BSL-4 lab. The building is being designed for blast resistance and the interior BSL-4 core walls are hardened. As a result of the surprise of noise and possible minor vibration from the explosion, the technician drops the vial on the floor. *All* of the spores in the vial are assumed to be released and the aerosolized spores filtered through the BSL-4 exhaust HEPA filters. The twice-filtered air released to the environment via the building's normal exhaust stack does not contain any respirable spores.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: None

Q: What is the probability of public health harm?
A: None

10. Bomb Breaches Lab Wall.

Q: What is the effect of the explosion on the BSL-4 lab? What is the potential for release of anthrax spores to the outdoor environment? What is the probability of public health harm?

A: The bomb is assumed to breach the wall; the wall is compromised, and all the spores are released. However, the building HVAC goes into fail-safe mode, i.e. shuts down, and no spores are released to the environment. There is no public health harm outside the building.

11. Bomb on Roof; Spill on Floor.

Q: What is the effect of the explosion on the BSL-4 lab? What is the potential for release of anthrax spores to the outdoor environment?

A: The explosion on the roof of the building has no appreciable structural effect on the BSL-4 lab due to the hardening of the building which simply forces the blast wave up and away from the labs. As a result of the surprise of noise and possible minor vibration from the explosion, the technician drops the vial on the floor. *All* of the spores in the vial are assumed to be released and the aerosolized spores are filtered through the BSL-4 laboratory exhaust HEPA filter. The worst-case scenario is that 377 spores could be released to the environment, which does not constitute a potentially hazardous exposure.

Q: What is the probability of public health harm beyond the perimeter fence?
A: None.

12. TOW Missile.

Outcome: The missile may or may not penetrate the outside wall of the building, as the missile is designed to penetrate 700-800 mm and then discharge a small explosive. The BUMC/NEIDL exterior will be blast hardened. The BSL-4 laboratories are planned to occupy the center of the building. No container of anthrax is damaged.

Q: What is the effect of the explosion on the BSL-4 lab?
A: Disruption of subsequent work.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: None

Q: What is the probability of public health harm within a one mile radius of the building?
A: None.

13. TOW Missile; Spill on Floor.

Q: What is the effect of the explosion on the BSL-4 lab?
A: As above, the missile may penetrate the outside wall of the building *but does not* penetrate the lab. The technician drops the vial at the sound of the explosion, and *all* spores from the vial are released inside the lab but not inside a BSC.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: Approximately 377 spores may be released to the environment.

Q: What is the probability of public health harm?
A: None

14. Arson; Major Fire In Lab.

Outcome: All spores in the lab are destroyed by the fire; the HVAC is shutdown and all vents are closed as per scenario 4.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: None.

Q: What is the probability of public health harm?
A: None.

15. Big Bomb on Roof.

Q: What is the effect of the explosion on the BSL-4 lab?
A: The explosion on the roof of the building may damage the roof, but explodes outward and upward because there is no shape charge (ASCE, 2001). Additionally, the roof will have a concrete deck which will further protect the mechanical space below. As a result of the surprise of noise and possible vibration from the explosion, the technician drops the vial on the floor. *All* of the spores in the vial are assumed to be released. Either (1) the HVAC goes into fail-safe, shut-down mode due to mechanical room damage or a direct hit, and no spores are released; OR (2) all the spores are filtered through the BSL-4 exhaust HEPA filter which is located in the interstitial space between floors, remote from the roof.

Q: What is the potential for release of anthrax spores to the outdoor environment?
A: None

Q: What is the probability of public health harm?
A: None.

6.2 Lessons from the Maximum Possible Risk (MPR) Model

Given the environmental viability of spores, the worldwide experience in BSL-4 risk assessment, and the potential virulence of aerosolized anthrax, a maximum possible risk (MPR) model for the safety at BUMC/NEIDL is to consider environmental release of anthrax spores. To create measurable scenarios in the geographic area around the lab, even harsher assumptions of lack of filtration and a massive number of spores in one release have been made. Using all of these MPR assumptions and unrealistic possibilities, it is possible to compute a transient spore concentration in the air outside the lab under certain conditions.

In conjunction with a spore concentration in the air, a conservative level of estimated pathogenic dose of spores was applied to compute exposure times of risk to the public under the release-event conditions. For all of the potential release events and ambient winds, and for all locations off-site, the duration of exposure would need to be hours or more. Even if such conditions and durations could exist, the lab would realize an event had occurred and take remedial action (stop further release), the spores would actually further dissipate in the environment, and/or affected individuals would evacuate the area.

The conclusion from this data is that the general public is not at risk for environmental exposure of pathogens from the construction or operation of the BSL-4 laboratory at BUMC.

The propriety of the MPR model, for this application, lies in the combined effect of three realities. First, the total volume of potentially-released material is several orders of magnitude lower than what it would take to form a plume that would be simultaneously concentrated enough to pose a risk to human health, and sustained, without dissipation, over a long enough time to negate avoidance behavior. If these factors were simultaneously present, for example, if the giant plume of dust associated with the collapse of the Trade Center had been anthrax spores, then a so-called "urban fluid mechanics" model might be a desirable, though unattainable, methodology.

The second reason the MPR model is appropriate is that a physics-based fluid mechanics model is virtually impossible to apply beyond small, tightly-controlled, simulated physical environments, e.g. inside jet engines, high-performance exhaust systems, or over portions of wing surfaces. Even for the latter, such models are not considered reliable and are supplemented by wind-tunnel testing and test-pilot bravado.

Finally, the MPR is appropriate because, at every step of calculations, assumptions have been applied which are unrealistically negative:

(a) that an entire vial of spores would all get released, when in fact, many spores would likely remain in the vial, in the lab, or in the building;

(b) the dispersion to the community would be relatively uni-directional toward the points of interest when, in fact, the much more likely scenario is that spores would be blown this way and that;

(c) that at the extreme reaches of the dispersion patterns and at the same point in time, the spores would be as concentrated as at the points closer to the release, when, in fact, by the time the concentrations reached the reported levels, some of the spores would be past that point and therefore the total possible exposure would be lower, and;

(d) that everything would happen instantly, without time for evacuation or closing off relevant areas near the lab.

It is, of course, impossible to account precisely for all these factors. This is precisely why the MPR approach was employed. It should be clear that the MPR approach is over-stating risks, perhaps by orders of magnitude. Even so, the analysis demonstrates that building and operating the BSL-4 facility at the BUMC will not cause an appreciable addition of risk of harm to the public health.

Section 7 Bibliography

References consulted for preparation of this Risk Assessment report are presented here.

Ad Hoc Group of the States Parties to the Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction, *Procedural Report of the Sixteenth Session,* Geneva, 13 September - 8 October 1999, *Part I, BWC/Ad Hoc Group/47, English version, 15 Oct. 1999,* Geneva: World Health Organization.,1999, pp. 140-143.

Albrink WS, Goodlow RJ. Experimental inhalation anthrax in the chimpanzee. *Am J Pathol* 1959;35:1055--65.

"Antiterrorism and Effective Death Penalty Act of 1996," *Pub. L. No. 104-132*, Section 511, 42 C.F.R., Part 72 RIN 0905-AE70.

Benjamin GS, Balmes J. The Lungs, Chapter 2, in Fundamentals of Industrial Hygiene, 5th ed., Plog B, Quinlan P, eds., National Safety Council, Itasca, IL, 2002

"Biological and Chemical Terrorism: Strategic Plan for Preparedness and Response, Recommendations of the CDC Strategic Planning Workgroup 2000," *Morbidity and Mortality Weekly Report,* 2000, 49(RR-4), pp. 1-14.

Brachman, P.S., A. Kaufman, and F.G. Dalldorf, "Industrial Inhalation Anthrax," *American Society of Microbiology*, vol. 30, no. 3, Sept. 1966.

Brachman PS, Kaufmann AF, Dalldorf FG. Industrial inhalation anthrax. Bacteriol Rev 1966;30:646–57.

Brachman, P.S., and A.S. Evans (eds.), *Bacterial Infections of Humans – Epidemiology and Control*, 2nd edition, Plenum Press, New York, 1993.

-------. Inhalation anthrax. *Ann NY Acad Sci* 1980;353:83--93.

Center for Strategic and International Studies (CSIS), "Report of the CSIS Homeland Defense Project: Combating Chemical, Biological, Radiological, and Nuclear Terrorism - A Comprehensive Strategy," December 2000, pp. 1-96. Available at: URL: http://www.csis.org/homeland/reports/combatchembiorad.pdf

Centers for Disease Control and Prevention, "Preventing Emerging Infectious Diseases: A Strategy for the 21st Century," U.S. Department of Health and Human Services,1998, pp. 1-74.

------, "Suspected Cutaneous Anthrax in a Laboratory Worker," *Morbidity and Mortality Weekly Report,* 2002, 51, pp. 279-280.

Churchill, Geoff, and Thomas Whalen, J. Kacprzyk, M. Krawczak and S. Zadrozny (eds.), "Decisions Under Uncertainty," *Issues in Information Technology*, EXIT, Warsaw, 2002, pp. 201-224.

Davis, C.J., "Nuclear Blindness: An Overview of the Biological Weapons Programs of the Former Soviet Union and Iraq," *Emerging Infectious Diseases,* 1999, 5, pp. 509-512.

Department of Defense, "Minimum Antiterrorism Standoff Distances for Building," *Unified Facilities Criteria*, 2002.

------, "Biological Defense Safety Program-Army Regulation 385-69, 1993

"Design of Buildings to Optimize Resistance to Blast Loading," *American Society of Civil Engineers,* 2001.

Federal Bureau of Investigation, "Terrorism in the United States," 1998, pp. 1-24. Available at: URL: http://fbi.gov/publications/terror/terror98.pdf

Gutteling, Jan M., and Oene Wiegman, *Exploring Risk Communication*, Kluwer Academic Publishers, Dordrecht, Boston, c1996.

Harding AL, Byers KB. Epidemiology of Laboratory-Associated Infections. In Biological Safety Principles and Practices, ASM Press, 2000

Hare, R., *Without Conscience: The Disturbing World of Psychopaths Among Us,* Simon and Schuster, NY, 1993.

Henderson, D.A., "Bioterrorism," *International Journal of Clinical Practice*, December 2000, pp. 32-36.

------, "Bioterrorism as a Public Health Threat," *Emerging Infectious Diseases*, July-September 1998, pp. 488-492.

Inglesby, T.V., D.A. Henderson, J.G. Bartlett, M.S. Ascher, E. Eitzen, A.M. Friedlander, J. Hauer, J. McDade, M.T. Osterholm, T. O'Toole, G. Parker, T.M. Perl, P.K. Russell, and K. Tonat, "Anthrax as a Biological Weapon, Medical and Public Health Management," *Journal of the American Medical Association*, May 12, 1999, pp. 1735-1745.

------, T. O'Toole, D.A. Henderson, J.G. Bartlett, M.S. Ascher, E. Eitzen, A.M. Friedlander, J. Gerberding, J. Hauer, J. Hughes, J. McDade, M.T. Osterholm, G. Parker, T.M. Perl, P.K. Russell, and K. Tonat, "Anthrax as a Biological Weapon, 2002: Updated Recommendations for Management," *Journal of the American Medical Association*, May 1, 2002, pp. 2236-2252.

Kasperson, Roger E., and Pieter Jan M. Stallen (eds.), *Communicating Risks to the Public: International Perspectives*, Kluwer Academic Publishers, Dordrecht, Boston, c1991.

Lundgren, Regina E., and Andrea H. McMakin, *Risk Communication: A Handbook for Communicating Environmental, Safety, and Health Risks*, 2nd edition, Battelle Press, Columbus, c1998.

Mandell, G.L., J.E. Bennett, and R. Dolin (eds.), *Principles and Practices of Infectious Diseases,* 5th edition, Churchill Livingstone, Philadelphia, 2000.

Morgan, M. Granger, et. al., *Risk Communication: A Mental Models Approach*, Cambridge University Press, Cambridge, N.Y., 2002.

Murray, P.R., E.J. Baron, M.A. Pfaller, F.C. Tenover, and R.H. Yolken (eds.), *Manual of Clinical Microbiology,* 7th edition, ASM Press, Washington, D.C., 1999.

National Sanitation Foundation, NSF Standard 49; 2002.

Rotz LD, Khan AS, Lillibridge SR, Ostroff SM, Hughes JM. Public Health Assessment of potential biological terrorism agents. Emerg Infec Dis. 2002 Feb; 8(2):225-30.

Shafer, Glenn, *A Mathematical Theory of Evidence,* Princeton University Press, Princeton, NJ, c1976.

"Specification for HEPA Filters used by DoE Contractors," *DOE Standard 3020-97,* Washington, DC, January 1987.

U.S. Department of Health and Human Services, *Biosafety in Microbiological and Biomedical Laboratories,* 4th edition, U.S. Government Printing Office, Washington, D.C., 1999.

Whalen, Thomas, "Achieving Synergy Between Computer Power and Human Reason," *Supplement to the Encyclopedia of Library and Information Science, Volume 71, Supplement 34,* Marcel Dekker, 2002, and *Supplement to the Encyclopedia of Microcomputers, Volume 27, Supplement 6,* Marcel Dekker, 2001, pp.1-14.

------, "Interval Probabilities Induced by Decision Problems," in Mario Fedrizzi, Janusz Kacprzyk and Ronald Yager (eds.), *Advances in the Dempster-Shafer Theory of Evidence*, John Wiley & Sons, 1994, pp.353-374.

------, and Bronn, C.Introduction to Decision Making Under Uncertainty," in J. Kacprzyk and S. Orlovski (eds.), *Optimization Models Using Fuzzy Sets and Possibility Theory*, Springer-Verlag, 1987.

------, "Decision Making Under Uncertainty With Ordinal Linguistic Data," in D. Ruan, J. Kacprzyk, M.Fedrizzi (eds.), *Soft Computing for Risk Evaluation and Management Applications in Technology, Environment and Finance*, Physica-Verlag, Heidelberg & New York, 2001, pp. 3-16.

------, and S. Samaddar, "Problem Solving: A Knowledge Management Process," *Knowledge Management Handbook*, Springer-Verlag, 2002, pp. 349-366.

Willis, William James, and Albert Adelowo Okunade, *Reporting on Risks : The Practice and Ethics of Health and Safety Communication*, Praeger, Westport, Conn., 1997.

World Health Organization, 2002. Guidelines for Safe Transport of Infectious Substances and Diagnostic Specimens.