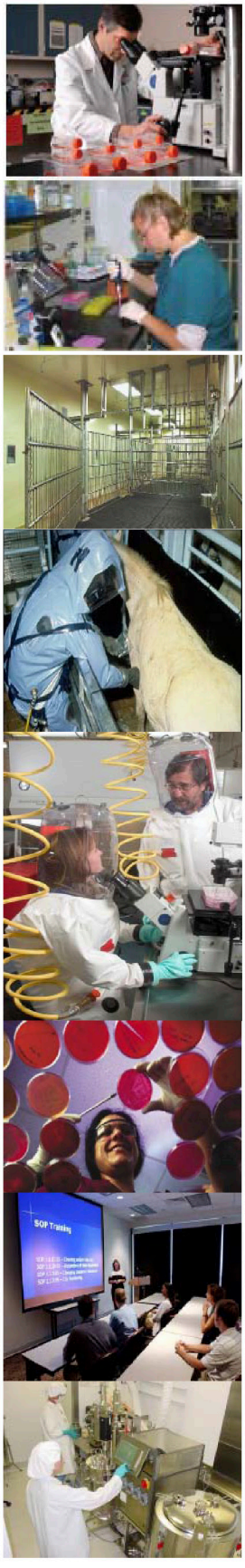
NATIONAL BIO AND AGRO-DEFENSE FACILITY

Science and Technology Directorate/Office of National Laboratories



US DEPARTMENT OF HOMELAND SECURITY NATIONAL BIO AND AGRO-DEFENSE FACILITY

APPENDIX E

ACCIDENTS METHODOLOGY

JUNE 2008

U.S. DEPARTMENT OF HOMELAND SECURITY

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APPENDIX E HAZARD AND ACCIDENT METHODOLOGY

E.1 INTRODUCTION

The purpose of the National Bio and Agro Defense Facility (NBAF) is currently in the conceptual design stage with six potential locations in the continental United States under consideration: San Antonio, TX; Plum Island, NY; Flora, MS; Athens, GA; Manhattan, KS; and Butner, NC. The potential NBAF mission is two-fold: maintaining the existing mission of the current Plum Island Animal Disease Center (PIADC) and expanding to new missions to include additional agricultural biocontainment laboratories at biosafety level 3 (BSL-3) agriculture (BSL-3Ag), BSL-3E, and BSL-4 for foreign animal and zoonotic diseases as called for in Homeland Security Presidential Directive (HSPD)-9. With the PIADC more than 50 years old, it is becoming ever more difficult and expensive to maintain in support of the scientific research, development, and diagnostic programs (NBAF-1). The new and unique government biocontainment infrastructure would

- Integrate those aspects of public and animal health research that have been determined to be central to national security;
- Assess and research evolving bioterrorism threats over the next five decades; and
- Enable the Departments of Homeland Security and Agriculture to fulfill their related homeland defense research, development, testing, and evaluation responsibilities.

With the potential operation of BSL-3Ag, BSL-3E, and BSL-4 laboratories, the NBAF could present significant hazards to both on-site personnel (employees), as well as the surrounding communities in which it could be built. Such hazards range from more frequent low-consequence events such as a laboratory-acquired infection (LAI) of an employee, which may not spread to the surrounding community, to a much less frequent high-consequence event such as an earthquake impacting the entire facility and releasing a significant amount of pathogens into the environment.

This appendix details the hazard assessment methodology used to determine the health and safety risks of the proposed NBAF sites. This hazard assessment starts by identifying potential hazards, screening the hazards for the ones that present the highest potential consequences to the workers and public, selecting from the list of screened hazards those that will be evaluated in more detail (called an accident selection), then performing a semiquantitative analysis of the chosen accidents. The final step and the end goal of any hazard assessment is to determine the type and number of controls (engineered barriers and administrative/procedural controls) that will prevent and/or mitigate the hazards to a reasonable and acceptable level of risk to the workers and the public given the operating mission objectives.

For this analysis, a hazard is considered any biological, physical, or chemical characteristic of a material, system, process, or facility that has the potential for causing harm. Hazards can present a risk (a combination of probability and consequences) to the workers and public from operational accidents, external man-made events (such as an airplane crash into the facility), natural phenomena events (such as an earthquake), or intentional acts (such as terrorism or a disgruntled employee purposefully releasing pathogens). All of these sources of risk are discussed in this appendix, and site-specific consequences and probabilities are presented for the chosen accidents to assist in determining whether the NBAF should be built and, if so, which site is preferable. The following illustration and flow chart describe the overall approach to evaluating human health and safety in the Draft Environmental Impact Statement (EIS) and the potential establishment of viruses in the environment that could adversely impact agriculture and wildlife in the United States.

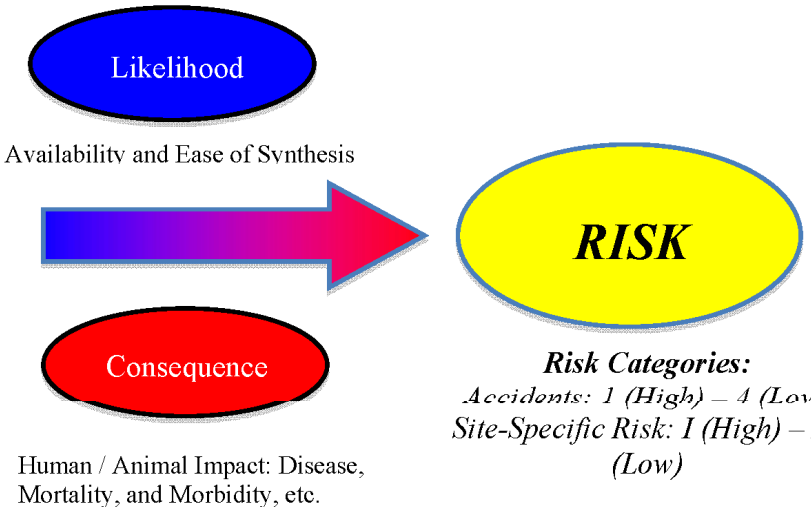
NBAF Biological Hazard / Accident / Threat / Risk Model

Likelihood is defined as the probability of a defined adverse consequence (accident results in release of pathogens or that an adversary acquires, produces, and disseminates a Biological Weapon)

- *Estimated based on qualitative frequency categories*
- *Event trees identify importance of controls*
- *Event trees developed for unmitigated and mitigated conditions*

Consequence is defined as the magnitude of the impact to the workers, public, and environment from the accident or intentional act

- *Consequences calculated using deterministic values*
- *Estimated based on a bounding parameter values*
- *Consequences developed for accidents and intentional acts for both unmitigated and mitigated conditions*

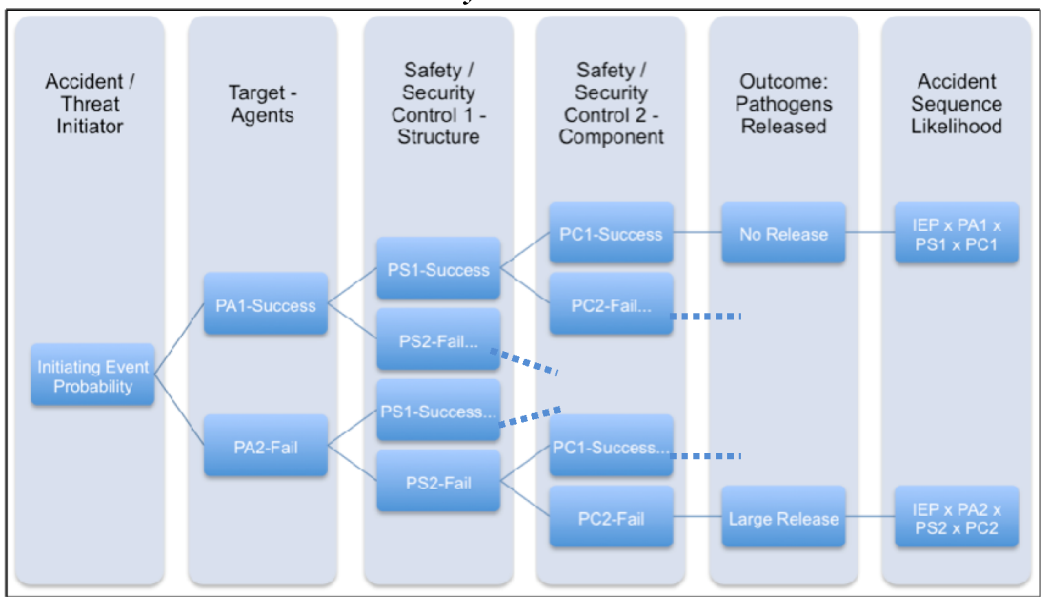


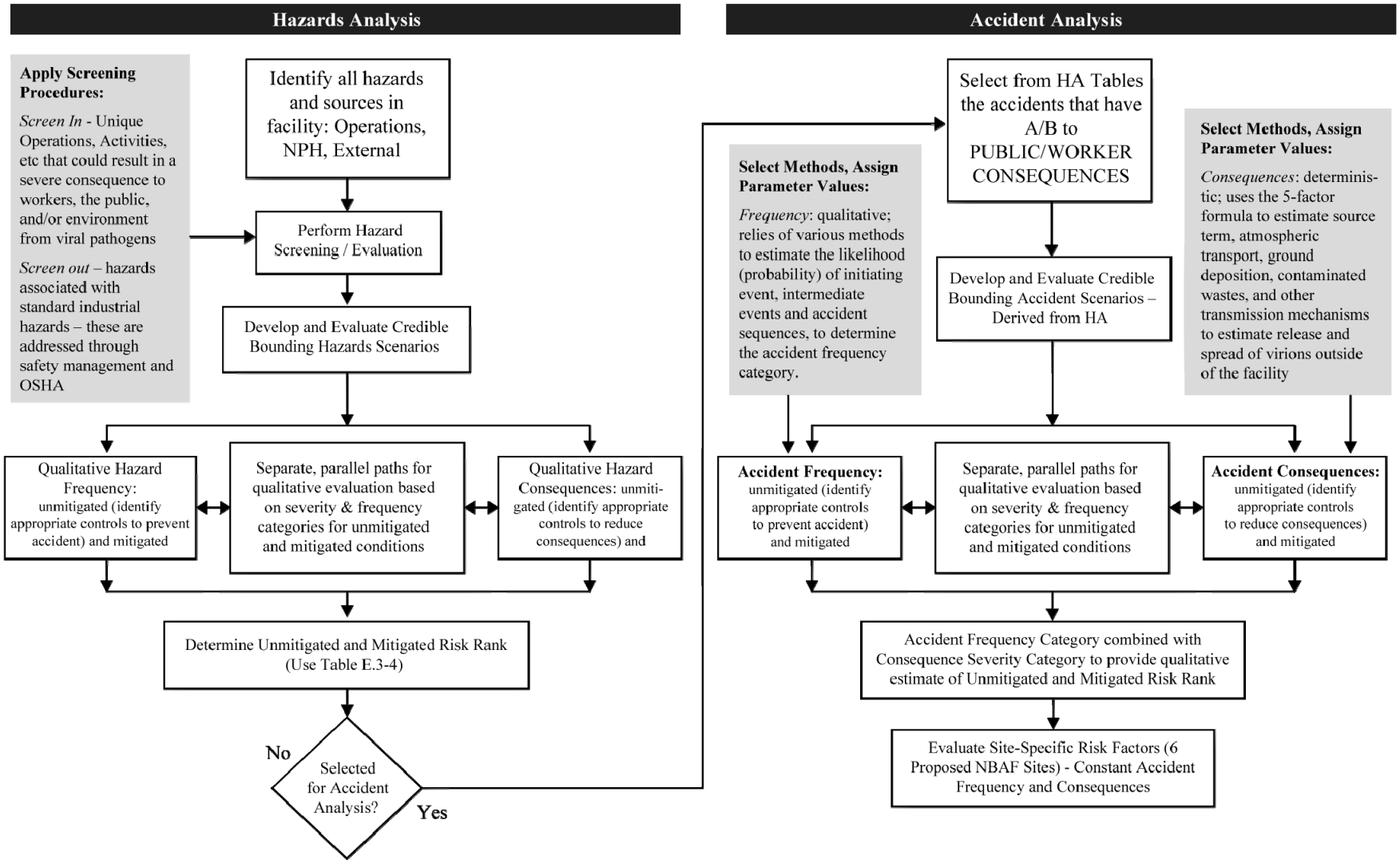
Phase I: Hazards / Threats / Vulnerability Evaluation

- Identify hazards / threats / vulnerabilities
- Develop & evaluate credible scenarios
- Determine qualitative likelihood / consequences
- Identify controls
- Identify potential candidates for detailed analysis

Phase II: Detailed Analysis of Selected Accidents / Threats for Consequence & Likelihood

Phase II: Accident / Threat Analysis Likelihood Estimation Event Tree





Hazard and Accident Frequency and Consequence Estimates:

Unmitigated: defined as a facility that is not designed, constructed, maintained, and operated at the level appropriate for high containment biological pathogens (e.g., typical laboratory setting, manufacturing operation, or facilities with low or no hazardous materials present)

Mitigated: defined to represent a facility that has robust design, construction, maintenance, and operation commensurate with a high containment biological hazard operation (BSL-3E, BSL-3Ag, & BSL-4) facility (e.g., on a similar level to that of a high hazard category 2 or 3 nuclear facility, high hazard chemical facility, or highly hazardous processing facility)

Hazards Evaluation, Accidcnt Analysis, and Risk Assessment Flow Diagram

The specific objective of this hazard identification, accident analysis, and risk assessment is to identify the likelihood and consequences from accidents or intentional subversive acts. In addition to identifying the potential for or likelihood of the scenarios leading to adverse consequences, this analysis provides support for the identification of specific engineering and administrative controls to either prevent a pathogen release or mitigate the consequences of such a release. The consequence analysis is related specifically to the accidental or intentional release of a pathogen and was developed and presented in a qualitative and or semiquantitative manner.

The fundamental questions addressed in this analysis are (NAS 2008)

- What could go wrong (the sequence of events that could cause an infectious pathogen to escape the laboratory, set up a chain of transmission, and cause infectious disease in the surrounding community)?
- What are the probabilities (likelihood for each type of release) of such a sequence of events?
- What would be the consequences of such a sequence of events (e.g., the impacts of a release including transmission of disease, morbidity, and mortality)?

To address these questions, a series of steps were involved as illustrated in the flow chart above. The NBAF analysis was prepared such that both a wide range of realistic hazard scenarios were considered, as well as the identification and detailed evaluation of a select number of high-consequence accidents. This approach provided a realistic assessment of risks associated with the NBAF in general and illustrated the comparative risks across the six proposed sites. The hazards analysis of the NBAF operations concentrated on identifying potential releases that required additional safety controls and determining those accidents that required additional evaluation.

In addition to the wide array of hazard scenarios, this risk assessment also evaluated those potential release scenarios that are highly unlikely but still provide credible high-consequence results. This method of approach was used for the NBAF where the selected accidents focused on the potential pathogen release from many diverse initiators such as procedural or work practice failures, including those that lead to worker exposures and infections, biocontainment system and equipment failures, and an appropriate array of intentional acts (addressed separately in the Threat Risk Assessment).

The methods used to identify and evaluate hazards included "what-if" scenario development and limited use of cause-consequence analysis (e.g., numerous hazard scenarios and the seismic, wind, and aircraft crash accidents). The most important aspect of selecting appropriate methods is to understand the objectives of the study and the expected results from applying the techniques, methods, and models.

The factors that influence the selection of the hazard evaluation and accident analysis technique include (CCPS 1992) the following:

- Motivation for the study;
- Type of results needed or desired (how will the information be used?);
- Type of information available to perform the study;
- Characteristics of the analysis problem;
- Perceived risk associated with the subject process or activity; and
- Resources available and analyst/management preferences.

Of these factors, the *motivation for the study* and *type of results needed* should be the most important factors that the analyst considers. The *motivation for the study* is particularly important when one considers different end uses of the risk information. This factor can play an entirely different role in the selection and application of various techniques and methods when consideration of the maturity of the process or activity is factored into the analysis. In this risk assessment, the methods and techniques were carefully selected to provide the results at the appropriate level and to balance the fidelity of the available information used in the analysis. The end use of the risk information from this study is to support a decision of whether to build the NBAF. In

addition, the risk information (hazards and accidents) was developed to support a decision of where to locate the NBAF, assuming that the facility is to be constructed. To meet the need for this level of decision making, it was imperative that defensible techniques and methods were used. However, given that the NBAF is currently only at the conceptual design stage, the application of the techniques needed to be more qualitative than quantitative. It was also important to present the methods, analyses, and results in a clear and understandable manner. To support all of these objectives, the approach or risk model used was based on two separate, yet parallel, paths towards estimating the primary components of a risk assessment.

The primary components of any risk assessment, as discussed above, are 1) determining the magnitude of potential adverse consequences resulting from accidents and intentional acts and 2) estimating the likelihood of those accidents that lead to adverse consequences. The overall approach used in the NBAF risk assessment involved two phases, each of which consisted of an unmitigated (uncontrolled) and a mitigated (controlled) condition state. These phases were 1) the hazards evaluation and 2) detailed accident analysis (DOE 2006).

Hazard analysis is the determination of material, system, process, and plant characteristics that can produce undesirable consequences, followed by the assessment of hazardous situations associated with a process or activity. Largely qualitative techniques are used to pinpoint weaknesses in design or operation of the facility that could lead to accidents. The hazards analysis examines the complete spectrum of potential accidents that could expose members of the public, on-site workers, facility workers, and the environment to hazardous materials (DOE 2006). The expected operations for the NBAF were obtained from knowledge of the activities at similar biological facilities, information contained in the NBAF Feasibility Report (presented in Section E.2 Facility Operations), and years of experience in operating laboratories and chemical and nuclear facilities.

Accident analysis has historically consisted of the formal development of numerical estimates of the expected consequence and probability of potential accidents associated with a facility. For the purposes of implementing the risk assessment for the NBAF, accident analysis is a follow-on effort to the hazard analysis—not a fundamentally new examination requiring extensive original work. As such, it requires documentation of the ***basis for assignment to a given likelihood of occurrence range*** in hazard analysis and performance of a formally documented consequence analysis. Consequences are compared with the minimum infectious dose (10 virions) to identify safety controls (including facility structure, various systems, and associated components) (CCPS 1992; DOE 2006; Ericson 2005).

Safety analyses specifically examine those hazards inherent in processes and related operations that can result in unmitigated (uncontrolled) release of hazardous material (i.e., biological, chemical, or radiological) or process-unique energy sources (e.g., high-pressure autoclave). Standard industrial hazards do not require explicit coverage in the accident analysis, since the concept of safety management programs is introduced to address these hazards. Standard industrial hazards, such as burns from hot objects, electrocution, falling objects, etc., are of concern only to the degree that they can be a contributor to a significant uncontrolled release of hazardous material (e.g., 115-volt wiring as initiator of a fire) or major energy sources such as explosive energy.

Unmitigated release is meant to consider material quantity, form, location, dispersability, and interaction with available energy sources; however, it is not to consider safety features (e.g., ventilation systems, fire suppression, etc.) that would prevent or mitigate a release. Final dose estimations representing the anticipated behavior of the facility under accident conditions were based on the mitigated accidents, wherein full or partial functionality of safety control or barrier is assumed.

In developing the application of techniques and methods, it was necessary to present the risks in this manner to emphasize the importance of the safety barriers and controls. Because the NBAF is at the conceptual design stage, there is less detailed information available for developing detailed system interaction models than would commonly be available with a final design or an operating facility. In addition, the end use of the risk information is not focused on the details of operation to, for example, improve performance in a particular

system or component. In this situation, the focus is on the significance or importance of the safety barriers in reducing risks. To address this difference, the concepts of unmitigated (uncontrolled) and mitigated (controlled) were employed.

Considering this model for hazards, accident, and risk analysis, the facility as unmitigated can be assumed to represent a condition where safety controls either do not operate reliably or effectively. In the case of reliability, a fully qualitative approach is used in the hazards evaluation, while a semiquantitative technique (event trees) was employed in the accident analysis. The benefit that can be gained by significantly improving preventative safety measures, such as procedures, quality assurance, and maintenance, is illustrated by comparing unmitigated frequency estimation with the mitigated frequency state. The event trees are used to demonstrate the various accident sequences and provide qualitative estimates of the change in accident frequency by improvement in the reliability (reducing the failure probability) of various safety barriers. The barriers that depend intrinsically on human control are assigned failure probabilities that are consistent with human reliability, whereas reliability of safety controls, which are primarily driven by mechanical failures, are assigned failure probabilities consistent with mechanical systems.

Failure data obtained from the study of nuclear facilities have provided insight into the likelihood of human error compared with that of mechanical systems. Examples of system failure data and human reliability data are provided in Exhibits 1 through 3. What is clearly seen is that the range of hazard rates and failure probabilities are quite large both in mechanical systems and human reliability. The types of components and systems that are expected in the NBAF will include pumps, valves, air handling units, and numerous electrical components. These systems, when appropriately designed for use in high-containment facilities, will exhibit similar reliability characteristics. Because the NBAF is currently at the conceptual design stage, much of the detail required to fully characterize the system failure probabilities does not yet exist. Information that is available can be used to construct generalized, credible bounding scenarios with upper-bound estimates of the failure probabilities for both mechanical systems and human reliability. This approach was used to evaluate the overall accident frequency for the six selected operational accidents analyzed for the NBAF. The nominal unmitigated human error likelihood was assigned a value of 0.1 and a mitigated (e.g., based on improved procedures, maintenance methods, two-person rule, training, etc.) value of 0.01. The nominal unmitigated failure probability for a essentially mechanical system or component was assigned a value of 0.01 and a mitigated value of 0.001. These values, as evidenced by Exhibits 1 through 3, provide a credible, yet bounding, estimate of individual event failure probabilities for use in estimating the overall frequency category that the accident falls within.

Table B-1 *Hazard Rates λ and Demand Failure Probabilities Q_d for Mechanical Hardware*[a,b]

Components	Failure mode	Assessed range on probability of occurrence	Computational median	Error factor
1. Pumps (includes driver)	Failure to start on demand Q_d[c]	$3 \times 10^{-4} - 3 \times 10^{-3}$/d	1×10^{-3}/d	3
	Failure to run, given start λ_0 (normal environments)	$3 \times 10^{-6} - 3 \times 10^{-4}$/hr	3×10^{-5}/hr	10
	Failure to run, given start λ_0 (extreme, post-accident environments inside containment)	$1 \times 10^{-4} - 1 \times 10^{-2}$/hr	1×10^{-3}/hr	10
	Failure to run, given start λ_0 (post-accident, after environmental recovery)	$3 \times 10^{-5} - 3 \times 10^{-3}$/hr	3×10^{-4}/hr	10
2. Valves				
a. Motor operated:	Failure to operate (includes driver) Q_d[d]	$3 \times 10^{-4} - 3 \times 10^{-3}$/d	1×10^{-3}/d	3
	Failure[e] to remain open (plug) Q_d	$3 \times 10^{-5} - 3 \times 10^{-4}$/d	1×10^{-4}/d	3
	λ_s	$1 \times 10^{-7} - 1 \times 10^{-6}$/hr	3×10^{-7}/hr	3
	Rupture λ_s	$1 \times 10^{-9} - 1 \times 10^{-7}$/hr	1×10^{-8}/hr	10
b. Solenoid operated:	Failure to operate Q_d	$3 \times 10^{-4} - 3 \times 10^{-3}$/d	1×10^{-3}/d	3
	Failure to remain open, Q_d (plug)	$3 \times 10^{-5} - 3 \times 10^{-4}$/d	1×10^{-4}/d	3
	Rupture λ_s	$1 \times 10^{-9} - 1 \times 10^{-7}$/hr	1×10^{-8}/hr	10
c. Air-fluid operated:	Failure to operate Q_d	$1 \times 10^{-4} - 1 \times 10^{-3}$/d	3×10^{-4}/d	3
	Failure to remain open Q_d (plug)	$3 \times 10^{-5} - 3 \times 10^{-4}$/d	1×10^{-4}/d	3
	λ_s	$1 \times 10^{-7} - 1 \times 10^{-6}$/hr	3×10^{-7}/hr	3
	Rupture λ_s	$1 \times 10^{-9} - 1 \times 10^{-7}$/hr	1×10^{-8}/hr	10
3. Check valves	Failure to open Q_d	$3 \times 10^{-5} - 3 \times 10^{-4}$/d	1×10^{-4}/d	3
	Internal leak λ_o (severe)	$1 \times 10^{-7} - 1 \times 10^{-6}$/hr	3×10^{-7}/hr	3
	Rupture λ_s	$1 \times 10^{-9} - 1 \times 10^{-7}$/hr	1×10^{-8}/hr	10
4. Vacuum valve	Failure to operate Q_d	$1 \times 10^{-5} - 1 \times 10^{-4}$/d	3×10^{-5}/d	3
5. Manual valve	Failure to remain open Q_d (plug)	$3 \times 10^{-5} - 3 \times 10^{-4}$/d	1×10^{-4}/d	3
	Rupture λ_s	$1 \times 10^{-9} - 1 \times 10^{-7}$/hr	1×10^{-8}/hr	10
6. Relief valves	Failure to open Q_d	$3 \times 10^{-6} - 3 \times 10^{-5}$/d	1×10^{-5}/d	3
	Premature open λ_o	$3 \times 10^{-6} - 3 \times 10^{-5}$/hr	1×10^{-5}/hr	3
7. Test valves, flow meters, orifices	Failure to remain open Q_d (plug)	$1 \times 10^{-4} - 1 \times 10^{-3}$/d	3×10^{-4}/d	3
	Rupture λ_s	$1 \times 10^{-9} - 1 \times 10^{-7}$/hr	1×10^{-8}/hr	10
8. *Pipes*				
a. Pipe ≤ 7.5 cm diam per section	Rupture/plug λ_s, λ_o	$3 \times 10^{-11} - 3 \times 10^{-8}$/hr	1×10^{-9}/hr	30

(*Continued*)

Exhibit 1 — Illustration of Hazard Rates and Demand Failure Probabilities for Hardware (McCormick, 1981). Original data table excerpted from NUREG 075.

Table B-3 *Human Error Probabilities*[a,b]

Demand failure probability	Activity
10^{-4}	Selection of a key-operated switch rather than a nonkey switch. (This value does not include the error of decision where the operator misinterprets situation and believes key switch is correct choice.)
10^{-3}	Selection of a switch (or pair of switches) dissimilar in shape or location to the desired switch (or pair of switches), assuming no decision error. For example, operator actuates large handled switch rather than small switch.
3×10^{-3}	General human error of commission, e.g., misreading label and, therefore, selecting wrong switch.
10^{-2}	General human error of omission when there is no display in the control room of the status of the item omitted, e.g., failure to return manually operated test valve to proper configuration after maintenance.
3×10^{-3}	Errors of omission where the items being omitted are embedded in a procedure rather than at the end as above.
3×10^{-2}	Simple arithmetic errors with self-checking but without repeating the calculation by redoing it on another piece of paper.
1/x	Given that an operator is reaching for an incorrect switch (or pair of switches), he or she selects a particular similar appearing switch (or pair of switches), where x = the number of incorrect switches (or pairs of switches) adjacent to the desired switch (or pair of switches). The $1/x$ applies up to 5 or 6 items. After that point the error rate would be lower because the operator would take more time to search. With up to 5 or 6 items, the operator doesn't expect to be wrong and therefore is more likely to do less deliberate searching.
10^{-1}	Given that an operator is reaching for a wrong motor operated valve MOV switch (or pair of switches), he or she fails to note from the indicator lamps that the MOV(s) is (are) already in the desired state and merely changes the status of the MOV(s) without recognizing that he or she had selected the wrong switch(es).
~1.0	Same as above, except that the state(s) of the incorrect switch(es) is (are) *not* the desired state.
~1.0	If an operator fails to operate correctly one of two closely coupled valves or switches in a procedural step, he or she also fails to correctly operate the other valve.
10^{-1}	Monitor or inspector fails to recognize initial error by operator. Note: With continuing feedback of the error on the annunciator panel, this high error rate would not apply.
10^{-1}	Personnel on different work shift fail to check condition of hardware unless required by checklist or written directive.

Exhibit 2 — Illustration of Human Error Probabilities for Various Activities (McCormick, 1981). Original data table excerpted from NUREG 075.

Table B-3 (*Continued*)

Demand failure probability	Activity
5×10^{-1}	Monitor fails to detect undesired position of valves, etc., during general walk-around inspections, assuming no check list is used.
0.2–0.3	General error rate, given very high stress levels, where dangerous activities are occurring rapidly
$2^{(n-1)}x$	Given severe time stress, as in trying to compensate for an error made in an emergency situation, the initial error rate x, for an activity doubles for each attempt, n, after a previous incorrect attempt, until the limiting condition of an error rate of 1.0 is reached or until time runs out. This limiting condition corresponds to an individual's becoming completely disorganized or ineffective.
~1.0	Operator fails to act correctly in the first 60 seconds after the onset of an extremely high stress condition, e.g., a large LOCA.
9×10^{-1}	Operator fails to act correctly after the first 5 minutes after the onset of an extremely high stress condition.
10^{-1}	Operator fails to act correctly after the first 30 minutes in an extreme stress condition.
10^{-2}	Operator fails to act correctly after the first several hours in a high stress condition.
x	After 7 days after a large LOCA, there is a complete recovery to the normal error rate x, for any task.

[a] Reactor Safety Study, Appendix III, Failure Data, WASH-1400 (October 1975).
[b] See Section 5-4 for discussion of use.

Exhibit 3 — Illustration of Human Error Probabilities for Various Activities (McCormick, 1981). Original data table excerpted from NUREG 075.

In the case of safety control effectiveness, the accident analysis relies on deterministic techniques to develop credible, yet bounding, scenarios that are used to examine the value or effectiveness of controls by comparing the unmitigated with the mitigated consequences. The difference between a facility that is considered to be in an unmitigated condition or state and one that is appropriately mitigated is characterized by the effectiveness of the safety controls. One can consider the unmitigated or uncontrolled state to reflect a facility without proper or effective ventilation, less stringent construction, and sometimes no critical safety controls. The mitigated case is a facility that has been appropriately designed, constructed, and operated to handle the high-containment pathogens proposed for study in the NBAF.

Using this model for evaluating the hazards, analyzing the accidents, and assessing the risk provides a comprehensive and bounding picture of the potential hazards, postulated accidents and consequences, and the possible risks. In addition, the analysis provides insight into those safety controls necessary to reduce the risk by orders of magnitude. The hazards evaluation, used for the NBAF analysis, identified and evaluated a wide range of realistic scenarios that were postulated to result in an adverse consequence, along with a qualitative evaluation of the protective features in place to prevent or mitigate the hazards and their adverse consequences. Safety controls include engineered safety systems (passive and active) and administrative controls (e.g., training and standard operating procedures, maintenance, and quality assurance).

The overall accident and risk analysis that examined possible sequences and post-release events focused attention on the magnitude of the possible consequences of a release, by considering mechanisms of transmission, susceptibility, virulence, and other aspects that influence the growth and spread of disease. The number of accident scenarios analyzed in detail was determined from the wide array of hazards scenarios that lead to high likelihood and consequences to the workers, public, and/or the environment.

Even with improved engineering and design of high-containment biological laboratories, accidental releases due to human error or maintenance failures still occur. Recent such events include the infection of workers with *Brucella* at one of Texas A&M University's BSL-3 laboratories in 2006; a 1-hour power outage in 2007 at the new BSL-4 facility of the Centers for Disease Control and Prevention (CDC) in Atlanta, before work with pathogens began, wherein the main and back-up power systems both failed and the negative air pressure system, a key element of pathogen containment, shut down; and, also in 2007, a release of foot and mouth disease to livestock on farms near the Pirbright high-containment laboratory in the United Kingdom due to a damaged and leaking drainage system at the facility (GAO 2007). Scenarios for evaluating the risks posed by the NBAF included potential realistic means of biological pathogen release and describing the various safety controls and barriers relied upon to protect laboratory workers, the public, and the environment.

Potential pathogen release included procedural and/or operational and procedural failures, including those that lead to worker exposures and infections, spills, loss of containment or control, and even large facility fires. In addition, consideration of contamination of the waste streams from the laboratory, intentional infection of laboratory workers, and unintentional release of laboratory animals or pests (such as mosquitoes, which are vectors for Rift Valley fever virus [RVFV]). Development of scenarios to address the numerous and varied situations that can lead to an adverse consequence provides insights for consideration of additional measures to enhance laboratory safety.

The NBAF risk assessment and accident analysis assumed, for purposes of providing an initial case for modeling, that a release occurred. Scenarios that include probabilistic evaluation of how a biological pathogen could be released lead to enhanced preventive measures. For example, the assessment of the spill accident highlighted the importance of laboratory worker training in reducing the likelihood of the event. In addition to laboratory-related interventions to *minimize the occurrence* of such events (that is, prevention measures), the risk assessment addressed, as an important safety control the response capabilities to *respond* to untoward events (that is, mitigating measures).

Without the discussion of preventive and mitigating measures, scenarios would not reflect necessary management and operational aspects of the NBAF, resulting in the loss or unavailability of vital risk information for decision making. Basing scenarios on as much factual information as possible provides relevance and ensures that the various accident scenarios portray more accurately the hazards associated with work in high-containment laboratories.

Pathogens Considered in the NBAF Analysis

The NBAF risk assessment was based on the selection of a variety of representative pathogens with appropriately diverse transmission characteristics (blood borne, transmitted on fomites, spread by aerosol, and/or requiring vectors, as well as the potential for maintenance in existing reservoir species). In addition, such aspects of transmission as high- or low-reproduction, latency, and incubation periods were considered in the assessment of risk at each of the six proposed NBAF sites. The pathogens considered in the NBAF risk assessment were foot and mouth disease virus (FMDV), RVFV, and Nipah virus.

The characteristics of the particular infectious pathogens considered in the NBAF risk assessment make it more likely that the pathogen could lend itself to the establishment of a chain of transmission that leads to the spread of infection in livestock and endemic species (Section 3.14.4). The NBAF risk assessment and accident analysis analyzed the potential for disease spread by three pathogens that all have relatively high transmissibility and are likely to spread beyond the animals initially infected.

These three pathogens require BSL-3 and BSL-4 protection levels, which include different factors for consideration. These factors include, for example, risk to laboratory workers (and uninfected animals) and whether the pathogen is endemic (neither FMDV, RVFV, nor Nipah virus are endemic viruses in the United States). BSL-3 laboratories are used to study biological pathogens that are potentially lethal and that are transmissible by the aerosol route (CDC 2007; NAS 2008). Consideration of the specific transmissibility, morbidity, and mortality—whether they are handled at the BSL-3 or BSL-4—is also important in evaluating risk. While engineered controls are typically more stringent (e.g., air line respirators in lieu of working in a biosafety cabinet [BSC]) and are greater in BSL-4 facilities, risks of human error maybe greater in BSL-3 laboratories.

Estimating the Probability of Release

The potential pathogen releases considered in the NBAF analysis included estimates of likelihood (probability), calculated using standard yet simple models with bounding values for the specific parameters. An infectious pathogen release could have a variety of consequences, including (NAS 2008) the following:

- No subsequent transmission, following a small initial pool of infection;
- Little or no subsequent transmission, following multiple exposures;
- Limited transmission that is contained by public health measures; and
- Amplified transmission.

Because of the pathogens selected for the NBAF risk assessment, the potential for amplified transmission outcome was the primary focus. The qualitative analysis of potential outcomes considered the impact of the local characteristics (population density, livestock availability, wildlife, and vector availability) for each of the six proposed sites as discussed in Section 3.14.4.

Risk assessment addresses both the probability and the consequences of adverse events. The scenarios and pathogens discussed were used in the risk assessment to analyze and present the likelihood of adverse events for both mitigated and unmitigated conditions. The qualitative evaluation of the likelihood of the impacts after a release was based on information available from the chemical, nuclear, and biological communities.

The amplified transmission outcome (consequence) is particularly important for the FMDV, RVFV, and Nipah virus since these pathogens could establish a successful chain of transmission in both livestock and wildlife species in the United States. Examples of foot and mouth disease (FMD) outbreaks in England and RVFV and Nipah virus outbreaks around the world illustrate the magnitude of the adverse consequences from a potential release. Drastic measures to control FMD outbreaks in cattle can and often do lead to great economic loss.

The consequences of a release of an infectious pathogen from a high-containment laboratory depends on numerous factors, such as the characteristics of the pathogen, the pathway by which it is spread, and the size and characteristics of the population that is exposed to it. The major concern for the NBAF analysis is the potential for outbreaks of disease in livestock, wildlife, and, to a lesser degree, the human population.

Modeling is another way of assessing how disease caused by a pathogen may be spread. Modeling may also be an important tool in devising appropriate mitigating strategies. Calculating the subsequent outcome, after a potential release of a biological pathogen, with models is difficult and uncertain. The process of *transmission*, which has a high degree of uncertainty, is a major parameter in determining the results of a release. It is also difficult and uncertain to estimate the number of contacts between animals, between people, or between animals and people (NAS 2008). In addition, since the RVFV is predominantly a vector-borne disease, the potential for widespread transmission in amplified by mosquitoes.

The accuracy and precision of a single model to simulate both the transmission of an aerosol-transmissible pathogen and that of a fomite-transmitted pathogen is uncertain and requires great effort to verify or validate results (NAS 2008). Simple descriptions and qualitative discussions have distinct advantages over the use of controversial and complex models. First, the behavior of simple models is relatively well understood because the mathematics are well established. The effect of changing inputs in simple models is relatively transparent as in the case of distinguishing between the mitigated and unmitigated accidents. More complexity and detail often does not add to confidence or accuracy of the results. The accuracy is most often determined by the data used to develop input. These data are often either not available or in a form that includes many uncertainties (NAS 2008). This is illustrated by the data available for livestock in the vicinity of each proposed NBAF site. The data were provided in terms of livestock per county without a differentiation as to the species of animal.

The focus of risk assessment, performed on the NBAF, was on potential bounding consequences and the identification of safety controls to prevent the release or mitigate the consequences, including the need for a robust and comprehensive emergency response program. A robust emergency response program and detailed implementation plans are an essential safety control and are identified as a practical aspect of managing an incident (Greenberg 1991).

The detailed analysis of potential consequences associated with operation of a NBAF was developed specifically for each of the six potential sites where the NBAF could be located. In the No Action Alternative, the risks and consequences specific to the NBAF would not occur. However, since PIADC currently operates a BSL-3Ag facility, the risks and consequences presented in this analysis would be applicable to the No Action Alternative, as well. The results and conclusions are presented to inform a decision to construct and operate the NBAF and to provide support for a final determination on which of the six sites is best suited to accommodate the facility, if the decision is made to construct and operate the NBAF. To support this critical decision, the analysis was developed around the specific hazards associated with the operation of a large high-containment biosafety laboratory. The hazards and the subsequent accident analyses focus on the potential for a release of the three representative viral pathogens and the types of safety controls that are to be incorporated into the design and operation of the NBAF that would be relied upon to prevent a release or to mitigate the consequences of a release. As stated in Chapter 1, the Department of Homeland Security (DHS) anticipates that the NBAF would initially focus BSL-3Ag research on African swine fever, classical swine fever, contagious bovine pleuropneumonia, FMDV, Japanese encephalitis, and RVFV, as well as BSL-4 research on Hendra and Nipah viruses. FMD, Rift Valley fever (RVF), and Nipah viruses present the most significant and

unique challenges compared with any of the other pathogens currently proposed for study at the NBAF. Therefore, the accidental or intentional (criminal or terrorist activity) act that results in the release of one or more of these three pathogens is used in the following consequence analysis. In conveying the critical information necessary for the decision makers and stakeholders to fully appreciate the overall potential impacts from operations of the NBAF, specific risk ranking strategies were applied to the evaluation of the hazards and accidents. The risk ranking is based first on the likelihood of an accident or intentional release occurring and, second, the subsequent consequences for both mitigated and unmitigated events. The differentiation between the unmitigated and mitigated events provides the decision makers and stakeholders the essential information to understand and appreciate the reduction in risk to the workers, the public, and the environment between the unmitigated and mitigated events (DOE 2006).

E.2 FACILITY OPERATIONS

In order to determine the NBAF hazards, a description of the facility and the proposed operations is warranted. The primary goal of the NBAF is to provide the United States with the first integrated agricultural, zoonotic disease RDT&E facility. The facility will ultimately be able to provide the capability to address high-consequence zoonotic agents and foreign animal diseases (FADs).

The current NBAF conceptual design considers the following programmatic needs:

- Nine BSL-3Ag and two BSL-4 modules to conduct three BSL-3Ag and two BSL-4 agro-countermeasure research and development programs simultaneously.
- Supporting the research and development activities are core laboratory Pathology and Analytical Chemistry modules that will include electron microscopy, other imaging capabilities, and a gamma irradiation capability to inactivate samples for shipment outside of biocontainment.
- Additional laboratory modules will include insectary spaces necessary to support primary research activities. The BSL-2 insectary combines the functions of breeding, rearing, manipulating, and pre-test and post-test holding/incubating of non-infected arthropods. Other insectary research spaces within BSL-3E and BSL-3Ag will be used for holding infected live insects and for virus transmission studies to and from both infected and non-infected large animals and small animals.
- A separate training module integrated within the facility will meet a primary mission requirement of the Animal and Plant Health Inspection Service (APHIS) to train veterinarians to recognize and diagnose FADs. This facility will have a modern infrastructure including a distance learning capability. Courses will operate anytime during the year and will be arranged to integrate with, and not conflict with, the separate security requirements necessary for the main research facility.
- A current good manufacturing practice (cGMP) module is needed for small-scale vaccine and reagent production. An industry partner will still be needed for large-scale manufacturing. This module will allow for production of two vaccine candidates at one time. Module components at BSL-2 will include a Viral Production Room, a Vaccine Sterile Assembly and Fill Room, a Vaccine Lyophilization Area, and a Diagnostic Reagent Production Room.

NBAF Biological Hazard

The hazard screening process was based on a thorough knowledge of the biological hazards that have been designated as research candidates for the NBAF. Representative worst-case non-zoonotic and zoonotic agents are identified for detailed analysis under operational, accidental, and intentional release scenarios.

The DHS foresees multiple uses and goals for the NBAF. These include

- Serving as a unique BSL-3Ag and BSL-4Ag livestock laboratory capable of developing countermeasures for FADs; and
- Providing advanced test and evaluation capability for threat detection, vulnerability assessment, and countermeasure assessment for animal and zoonotic diseases.

Microorganisms that cause human infectious diseases are acquired from two major sources: outside the body (exogenous) and ones that inhabit certain body sites (endogenous). Exogenous sources are the ones of concern from the NBAF. Most exogenous infections are acquired from other individuals by direct contact, by aerosol transmission of infectious respiratory secretions, by ingestion of contaminated food or drink, or indirectly through contact with contaminated inanimate objects (e.g., fomites) (Fleming 2006).

DHS anticipates that the facility would focus on FMD, classical swine fever, African swine fever, RVF, Nipah virus, Hendra virus, contagious bovine pleuropneumonia, and Japanese encephalitis. DHS plans to perform research at the NBAF to study how these pathogens enter the animal, what types of cell the pathogen affects, what effects the pathogen has on cells and animals, how newly developed countermeasures help protect the animal against the pathogen and prevent disease, and what new detection methodologies are (CRS 2007). To evaluate the hazards posed by these potential research areas at the NBAF, representative pathogens that bound the range of potential consequences were identified. The representative pathogens selected for the detailed hazards and accident analysis are FMDV, RVFV, and Nipah virus. The basis for the selection of these pathogens is presented below.

FMDV

FMDV are viral pathogens handled at the BSL-3Ag biological safety protective level and deserve specific discussion in the NBAF EIS. FMDV causes debilitating vesicular disease and death in all cloven-hoofed livestock and wildlife, i.e., ruminants and ungulates (hoofed animals). With seven serotypes of FMDV, each of which causes FMD, it is internationally the most feared disease of livestock and wildlife. The viruses spread with alarming speed through herds and flocks of susceptible animals. The disease causes high morbidity and clinical disease that results in dramatic losses of condition and productivity, from which most infected stock never fully recover. The economic consequences are huge, and the loss of international markets is devastating. Equines, poultry and fowl, and humans are not infected. Although humans are not considered susceptible to infection, the viruses can persist in the human upper respiratory tract for up to 48 hours, making them potential vectors if they are exposed.

FMDV are highly infectious and are transmitted mainly by aerosols and simple contact with fomites (contaminated materials, inanimate objects, clothing, veterinary equipment, vehicles, foodstuffs, manure, soil, and vegetation). Viruses are excreted from and present in blood and body fluids, including respired air, saliva, vesicular fluids, and tissues of the vesicles, which are a hallmark of the infection; semen; vaginal fluids; urine; feces; meats; and milk. Infected animals can excrete high concentrations of virus in respired air, secretions, and fluids. For example, cattle may excrete up to 126,000 $TCID_{50}$ virions/24 hours in expired air. Swine (pigs) have been measured at rates up to 3.98×10^8 $TCID_{50}$ virions/24 hours in expired air. Pathogen doses as low as 10 to 20 $TCID_{50}$ could infect sheep and steer populations, respectively (Sorensen 1999). In other words, cattle can respire in a 24-hour period sufficient FMD virions to result in 100,000 doses. The infectious dose for FMDV, as reported in the Canadian Food Inspection Agency's Pathogen Safety Data Sheets, is 10 virions. There is no minimum infectious dose (MID) provided for either RVFV or Nipah virus (CFIA 2005). The MID for these viruses is assumed to be equivalent to that for FMDV. The Pathogen Safety Data Sheets for Nipah virus, FMDV, and RVFV are attached to this appendix.

The minimum dose of natural aerosol to infect a pig has not been determined, but some observations suggest that it is probably much higher than that for other species (Donaldson 1999). The virus measures 27-28

nanometer (nm), are notoriously resistant to inactivation, and are extremely difficult to contain. Numerous releases and exposures have been documented from laboratories and facilities, with movement up to 50 kilometers (km) having been reported under favorable environmental conditions (Sorensen 1999). Viruses will survive in moist environments such as manure, soil, and organic materials. Acidic and alkaline conditions and sunlight (ultraviolet light) will inactivate the viruses (inactivation parameters include time, concentration, and temperature, as well as humidity). Farms, ranches, and agricultural premises are normally held fallow for 3 months before sentinel susceptible livestock are reintroduced to contaminated environments. FMDV is particularly important to evaluate because inhaled viruses can be trapped by airway mucous and be swept from the lungs into the gastrointestinal tract, leading to a fatal result for the animal. In addition, FMDV can be aerosolized and exhaled in the time necessary for the disease to take its course. Laboratory workers who come into contact with excretions or respired virions can have the virus surviving in their respiratory tracts for up to 48 hours, thereby becoming a potential vector in the spread of the disease.

RVFV

RVFV deserves specific discussion in the NBAF EIS for several reasons as presented below. RVFV is a viral pathogen handled at the BSL-3E and BSL-3Ag (for work with infected animals) biological safety protective levels. RVFV causes disease and death in cattle, sheep, and goats. Abortion rates in pregnant sheep are nearly 100%, and about 90% of infected lambs die. Cattle and calves also suffer but at less dramatic clinical rates. Literature from Africa does not address infections in ruminant or other ungulate wildlife, except for antelope. However, there will be concern within the game/wildlife community because RVFV infection in United States (U.S.) wildlife species in the same genera as livestock species is possible (e.g., the genus *Ovis* includes domestic sheep and bighorn sheep, and the genus *Capra* includes the domestic goat and mountain goats). The pronghorn is the only living representative of the genus, *Antilocapra* (pronghorn are not antelope), and cervids include deer and elk. The susceptibility of any of these species or genera to RVFV is unknown. RVFV also can infect rodents (such as field mice, squirrels, voles, and rats), cats, and dogs.

The virus averages 100 nm in size and is transmitted to animals and humans by infected mosquitoes and possibly biting flies. Other biting insects such as ticks and black flies appear able to harbor and transmit the virus during epidemic outbreaks. Several North American species have been shown experimentally to be infectable and capable of transmitting the virus. Certain *Aedes* mosquitoes in Africa are known to transmit virus through their eggs. Thus, there is potential that RVFV could establish a continuous ecological cycle in the United States if it escaped from a research laboratory. One to three percent of infected humans develop severe hemorrhagic fever and/or encephalitis that may be fatal. These patients often have sufficient virus in their blood to permit mosquito infection and transmission to other humans and animals. Contact with, or consumption of meat from, infected domestic animals also is a source of infection. Virus is present in blood and body fluids that are highly infectious for humans at risk humans, such as veterinarians and abattoir workers, and livestock via aerosols (respiratory route of transmission). RVFV from blood, body fluids, and tissues is a significant hazard because the virus can be aerosolized from animal activity and room, laboratory, or cage wash-down operations.

Nipah Virus

Nipah viruses are pathogens handled at the BSL-4 biological safety protective level and deserve specific discussion in the NBAF EIS for several reasons. Nipah viruses are recently described zoonotic viruses that cause highly fatal encephalitis in humans.

Under particular limited circumstances, the virus can be contagious among humans. In Malaysia, 265 cases of encephalitis with a 40% death rate were reported primarily among pig farmers (Chua 1999; Goh 2000). In this outbreak, it was shown that close contact with pigs, especially sick pigs, was the major risk factor for human infection. Respiratory infection of humans by aerosols from infected pigs is suspected.

Nipah viruses exhibit an extended host range, with natural infections including swine, humans, and, to a minor extent, cats and dogs. Serologic studies imply that infection can occur in horses and bats. The viruses are carried by fruit-eating bats (absent from the western hemisphere), and infections in humans and animals can be contracted from bats via fruit or other fomites contaminated by infected bats.
Nipah virus' average size is 500 nm. The viruses have been detected in respiratory secretions and urine of infected patients in Malaysia, suggesting that person-to-person transmission might be possible in some situations. None of the patients showed obvious pulmonary symptoms.

Secondary human-to-human transmission of Nipah virus was not shown for outbreaks in Malaysia or Singapore, but findings from outbreaks in Bangladesh from 2001 to 2007 suggested that close family contact can result in transmission. Dr. Pierre Rollin of the CDC indicated that of the 35 or so cases of Nipah virus infection acquired from humans, most were linked to cutaneous infection of caregivers who had held open the mouth of the patient while giving food. The virus is presumed to have entered breaks in the skin barrier from the saliva.

Recent infections among humans in Bangladesh present new evidence regarding epidemiology, virulence, and contagiosity including those listed below.

- Pigs were not involved. Humans are believed to have been infected by consuming date palm sap contaminated by fruit-eating bats.
- Pulmonary infection was followed by encephalitis and death in as little as 48 hours.
- The reproduction ratio was found to be 0.51, meaning that 0.51 additional infections were believed to have been contracted from each primary infectious person.
- Human-to-human transmission and the higher fatality rate (86 of 122, i.e., 70%) might be the result of poor sanitary conditions and lack of health care resources.
- The strains of viruses from humans in Malaysia and Bangladesh are genetically different.

E.2.1 BSL-4 Laboratory and Animal Biocontainment Facilities

BSL-4 is required for work with dangerous and exotic agents that pose a high risk of aerosol-transmitted laboratory infections and life-threatening disease to humans. The BSL-4 biocontainment area of the NBAF will be designed with the concept of maximum flexibility. Each BSL-4 laboratory/BSL-4 animal area is designed to operate in combination with or separately from the other. This further flexibility allows each of the suites to allocate additional animal holding capability from the other in support of their program if the need arises. Each of the two BSL-4 laboratory/BSL-4 animal suites will have a dedicated Change/Suit Change Room that will provide the ability to separately enter into and egress out of the BSL-4 laboratory and BSL-4 animal space through dedicated chemical shower/airlocks. The proposed design will provide enhanced operational flexibility and adaptability of valuable research space.

Program requirements/net square foot areas for the BSL-4 laboratory/BSL-4 animal suites included are based on the defined needs by the DHS/U.S. Department of Agriculture scientific research user group for two stand-alone, completely redundant, BSL-4 laboratory/BSL-4 animal suites each comprised of the following:

BSL-4 Laboratory Area	BSL-4 Animal Area
• Men's and Women's Change/Suit Change Room (shared with adjacent BSL-4 animal area within the suite) • BSL-4 Chemical Shower • BSL-4 Laboratory • BSL-4 Autoclave and Dunk Tank • BSL-4 Fumigation Vestibule (shared with adjacent BSL-4 animal area within the suite) • BSL-4 Virus Collection/Equipment Room • BSL-4 Cabinet Lab (shared with laboratory area of adjacent suite) • BSL-4 Cabinet Lab Change Room • BSL-4 Staff Corridor	• Men's and Women's Change/Suit Change Room (shared with adjacent BSL-4 laboratory area within the suite) • BSL-4 Chemical Shower • Two BSL-4 Large Animal Holding Rooms (including Body Shower/Feed Storage) • BSL-4 Animal Holding Room (Rodents) • BSL-4 Procedure Room • Two BSL-4 Fumigation Vestibules (one is shared with BSL-4 laboratory area within the suite) • BSL-4 Necropsy (including Cold Storage space, shared with animal area of adjacent suite) • BSL-4 Staff Corridor • BSL-4 Animal Corridor

In addition, the BSL-4 suites will be supported by a protective suit storage and supply room and an operational monitoring room located immediately adjacent to, but outside of, the biocontainment perimeter.

Each BSL-4 (non-rodent) animal holding room will potentially accommodate the following number of animals for a given species:

Animal Species	Species Size Pounds	Animal Count Per Room
Dairy/beef cattle	1,400	2
	800	4
	440	6
Sheep	<100	16
Swine	<200	14

Each subsection to follow will provide a brief statement as to how the subsection impacts the hazards analysis, where applicable.

E.2.1.1 BSL-3Ag Animal Biocontainment Facilities (Agro-Countermeasure Program)

BSL-3Ag is required to protect the environment from a higher economically important risk pathogen where research studies utilize large agricultural animals and where the walls/ceilings/floors of the animal isolation room now serve as the primary biocontainment. The table below is a representation of the anticipated animal species and sizes likely to be housed in NBAF.

Animal Species	Species Size Pounds	Minimum Space Required per Animal Feet Squared
Dairy/beef cattle	484 – 1,430	48 – 144
Sheep	55 – 110	10 – 15
Swine	110 – 440	15 – 48
Whitetail deer	150	48 – 144
Poultry (chickens & ducks)	6.6	3
Mice/rats	<200 g	23 in^2
Bison	440 – 1,400	48 – 144
Equine	—	144

Handling and housing methods vary largely based on the characteristic of each animal species. The design of the animal holding areas will accommodate safe working zones around the perimeter of the pens for research staff. Some of the key animal behavioral considerations that will impact the design characteristics of the NBAF include the following:

- Dairy cattle – Large and potentially dangerous to staff. Means of worker safety include squeeze chutes and penning and gating. These configurations allow animals to be maneuvered with minimal risk to staff. Produce large amounts of manure waste and will require significant amounts of water for cleaning.
- Beef cattle – Large and potentially dangerous; more aggressive than dairy cattle. Will also produce large amounts of waste.
- Bison – Very powerful strong and aggressive animals. Will require reinforced penning systems to maintain control for safety.
- Equine – Can be a nervous species. Skilled caretakers required to maintain known relationship. Ceiling height and safe work zones are required.

It is assumed that the animal areas will be occupied only intermittently during the day and night when training classes are not being held. The animal handlers visit at least twice a day to feed and care for the animals and clean the rooms. The program staff visits the rooms on an as-required basis, which may be daily or a few times a week.

In addition to the mission and educational requirements of the BSL-3Ag facilities, there are additional support operations that must be considered. Among them are necropsy, personnel, space decontamination, and waste management described below.

The NABF facility will utilize a standard pen size designed around the use of large animals at 144 square feet (ft^2) for flexibility. The standardization to one size will allow the facility to accommodate more animals at lower weight ranges as long as the weight of one individual does not exceed the minimum required by the National Research Council guide. From the Feasiblity Study, the following table gives an approximate bounding number of animals in the NBAF:

	Large Cows (up to 1,430 Pounds)	Medium Cows (up to 730 Pounds)	Small Cows (up to 440 Pounds)	Swine	Sheep
BLS-3Ag	138	276	414	798	912
BSL-4	28	56	84	196	224
Total	166	332	498	994	1,136

Relationship to Hazards Analysis: The number and type of animals affect the amount of virions that are expelled by infected in the facility. For example, animals can expel virions by respiration, urination, and defecation.

E.2.1.2 BSL-3Ag Necropsy

Currently, there is a need for two similarly sized necropsy suites. One necropsy suite shall serve both the general vivarium, as well as the FAD diagnostic training facility; the second necropsy will have two separated procedure areas that will serve the bulk of the general vivarium operations. The necropsy rooms will be built with the same BSL-3Ag biocontainment systems as the animal rooms. As the dirtiest rooms in the complex, necropsy is totally sealed and easily decontaminated. The necropsy rooms are required to have a euthanasia room, a minimum of two necropsy tables, a formalin preparation lab, a carcass cooler, and separate shower-

out locker facilities. While it is not anticipated that a necropsy room will be dedicated for the FAD diagnostic purposes, one necropsy room will be provided with a fixed necropsy table and up to eight portable tables for use by students and instructors. The requirements for this room are similar to those for other necropsy suites, except that this room will accommodate a minimum of 10 to 15 students.

Because training will be performed with select agents, appropriate requirements for security, storage, inventory control, and other features will be included in the design. In addition, capability will be allowed for video presentation to a classroom or associated lecture room as part of the FAD diagnostic training program. Additional functional requirements include access to an autoclave, dunk tank, and pass box for decontaminating and distributing samples for use in the BSL3-Ag animal facilities. A method for decontaminating respirators will be located adjacent to the necropsy shower block.

A 2-ton capacity monorail with trolley and electric hoist will be provided in the necropsy suite and cooler room for transporting carcasses.

The training is intended as a hands-on experience. For a typical class, students would change clothes in the main locker room and enter the animal rooms through a second shower room from the clean corridor. After observing and diagnosing infected animals, the students move through and stay within the dirty corridors. Because of the length of the course and the topics of study, normal protocols to prevent cross-contamination between rooms would not be observed (DHS 2007).

Decontamination: High-pressure washing – portable or central high-pressure wash stations are commonly used for moving and removing materials adhered to surfaces, walls, ceilings, and floors. Hot water (70°C to 90°C [158°F to 194°F]) is pressurized at 8.5 to 10.5 MPa (1,200 to 1,500 psi) and delivered via hard and flexible pipe and hoses to a wand with hand lever control. High-pressure systems can be combined with detergents or chemicals to aid in the cleaning or disinfection process. Portable or localized addition of chemicals is preferred over central mixing of chemicals. Wands with manual hand controls are required to reach surfaces with a spray pattern effective for cleaning. High ceiling areas are difficult to reach, and wand extensions or raised platforms, such as scaffolds, are necessary for cleaning these areas.

Decontamination: Equipment wash room – an equipment wash room will be provided for various pieces of equipment including socialization toys, penning, animal caging systems, and other reusable animal supplies. Typically, this equipment is capable of washing material in 180°F water as recommended in the Nuclear Regulatory Commission (NRC) guide and supported with redundant instantaneous water heaters and will include the following:

- Bulk pass-through type equipment and cage washing systems;
- Staff entry and gowning as the primary entry point, with airlock and personal protective equipment (PPE) changing station;
- Gross wash for initial spray-down and acid soak of equipment, animal racks, caging, and penning;
- Staging for dirty and clean cages;
- Equipment zones and dedicated space for placing washing equipment, with floor pits and overhead clearance for utility services; and
- Detergent storage, located directly adjacent to the equipment zones to stage and pump chemical detergents to the washing equipment.

Decontamination: Space – primary and secondary biocontainment envelopes need to be able to pass various types and sizes of materials, tools, equipment, and waste out of the biocontainment envelope from one area to another. Current biocontainment laboratories adopt several technologies and solutions.

- *Dunk tanks:* A barrier-designed dunk tank allows for the passage of materials that are heat sensitive or capable of being decontaminated using a liquid disinfectant or virucide across the biocontainment barrier. The types of disinfectants (phenolics, glutaraldehydes, quaternary ammonium compounds, hydrogen peroxide, alcohols, proteinated iodines, and sodium hypochlorite) vary both for the types of infectious agents and their characteristics, such as corrosiveness, viability over time, and concentrations in use. Biosafety protocols will determine which disinfectant is used, when it is replenished, and what concentrations are required. Dunk tanks will be provided at all necropsy rooms.
- *Autoclaves:* Materials taken from primary biocontainment zones must be decontaminated including waste (disposable PPE, paper goods, and medical supplies); mobile and shared equipment; isolators, cages, racks, and penning; medical and procedural supplies (clinical waste); and samples (pathologic waste). For most materials, decontamination can be achieved via a steam autoclave. For certain sensitive items, alternate methods of decontamination including vaporized hydrogen peroxide (VHP), chlorine dioxide, paraformaldehyde burn, and ethylene oxide are available. Double-door autoclaves located at the biocontainment barrier envelope allow material to be passed from the dirty side to the clean side with a full sterilization cycle. Interlocking doors also prevent both doors from being opened at once. The double-door barrier autoclave has two types of barrier seal. It is recommended that the tight seal is pressure capable to at least 500 Pa (2 in. wg), has a flange that is bolted with a flexible neoprene (or silicone) seal, and has a receiving flange that is cast into the wall cavity. The location of the flange seal with respect to the autoclave body is important to consider in terms of maintenance requirements. Some autoclaves have close to 30 valves, numerous filters, and high-maintenance door seals. This combination requires that maintenance be both preventative and corrective. The autoclave body should be located on the clean side of the biocontainment barrier and the chamber condensate hard-piped directly to the waste treatment system. Autoclaves are required inside the biocontainment zones of the necropsy rooms (primary containment), and along the secondary biocontainment corridor leading to the non-contained zones. Each zone is considering two autoclaves for redundancy and is currently considering three sets of redundant bulk autoclaves serving the BSL-3Ag facility including three medium-size autoclaves to serve smaller loads, when needed.
- *Gas Decontamination:* Gas decontamination will be considered for large pieces of equipment (such as penning, BSCs, and carts) as they pass between barriers of biocontainment. Both VHP and paraformaldehyde are gases effective for this application, which is dependent on room size. A paraformaldehyde gas-generating machine capable of decontaminating large room spaces will also be necessary. This piece of equipment also incorporates gas neutralization (ammonium carbonate) as part of the sterilization cycle. The humidity levels and the temperature are important for effective sterilization (70% RH and 20°C [68°F]). The decontamination rooms are designed for tightness with bioseal dampers on the ventilation ducts, tight barrier doors with specialized seals, and tight service penetrations. Fans, which are used to circulate the gas within the room, can either be permanently mounted or portable. These rooms can also be used for transferring materials and animals into the facility and will require interlocking doors, penning, and door windows. Animal air locks can be designed to accommodate gaseous decontamination of equipment. VHP is an alternative for room decontamination within the facility. Infrastructure will be required to be in place to support VHP equipment, including supply and exhaust ports into the room, circulating fans, vaporizer equipment, and dehumidification equipment. Since this infrastructure will be provided in the facility, it is intended to utilize certain rooms or airlocks as a means to decontaminate large pieces of equipment on a periodic basis. One disadvantage to gas-phase decontamination is that it is best served for surface treatment and does not kill agents that are sealed off from exposure. For this reason, autoclaves are provided.

Decontamination: Waste Treatment – solid waste and liquid effluent decontamination is required of all materials infected with pathogens, including animal carcasses. Any waste disposal technology must consider the following design criteria:

- Ease of transport and loading into treatment equipment;
- Worker protection and reduction of biohazard aerosol generation;
- Decontamination effectiveness of given technologies;
- Consistent and repeatable performance;
- Volume reduction for final disposal;
- Compliance with local, state, and federal environmental requirements;
- Cost-effectiveness (capital and operating);
- Technical maturity and degree of automation to achieve effective labor savings; and
- Reliability and maintainability.

Several decontamination and sterilization technologies were initially reviewed and will be studied further: chemical, incineration, rendering, autoclave, and alkaline digestion.

Relationship to Hazards Analysis: Activities during necropsy lead to the potential for an LAI from personnel errors such as a procedural violation or a mechanical failure resulting in a cut or inhalation. Since training activities will be conducted in the necropsy suites, the inexperience of a trainee could increase the probability of an LAI.

E.2.1.3 Support Laboratories at the BSL-2 Level

To support the current and projected scientific programs, there will be more BSL-3E laboratories than BSL-2 laboratories at the facility. It has also been determined that the programs within the BSL-3E and BSL-2 labs will share "CORE laboratories" to help maximize space and provide for an efficiency of building systems. Programs that will need support from BSL-2 activities are the programs in BSL-4 suites and, possibly, in the BSL-3Ag animal holding rooms.

BSL-2 Insectary for Rearing – A vector-borne disease program will use insects and arthropods procured from vendors or other laboratories and/or reared only in this BSL-2 facility; arthropods reared and held in the BSL-2 insectaries are not infected with pathogens. The inclusion of insectaries at the NBAF will provide Agricultural Research Service (ARS) scientists with the option to move other laboratories to the NBAF and allow DHS to conduct countermeasure efficacy trials using natural challenge models. The BSL-2 insectaries would be in the same area as the BSL-2 laboratories; clean insect/arthropod rearing and holding will be done in this BSL-2 space.

Insects/arthropods will be moved into BSL-3E, BSL-3Ag, or BSL-4 biocontainment for infection with pathogens; at least one ARS program and at least one DHS program will involve arthropods as vectors. Infected insects/arthropods will be sorted microscopically (for sexing, counting, and blood meal feeding) in modified BSCs and incubated prior to use in animal transmission and laboratory studies. Studies may include virus-vector interactions and vector-host interactions in which non-infected arthropods are fed on infected hosts or infected arthropods are fed on non-infected hosts, as well as virus-host interactions. Holding of infected vectors and infecting of vectors will be performed in the BSL-3Ag and BSL-4 animal rooms or laboratories. Vector-specific studies may include vector biology, vector competence, vector capacity, and vector genetics.

BSL-2 NAFMDVB (North American Foot-and-Mouth Disease Vaccine Bank) – The room will be at positive pressure in relation to the corridor, which is not desired and leads to the determination and basis for recommending improved safety controls. It is these types of configurations that are so vital to development of the wide array of hazard scenarios. For example, a need for liquid nitrogen (LN2) freezers for storage of vaccines was identified, and this lead to the evaluation of cryogenic hazards. While these ultimately are screened as standard industrial hazards, it is important to understand all hazards in the development of the risk assessment.

BSL-2 Core Tissue Media Preparation – This area will include a cell culture facility, a media preparation facility, an area in BSL-2 for production of non-infectious reagents and reference panels (nucleic acids and inactivated viruses), and an area for working with non-infectious vectors (viruses and bacteria).

BSL-2 Core Cell Culture and Media Preparation – This is a larger laboratory with two 6-feet wide BSCs and sinks near the columns, and the remaining case work will be movable for flexibility.

BSL-2 Glassware/Metal Wash – The trend is toward the usage of more disposable materials instead of glassware. These rooms will be shared core laboratory spaces.

BSL-2 Core Storage – This will be a shared core storage area. Sometimes when a new piece of equipment is procured, there is a need to set it up, calibrate it, and test its function prior to moving it into biocontainment.

BSL-2 Core Packaging and Shipping Reagents – This area will be utilized for packaging and shipping reagents to the National Animal Health Laboratory Network laboratories and/or to the National Veterinary Services Laboratories,, to international reference laboratories, and to other collaborators, as required. Permits will be required for shipping.

BSL-2 ARS Microbiology/Molecular Biology – This will be a large open laboratory that can function as an high throughput testing (HTP) laboratory, if necessary.

BSL-2 APHIS Microbiology/Molecular Biology – This laboratory will serve for reagent production, proficiency panel development, and other molecular techniques.

BSL-2 DHS Microbiology/Molecular Biology – This is a large open laboratory specific for DHS research and development.

BSL-2 APHIS Class III BSC/Processing Rooms for Diagnostic Samples – The Class III BSC will be utilized for the sorting, examination, and processing of samples (diagnostic accessions, safety test accessions, and forensics samples). The Class III BSC will allow safe "splitting" and processing of samples prior to the entry into the BSL-3E laboratories. There will be a need for an anteroom and walk-in cooler and freezer storage for samples that are processed and stored in the BSL-2 space. The Class III BSC will have a direct pass-through to the BSL-3E laboratories. There will also be a need for an autoclave to process waste material and move it outside of the Class III BSC.

Relationship to Hazards Analysis: The existence of an insectary, for example, provides an opportunity for infected insects to escape from the facility, particularly during transport to/from different sections (biosafety levels) in the facility. Smaller organisms like insects are more probable to escape from the facility than larger animals such as swine or cattle.

E.2.1.4 Support Laboratories at the BSL-3E Level

BSL-3E provides the necessary biocontainment for laboratory agents that may be indigenous or exotic to the United States and can be contracted by the respiratory route. They may cause serious or lethal diseases to animals or cause moderate economic losses to the animal industries. The BSL-3E laboratories will directly support the BSL-3Ag program spaces and will consist of two types of BSL-3E laboratory spaces. The primary type will be a typical BSL-3E laboratory with filtration and ventilation enhancements described elsewhere. A second type is denoted as BSL-3E "isolation" laboratory, and it will also have additional filtration and ventilation enhancements to support work with FMDV. A subset of the BSL-3E isolation laboratory is a "high-risk" laboratory with additional enhancements that are required for spaces in which centrifugation and other potential aerosol-generating activities are conducted outside a BSC.

The standard BSL-3E laboratories will have a bubble-tight isolation damper and no high-efficiency particulate air (HEPA) filters in the supply air ducts, but the BSL-3E isolation laboratories will have HEPA filters in the supply air ducts. Air pressure–resistant (APR) doors and a shower-out capability are also being studied for the BSL-3 isolation spaces. BSL-3E spaces will not be located directly on the exterior walls. A surrounding corridor for the BSL-3E space that is outside of biocontainment might be desirable for management of autoclave out, fumigation, etc. It has been determined that pressure decay testing will not be required for any of the BSL-3E biocontainment.

BSL-3E Break Room – It is intended to be in biocontainment, as exists at PIADC (Plum Island Animal Disease Center). (This is problematic since co-mingling break rooms with areas where pathogens are expected can lead to potential release scenarios. This is particularly the case for viruses, like FMDV, which can survive for extended periods as easily transmitted by contaminated fomites.) This will allow people to get food and drink throughout the day without having to leave the BSL-3E area, which requires showering out. The space will connect via a pass through to the BSL-2 area cafeteria. These spaces should be near or along an outside wall to allow for natural light into the spaces and views out to the campus. APHIS suggests 50 employees in BSL-2 and 70 in BSL-3E.

Offices in or Near BSL-3 Laboratory Space – The offices will be located inside the biocontainment barrier to enable the researchers to go from their laboratories to their offices without having to shower out to move between spaces. (This is problematic for the same reason that break rooms need to be outside of containment areas.)

BSL-3E Cage Wash – Include cage wash for smaller animal cages, etc., which may be utilized for animal studies in BSL-3E and particularly in the BSL-4 space. There is very little small animal work anticipated. The cage wash will be located behind the BSL-3E biocontainment barrier.

BSL-3E DHS R&D Laboratory and Support Suite – Three of these suites will be required. This suite is a typical BSL-3E layout that will be consistent with the other BSL-3E suites in the program. Each is a separate suite with three support laboratories and a vestibule/anteroom through which the suite is entered. The vestibule/anteroom will have a sink for hand washing as employees leave the laboratories; anterooms also provide storage for PPE. The support laboratories will have necessary equipment and be designed for flexibility. The main laboratory will have a sink for the research activities. The only fixed casework will be the sink cabinet. The ability to locate fume hoods and BSCs in several locations to support each research program will be incorporated into the design of these laboratories.

BSL-3E ARS Pathogen Research and Support Laboratory – There will be six separate laboratories required to focus on different pathogens. This is a typical BSL-3E laboratory design as discussed above.

BSL-3E ARS Immunology Research and Support Laboratory – This is a typical BSL-3E laboratory suite.

BSL-3E Core Pathology Suite and Support – This suite consists of six support laboratories that focus on specific tasks. The laboratories are designed along a common corridor with exit doors at the ends of both sides of the corridor to allow for an alternate means of egress in an emergency.

BSL-3E Core Freezer Storage – Will require negative pressure for the air flow and hold 52 3-foot wide each freezers. This space will hold select agent, LN2, and −70°C freezers. The mechanical systems will be designed to appropriately address the heat loads generated by this equipment.

BSL-3E Core Analytical Chemistry – Has one laboratory for a mass spectrometer, electron microscope, and high-pressure–high-performance liquid chromatograph (HPLC). There will be two bio-imaging laboratories. These spaces will have special vibration and lighting requirements that will be addressed in the next design phase.

BSL-3E Insect Holding and Experiments (Infecting)

BSL-3E Fumigation

BSL-3E Core Quality Control

BSL-3E Clean Reagent Set Up

BSL-3E HTP Support Laboratories – Will be located off of the main laboratory and designed to allow for the separation of molecular functions and/or processes. The core HTP Laboratory will be the largest BSL-3E laboratory with smaller support laboratories off this space.

BSL-3E APHIS Vaccine Bank Testing Laboratory

BSL-3E APHIS Reagent Production Laboratory

Changing Rooms – There are separate changing rooms for men and women. The location of the changing rooms is critical to the success and efficiency of the BSL-3E and BSL-3Ag research. One option is to have one large changing room suite that will serve the BSL-3E and BSL-3Ag spaces, which will allow people to go between the two spaces without having to shower-out each time. The changing rooms will include the restrooms, lockers, clothing storage, and showers. There will need to be strict protocols established to ensure that cross-contamination does not occur between the BSL-3Ag animal rooms and BSL-3E laboratories.

Redundant autoclaves will be located within reasonable access from all the laboratories. Given the BSL-3E enhancements, the autoclaves will need to be the pass-thru/thruwall type. During the schematic design phase, care will be taken to ensure adequate service space around these units.

BSL-3E Isolation Laboratory's Space Requirements – These laboratory spaces focus on FMDV research. The following spaces will be adjacent to each other in a wing of the building and will require isolation enhancements.

BSL-3E (Isolation) Molecular Suite – The Amplification Laboratory is the main open laboratory with the support laboratories directly off this space. The support laboratories include Sample Preparation, Clean and Dirty, and Template Addition and will contain two fume hoods.

BSL-3E (Isolation) Serology – Will include enzyme-linked immunosorbent assay, Luminex, and immunohistochemistry spaces. Two of these spaces will require more enhancements.

BSL-3E (Isolation) Virus Isolation – Individual rooms with BSCs, sinks, mobile casework, and an equipment area.

BSL-3E (Isolation) Sample Receiving – Two sample receiving rooms are necessary. One sample receiving room (clean) will be utilized to handle diagnostic specimens sent to FAD diagnostic laboratories for testing and the other sample receiving room (dirty) will be utilized to receive samples that are suspected or known to contain a select agent and will be utilized for validation or as reference material. Sample receiving will have an autoclave, computers, and other equipment.

BSL-3E (Isolation) Autoclave

BSL-3E (Isolation) Support Lab for BSL-3E (High Risk)
Training Module

The APHIS training facility is designed to teach veterinarians to identify various foreign animal diseases and will be part of the overall NBAF in support of the FAD diagnostic mission. Veterinarians will be trained in the diagnosis of FADs such as FMD, classical swine fever, and other pathogens of interest. APHIS will conduct five to six FAD diagnostic training courses per year with approximately 35 students in each class. In addition, there will be approximately six instructors and three animal caretakers associated with each school. The primary components of the training facility will include the below items.

10 BSL-3Ag Holding Rooms for Animals – Ten BSL-3Ag holding rooms for animals infected with the disease agents of interest. Each room must be capable of holding at least four to six livestock animals, including poultry, and 5-10 students. Ten rooms are needed to display and concentrate the diagnostic training on particular aspects of the diagnostic evaluation and to limit the number of students per room for direct educational contact. It is understood that the rooms will be used by other programs when not in use by the training programs.

Lecture Rooms – Lecture rooms will be provided for presentation sessions. The desire is to have a raised floor design for 35-40 students. The lecture room will have a continuous fixed work table and chairs to allow for sufficient individual layout space of approximately 42 inches per student. The lecture hall would also serve other programs in the facility. In addition, at least two smaller training rooms for up to 15 people each would be needed; these would also serve the larger facility mission needs.

Audio Visual Capability – The lecture room would include the capability to provide multiple image sources including video projection capability and live imagery from at least two animal holding rooms and the necropsy facility with remotely controlled cameras (minimum two per room with two-way communications). Lecterns will be provided with full remote control capability. In addition to the projection capability, sliding white boards will be provided.

Pre-Function Space – Pre-function is a multipurpose space that will provide several functions. It will serve the lecture room as break space and include a small catering kitchen with vending machines. In addition, it will function as a security check point and sign-in station for students attending the training programs. The NBAF primary facility entrance will serve the entire facility. Direct linkage to the training facility by way of a "main street" type connection is the preferred method for maintaining a secure facility.

Locker Facilities – A separate locker facility will be provided for security and when considering the time and motion aspects of the training operation. The locker facilities would include the same amenities as the primary locker facility but be at a much smaller scale commensurate with the number of students using the space.

Necropsy – As part of observed elements of the training courses, a necropsy room will be needed for animal euthanasia, necropsy, and sample preparation. While it is not anticipated that a necropsy room will be dedicated for training purposes, it is suggested that one necropsy room be provided with a fixed necropsy table and approximately eight portable tables for use by the students and instructors. The requirements for this room will be similar to those for other necropsy suites, except that this room must accommodate a larger number of people. Because training will be performed with select agents, appropriate requirements for security, access, storage, inventory control, and other features should be included in the design.

General Area – Support areas will include toilet rooms, coat room, and general storage space.

cGMP Laboratory

To support the development and eventual licensure of products/reagents discovered at the NBAF, the cGMP module supports translational studies by producing materials and documenting processes and results. Efficacy studies will provide preliminary toxicology/general safety data to allow for larger volumes of early clinical phase materials to be manufactured. The discovery model is to create small quantities of materials through

proof of concept. The clinical processing will provide consistent/reproducible products and processes to confirm drug safety and effectiveness, which will allow technology transfer to industry partners and/or contract manufacturers for scale-up and commercial product manufacturing. Clinical investigations focus on safety, purity, potency, and efficacy of licensed products; the cGMP module must provide the controlled environment to conduct these tests.

The amount of materials required is based on the size of the study and will vary based upon the developmental phase of the product. Batch sizes are difficult to predict, as are yields anticipated for the variety of products and technology platforms used to create them. The cGMP facility will support the growth and purification of agents in Viral Production and Diagnostic Reagents Production suites. Based on users' past experience, the largest scale envisioned for manufacturing needs in this facility is 30L – 50L. The Sterile Fill and Assembly function will support the capability to apply the agent into a delivery system for use in the study model. The primary current application for vaccines is direct injection; however, other delivery forms may be considered in the future (ingestion – solid dose, aerosol, transdermal). It is assumed that the QC Testing component to meet cGMP requirements will be supported by dedicated space and equipment located within the laboratory blocks at the NBAF.

The proposed cGMP module is intended to provide small-scale production of biological countermeasure materials for supporting efficiency studies and early phase clinical trials responding to DHS programs and small-scale production of biological reagents for DHS, ARS, and APHIS programs. It will operate in accordance with cGMPs as described in U.S. Code of Federal Regulations (21 CFR, Parts 210/211/600 and 610) and be dedicated to the manufacture of experimental cell therapy, diagnostic, and vaccine-related products. Some specific biological products have been selected to date; however, the design of the facility has been planned to provide flexibility in the future for a variety of product types and manufacturing processes. Some general process areas include the following:

- Production of plasmid DNA products and natural antigens;
- Production of monoclonal antibodies;
- Production of diagnostic reagents;
- Production of recombinant protein therapeutics/diagnostics;
- Production of attenuated and inactivated viral and bacterial vaccine; and
- Dedicated Formulations/Aseptic Fill area.

Module components will include a Viral Production Area, Diagnostic Reagent Production Area, Vaccine Sterile Assembly and Fill Room with lyophilization capability, and manufacturing support areas. The facility will need to allow simultaneous production of multiple diagnostic reagents and vaccine candidates.

Restricted personnel access and full gowning procedures will be required for classified manufacturing areas. The facility is assumed to be utilized 24 hours per day, based on a year-round production schedule (365 days), with periodic shutdowns for maintenance and validation. A BSL-2 biocontainment facility is envisioned for the majority of manufacturing and support space with a BSL-3 Enhanced Viral Production Area. The ability to respond to a national emergency for zoonotic-type diseases is anticipated, which will require BSL-4 biocontainment and cGMP. For the initial program, however, BSL-4 vaccine capability will not be provided.

Process Descriptions – Typical biological product processes utilize a variety of technology platforms for growth and purification of targeted organisms. Expansion systems most commonly used are either cell cultures or microbial fermentation. Vaccine candidates may use whole cell organisms, DNA fragments or surface antigens/proteins, or excretions produced by the organism. The following general designations are provided to help identify the potential unit operations required and most common technology platforms in use today.

Cell Culture and Primary Recovery (Viral Production) – Cell culture operations may be traditional cell culture work with anchorage-dependant cells in plastic containers or cell cubes or in bioreactors using suspension cell cultures. Contained volumes may reach as high as 50 liters (L).

Roller Bottle Production – Typical roller bottle production utilizes pre-sterilized plastic roller bottles holding 700 to 1,000 milliliters (mL) of cell culture medium. Several roller bottles can be placed on a roller machine to slowly turn the bottles, bathing the inside surface of the container. Cells attach themselves to the inside surface of the container and grow into a confluent monolayer. Passage of cells occurs by gently removing the monolayer by mechanical and/or enzymatic methods and transferring the cell-laden fluids into new sterile bottles. Scale-up consists of multiple roller bottles to obtain the desired volume of harvested fluids.

Cell Cube Production (Hollow Fiber) – Each cube system has a selection of stacking configurations (25 stack, 50 stack, and 100 stack). The surface area capacity of the 100 stack is 85,000 square centimeters (equivalent to 100 roller bottles) to grow the cells. Scale-up, if required, is a multiple of the cell cube units or potentially a 30-L bioreactor.

Bioreactor Operations – Mobile Bioreactors/Wave Bag – The anticipated bioreactors may be 1 L, 10 L, or 30 L in volume, or wave bags may be 20 L or 50 L in volume.

After harvesting, the cell cultures generally pass through a micro-filtration system to retain the liquid portion of the product stream. The product stream is filtered and further processed to obtain the final product. Cells may be broken by mechanical or chemical methods if the product is found inside the cells rather than the extra-cellular fluids. Further processing of the product stream is completed to obtain the final product.

Microbial fermentation may be yeast or bacterial cultures engineered to express desired gene products. Flexibility in the cGMP suite is necessary to accommodate a variety of production processes. Conceptual design plans call for one production suite to handle multiple small-scale mobile bioreactors (up to 10 L each). Microbial production may be a batch, fed-batch, or a continuous process depending on the organism and process under development.

Portable nutrient feeding solution vessels with steam-sterilization connection ports are coupled to the fermentor. Solvents (e.g., methanol, ethanol, etc.) may be required during the fermentation process, and provisions for a solvent-rated area (fume hoods) for preparation and use is provided in the cGMP concept. Inoculum for the fermentor will be prepared in a BSC and prior to transfer to a seed fermentor. The seed culture will be incubated for a specific time before transfer to production. Recovery of product from the harvested material uses centrifugation, ultrafiltration, and homogenization or a combination of these methods, depending on the process. Generally, the microbial cells are separated from the liquid portion of the harvested material using centrifugation or filtration. If the desired product is contained within the microbial cells, the supernatant fluid is discarded and the cell mass is retained.

Recovery – The recovered cells may be washed with buffer one or more times and held frozen at -70^{o}C until further processing. The microbial cells are lysed to release the intracellular proteins. Cell lysis will be performed by mechanical, chemical, or biochemical means. Yeast and some microbial cells can be homogenized using a high-pressure homogenizer or insonator to break up the cells. Centrifugation or filtration methods remove the unwanted portions of the product stream. The retained process stream is further processed to obtain the desired product.

Alternatively, if the desired product is contained in the liquid portion (supernatant) of the harvested material, the cell mass is discarded and the supernatant fluid retained. The supernatant fluid may be diafiltered to optimize the recovery process. The recovered material may be held at 2^{o}C to 8^{o}C for a short period or processed immediately if the product is not stable.

Purification – This operation applies to either microbial-derived fermentation product or cell culture–derived product streams. One purification area is provided with the cell culture production area and is flexible in terms of equipment and conditions. Operations in ISO-7/Class 10,000/Grade C air space will accommodate cGMP processes on a campaign basis. It is common to conduct fermentation and purification operations in the same room with small scale operations and proper clean-up and campaign change-over of the space and equipment. The room must be designed for the cleanest operation (purification). The most acceptable methodology works when the room is used for a dedicated single product. Utility/service panels will be ubiquitous for flexibility. There will be provisions for a solvent-rated area (fume hood) in each suite, if required.

Purification equipment may consist of the following:

- HPLC systems;
- Liquid chromatography affinity, gel, ion exchange, and hydrophobic interaction systems;
- Other chromatographic technologies;
- Different processing conditions (cold room processing vs. ambient temperature processing);
- A range of solvent and buffer solutions may be used in the downstream purification processes; and
- Additional steps such as virus removal, refolding, ultrafiltration and diafiltration, centrifugation, and sterile filtration may be required.

Typical unit operations might include the following:

- An ion exchange column;
- Chemical treatment of the product stream;
- Hydrophobic Interaction Chromatography (HIC) column, refold step;
- One or two other chromatography steps;
- Concentration/buffer exchange step;
- Virus removal;
- Sterile filtration of the final product prior to bulk fill (typically done in the same room); and
- Modular portable equipment systems and units moved in and out of the open/flexible purification area will accommodate various downstream purification protocols. Portable vessels of buffer solutions, plus collection and check tanks, aseptically connected to the equipment or system allow the proper sequence of operations to proceed.

Sterile Assembly and Fill – The aseptic preparation and formulations/fill room are designed for maximum flexibility. The fill/finish process room contains a Class 100 laminar flow hood for aseptic operations and vial/syringe filling. Due to volume and size of operations, formulations, fill, and lyophilization are all planned for the same room. Equipment instrumentation is controlled using local control modules. Fill/finish liquid component(s) are transferred to a mixing tank in a process room, diluted, and adjusted as required depending on the product formulation. The estimated average batch is assumed to be small, approximately 20 L or less. The blended liquid components are passed through an emulsification machine with specific emulsifying agents that may require recirculation through the unit until the desired emulsion characteristics are produced. Labeling and packaging of product will be conducted in the finishing area in this room.

Filling/Lyophilization – The filling and lyophilization areas operate under ISO 5, Class 100, Grade A conditions. Sterile vials, typically ranging from about 1 mL to 30 mL, are aseptically filled under a laminar flow hood by hand filling or using a single-head filling machine, then plugged, sealed, and capped. Products that require lyophilization are filled as described above, and special fluted stoppers are partially inserted into each vial. Trays of filled, and partially stoppered vials are transferred to a lyophilization machine and frozen on the shelves at –45°C to –65°C. The chamber is evacuated to a deep vacuum, and the shelves are slowly heated for a prescribed time. The frozen liquid transforms to a gaseous state (sublimation) as the temperature

of the product increases under vacuum. The proteins and other components remain as the water vapor is condensed in a remote location. Dried product is stoppered and capped. Nitrogen may or may not be used to purge the vials during the lyophilization process. An after-seal may be applied as required in the finishing area. This room must be designed to handle active products, which will require biocontainment air locks (referred to as sinks) at both sides of the room (entry/exit) and inactivated products. Aseptic fill requires rooms to be positively pressured for cleanliness to meet cGMPs.

Glassware Operations – Dirty glassware and equipment collected from the production suites is disinfected in an acid bath, decontaminated in an autoclave, and delabeled. Large double-door glassware washers are loaded from the preparation side. Clean glassware and equipment is unloaded from the preparation side, dried in ovens, appropriately wrapped, and sterilized in a separate autoclave. Portable tanks are cleaned-out-of-place and sterilized-in-place at a tank cleaning and sterilization station. Plastic carboys are washed at a carboy wash station and sterilized in an autoclave for reuse. Sterile glassware, plastic ware, and equipment are staged in an ISO 8, Class 100,000, Grade D room and distributed back to the production suites by the operational personnel. Equipment and supplies that are being taken out of campaign use are cleaned, dried, wrapped, sterilized, and then transferred to be held in controlled storage for future campaigns.

Reagent/Media Preparation – A dedicated or specific room for reagent/media preparation is not anticipated. Cell culture media, typically stored as purchased in pre-sterilized containers, is shared and distributed to production areas. For media not available or desired in this form, such as media containing custom components, media ingredients are weighed in a central weigh-out area and batched in the production rooms. Media batches are prepared according to standard operating procedures supplied by the researcher and sterilized either by filtration or in autoclaves and stored in the appropriate production suite. Aseptic preparation of media takes place in laminar flow hoods. Reagent/buffer ingredients are weighed in the same area, on a schedule such that media ingredients are not being handled concurrently. Reagent/buffer concentrates for production are prepared in buffer compounding tanks, transferred into portable tanks and taken to the appropriate production equipment. Small volumes of stock solutions are stored in a reagent/media preparation area and in each production area. Aseptic preparation of solutions takes place in laminar flow hoods.

Relationship to Hazards Analysis: The conceptual design includes a break room within biocontainment to allow employees to get food and drinks without leaving the BSL-3E area. Such a design leads to potential cross-contamination and resulting ingestion of contaminated foods or potential intentional acts such as the infections resulting from a disgruntled employee contaminating pastries in a break room (Harding and Byers 2006). Another example hazard is a release from a drainage system such as what occurred in August 2007 at the Pirbright site in the United Kingdom, resulting in the probable release of FMDV (NEEG 2007).

E.2.2 Safety Barriers and Equipment

This section discusses all of the safety barriers within the NBAF, including water, air handling, and waste (liquid and solid), etc., necessary to evaluate and analyze consequences associated with operation of the facility.

Safety Equipment (Primary Barriers And Personal Protective Equipment)

Facility Design and Construction (Secondary Barriers)

Biocontainment Systems

Biocontainment is one of the fundamental principles of biosafety. As described in the Biosafety in Microbiological and Biomedical Laboratories (BMBL) (CDC [BMBL] 2007) below.

> "The principles of biosafety introduced in 1984 in the first edition of BMBL[1] and carried through in this fifth edition remain steadfast. These principles are containment and risk assessment. The fundamentals of containment include the microbiological practices, safety equipment, and facility safeguards that protect laboratory workers, the environment, and the public from exposure to infectious microorganisms that are handled and stored in the laboratory."

Safety equipment and facility safeguards can be described in terms of primary and secondary barriers to protect against exposure to such infectious microorganisms.

E.2.2.1 Primary Barriers

Primary barriers include BSCs (or other containment systems used for open handling of agents) and full-body, air-supplied, positive-pressure suits. The type of BSC used depends on the agents being handled. In general, the BMBL recommends Class I or II BSCs for BSL-2 and BSL-3 areas and Class III BSCs (or Class I or II BSCs with positive-pressure suits) for BSL-4 areas. The NBAF Feasibility Study (ref. 2) anticipates usage of Class III BSCs for the BSL-4 cabinet laboratory and the BSL-2 APHIS Class III BSC/Processing Rooms for Diagnostic Samples; reference 2 also anticipates usage of Class II Type A2 BSC and/or Class II Type B2 BSCs in the BSL-4 laboratories and necropsy room. Diagrams and brief descriptions of each of the above described BSCs follow (ref. 1).

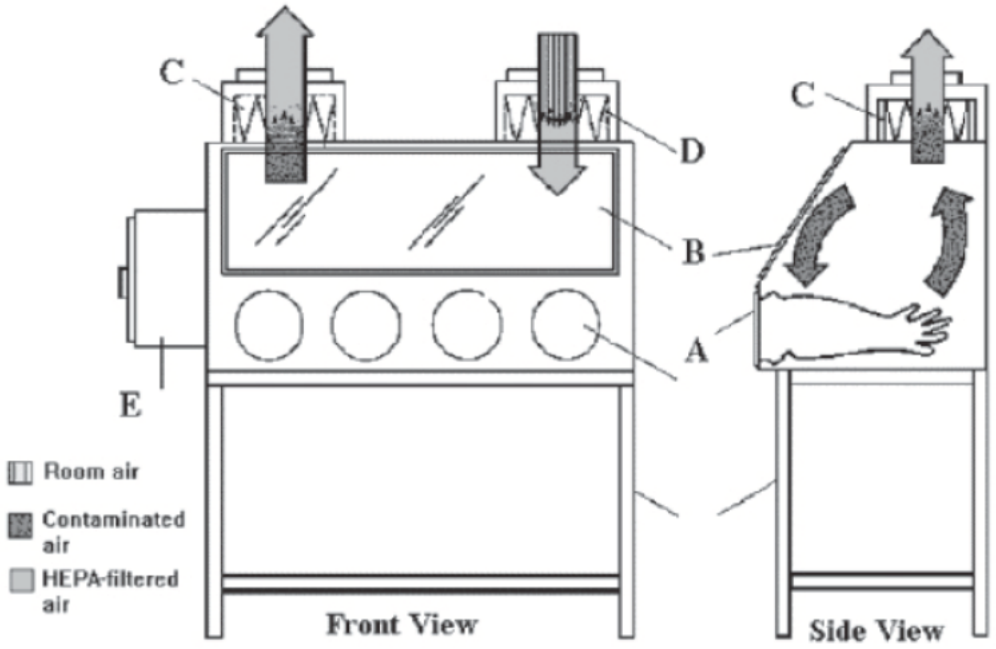


Figure E.2.2.1-1 — Class III BSC. A. glove ports with O-ring for attaching arm-length gloves to cabinet; B. sash; C. exhaust HEPA filter; D. supply HEPA filter; E. double-ended autoclave or pass-through box. Note: A chemical dunk tank may be installed, which would be located beneath the work surface of the BSC with access from above. The cabinet exhaust needs to be hard connected to an independent dedicated exhaust system. The exhaust air must be double-HEPA filtered or HEPA filtered and incinerated.

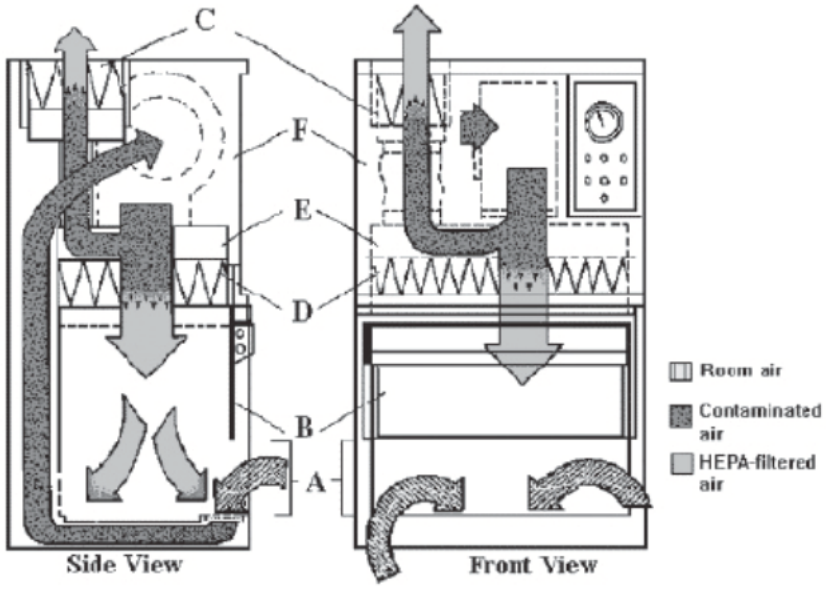


Figure E.2.2.1-2 — The Class II, Type B2 BSC. A. front opening; B. sash; C. exhaust HEPA filter; D. supply HEPA filter; E. negative pressure exhaust plenum; F. filter screen. Note: The carbon filter in the exhaust system is not shown. The cabinet needs to be hard connected to the building exhaust system.

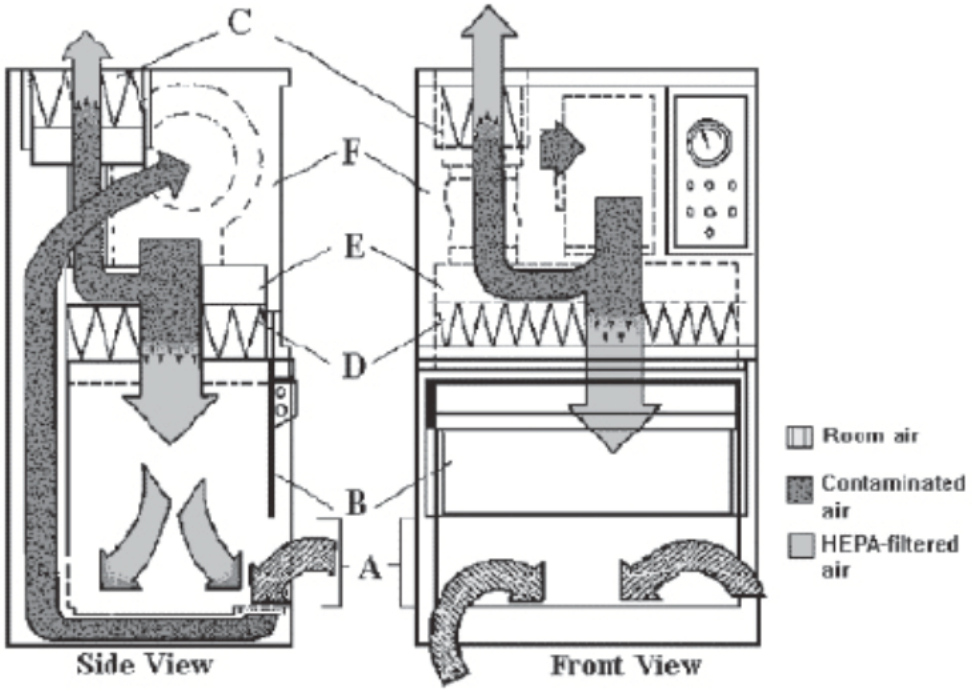


Figure E.2.2.1-3 — The tabletop model of a Class II, Type A2 BSC. A. front opening; B. sash; C. exhaust HEPA filter; D. supply HEPA filter; E. positive pressure common plenum; F. negative pressure plenum. The Class II Type A2 BSC is not equivalent to what was formerly called a Class II Type B3 unless it is connected to the building exhaust system. Note: The A2 BSC should be canopy connected to the exhaust system.

E.2.2.2 Secondary Barriers

Secondary barriers include the facility layout with separate zones for laboratories of various biosafety levels, dedicated supply and exhaust ventilation systems for each zone, and/or negative pressure in the laboratories.

Facility Layout (Conceptual)

The NBAF Feasibility Study (NBAF-1) describes two building concepts that have been developed and will be evaluated further during design: a linear scheme and a radial scheme.

In the linear scheme, a central spine housing the BSL-2 laboratory and office spaces feeds BSL-3E and BSL-4 wings on both sides and the larger BSL-3Ag block at the end. This layout segregates the different BSLs into distinct zones, while at the same time maintaining a strong functional connection between them as required by the research program.

Figure E.2.2.2-1 — Linear Scheme – First Floor

In the radial scheme, the BSL-4, BSL-3Ag, and BSL-3E wings radiate from a central hub at the front of the building consisting of BSL-2 laboratory and office space. Similar to the linear scheme, the different BSLs are segregated into zones, while maintaining the functional connections required by the research program.

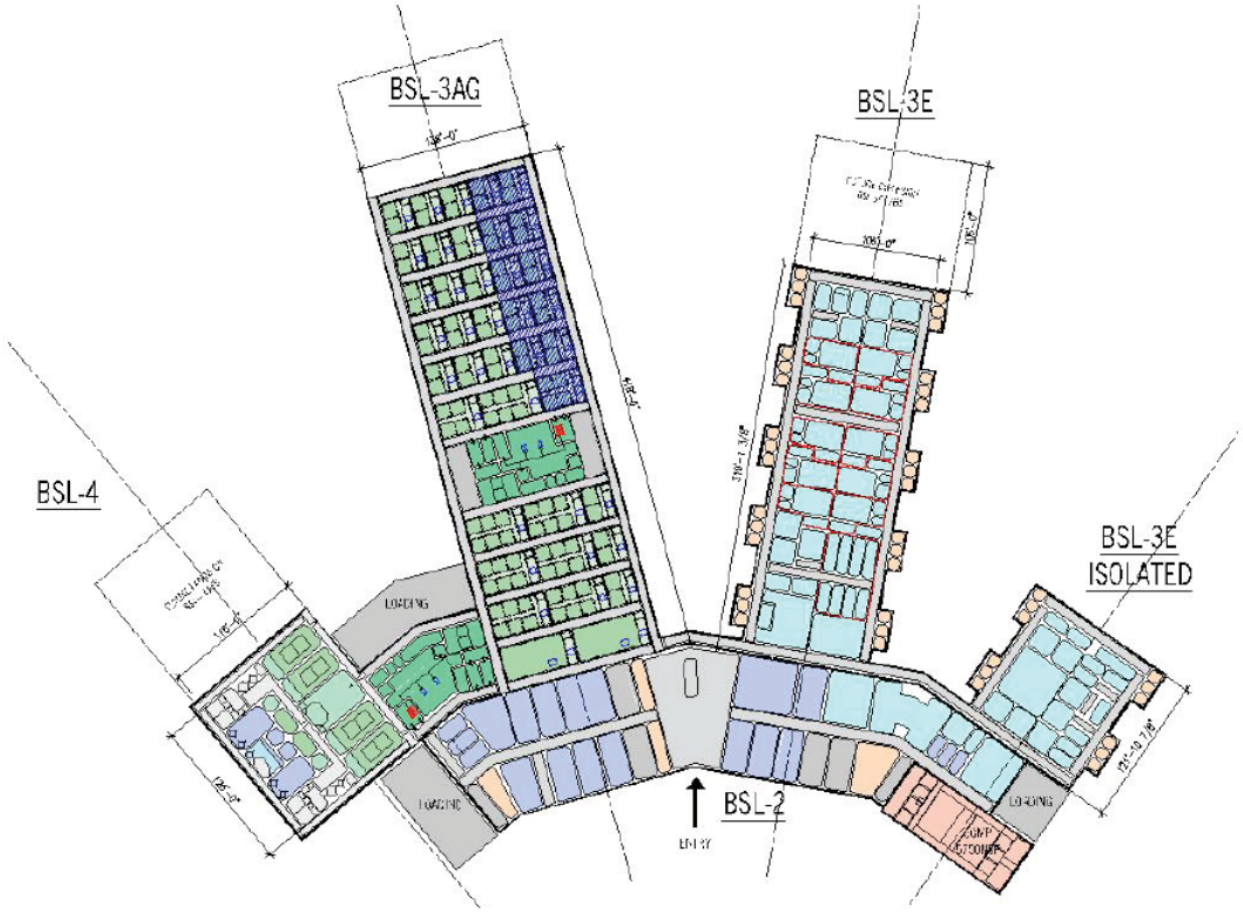


Figure E.2.2.2-2 — Radial Scheme – First Floor

Relationship to Hazards Analysis: Both radial and linear conceptual floor plans show the highest hazard BSL laboratories on the exterior of the building. Such a layout is potentially more likely to result in aircraft crash accidents or be a more likely terrorist target than if these laboratories were located in interior laboratory spaces (i.e., not exposed directly to the outside).

Process Flow

The ability to maneuver people, equipment, supplies, and animals throughout the facility efficiently, without compromising the integrity of the research programs or creating an unsafe environment for building occupants, is extremely important in the design of the facility. Proper design of such process flows prevents cross-contamination of vital research/diagnostic programs and allows for compartmentalization of rooms and suites for decontamination purposes. An example process flow diagram for a conceptual BSL-4 module is shown below, followed by a brief description (NBAF-1).

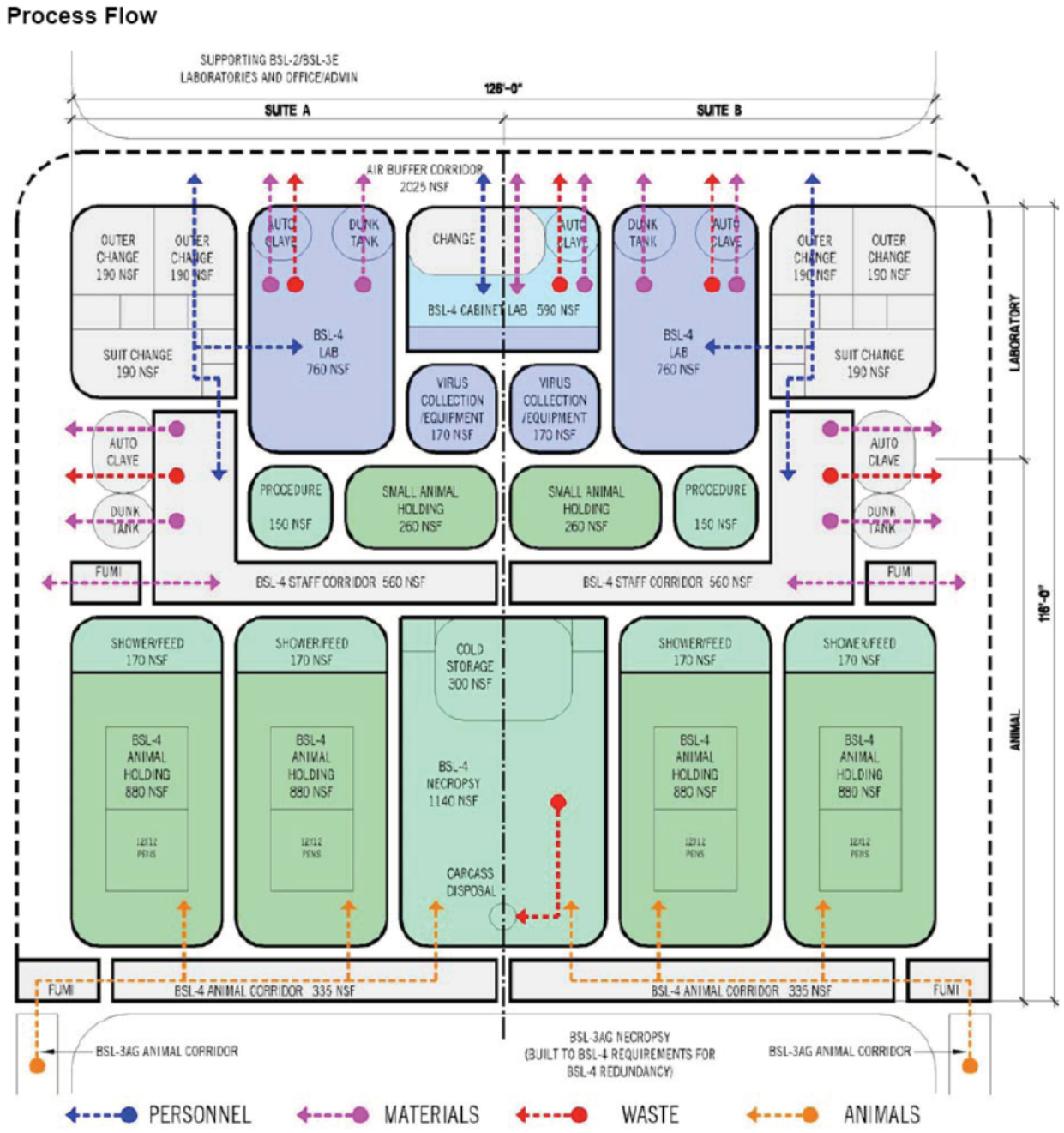


Figure E.2.2.2-3 — NBAF BSL-4 Process Flow Diagram (NBAF,2007)

Personnel will enter/exit through the change facilities that serve the respective suites. The entry process begins at the outer change room, continues through a body shower, and moves into the suit change room. At the suit change room, there will be two chemical showers, one leading to the laboratory area of the suite and the other leading to the animal area of the suite. The chemical showers will typically serve as only an airlock during the entry procedure. Once personnel have passed through the chemical shower airlock, they may freely circulate within the respective area they've entered. Depending on the mode of operation, personnel may also circulate between laboratory/animal areas and between suites, as need and protocol dictates.

Materials and/or equipment entering/leaving the BSL-4 suites may do so through a variety of means depending on the specifics of the particular item. Stainless steel chemical dunk tanks, pass-thru double-door autoclaves, and fumigation vestibules will be provided for each BSL-4 laboratory and each BSL-4 animal area. Smaller samples and other materials may enter/exit via any one of the three means. Large and/or sensitive pieces of equipment will enter/exit through the fumigation vestibules. When any item exits via the fumigation vestibule, the item will be decontaminated inside the fumigation vestibule prior to final exit out of the BSL-4 suite.

Waste materials and contaminated instruments will exit via a pass-thru autoclave. Infected animal carcasses will exit via the carcass disposal chute located inside the necropsy room. Animal access will be achieved at the main research floor via an adjacent animal loading dock that is located outside biocontainment, yet secured within the building. Animals will be directed from the dock into the BSL-4 animal corridor serving each suite via a fumigation vestibule equipped with APR doors. Access from the BSL-4 animal corridor into the holding rooms will be via an APR door that is opened only once the rooms have been cleaned, decontaminated, and isolated from the remainder of the BSL-4 space in anticipation of animal set-up. Once the animals are secured, the APR doors to the animal corridor will be sealed.

Ventilation System Descriptions (Conceptual)

Laboratory Supply Systems

The supply air system for BSL-2, BSL-3E, BSL-3E (Isolation), BSL-3E (Isolation High-Risk), BSL-3Ag, and BSL-4 laboratories will consist of multiple 100% outside air, air-handling units connected to a common supply manifold. Equipment sizing and selection will be such that the design loads will be met with one air-handling unit off-line for service. The system will be a single duct variable air volume reheat system, providing heating and cooling to the spaces. Supply fans will be provided with variable frequency dampers for volume control. Each supply air terminal unit will be provided with a hot water reheat coil. Air handling units will be factory fabricated custom units. The air-handling system will operate continuously. All air-handling units will be served by stand-by power.

The BSL-3E (Isolation) and BSL-3E (Isolation High-Risk) laboratory areas will be served by a dedicated central supply air system. The BSL-3Ag animal holding rooms will be served by a dedicated central supply air system. The BSL-4 laboratory areas/animal holding rooms will be served by a dedicated central supply air system. Each laboratory suite/animal holding room will be supplied air from the supply header and through a control air valve assembly, reheat coil, single HEPA filter and a bubble-tight damper arrangement. Filtration efficiency will be to 99.97% [SIC error in original document] (at 0.3 microns) at the point of exit from the HEPA filter housing.

Relationship to Hazards Analysis: HEPA filters provide a final removal of pathogens prior to being released to the environment. The higher the filtration efficiency and/or more filters in series provide a more effective reduction pathogen concentration released in the event of an accident.

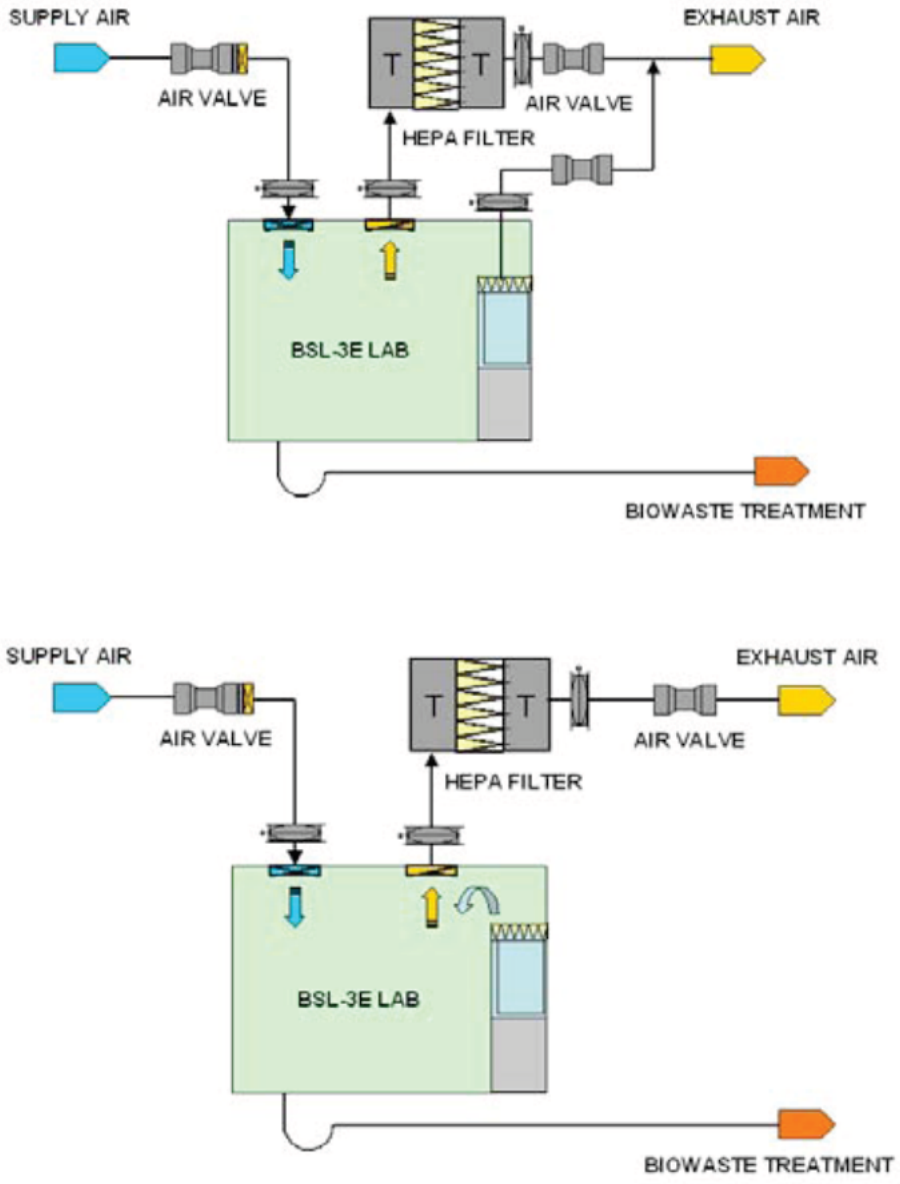


Figure E.2.2.2-4 — BSL-3E Conceptual Ventilation Flow Diagram

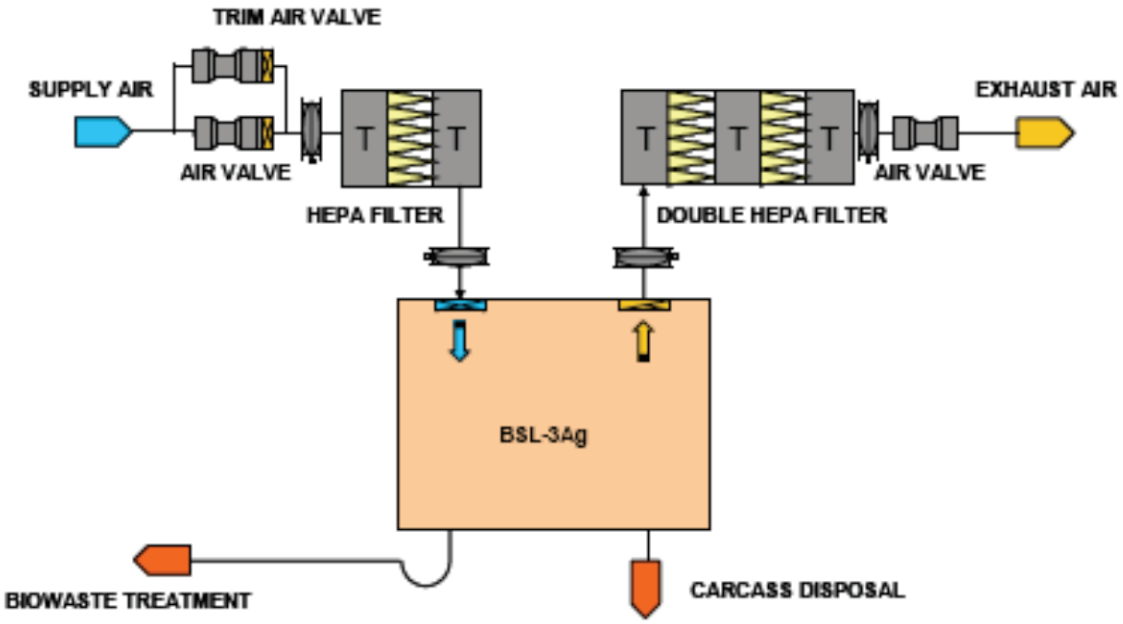


Figure E.2.2.2-4 — BSL-3Ag Conceptual Ventilation Flow Diagram

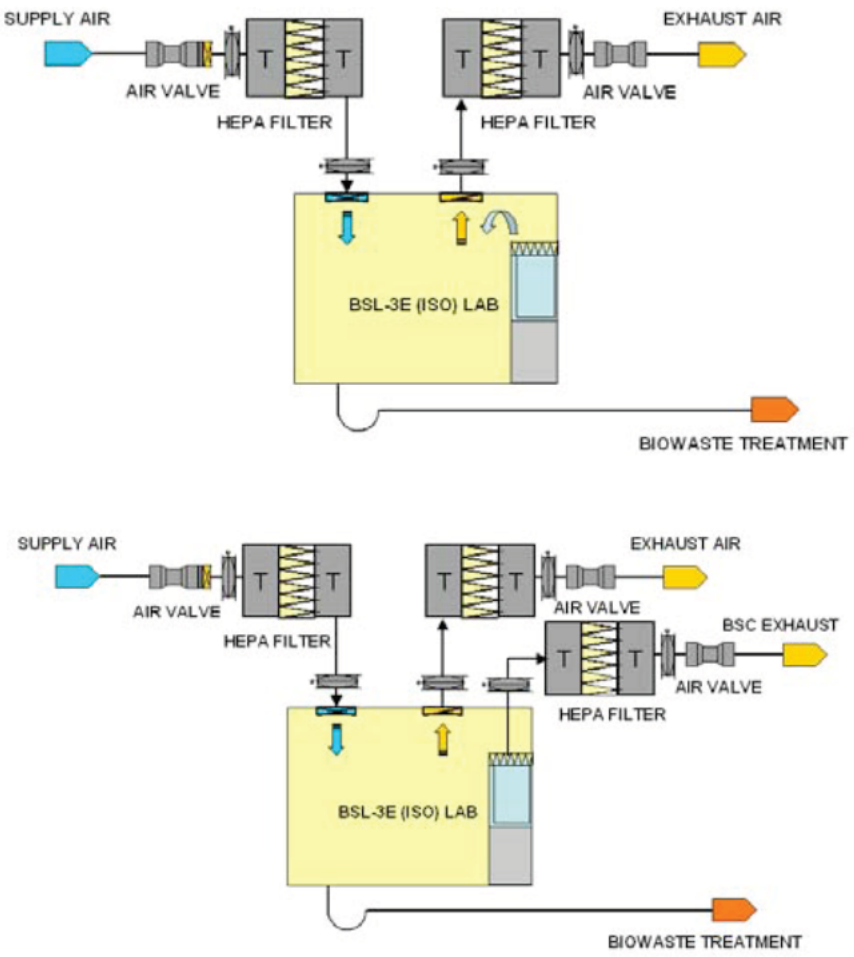


Figure E.2.2.2-5 — BSL-3E (ISO) Conceptual Ventilation Flow Diagram

Laboratory Exhaust Systems

BSL-2 Laboratory Exhaust System

The laboratory areas will be served by a central exhaust air system. The system will accommodate laboratory fume hoods, snorkels, and canopy hoods with general exhaust air. The system will consist of multiple exhaust fans connected to a common exhaust fan inlet plenum and will be located in the penthouse or on the roof. One of the fans in the manifold will be a redundant fan. The system will operate continuously in conjunction with the laboratory supply air system. All fans in the system will be served by stand-by power.

BSL-3E, BSL-3E (Isolation), BSL-3E (Isolation High-Risk), BSL-3Ag, and BSL-4 Laboratory Exhaust Systems

The BSL-3E, BSL-3E (Isolation), and BSL-3E (Isolation High-Risk) laboratory areas will be served by a dedicated central exhaust air system. The system will accommodate snorkels, BSCs, and canopy hoods with general exhaust air.

The BSL-3Ag animal holding rooms will be served by a dedicated central exhaust air system. The system will accommodate BSCs and canopy hoods with general exhaust air. The BSL-4 laboratory areas/animal holding

rooms will be served by a dedicated central exhaust air system. The system will accommodate snorkels, BSCs, and canopy hoods with general exhaust air.

The system will consist of multiple exhaust fans connected to a common exhaust fan inlet plenum and will be located in the penthouse or on the roof. One of the fans in the manifold will be a redundant fan. The system will operate 24 hours per day, every day of the year. The laboratory exhaust system will be a variable air volume (VAV) system. While the system is VAV, the exhaust fans will operate at constant volume to maintain a constant stack discharge velocity. A static pressure sensor in the exhaust fan inlet plenum will modulate an outside air bypass damper, introducing the required outside air into the plenum to maintain a constant flow rate through the fans. Fans will have packless type sound-attenuating devices on the exhaust main and the outside air by-pass duct. The fan system will be provided with stand-by power to operate at full capacity in the event of normal power failure.

Each BSL-3E (Isolation High-Risk), BSL-3Ag, and BSL-4 laboratory/animal holding room will be exhausted through double-HEPA filter arrangement complete with bubble-tight dampers, filtration efficiency will be to 99.97% (at 0.3 microns) [sic corrected] at the point of exit from the HEPA filter housing.

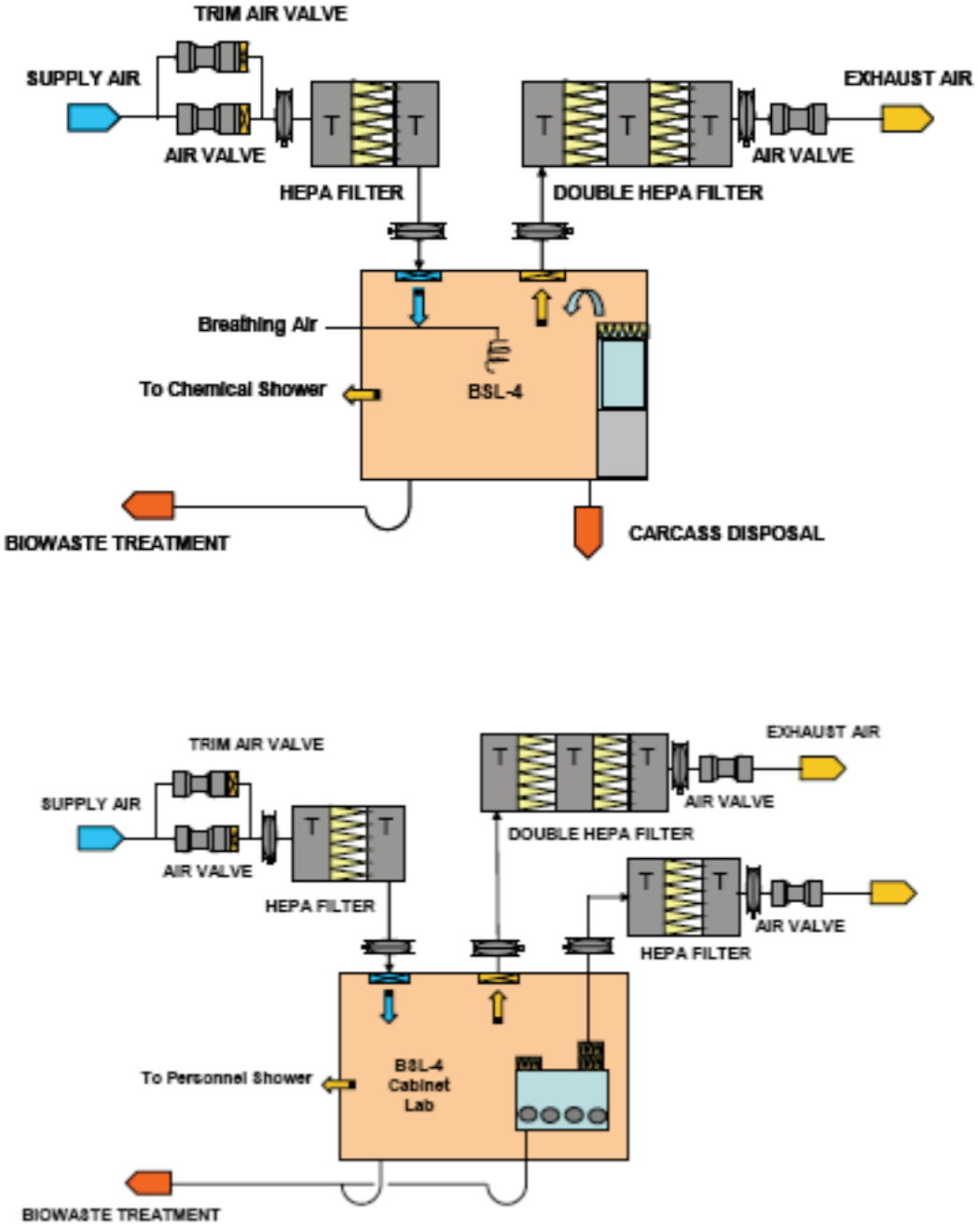


Figure E.2.2.2-6 — BSL-4 Conceptual Ventilation Flow Diagram

Building Automation System (BAS) (BSL-2, BSL-3E, BSL-3E [Isolation], and BSL-3E [Isolation High-Risk])

The automation system for the laboratories will consist of a series of stand-alone direct digital controllers (DDC), integrated together with a local area network. The local area network will integrate with the overall building automation system to provide a single total building control system. In individual laboratory suites, rooms/spaces within the suite will be controlled by individual DDC controllers utilizing solid-state electronic sensing and rapid-response pneumatic or electronic actuation.

Temperature and airflow controls will include DDC-based room temperature sensor and control of supply air terminal unit and reheat coils and exhaust air valves to maintain relative room pressurization through air flow tracking.

BAS (BSL-3Ag and BSL-4)

The automation system for the high-biocontainment BSL-3Ag/BSL-4 spaces will consist of a series of stand-alone DDC, integrated together with a local area network. The local area network will integrate with the overall building automation system to provide a single total building control system. In individual BSL-3Ag/BSL-4 suites (cell), rooms/spaces within the suite will be controlled by individual DDC controllers utilizing solid-state electronic sensing and rapid-response pneumatic actuation.

Two options will be considered to maintain individual space pressurization: pressure differential control and differential airflow control (ref. 2). In either case, each BSL-3Ag and BSL-4 room will be equipped with air flow valves on the supply and exhaust ducts. All input and output devices required for the monitoring and control of individual spaces will be wired to controllers dedicated to the individual spaces. (Note, using the inlet fans to control pressure can lead to an over-pressurization event that may have a higher likelihood of failing the HEPAs, so consider using the exhaust fans for pressure control.)

The supply air will be volume tracked to the summation of the room exhausts to within an adjustable negative offset. For pressure differential control, the remaining supply volume will be provided by a trim valve adjustment to maintain room differential pressure set point. For differential airflow control, the remaining supply volume will be provided by a make-up air opening protected by a HEPA filter and bioseal damper. Negative offset air may be adjusted to maintain desired pressure differential.

All room pressure control devices will be independently referenced to a common building pressure pipe loop (outdoor atmospheric) to establish the desired room pressures. A “cascading” room-to-room system will not be used, so that a failure in any given room will leave the remaining areas unaffected.

Pressure gradients will be adjustable from the BAS. The two-stage monitoring will initiate the initial warning alarm upon rise of pressure in an area relative to the pressure of the adjacent space and record alarm on subsequent pressure deviations from programmed boundaries set point.

Relationship to Hazard Analysis: Maintaining increasingly negative pressure differentials as one goes from areas of lower hazard to areas of higher hazard is effective in mitigating the effects of a release of aerosolized pathogens. For example, if a BSL-4 laboratory connects to a BSL-2 laboratory with a lower pressure in the BSL-4 laboratory, then airflow will be in the direction from BSL-2 to BSL-4; thus, a pathogen spilled, for instance, will tend to be routed to the BSL-4 exhaust HEPA filtration system instead of diffusing into the BSL-2 laboratory space and infecting co-located workers in that area.

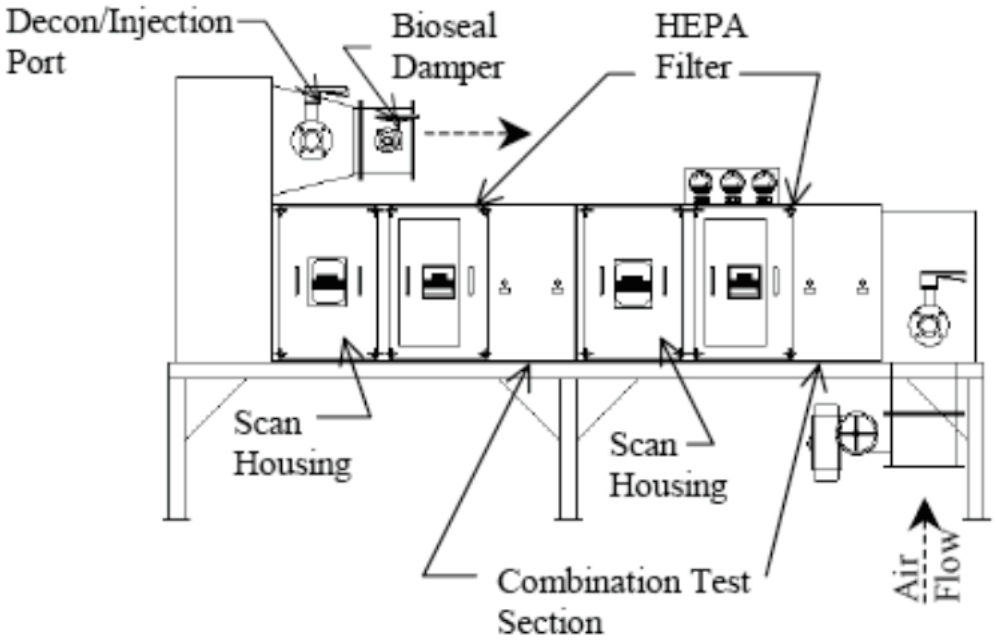


Figure E.2.2.2-7 — HEPA Housing

E.3 HAZARD EVALUATION AND ACCIDENT ANALYSIS METHODOLOGY

To support any hazard evaluation and analysis effort, an identification of potential hazards must be completed. For this exercise, a hazard is a biological, physical, or chemical characteristic of a material, system, process, or facility that has the potential for causing harm. Hazard identification, therefore, involves two key tasks: 1) identification of specific undesirable consequences and 2) identification of materials, systems, processes, and facility characteristics that could produce those consequences (CCPS-1).

This hazards assessment is developed utilizing information from the NBAF initial feasibility study (NBAF-1) and identifies potential hazards inherent in the anticipated NBAF processes or activities. This hazards listing consists of broad categories of factors that are associated with accident initiation or magnitude and include pathogenic, toxicologic, energetic, mechanical, human error, and others.

The methodology used for the hazard evaluation is based primarily on the method referred to as "*what if?/checklist"* analysis technique (CCPS-1). This technique is first applied in brainstorming the identification of various types of failures and scenarios that could conceivably occur in a process or facility. Once the failures and scenarios have been identified in a particular area or step of the process or activity, all pertinent aspects of the operation are considered for potential accident initiators and failure modes. After developing and listing potential failures and accident scenarios, each scenario is qualitatively evaluated to determine the potential consequences of the scenario. Safeguards that prevent, mitigate, or contain the effects of the potential accident are detailed, and each accident scenario is evaluated to determine whether additional improvements or controls should be recommended. All scenarios from the table that have adverse consequences of interest are identified. From this list, the safeguards for each selected accident scenario are categorized as primary and secondary containment barriers and procedural controls. Primary barriers are those engineered protective features that include safety equipment and personal protective equipment (BSCs, special process equipment, personnel safety suits, etc.), whereas secondary containment barriers are those intrinsic protective systems designed and constructed into the facility (structure, ventilation, fire suppression, etc.). Procedural controls by their design are administrative in nature.

Safeguard	Description
Primary Containment Barrier (Protective Feature)	Specific or intrinsic to the process or design element.
Secondary Containment Barrier (Protective System)	Provided by the facility and not the system and is intrinsic to the process or design element.
Procedural Control (Administrative)	Procedural in nature. May be a protective safety management program, a procedure, or a specific procedural step (directive language).

Each scenario is analyzed in an unmitigated fashion where the effects of any primary or secondary containment barriers or procedural controls are discounted to determine the uncontrolled impact of the accident scenario on the worker, the public, and the environment. Based on the consequence severity definitions listed in the following Tables (E.3-1 and E.3-2), categories are qualitatively assigned to each accident scenario.

The expected frequency of an occurrence for each scenario including such factors as the number of operations conducted each year, complexity of the operation, failure-rate data for any equipment involved, operator-error rates, operational experience, and expert judgment is qualitatively assessed. A frequency estimate is determined for each scenario using the likelihood categories from Table E.3-3. The overall risk for that particular accident scenario to both the public and the worker is then determined from the qualitative estimates of consequence (Tables E.3-1 and E.3-2) and the frequency of occurrence (Table E.3-3). These risk ranking values are given in Table E.3-4 showing the values of both public and worker in the form public/worker. To support unmitigated accident analyses, the accident scenarios are evaluated without primary or secondary containment barriers or procedural controls in place. That is, the consequence of each unmitigated accident scenario is based on the assumption that none of the controls mitigate any of the consequences.

Table E.3-1 — Public and Environmental Consequence Categories and Definitions

Category	Definition
A	**Substantial Off-Site Consequences** • *Biological hazard*: high probability or likelihood for human life-threatening health effects (RVFV and Nipah virus) and spread of animal pathogens (FMDV, RVFV, and Nipah virus) • *Chemical hazard*: off-site concentration Emergency Response Planning Guideline (ERPG) and/or Temporary Emergency Exposure Limit (TEEL) of ≥ EPRG/TEEL-3 • *Radiological hazard:* total effective dose equivalent (TEDE) ≥25 rem based on 10CFR830
B	**Moderate Off-Site Consequences** • *Biological hazard*: low probability or likelihood for human life-threatening health effects (RVFV and Nipah virus) and spread of animal pathogens (FMDV, RVFV, and Nipah virus) • *Chemical hazard*: EPRG/TEEL-3 > off-site concentration ≥ EPRG/TEEL-2 • *Radiological hazard:* 25 rem > TEDE ≥5 rem
C	**Minimal Off-Site Consequences** • *Biological hazard*: contamination occurs with no or minimal human life-threatening health effects (RVFV and Nipah virus) and spread of animal pathogens (FMDV, RVFV, and Nipah virus) • *Chemical hazard*: EPRG/TEEL-2 > off-site concentration ≥ EPRG/TEEL-1 • *Radiological hazard:* 5 rem > TEDE ≥0.1 rem
D	**Negligible Off-Site Consequences** • *Biological hazard*: little contamination with little or no potential for transient human life-threatening health effects (RVFV and Nipah virus) and spread of animal pathogens (FMDV, RVFV, and Nipah virus) • *Chemical hazard*: EPRG/TEEL-1 > off-site concentration ≥ EPRG/TEEL-1 • *Radiological hazard:* 0.1 rem > TEDE ≥0.01 rem
E	**No Measurable Off-Site Consequences** • *Biological hazard*: none • *Chemical hazard*: off-site concentration < TEEL-0 and < ERPG-1 • *Radiological hazard:* TEDE <0.01 rem

Table E.3-2 — Worker Consequence Categories and Definitions

Category	Definition
A	Immediate high probability of health effects leading to loss of life
B	Long-term health effects, disability, or severe injury (possibly life threatening)
C	Lost time injury but no disability (work restriction, not life threatening)
D	Minor injury with no disability and no work restriction
E	No measurable consequences

Table E.3-3 — Frequency Categories and Definitions

Frequency Category	Approximate Range	Label	Description
I	$\geq 10^{0}$/yr	Frequent	**Likely to occur often during the life of the facility** Incidents that occur during normal operations.
II	$<10^{0}$/yr to $\geq 10^{-2}$/yr	Occasional	**Likely to occur several times during the life of the facility** Incidents that may occur during the lifetime of the facility. These are incidents with a mean expected likelihood of occurring several times (≤50) in 50 operating years.
III	$<10^{-2}$/yr to $\geq 10^{-4}$/yr	Probable	**Unlikely but possible to occur during the life of the facility** Incidents that are not anticipated to occur during the lifetime of the facility but could. These are incidents having a likelihood of occurring between 1 time in 100 operating years to between 1 time in 10,000 operating years.
IV	$<10^{-4}$/yr to $\geq 10^{-6}$/yr	Improbable	**Unlikely to occur during the life of the facility** Incidents that will probably not occur during the lifetime of the facility. These are incidents having a likelihood of occurring 1 time in 10,000 years to between 1 time in 1 million operating years.
V	$<10^{-6}$/yr	Remote	**Should not occur during the life of the facility** These remaining incidents have a likelihood of occurring with a frequency of less than 1 time in 1 million operating years.

Table E.3-4 — Public/Worker Risk Ranking

Matrix of Risk Rank Values Public/Worker: 1 = High Risk and 4 = Low Risk					
Consequence Severity	Likelihood Category I	Likelihood Category II	Likelihood Category III	Likelihood Category IV	Likelihood Category V
A	1/1	1/1	2/2	2/2	3/3
B	1/1	2/1	2/2	3/3	3/4
C	1/1	2/2	3/3	3/4	4/4
D	3/2	3/3	3/4	4/4	4/4
E	4/4	4/4	4/4	4/4	4/4

E.3.1 Hazard Screening Analysis

Initially, hazard screening is the process of identifying the scenarios producing the highest pathogenic consequence impact to the public. Characterization of these scenarios is necessary to bound all NBAF operations in hazard space. Once this has been accomplished and the desired operational envelope has been defined, the selection process will identify design-basis accidents representative of the high-consequence public scenarios. These accidents are analyzed in detail to evaluate and determine the controls required to protect the public, the worker, and the environment in the event of an accident or unplanned event. The selection and evaluation process is used to define and evaluate bounding design-basis accidents and select specific controls to prevent the accident or to mitigate the accident consequence significantly. Once complete, lower-tier accidents within the same accident family are adequately and sufficiently prevented or mitigated.

Standard industrial hazards (slip, trips, falls, wounds, electrical hazards, chemical toxicity, fire hazards, and traumatic injuries) are not included in the hazard identification and evaluation process unless the hazard directly contributes to a pathogen release. Table E.3-5 presents the hazard analysis summary.

The following are a few of the identified hazard scenarios considered in the evaluation of the consequence from an inadvertent release of biological agents.

Surface Obstructions (Slipping, Tripping, Bumping, and Dropping) – These scenarios involve human errors and procedural violations, or possibly an incident initiated by a standard industrial hazard, such as slippery floors from cleaning. The scenario postulates a spill or splash, releasing an aerosolized microbiologic hazard or a surface contamination source with the potential for exposure to the laboratory workers. This scenario was evaluated in terms of the potential for material to be released from the NBAF. Due to the frequency of these types of hazard scenarios, a spill accident was evaluated specifically.

Biological Contamination and Worker Infection – A worker is postulated to become contaminated and infected by a microbiologic agent, resulting in the spread of a transmissible infectious disease to other workers, co-located workers, the public, or susceptible animals hosts. The origin of the infection could be from an undetected spill or surface contamination or the work area or equipment. This scenario represents a significant source of risk for the laboratory workers and is specifically evaluated.

Internal Leaks or Flooding – A break or leak in sprinkler piping or other internal plumbing is postulated to cause water to drip or pour onto experimental or storage equipment containing microbiologic hazards and/or cause an electrical short, resulting in a release of a microbiologic hazard with the potential for direct or indirect exposure. Due to the potential for a release to the environment, this scenario was considered explicitly.

Sharps (Cuts) – A worker is postulated to be inadvertently cut with a contaminated sharp object (broken glass, scalpel, scissors, microscope slide, or other sharps). This scenario is a biological contamination through incision, puncture, or abrasion.

Centrifuge, Incubator, Vacuum Pumps, and Other Instrumentation Sources – A procedural violation or equipment malfunction is postulated to result in a release of aerosolized microbiologic hazard with the potential for direct or indirect exposure. A centrifuge, vortexer, shaker, or incubator, etc., could malfunction or lose biocontainment as the result of the programming of inappropriate operation parameters, improper operation, equipment malfunction, improper maintenance, etc.

Biological Safety Cabinet – While performing open manipulations with a microbiologic agent within a BSC, an equipment malfunction (HEPA filter, fan failure, loss of power, or any activity that disrupts the inward directional laminar airflow of the BSC) occurs and results in a release of a microbiological hazard with the potential for direct or indirect exposure. This scenario was evaluated further in the accident analysis due to the impact from a system failure.

Heating, Ventilating, and Air Conditioning (HVAC) System Failure – A malfunction of the ventilation or HEPA filtration system, such as component failure or control malfunction, is postulated to result in a loss of building pressure control, which can contribute to a potential release. In addition, the potential of losing the hard ducted connection from a BSC resulting in direct exposure was evaluated. Events that may result in a malfunction of ventilation system include facility loss-of-power, door interlocks failing or malfunctioning, control system error, and improper maintenance. This scenario was further evaluated in the accident analysis due to the impact from a system failure.

Autoclave or Other Decontamination Equipment – A procedural violation, malfunction of boiler or steam lines, or other equipment malfunction while operating the autoclave or other steam disinfection or sterilization equipment is postulated to result in either equipment breach or incomplete decontamination with the potential for direct or indirect exposure.

Compressed Gas Cylinder Manifold Valve – A malfunction of a compressed gas cylinder manifold valve is postulated to lead to over-pressurization of equipment, resulting in a release of a microbiological hazard with the potential for direct or indirect exposure. Explosive detonation of gas cylinders from overfilling or unnoticed damage to the cylinder does occur. A nitrogen cylinder explosion occurred at the NADC, Ames, Iowa.

Laboratory or Room Fire – A procedural violation or inadequate combustible loading program leads to an accumulation of combustible fuel in an area (BSL, laboratory area, closet, cabinet, etc.). This coupled with any ignition source causes a fire that breaches containment within the NBAF and causes inter-laboratory contamination or may cause a fire large enough to breach facility containment by failing the ventilation and filtration system leading to a pathogen release to the environment. This scenario was further evaluated in the accident analysis due to the impact from a system failure.

Deflagration Leading to an Overpressure Event or a Laboratory Fire – The use of volatile and flammable chemicals as a part of routine NBAF operations has the possibility to lead to a deflagration accident scenario through either procedural violation or equipment malfunction. Formaldehyde and ethylene oxide are flammable and are candidates for use in large-volume disinfection operations. Alcohol and acetone are also used in routine process operations. Any use of these flammable chemicals could lead to deflagration scenarios resulting in overpressure events or laboratory fires that could challenge laboratory containment or facility confinement integrity. These scenarios were further evaluated in the accident analysis due to their impacts to safety systems.

Earthquake, Lightning, and High Winds – An earthquake is postulated to upset experimental and safety equipment; damage facility barriers such as the HEPA filters, plenums, or other elements of the ventilation system; and/or impair or eliminate utility services (power or fire suppression) and potentially fail the building structure, resulting in a release of a microbiologic hazard with the potential for direct or indirect exposure. This scenario was further evaluated in the accident analysis due to the impact from a system failure.

Although lightning strikes and high winds may be less likely to upset experimental and safety equipment, damage barriers such as the HEPA filters and HVAC system and/or impair or eliminate utility services compared with an earthquake, it is conservatively assumed that all three accident initiators result in the same equipment failures and consequences. It is also postulated that lightning strikes and earthquakes have sufficient energy to be considered as fire initiators.

Table E.3-5 — Hazard Analysis Table Developed to Support Health and Safety Section 3.14

Accident Number	Hazard	Accident Type	What-if (initiating event)	Outcome (accident progression)	Freq	Unmitigated (uncontrolled)			Existing Controls	Freq	Mitigated (controlled)				Recommended Additional Controls
						Consequence		Qualitative Risk			Consequence		Qualitative Risk		
						P/E	W	highest of P/E or W			P/E	W	P/E	W	
LAI-1	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**procedural violation** creates sharps (scissors, scalpels, sharp lab surfaces, other glass items including reagent bottles, vials, blood tubes, capillary tubes, microscope slides)	personnel infection (autoinoculation)	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for sharps handling and control; PPE; incident reporting requirements; incident response; security protocol; human reliability program (HRP)	Occasional (1.0 / yr to E-2 / yr)	E	C	4	2	2-person rule for procedure compliance and equipment use; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-2	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**equipment malfunction** creates sharps (scissors, scalpels, sharp lab surfaces, other glass items including reagent bottles, vials, blood tubes, capillary tubes, microscope slides)	personnel infection (autoinoculation)	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for equipment use; equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE and sharps containers; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	C	4	3	2-person rule for procedure compliance and equipment use; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-3	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**procedural violation** results in ingestion from pipette aspiration	personnel infection	Occasional (1.0 / yr to E-2 / yr)	B	A	1	procedures and training for pipette use; PPE; pipette aids; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	2-person rule for procedure compliance and equipment use; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-4	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**procedural violation** results in ingestion from inadvertent contact between mucous membranes and contaminated surfaces or hands	personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for contamination recognition and control; procedures against eating, drinking, cosmetics application, gum, tobacco, eye drops, open wounds, etc in facility; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	C	4	3	2-person rule for procedure compliance and equipment use; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-5	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**equipment malfunction** results in ingestion from inadvertent contact between mucous membranes and contaminated surfaces or hands	personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for contamination recognition and control; equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; procedures against eating, drinking, cosmetics application, gum, tobacco, eye drops, open wounds, etc in facility; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	C	4	3	2-person rule for procedure compliance and equipment use; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-6	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**procedural violation** results in aerosol production and inhalation (centrifuge, grinding, homogenizing, blending, vigorous shaking or mixing, sonic disruption, cell separator, etc)	personnel infection	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training for recognizing and controlling aerosol production in routine lab operations (culture prep and handling, pipette use, sampling, etc) in addition to lab equipment use (centrifuge, blending, grinding, mixing, shaking, etc); PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation;incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-7	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**equipment malfunction** results in aerosol production and inhalation (centrifuge, grinding, homogenizing, blending, vigorous shaking or mixing, sonic disruption, cell separator, etc)	personnel infection	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training for recognizing and controlling aerosol production in routine lab operations (culture prep and handling, pipette use, sampling, etc) in addition to lab equipment use (centrifuge, blending, grinding, mixing, shaking, etc); equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; configuration management governs maintenance type and frequency or equipment replacement; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-8	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**procedure violation or shipping-receiving violation** results in aerosol production and inhalation from opening pressurized containers	personnel infection	Probable (E-2 / yr to E-4 / yr)	A	A	1	procedures and training for recognizing and controlling aerosol production in routine lab operations; rigorous transportation requirements including shipper disclosure, packaging requirements for infectious materials; procedures, training, and equipment for packing and unpacking shipped biomaterials; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Remote (<E-6 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-9	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**equipment malfunction** results in aerosol production and inhalation from opening pressurized containers	personnel infection	Probable (E-2 / yr to E-4 / yr)	A	A	1	procedures and training for recognizing and controlling aerosol production in routine lab operations; rigorous transportation requirements including shipper disclosure, packaging requirements for infectious materials; procedures, training, and equipment for packing and unpacking shipped biomaterials; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Remote (<E-6 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; configuration management governs maintenance type and frequency or equipment replacement; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-10	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**animal handling procedural violation** results in bites, scratches	personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for animal handling and control; PPE; incident reporting requirements; incident response; security protocol; HRP	Occasional (1.0 / yr to E-2 / yr)	E	C	4	2	2-person rule for procedure compliance and equipment use; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-11	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**animal handling equipment malfunction** results in bites, scratches	personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for animal handling equipment use; procedures and training for equipment maintenance; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Occasional (1.0 / yr to E-2 / yr)	E	C	4	2	2-person rule for procedure compliance and equipment use; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-12	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**animal handling procedural violation** results in needle sticks	personnel infection (autoinoculation)	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for animal handling and control; PPE; incident reporting requirements; incident response; security protocol; HRP	Occasional (1.0 / yr to E-2 / yr)	E	C	4	2	2-person rule for procedure compliance and equipment use; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-13	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**animal handling equipment malfunction** results in needle sticks	personnel infection (autoinoculation)	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for animal handling equipment use; equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Occasional (1.0 / yr to E-2 / yr)	E	C	4	2	2-person rule for procedure compliance and equipment use; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-14	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**animal handling procedural violation** results in ingestion from inadvertent contact between mucous membranes and contaminated surfaces or hands	personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for animal handling and contamination recognition and control; procedures against eating, drinking, cosmetics application, gum, tobacco, eye drops, open wounds, etc in facility; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	C	4	3	2-person rule for procedure compliance and equipment use; need for monitoring or detection capability to control contamination spread (fluorescence?)

Table E.3-5 — Hazard Analysis Table Developed to Support Health and Safety Section 3.14 (Continued)

Accident Number	Hazard	Accident Type	What-if (initiating event)	Outcome (accident progression)	Freq	Unmitigated (uncontrolled)			Existing Controls	Freq	Mitigated (controlled)				Recommended Additional Controls
						Consequence		Qualitative Risk			Consequence		Qualitative Risk		
						P/E	W	highest of P/E or W			P/E	W	P/E	W	
LAI-15	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**animal handling equipment malfunction** results in ingestion from inadvertent contact between mucous membranes and contaminated surfaces or hands	personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for animal handling and contamination recognition and control; equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; procedures against eating, drinking, cosmetics application, gum, tobacco, eye drops, open wounds, etc in facility; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	C	4	3	2-person rule for procedure compliance, equipment use, configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-16	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**animal handling procedural violation** results in aerosol production and inhalation (inoculating animals intranasally, harvesting infected tissue from animals or eggs)	personnel infection	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training for recognizing and controlling aerosol generation during animal handling operations; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
LAI-17	Uncontrolled *known or unknown* exposure to pathogen	Laboratory acquired infections (LAI)	**animal handling equipment malfunction** results in aerosol production and inhalation (inoculating animals intranasally, harvesting infected tissue from animals or eggs)	personnel infection	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training for recognizing and controlling aerosol generation during animal handling operations; equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; configuration management governs maintenance type and frequency or equipment replacement; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
CONT-1	Uncontrolled *known or unknown* exposure to pathogen	Loss of containment	**animal handling or insectary procedural violation** results in escaped animal or insect	environmental contamination	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training for animal handling and husbandry as well as for insectary operations; appropriate animal and insect facilities are provided and personnel are trained on procedures for their use and maintenance; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	D	E	3	4	2-person rule for procedure compliance and facility use, especially the insectary; BSC enclosures for animal and insectary operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
CONT-2	Uncontrolled *known or unknown* exposure to pathogen	Loss of containment	**animal handling or insectary equipment malfunction** results in escaped animal or insect	environmental contamination	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training for animal handling and husbandry as well as for insectary operations; appropriate animal and insect facilities are provided and personnel are trained on procedures for their use and maintenance to procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	D	E	4	4	2-person rule for procedure compliance and facility use, especially the insectary; configuration management governs maintenance type and frequency or equipment replacement; BSC enclosures for animal and insectary operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
CONT-3	Uncontrolled *known or unknown* exposure to pathogen	contaminated solid waste (including animal)	**procedure violation** results in incomplete sterilization/disinfection of solid waste	contamination, possible personnel infection, possible environmental contamination	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training exist for pre- and post-treatment waste handling; for preparing and transferring the waste for treatment; and for sampling and (assumed) confirming sterile prior to discharge to environment; treated waste is transferred and retained in a controlled repository; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	D	D	3	4	2-person rule for procedure compliance and equipment use; ifthere is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; need for monitoring or detection capability to control contamination spread (fluorescence?)
CONT-4	Uncontrolled *known or unknown* exposure to pathogen	contaminated solid waste (including animal)	**equipment malfunction** results in incomplete sterilization/disinfection of solid waste	contamination, possible personnel infection, possible environmental contamination	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training exist for the use and maintenance of pre- and post-treatment waste handling and transfer equipment; procedures and training exist for the use and maintenance of sterilization equipment and process equipment; and for sampling and (assumed) confirming sterile prior to discharge to environment; equipment/process used to transfer treated waste to controlled repository is properly maintained; all equipment has proper maintenance and use procedures to prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	D	D	4	4	2-person rule for procedure compliance and equipment use; ifthere is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
CONT-5	Uncontrolled *known or unknown* exposure to pathogen	contaminated liquid waste (including shower effluent, disinfectant wash-down, animal)	**procedure violation** results in incomplete sterilization/disinfection of liquid waste	contamination, possible personnel infection, possible environmental contamination	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training exist for pre- and post-treatment waste handling; for preparing and transferring the waste for treatment; and for sampling and (assumed) confirming sterile prior to discharge to environment; treated waste is transferred and (assumed) treated again in a commercial liquid waste treatment facility; PPE; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	D	D	4	4	2-person rule for procedure compliance and equipment use; ifthere is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; need for monitoring or detection capability to control contamination spread (fluorescence?)
CONT-6	Uncontrolled *known or unknown* exposure to pathogen	contaminated liquid waste (including shower effluent, disinfectant wash-down, animal)	**equipment malfunction** results in incomplete sterilization/disinfection of liquid waste	contamination, possible personnel infection, possible environmental contamination	Frequent (≥ 1.0 / yr)	A	A	1	procedures and training exist for the use and maintenance of pre- and post-treatment waste handling and transfer equipment; procedures and training exist for the use and maintenance of sterilization equipment and process equipment; and for sampling and (assumed) confirming sterile prior to discharge to environment; equipment/process used to handle and transfer treated waste to a second commercial effluent treatment facility is properly maintained; all equipment has proper maintenance and use procedures to prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Remote (<E-6 / yr)	D	D	4	4	2-person rule for procedure compliance and equipment use; ifthere is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
SUIT-1	Uncontrolled *known or unknog* exposure to pathogen	suit-specific hazards	**suit breach** from crush, pinch, puncture (air-lock doors, quick disconnects, movement of equipment, suit puncture or tear)	personnel contamination	Frequent (≥ 1.0 / yr)	C	A	1	procedures and training for suit use and for recognizing and controlling pinch points; procedures and training for minimizing and recognizing aerosol production in routine lab operations (culture prep and handling, pipette use, sampling, etc) in addition to lab equipment use (centrifuge, blending, grinding, mixing, shaking, etc); suit maintenance and use procedures prevent misuse and proper equipment replacement protocol; redundant PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance, equipment use, and for suit damage hazard control; configuration management governs maintenance type and frequency or equipment replacement; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)

Table E.3-5 — Hazard Analysis Table Developed to Support Health and Safety Section 3.14 (Continued)

Accident Number	Hazard	Accident Type	What-if (initiating event)	Outcome (accident progression)	Freq	Unmitigated (uncontrolled)			Existing Controls	Freq	Mitigated (controlled)				Recommended Additional Controls
						Consequence		Qualitative Risk			Consequence		Qualitative Risk		
						P/E	W	highest of P/E or W			P/E	W	P/E	W	
SUIT-2	Uncontrolled *known or unknown* exposure to pathogen	suit-specific hazards	**personnel error leads to suit breach** from heat/cold, dehydration from physical exertion and dry air supply, hypothermia and hot surfaces from autoclaves and other surfaces, hypoxia (air flow restriction)	personnel contamination	Occasional (1.0 / yr to E-2 / yr)	C	A	1	procedures and training for suit use and for recognizing physical distress and attention-to-detail hazards; procedures and training for minimizing and recognizing aerosol production in routine lab operations (culture prep and handling, pipette use, sampling, etc) in addition to lab equipment use (centrifuge, blending, grinding, mixing, shaking, etc); suit maintenance and use procedures prevent misuse and proper equipment replacement protocol; redundant PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	B	4	3	2-person rule for procedure compliance, equipment use, and for suit damage hazard control; configuration management governs maintenance type and frequency or equipment replacement; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
SUIT-3	Uncontrolled *known or unknown* exposure to pathogen	suit-specific hazards	**personnel error leads to suit breach** from physical and sensory isolation, claustrophobia	personnel contamination	Probable (E-2 / yr to E-4 / yr)	C	A	1	procedures and training for suit use and for recognizing physical distress and attention-to-detail hazards; procedures and training for minimizing and recognizing aerosol production in routine lab operations (culture prep and handling, pipette use, sampling, etc) in addition to lab equipment use (centrifuge, blending, grinding, mixing, shaking, etc); suit maintenance and use procedures prevent misuse and proper equipment replacement protocol; redundant PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Remote (<E-6 / yr)	E	B	4	4	2-person rule for procedure compliance, equipment use, and for suit damage hazard control; configuration management governs maintenance type and frequency or equipment replacement; BSC enclosures for aerosol-generating operations and equipment; need for monitoring or detection capability to control contamination spread (fluorescence?)
SPIL-1	Uncontrolled *known or unknown* exposure to pathogen	spill, small sample	**procedural violation during specimen transport** results in spill (slip, trip, fall, drop, jostle, jar, impact)	contamination, aerosol generation, and possible personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for packaging and transporting or transferring small samples intra-site and inter-laboratory; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)
SPIL-2	Uncontrolled *known or unknown* exposure to pathogen	spill, small sample	**equipment malfunction during specimen transport/storage** results in spill (slip, trip, fall, drop, jostle, jar, impact) poor or inadequate packaging/transport system, or failure of storage environment	contamination, aerosol generation, and possible personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for packaging and transporting or transferring small samples intra-site and inter-laboratory; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; transport system and storage equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	B	4	3	2-person rule for procedure compliance and equipment use; immediate decontamination available; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
SPIL-3	Uncontrolled *known or unknown* exposure to pathogen	spill, small-to-medium volume	**procedural violation during specimen transport** results in spill (slip, trip, fall, drop, jostle, jar, impact)	contamination, aerosol generation, and possible personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for packaging and transporting or transferring medium-volume samples intra-site and inter-laboratory; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)
SPIL-4	Uncontrolled *known or unknown* exposure to pathogen	spill, small-to-medium volume	**equipment malfunction during specimen transport/storage** results in spill (slip, trip, fall, drop, jostle, jar, impact) poor or inadequate packaging/transport system, or failure of storage environment	contamination, aerosol generation, and possible personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for packaging and transporting or transferring medium-volume samples intra-site and inter-laboratory; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; transport system and storage equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	B	4	3	2-person rule for procedure compliance and equipment use; immediate decontamination available; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
SPIL-5	Uncontrolled *known or unknown* exposure to pathogen	spill, large volume	**procedural violation during specimen transport** results in spill (slip, trip, fall, drop, jostle, jar, impact)	contamination, aerosol generation, and possible personnel infection	Probable (E-2 / yr to E-4 / yr)	A	A	1	procedures and training for packaging and transporting or transferring medium-volume samples intra-site and inter-laboratory; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; PPE; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	B	4	3	2-person rule for procedure compliance and equipment use; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)
SPIL-6	Uncontrolled *known or unknown* exposure to pathogen	spill, large volume	**equipment malfunction during specimen transport/storage** results in spill (slip, trip, fall, drop, jostle, jar, impact) poor or inadequate packaging/transport system, or failure of storage environment	contamination, aerosol generation, and possible personnel infection	Probable (E-2 / yr to E-4 / yr)	A	A	1	procedures and training for packaging and transporting or transferring medium-volume samples intra-site and inter-laboratory; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; transport system and storage equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Remote (<E-6 / yr)	E	B	4	3	2-person rule for procedure compliance and equipment use; immediate decontamination available; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
SPIL-7	Uncontrolled *known or unknown* exposure to pathogen	release from internal flooding	**internal flooding from failure** of process piping, fire suppression piping, or similar system (see CONT-4)	contamination of laboratory water or solution accumulation; improper collection and treatment leads to worker contamination or possible environmental release	Probable (E-2 / yr to E-4 / yr)	A	A	1	procedures and training exist for liquid waste handling for preparing and transferring the waste for treatment; and for sampling and (assumed) confirming sterile prior to discharge to environment; treated waste is transferred and treated again in a commercial liquid waste treatment facility (true?); PPE; incident reporting requirements; incident response; security protocol; HRP	Remote (<E-6 / yr)	D	D	4	4	2-person rule for procedure compliance and equipment use; if there is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; need for monitoring or detection capability to control contamination spread (fluorescence?)
RAD-1	Uncontrolled *known or unknown* exposure to pathogen	contaminated radioactive waste (solid or liquid)	**procedural violation when handling, processing, sterilizing mixed rad/bio waste/equipment** (solid or liquid) resulting in incomplete pathogen destruction	contamination, possible personnel infection, possible environmental contamination (both pathogen and radioactive)	Occasional (1.0 / yr to E-2 / yr)	C	C	2	because of the radioactive component of the waste, procedures and training will be specialized for use, collection, segregation, treatment, and disposal; volumes are low; PPE; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	D	D	4	4	2-person rule for procedure compliance and equipment use; if there is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; need for monitoring or detection capability to control contamination spread is available for the radioactive component

Table E.3-5 — Hazard Analysis Table Developed to Support Health and Safety Section 3.14 (Continued)

Accident Number	Hazard	Accident Type	What-if (initiating event)	Outcome (accident progression)	Freq	Unmitigated (uncontrolled)			Existing Controls	Freq	Mitigated (controlled)				Recommended Additional Controls
						Consequence		Qualitative Risk			Consequence		Qualitative Risk		
						P/E	W	highest of P/E or W			P/E	W	P/E	W	
RAD-2	Uncontrolled *known or unknown* exposure to pathogen	contaminated radioactive waste (solid or liquid)	**equipment violation when handling, processing, sterilizing mixed rad/bio waste/equipment** (solid or liquid) resulting in incomplete pathogen destruction	contamination, possible personnel infection, possible environmental contamination (both pathogen and radioactive)	Occasional (1.0 / yr to E-2 / yr)	C	C	2	because of the radioactive component of the waste, procedures and training will be specialized for use, collection, segregation, treatment, and disposal; volumes are low; procedures and training exist for the use and maintenance of sterilization equipment and process equipment; equipment/process used to handle and transfer treated radioactive waste is properly maintained; all equipment has proper maintenance and use procedures to prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	D	D	4	4	2-person rule for procedure compliance and equipment use; if there is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; need for monitoring or detection capability to control contamination spread is available for the radioactive component
RAD-3	Uncontrolled *known or unknown* exposure to pathogen	ionizing radiation or radioactive material contamination	**procedural violation using radioactive materials** creates mechanism for contamination, aerosol generation, ingestion, inoculation	personnel exposure to pathogen (inhalation, contamination, ingestion, etc) and exposure to ionizing radiation (no contamination)	Probable (E-2 / yr to E-4 / yr)	B	A	1	procedures and training for pathogen handling and control; procedures for handling and use of radioactive materials, PPE; incident reporting requirements; incident response; security protocol; human reliability program (HRP)	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	2-person rule for procedure compliance and equipment use similar to the suite of controls recommended for non-radioactive pathogen use; use of radioactive material monitoring and detection equipment to detect and control contamination spread
RAD-4	Uncontrolled *known or unknown* exposure to pathogen	ionizing radiation or radioactive material contamination	**equipment malfunction using radioactive materials** creates mechanism for contamination, aerosol generation, ingestion, inoculation	personnel exposure to pathogen (inhalation, contamination, ingestion, etc) and exposure to ionizing radiation (no contamination)	Probable (E-2 / yr to E-4 / yr)	B	A	1	procedures and training for equipment use; procedures and training in place and used for radioactive materials; equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE and sharps containers; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Remote (<E-6 / yr)	E	C	4	4	2-person rule for procedure compliance and equipment use similar to the suite of controls recommended for non-radioactive pathogen use; configuration management governs maintenance type and frequency or equipment replacement; use of radioactive material monitoring and detection capability to control contamination spread
NECR-1	Uncontrolled *known or unknown* exposure to pathogen	necropsy safety	**procedure violation during necropsy** results in LAI due to cut/puncture, ingestion, or inhalation	contamination and possible personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training in use for sharps use and handling/disposal, for contamination control to prevent inadvertent ingestion (no eating, drinking, cosmetics, tobacco, etc.), and for recognizing and controlling aerosol production in routine lab operations (culture prep and handling, pipette use, sampling, etc) in addition to lab equipment use (centrifuge, blending, grinding, mixing, shaking, etc); PPE; incident reporting requirements; incident response; security protocol; HRP	Occasional (1.0 / yr to E-2 / yr)	E	C	4	2	2-person rule for procedure compliance and equipment use; if there is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; need for monitoring or detection capability to control contamination spread (fluorescence?)
NECR-2	Uncontrolled *known or unknown* exposure to pathogen	necropsy safety	**equipment malfunction during necropsy** results in LAI due to cut/puncture, ingestion, or inhalation	contamination and possible personnel infection	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for equipment use; equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE and sharps containers; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	C	4	3	2-person rule for procedure compliance and equipment use; if there is no QC on sterilization effectiveness, the mitigated half of this scenario needs updating; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
ENER-1	Uncontrolled *known or unknown* exposure to pathogen	energetic event causing release	**deflagration of natural gas or other flammable process gas leak** causing BSC failure, laboratory, or main structure failure; personnel contamination, room contamination, ventilation system leakage around, through HEPA filters	contamination, personnel infection, laboratory contamination, possible environmental contamination	Occasional (1.0 / yr to E-2 / yr)	A	A	1	procedures and training for equipment use, open flame and spark control; equipment maintenance and use procedures prevent facility gas leak and accumulation; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	A	A	2	2	currently, natural gas is available to the central utility plant and should be precluded from the NBAF; flammable gas cylinders should contain limited volume if required at all for processes
ENER-2	Uncontrolled *known or unknown* exposure to pathogen	energetic event causing release	**overpressure from blockage in steam line** leading to autoclave failure or process steam line failure, personnel contamination, room contamination, ventilation system leakage around, through HEPA filters, environmental contamination	contamination, personnel infection, laboratory contamination, possible environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	modern autoclave and process steam piping instrumentation and control prevent catastrophic failure if procedures and maintenance protocol exist and personnel are trained and follow procedures; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	reliance on preventive and corrective maintenance procedures; frequent inspections; trained and experienced operators and maintenance personnel; redundant equipment
ENER-3	Uncontrolled *known or unknown* exposure to pathogen	energetic event causing release	**deflagration of formaldehyde, ethylene oxide, or other flammable agent during laboratory disinfection or sanitization**, personnel contamination, room contamination, structural failure, loss of containment, ventilation system leakage around, through HEPA filters	contamination, personnel infection, laboratory contamination, loss of containment, environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	modern disinfection / sanitization procedures, equipment, process instrumentation and control are available; training and maintenance procedures developed and used; flammable gas controls in place including detection, ventilation, recognition and control of ignition source used to prevent catastrophic consequences; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	reliance on preventive and corrective maintenance procedures; frequent inspections; recognition of flammable and toxic gases; trained and experienced operators and maintenance personnel
ENER-4	Uncontrolled *known or unknown* exposure to pathogen	energetic event causing release	**deflagration of unanticipated chemical reaction** leading to BSC failure, personnel contamination, room contamination, ventilation system leakage around, through HEPA filters	contamination, personnel infection, laboratory contamination, possible environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	training and maintenance procedures developed and used; flammable gas controls in place including recognition and control of flammable gases and ignition sources, gas detection, BSC ventilation used to prevent accumulation and catastrophic consequences; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	reliance on preventive and corrective maintenance procedures; frequent inspections; recognition and control of flammable and toxic gases; trained and experienced operators and maintenance personnel
ENER-5	Uncontrolled *known or unknown* exposure to pathogen	energetic event causing release	**deflagration/explosion/fire external (to the facility) of the supply of diesel, fuel oil, gasoline** leading to facility breach, personnel contamination, room contamination, possible environmental contamination	contamination, personnel infection, laboratory contamination, possible environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	training and maintenance procedures developed and used; combustible control program developed and implemented; ventilation in central utility plant; recognition and control of flammable gases and ignition sources; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	A	A	2	2	Central utility plant to store 500,000 gal of diesel (feasibility study, section 4.10, pg 2); proximity of diesel storage to main laboratories needs to be increased
FIRE-1	Uncontrolled *known or unknown* exposure to pathogen	fire (inside BSC or outside BSC but inside laboratory)	**fire from deflagration of natural gas or other flammable process gas leak** causing BSC failure, personnel contamination, room contamination, ventilation system leakage around, through HEPA filters	contamination, personnel infection, laboratory contamination, possible environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	training and maintenance procedures developed and used; combustible loading controls; flammable gas controls in place including recognition and control of flammable gases and ignition sources, gas detection, BSC ventilation used to prevent accumulation and catastrophic consequences; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	reliance on operating and maintenance procedures, stored energy control, and combustible loading controls to prevent and mitigate fires; frequent inspections; trained and experienced operators and maintenance personnel

Table E.3-5 — Hazard Analysis Table Developed to Support Health and Safety Section 3.14 (Continued)

Accident Number	Hazard	Accident Type	What-if (initiating event)	Outcome (accident progression)	Freq	Unmitigated (uncontrolled)			Existing Controls	Freq	Mitigated (controlled)				Recommended Additional Controls
						Consequence		Qualitative Risk			Consequence		Qualitative Risk		
						P/E	W	highest of P/E or W			P/E	W	P/E	W	
FIRE-2	Uncontrolled *known or unknown* exposure to pathogen	fire (inside BSC or outside BSC but inside laboratory)	**deflagration of anticipated or unanticipated chemical reaction** leading to BSC failure, personnel contamination, room contamination, possible ventilation system leakage around, through HEPA filters	contamination, personnel infection, laboratory contamination, possible environmental contamination	Occasional (1.0 / yr to E-2 / yr)	A	A	1	combustible loading controls developed and implemented; training and maintenance procedures developed and used for equipment and process use; volume / mass control of chemicals to minimize stored energy; flammable gas controls in place including recognition and control of flammable gases and ignition sources, gas detection, BSC ventilation used to prevent accumulation and catastrophic consequences; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	reliance on operating and maintenance procedures, stored energy control, and combustible loading controls to prevent and mitigate fires; frequent inspections; trained and experienced operators and maintenance personnel
FIRE-3	Uncontrolled *known or unknown* exposure to pathogen	fire (inside BSC or outside BSC but inside laboratory)	**fire from flammable process liquids** causing BSC failure, personnel contamination, room contamination, possible ventilation system leakage around, through HEPA filters	contamination, personnel infection, laboratory contamination, possible environmental contamination	Occasional (1.0 / yr to E-2 / yr)	A	A	1	combustible loading controls developed and implemented; training and maintenance procedures developed and used for equipment and process use; volume / mass control of chemicals to minimize stored energy; flammable gas controls in place including recognition and control of flammable gases and ignition sources, gas detection, BSC ventilation used to prevent accumulation and catastrophic consequences; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	reliance on operating and maintenance procedures, stored energy control, and combustible loading controls to prevent and mitigate fires; frequent inspections; trained and experienced operators and maintenance personnel
FIRE-4	Uncontrolled *known or unknown* exposure to pathogen	fire (inside BSC or outside BSC but inside laboratory)	**fire from buildup of combustibles (poor combustible control in laboratories)** causing BSC failure, personnel contamination, room contamination, possible ventilation system leakage around, through HEPA filters	contamination, personnel infection, laboratory contamination, possible environmental contamination	Occasional (1.0 / yr to E-2 / yr)	A	A	1	combustible loading controls developed and implemented; training and maintenance procedures developed and used for equipment and process use; volume / mass control of chemicals to minimize stored energy; flammable gas controls in place including recognition and control of flammable gases and ignition sources, gas detection, BSC ventilation used to prevent accumulation and catastrophic consequences; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	C	4	4	reliance on operating and maintenance procedures, stored energy control, and combustible loading controls to prevent and mitigate fires; frequent inspections; trained and experienced operators and maintenance personnel
EXT-1	Uncontrolled *known or unknown* exposure to pathogen	fire (external event)	**fire from fuel accumulation external to the facility; supply of diesel, fuel oil, gasoline burns** leading to facility breach, personnel contamination, room contamination, possible environmental contamination	contamination, personnel infection, laboratory contamination, possible environmental contamination	Occasional (1.0 / yr to E-2 / yr)	A	A	1	training and maintenance procedures developed and used; combustible control program developed and implemented; ventilation in central utility plant; recognition and control of flammable gases and ignition sources; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	A	A	2	2	Central utility plant to store 500,000 gal of diesel (feasibility study, section 4.10, pg 2); proximity of diesel storage to main laboratories needs to be increased
EXT-2	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**small airplane crash into facility (DOE-STD-3014 scenario)** causes structure failure; significant environmental and public contamination	personnel and environmental contamination	Improbable (E-4 / yr to E-6 / yr)	A	A	1	no different than for seismic with fire, wind, missile, or other NPH	Improbable (E-4 / yr to E-6 / yr)	A	A	1	1	as with seismic with the potential for fire, increase structural design, ventilation fans, filter plenums, filter housings, etc., to accept higher accelerations (~0.5g); facility to maintain integrity and negative pressure during and after impact event; seismic controls mesh with combustible loading controls and program to prevent or significantly mitigate attendant fires
EXT-3	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**wildland fire breaches facility boundary and reaches fuel accumulation external to the facility; supply of diesel, fuel oil, gasoline burns** leading to facility breach, personnel contamination, room contamination, possible environmental contamination	contamination, personnel infection, laboratory contamination, possible environmental contamination	Improbable (E-4 / yr to E-6 / yr)	A	A	1	training and maintenance procedures developed and used; combustible control program developed and implemented; facility grounds maintained to prevent fuel; incident reporting requirements; incident response; security protocol; HRP	Remote (<E-6 / yr)	A	A	2	2	Central utility plant to store 500,000 gal of diesel (feasibility study, section 4.10, pg 2); proximity of diesel storage to main laboratories needs to be increased
LEAK-1	Uncontrolled *known or unknown* exposure to pathogen	process leak, handling error, or poor housekeeping	**unknown process piping leak or other source of contamination (equipment malfunction)** leads to contamination spread	contamination, personnel infection, laboratory contamination, possible environmental contamination	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for equipment use; equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE and sharps containers; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; immediate decontamination available; configuration management governs maintenance type and frequency or equipment replacement; need for monitoring or detection capability to control contamination spread (fluorescence?)
LEAK-2	Uncontrolled *known or unknown* exposure to pathogen	process leak, handling error, or poor housekeeping	**procedure violation during material or waste handling or transfer** leads to contamination spread	contamination, personnel infection, laboratory contamination, possible environmental contamination	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training exist for waste handling prior to treatment; for preparing and transferring the waste for treatment; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; need for monitoring or detection capability to control contamination spread (fluorescence?)
LEAK-3	Uncontrolled *known or unknown* exposure to pathogen	process leak, handling error, or poor housekeeping	**equipment malfunction during material or waste handling or transfer** leads to contamination spread	contamination, personnel infection, laboratory contamination, possible environmental contamination	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training exist for material or waste handling prior to transferring, processing, or treatment; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; need for monitoring or detection capability to control contamination spread (fluorescence?)
LEAK-4	Uncontrolled *known or unknown* exposure to pathogen	process leak, handling error, or poor housekeeping	**procedural violation leads to poor housekeeping and** contamination spread	contamination, personnel infection, laboratory contamination, possible environmental contamination	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training exist for housekeeping to ensure contamination mitigation; waste management and material handling, transferring, and processing practices aid with contamination control; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance with housekeeping protocol and other contamination control practice; need for monitoring or detection capability to control contamination spread (fluorescence?)
TRAN-1	Uncontrolled *known or unknown* exposure to pathogen	transportation	**shipment handling violation results in facility contamination** (failure to meet Federal biomaterial transportation requirements) results in shipment with broken containers, external contamination, site and personnel contamination	contamination, personnel infection, equipment contamination, environmental contamination	Occasional (1.0 / yr to E-2 / yr)	A	A	1	procedures and training for packaging and transporting or transferring samples inter-laboratory; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; transport system and storage equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	B	4	3	2-person rule for procedure compliance and equipment use; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)

Table E.3-5 — Hazard Analysis Table Developed to Support Health and Safety Section 3.14 (Continued)

Accident Number	Hazard	Accident Type	What-if (initiating event)	Outcome (accident progression)	Freq	Unmitigated (uncontrolled)			Existing Controls	Freq	Mitigated (controlled)				Recommended Additional Controls
						Consequence		Qualitative Risk			Consequence		Qualitative Risk		
						P/E	W	highest of P/E or W			P/E	W	P/E	W	
TRAN-2	Uncontrolled *known or unknown* exposure to pathogen	transportation and handling	**mis-identification and site contamination** (failure to meet Federal biomaterial transportation requirements) results in inadequate handling and personnel contamination (high-level pathogen in low-level confinement with inadequate PPE)	contamination, personnel infection, equipment contamination, environmental contamination	Occasional (1.0 / yr to E-2 / yr)	A	A	1	procedures and training for packaging, identifying (manifest), and transporting or transferring samples inter-laboratory; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; transport system and storage equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; BSC, laboratory, facility containment; HEPA-filtered negative-pressure ventilation; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	E	B	4	3	2-person rule for procedure compliance and equipment use; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)
TRAN-3	Uncontrolled *known or unknown* exposure to pathogen	transportation	**over-the-road** (failure to meet Federal biomaterial transportation requirements) results in shipment with broken containers and external contamination not confined to site	contamination, personnel infection, equipment contamination, environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	procedures and training for packaging, identifying (manifest), and transporting or transferring samples inter-laboratory; procedures and training exist for transportation operators to load, secure, transport sample containers; procedures and training for recognizing and controlling contamination during post-transport handling; packaging materials and equipment available and used; transport system and storage equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	C	B	3	3	2-person rule for procedure compliance and equipment use; procedures and training for shipping and receiving personnel at receiving site; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)
TRAN-4	Uncontrolled *known or unknown* exposure to pathogen	transportation	**air cargo contamination** (failure to meet Federal or International biomaterial transportation requirements) results in shipment with broken containers, external contamination, and greater extent of contamination due to lack of discovery after many airports affected	contamination, personnel infection, equipment contamination, environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	procedures and training for packaging, identifying (manifest), and transporting or transferring samples inter-laboratory; procedures and training exist for transportation operators to load, secure, transport sample containers; procedures and training for recognizing and controlling contamination during post-transport handling; packaging materials and equipment available and used; transport system and storage equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	C	B	3	3	2-person rule for procedure compliance and equipment use (different packaging for air transport?); procedures and training for shipping and receiving personnel at intermediate and final receiving site; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)
TRAN-5	Uncontrolled *known or unknown* exposure to pathogen	transportation	**ocean-going contamination** (failure to meet Federal or International biomaterial transportation requirements) results in shipment with broken containers and external contamination	contamination, personnel infection, equipment contamination, environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	procedures and training for packaging, identifying (manifest), and transporting or transferring samples inter-laboratory; procedures and training exist for transportation operators to load, secure, transport sample containers; procedures and training for recognizing and controlling contamination during post-transport handling; packaging materials and equipment available and used; transport system and storage equipment maintenance and use procedures prevent misuse and proper equipment replacement protocol; PPE; incident reporting requirements; incident response; security protocol; HRP	Improbable (E-4 / yr to E-6 / yr)	C	B	3	3	2-person rule for procedure compliance and equipment use (different packaging for ocean-going transport?); procedures and training for shipping and receiving personnel at receiving site; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)
TRAN-6	Uncontrolled *known or unknown* exposure to pathogen	transportation	**procedural violation and improper intra-site packaging, unpackaging, material handling** results in broken containers, personnel contamination, and external contamination	contamination, personnel infection, equipment contamination, environmental contamination	Frequent (≥ 1.0 / yr)	B	A	1	procedures and training for packaging and transporting or transferring samples intra-site; procedures and training for recognizing and controlling aerosol generation; packaging materials and equipment available and used; PPE; incident reporting requirements; incident response; security protocol; HRP	Probable (E-2 / yr to E-4 / yr)	E	B	4	2	2-person rule for procedure compliance and equipment use; immediate decontamination available; need for monitoring or detection capability to control contamination spread (fluorescence?)
NPH-1	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**seismic event exceeds facility design criteria** and structure fails; significant environmental and public contamination	personnel and environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	no seismic controls; feasibility study indicates spectral acceleration of 0.06g to 0.19g -- equivalent of light-laboratory seismic resistance	Probable (E-2 / yr to E-4 / yr)	A	A	1	1	increase structural design, ventilation fans, filter plenums, filter housings, etc., to accept higher accelerations (~0.5g); facility to maintain integrity and negative pressure during and after seismic event
NPH-2	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**seismic event challenges or exceeds facility design criteria** and structure fails, **subsequent fire(s) start** from ignition sources in laboratories; significant environmental and public contamination	personnel and environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	no seismic controls; feasibility study indicates spectral acceleration of 0.06g to 0.19g -- equivalent of light-laboratory seismic resistance; with no seismic controls, ignition sources in laboratories and outside (500,000-gal diesel storage) assumed to result in fires. Performance Category 3 for High containment, High Hazard Facilities: design for seismic events > 100 yrs;	Probable (E-2 / yr to E-4 / yr)	A	A	1	1	increase structural design, ventilation fans, filter plenums, filter housings, etc., to accept higher accelerations (~0.5g); facility to maintain integrity and negative pressure during and after seismic event; seismic controls mesh with combustible loading controls and program to prevent or significantly mitigate attendant fires
NPH-3	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**high winds (tornado) challenge or exceed facility design criteria** and structure fails; significant environmental and public contamination	personnel and environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	facility wind resistance (90-mph), no tornado (readily apparent) considered in feasibility study; Performance Category 3 for High containment, High Hazard Facilities: design for wind speed > 117-mph & tornado exposure credible for example facility;	Probable (E-2 / yr to E-4 / yr)	A	A	1	1	increase structural design to withstand credible winds for the site; facility to maintain integrity and negative pressure during and after high-wind exposure
NPH-4	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**high winds (tornado) generate missiles that challenge or exceed facility design criteria** and structure fails; significant environmental and public contamination	personnel and environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	facility wind resistance (90-mph), no tornado (readily apparent) considered in feasibility study; PC3 designed to withstand (at a minimum) a 2-in. by 4-in. plank missile weighing 15 lb traveling at 50 mph at a maximum height of 30 ft above grade	Probable (E-2 / yr to E-4 / yr)	A	A	1	1	increase structural design to withstand credible wind-generated missiles for the site; facility to maintain integrity and negative pressure during and after high-wind exposure and missile impact
NPH-5	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**high water (floods) challenge or exceed facility design criteria** and structure damaged; significant environmental and public contamination	personnel and environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	site-specific controls required and developed as a result of standard construction methodology	Improbable (E-4 / yr to E-6 / yr)	C	B	3	3	reviewexisting construction standards and NBAF operations to determine if additional controls are appropriate to justify mitigated levels
NPH-6	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**snow and ice challenge or exceed facility design criteria** and structure fails; significant environmental and public contamination	personnel and environmental contamination	Probable (E-2 / yr to E-4 / yr)	A	A	1	site-specific controls required and developed as a result of standard construction methodology	Improbable (E-4 / yr to E-6 / yr)	C	B	3	3	reviewexisting construction standards and NBAF operations to determine if additional controls are appropriate to justify mitigated levels
NPH-7	Uncontrolled *known or unknown* exposure to pathogen	external events and natural phenomena	**loss-of-power from lightening or other source** causes loss of negativity; environmental and public contamination	personnel and environmental contamination	Frequent (≥ 1.0 / yr)	A	A	1	emergency generators available to support the facility for 30-days (feasibility study, section 5.2.3, pg 5) using the 500,000-gal diesel inventory in the central utility plant	Occasional (1.0 / yr to E-2 / yr)	B	A	2	1	not clear if the emergency power is dedicated to safety systems (ventilation, fire suppression, controls, decontamination, etc); not clear whether normal facility operations continue or if emergency procedures are implemented to achieve safe stand-down and confinement maintenance; may want to consider passive confinement design strategy in the event back-up power fails

E.3.2 Accident Selection Methodology

From the identification of hazards and the listing of potential accident initiating events, accident scenarios are postulated. For the NBAF, the scenarios producing the consequence of an uncontrolled pathogen release are presented in the hazards analysis summary Table E.3-5. From this listing, a unique set of accidents to be considered bounding is selected from the hazard analysis summary. Rationale for selecting a bounding accident is based semiquantitatively on the mitigated frequency and consequences of the accident after considering the existing controls in place used for mitigation or prevention.

Table E.3.2-1 — Accident Categories

Type of Event	Examples	Bounding Accident Candidates
Spill or uncontrolled release of aerosolized pathogens (includes *known and unknown* releases)	• Loss of containment • Over-pressurization • Personnel error leading to LAI • Equipment failure leading to laboratory-acquired infection (LAI)	• LAI – autoinoculation due to personnel error • LAI – aerosol uptake by personnel from centrifuge failure • Small spill resulting in loss of containment, personnel and area biocontamination, but no environmental contamination • Medium-level spill resulting in loss of biocontainment, personnel and area contamination, but no environmental contamination • Loss of animal/insect control resulting in environmental contamination • Improper sterilization/disinfection of solid waste results in environmental contamination • Improper sterilization/disinfection of liquid waste results in environmental contamination
Chemical release	• Spill • Over-pressurization • Personnel error	• Decontamination or disinfectant failure (e.g., chlorine dioxide generator malfunction) during disinfection process resulting in incomplete sterilization and personnel exposure
Fire	• Furnace • Mechanical or electrical • Flammable gas • Exothermic chemical reaction	• Large room or facility fire resulting in the loss of facility structure and large environmental releases
Deflagration	• Flammable gas • Exothermic chemical reaction • Flammable liquids • Steam	• Ethylene oxide deflagration in confined space during sterilization operation results in loss of containment • Over-pressure event from steam feeding an autoclave results in loss of containment
Natural phenomena events	• Seismic • High wind • Flood • Snow and ice	• Large, multi-laboratory spill as the result of a seismic event with and without an accompanying fire • Large, multi-laboratory spill as the result of structural damage from high winds (tornado) to a BSL-3Ag laboratory
External events	• Airplane crash • Wildfire • Transportation • Adjacent facility accidents	• Aircraft crash into the NBAF with subsequent release of pathogens • Transportation accident resulting when an improperly packaged sample arrives and is handled at a BSL level lower than is required • External fuel storage (diesel or fuel oil) explodes and causes loss of facility containment and environmental contamination

Once this rationale is complete for a given set of operational hazards or accident-initiating events, the bounding accidents can be selected by sorting the table based on hazard or accident type or consequence, etc. For the NBAF, the proposed scenarios were evaluated based on accident type and integrating unmitigated P/E consequence with the existing control set to determine its effect on risk (consequence and frequency). Generally one (maybe two) accidents are selected from each accident family for further quantitative analysis, as well as any unique accidents that might stand out from the others based on requiring specific controls or caused by specific phenomena. The selected accidents were evaluated in detail and are presented below.

E.3.3 Accident Analysis Methodology

After bounding and unique accidents have been selected, they are subjected to quantitative consequence analysis to determine if the control set used to prevent or mitigate the consequences contains the following:

- The correct type of control (engineered or procedural),
- A sufficient number of controls, and
- The correct safety designation for the particular accident under consideration.

The accident analysis methodology used in this section consists of the following steps, consistent with Nuclear and Chemical Industry standards for format and content:

- Accident scenario description and development,
- Semiquantitative scenario probability description using event and fault trees,
- Source term analysis,
- Consequence analysis, and
- Comparison of the quantity of pathogens released to the infectious dose to support identification of suitable engineered or procedural controls.

The first is to identify and describe each accident scenario that falls into the accident category address accident analysis. The accident analysis process begins with the description of accident scenarios from selected accident categories identified individually or as a group from the hazards analysis. Initiating events and the various controls identified in the hazards analysis are linked to formally describe the accident scenarios with respect to the accident progression and to qualitatively determine the likelihood of occurrence for the bounding accident in each accident category.

The likelihood of occurrence is addressed in a semiquantitative manner based on an assessment of the number and the effectiveness of controls that must be defeated for the accident scenario to occur. The semiquantitative approach relies on the use of event trees with best estimates for the probability of failure for each type of control. The effectiveness of the various controls is assessed semiquantitatively based on engineering judgment after review of operations, their procedures, and the conceptual design presented in the NBAF Feasibility Study (NBAF-1).

The accident categories are identified as representative examples of the accident families with potential impacts on NBAF operations. Secondary events caused by either natural phenomena or external events are considered on a case-by-case basis. External events including a small aircraft crash are considered potential conservative accidents as long as external event frequencies exceed 1×10^{-6} per year. Natural phenomena events are based on the return periods and magnitudes (ground acceleration, wind speed, etc.) as defined by site-specific evaluations.

The accident scenarios that meet the screening criteria are collected into major accident categories representative of accidents with unique characteristics (such as specific controls or caused by specific phenomena). Unmitigated consequences from accident scenarios that result in pathogen exposure to the worker or to the public and the environment are presented there. Numerous accident scenarios were identified as potentially having such consequences, and many of these accident scenarios were attributable to a single process or activity (a single process or activity could lead to several accident scenarios that might result in unacceptable consequences).

E.3.3.1 Source Term Analysis

The consequence to the public or environment of an accident involving the release of a pathogen is calculated by defining the level of exposure (virions inhaled, ingested, etc.), the infectivity of the pathogen (relative ability to produce an infection), and pathogenicity (relative ability for an infection to lead to a fatal disease). Pathogenicity is the ability of an organism to cause disease in another organism; thus, it is called a pathogen.

It is often used interchangeably with the term "virulence," although some authors prefer to reserve the latter term for descriptions of the relative degree of damage done by a pathogen. Pathogens are infectious agents that cause disease and include viruses, bacteria, fungi, protozoa, and higher parasites. The agents responsible for prion diseases such as Creutzfeld-Jakob disease in humans and Bovine Spongiform Encephalopathy (BCE) are also pathogenic. Pathogenicity is used to describe the capacity of microbes to cause disease (Talaro 2008).

The combination of the factors represents the potential consequences resulting from an exposure to a specified pathogen. The exposure is related to the quantity of a pathogen that is available for release or exposure. This term is often referred to as a source term and is typically measured in units of viral particles or virions.

The source term (amount of material released to the environment as a respirable aerosol) can be calculated by considering such factors as the material at risk (MAR); the damage ratio (DR), which is the amount of MAR actually released in situations where the MAR is contained or confined; an airborne release fraction (ARF); and a leak path factor (LPF). A respirable fraction (RF) is often included for particulates that have a range of sizes in order to address how much of the agent can reach the lungs when inhaled. Because virions have a typical size (Nipah virus averages 500 nm [range 180-1,900 nm]; RVFV averages 100 nm; FMD is about 30 nm) on the order of 0.1 microns (1/10,000,000 of a meter or 100 nm), the RF is essentially equal to unity (1.0).

The following five-factor formula represents the calculation for determining the source term, which is referred to as Q,

$$Q=MAR\times DR\times ARF\times RF\times LPF$$

Where:

Q = source term to the outdoor atmosphere [units of MAR]
MAR = material at risk [mass, concentration,]
DR = damage ratio [dimensionless]
ARF = airborne release fraction [dimensionless]
RF = respirable fraction [dimensionless]
LPF = leak path factor [dimensionless]

MAR – MAR is defined as the amount of hazardous material available to be acted on by a given physical stress. Facility operational limits and inventory information are considered in defining the MAR for each accident scenario to be evaluated. Because the inventory in any individual process, activity, or room is subject to day-to-day fluctuations from routine transfers that are necessary to support operations, upper-bound material inventories were used. In addition to the pathogen content of the MAR, it is necessary to define its form. For a single process or activity in which various material forms could be present, the MAR was assumed to be composed of the material form that yielded the highest value of ARF×RF. This form of material is typically a viable aerosol for the specified pathogens.

DR – DR represents the fraction of the MAR that is affected by the accident and with which given values of ARF×RF can be associated. DRs are scenario dependent, and their development is described in each accident

scenario section. This means that phenomenological characteristics (such as temperatures and pressures) of the accident scenario must be considered. State-of-the-art models (e.g., CFAST or FDS for fires) are used to support such analysis when required. Other computer codes are used if the potential for an explosion is assessed as large and the magnitude of the explosion expected to be sufficiently large to cause structural damage to containment or equipment in the vicinity of the explosion. Otherwise, analytical expressions are used to perform calculations necessary to support the evaluation of the DR. For the unmitigated release calculations, a DR of 1 is used unless otherwise stated and justified.

ARF and RF – ARF is that fraction of MAR×DR that is aerosolized. The RF is the fraction of the airborne material that is respirable (inhalable into the deep lung). This is assumed to include particles with an aerodynamic equivalent diameter (AED) of 10 micrometers (μm) or less. (The AED is the diameter of a sphere of density 1 g/cm^3 that has the same terminal gravitational settling velocity as the particle in question.) The values of ARF and RF for each postulated accident were selected based on best available data. They were chosen to be the bounding values unless otherwise noted.

The constraints placed on the amount of biological material that can be present for the postulated hazard and accident scenarios depends on the number of biological agents in the laboratory at any one time, coupled with the amount of storage space available. Scenarios that involve the entire facility, such as facility-wide fires, earthquakes (and other natural phenomena), terrorist attacks, or vehicle collisions, would require that the entire inventory is available for potential release. On the other hand, operational accident scenarios need only consider the amount of material involved with the specific operation.

One of the more important parameters in the analysis of potential release and subsequent exposure to biological pathogens is the ARF. This parameter modifies the total quantity of biological material available in any particular accident to provide an upper-bound estimate of the source term (the quantity of material released from the facility). The physical stresses and forces acting on a specific material determine the fraction of material that becomes airborne and can potentially escape the facility in an accident. These stresses include the energy associated with drops, spills, deflagrations, and fires. The form of the material is also an important factor in estimating the fraction that will become airborne. It is easy to appreciate that a spill of 1,000 g of biological material in liquid form that much less material is likely to become airborne than if the material is in a powder form. Similarly, less material will become airborne as a result of a spill from a height of 1 m (3.28 feet) than from a height of 3 m (9.8 feet). The choice for an appropriately bounding ARF is therefore dependent on the type of material, the physical form, and specific characteristics such as density, viscosity, etc. The choice for the ARF for the analysis of the potential release of virions of FMDV, RVFV, and Nipah virus was based on conservative estimates for these physical and chemical characteristics. The objective was to ensure that there was little chance that the ARF would be greater, and therefore the estimated consequences would be bounding.

One of the critical assumptions was that the material form is that of a solution with an assumed density and viscosity of water. This is a highly conservative assumption since most viral pathogens are stored, grown, and handled in gelatins or agar, which often have densities above that of water and viscosity that is much greater than that of water. Another factor that was considered in the choice of an appropriately bounding ARF value was actual data for the release of a powdered form of bacteria in the 2001 terrorist attack involving letters sent to the Senate. In 2001, five terrorist letters containing *B. anthracis* spores were sent to members of Congress, having passed through two separate mail facilities with at least one letter opened in the Hart Senate Building, resulted in 5 deaths and 17 confirmed or suspected sub-lethal anthrax infections (Weis 2002). An estimate of *B. anthracis* spore counts in each of the five delivered anthrax attack envelopes was based on one unopened letter discovered in a Congressional mail bin. The amount of material in the unopened letter contained approximately 2 g of powdered material, containing approximately 100 billion (1×10^{11}) to 1 trillion (1×10^{12}) *B. anthracis* spores per gram (Fennelly 2004). It was also estimated the 8-hour cumulative production of infectious aerosol, in the U.S. Postal Service (USPS) distribution center in Trenton, New Jersey, to be in the range from nearly 200,000 to as many as 8,610,000 spores that were less than 5 μm (Fennelly 2004).

To conservatively estimate the amount of the *B. anthracis* spores that could become airborne, from the original source that was specifically manipulated to be easily aerosolized, the total source term for the USPS is taken to be just one letter with 2 g of material. This would provide an initial source term between 200 billion (2×10^{11}) and 2 trillion (2×10^{12}) *B. anthracis* spores, as estimated from the unopened letter. Since the swipe, vacuum, and air sampling results provided a range of spores that were aerosolized between 200,000 and 8,610,000 spores, then the subsequent conservative estimate of the fraction that became airborne is the ratio of the aerosolized quantity to the initial source term, which results in a airborne fraction that ranges from a low of 1×10^{-6} to a high of 4×10^{-5}. These results show that even for a material, specifically manipulated to be easily aerosolized, the fraction that becomes airborne as a result of processing activities at the USPS distribution center is actually very low. This information was used to determine a realistic source term and release fraction for materials that would likely be used in proposed operations of the NBAF.

Even though *B. anthracis* is not an agent that one of the pathogens designated to be handled at the NBAF, the relationship between powdered materials and an appropriately bounding ARF is of value. The biological materials expected to be used in normal operations at the NBAF would be in a form that maintains the viral agent's viability, such as in a gelatin, agar, or other appropriate support media. The material modeled for purposes of hazards and accident analysis was considered to be in a form that is not easily aerosolized. This is in contrast to the type of material identified as having been mailed to the U.S. Senate during the anthrax attack that occurred in the fall of 2001. The powdered material in the 2001 terrorist attacks was specifically manipulated to be easily aerosolized (Weis 2002).

In addition to the information relative to the terrorist attack on the U.S. Senate and as a point of comparison, simulations previously conducted by the National Institutes of Health (NIH) for laboratory accidental releases of biological materials have been shown to result in low release fractions. As an example, a source strength of 1×10^{10} dry powdered *B. anthracis* spores have been shown to result in approximately 10^5 to 10^6 respirable particles that become and remain airborne for extended periods (DHHS-NIH 2005). Based on these results, the release fraction has a range between 1×10^{-5} and 1×10^{-4} spores.

Another source of information available for estimating an appropriately bounding ARF value is the experimental data obtained for spills of liquids and powders in the nuclear facilities operated by the Department of Energy (DOE). These data are provided in the two-volume DOE Handbook 3010-1994, *ARFs/Rates and RFs For Nonreactor Nuclear Facilities*, dated December 1994. It has been shown (Laul 2006) that for spills, the ARF is mostly dependant on density and height and that the ARF values are applicable to chemicals other than just plutonium and uranium, as originally tested in DOE Handbook 3010-94 (DOE-HDBK-3010). For example, DOE Handbook 3010-94 gives the following relationship for the free-fall spills of powder from up to 3 m in height:

$$ARF = 0.1064(M_0{}^{0.125})\frac{(H^{2.37})}{(\rho_{BP}{}^{1.02})}$$

Where: M_0 = mass of the powder spilled (kg)

H = spill height (m)

ρ_{BP} = bulk density of the powder (kg/m^3)

If one assumes a drop of a virus in powder form of mass 1,000 g (1 kg) from a height of 1 m (approximate height at which a container would typically be handled) and a nominal powder bulk density of a typical gelatin is approximately 720 kg/m^3, then the resulting ARF is 1.3×10^{-4}. This corresponds sufficiently well with the 1×10^{-4} upper range from the NIH laboratory simulations.

Also, DOE-Handbook 3010-94 provides a relation for the ARF resulting from the spill of a liquid, which is the more likely form for materials involved in accidents in the NBAF. DOE Handbook provides the following relation for the ARF value for a liquid spill from a height up to 3 m:

$$ARF = 8.9x10^{-10}\left[\rho_{air}{}^{2} * H_{sp}{}^{3}\frac{g}{(\mu_{sv})^{2}}\right]^{0.55}$$

Where:

H_{sp} = spill height (cm)

g = acceleration due to gravity (981 cm/s^2)

ρ_{air} = density of air (1.3×10^{-3} g/cm^3)

μ_{sv} = solution viscosity (poise)

Therefore, a spill of 1 kg of a liquid material containing virions, with a viscosity of water (0.01 poise) from a height of 1 m would result in an ARF of approximately 8×10^{-6}, which is more than an order of magnitude lower than the 1×10^{-4} ARF value used for spill accidents for the NBAF. While the form of the pathogens is more likely to be in forms such as gels, solutions, cultures, etc., instead of powder form, the use of the powder spill relation is representative and conservatively bounding for the forms expected to be handled in the NBAF. In conclusion, the ARF for spills, impacts, and other mechanical release initiators is conservatively assumed to be on the order of 1×10^{-4}. This assumption will provide a conservative basis for evaluating the potential consequences of the various accidents. The ARF values for fires and deflagrations were similarly developed based on the information provided in the DOE Handbook 3010-94.

LPF – LPF is the fraction of the locally aerosolized material released to the environment. The LPF is dependent on the nature and location of the accident, as well as the condition (open or closed) of various interior and exterior doors. The LPF is also particularly sensitive to whether a fire is associated with the accident and on external wind conditions because these two aspects provide major motive forces for the source aerosol. Whether doors can be assumed open or closed during an accident is determined by whether they have automatic closing mechanisms and by what is assumed about emergency egress behavior. Doors normally have closing mechanisms because closed doors are critical to air balance. On interlocked and gasketed APR doors, the decision needs to be made as to whether they fail locked or unlocked in an emergency. In one situation, biocontainment is improved; in the other situation, there is a significant risk to workers from life safety issues.

In most cases, the LPF values for the accident scenarios developed in this section were qualitatively estimated based on the conceptual design of the NBAF as presented in the Feasibility Study. An unmitigated accident is by definition one in which the aerosolized material is assumed to exit to the atmosphere without retention or mitigation (LPF = 1). This unmitigated case is of formal significance because the consequence of such a release is the basis for functionally classifying controls needed to ensure that the postulated accidental release to the atmosphere is sufficiently mitigated. For a well-designed facility with a normally operating active ventilation system and HEPA filtration system with redundant filters, the LPF can be estimated to be on the order of LPF = 0.001% or 1×10^{-5}. This is based on the building being leak tight and HEPA filter efficiencies at minimum 99.97% (Plog 2002).

Because the NBAF is at the conceptual design stage, the estimation of the building-wide LPF is based on known or expected design standards, testing methods, and operational conditions. Review of literature with respect to the design, testing, and operations of ventilation systems in high-containment facilities (biological, nuclear, and chemical) shows that leak rate testing of duct work, plenums, and filters requires very strict

standards for design, manufacture, and operation. Gas-tight duct work acceptance criteria requires no leaks greater than 1×10^{-5} cm^3/s. Therefore for an entire facility to be assigned a value of 1×10^{-5} is very conservative. The objective for choosing the 1×10^{-5} value for the LPF is to illustrate the importance of the pressure boundary and not just the efficiency of the HEPA filters (Fleming 2006). The Feasibility Study specifies use of standard HEPA with an efficiency of 99.97% at 0.3 μm; however, no specific criteria have yet been established for the NBAF. The purpose of the analysis and the evaluation of risks are to evaluate the effect of mitigation and to support potential future design considerations.

E.3.3.2 Fire Analysis Methodology

For a fire to occur, there must be an ignition source with sufficient energy (fuel), oxygen, and heat to sustain the reaction. Each element is as important as the other. In these analyzes, an ignition source was assumed to always be present, and heat was assumed not to be removed at rates that affect the fire source. Under these assumptions, the growth rate, peak size, and duration of a fire are wholly and equally dependent on fuel and oxygen availability.

This section documents the method used to evaluate fire scenarios based on the types of fuels potentially found in any laboratory room of interest. Various models were considered for prediction of the important fire parameters including the following:

- Maximum fire duration,
- Upper-layer temperature in the fire room,
- Upper-layer temperature in adjacent compartments,
- Maximum temperature at HEPA filters,
- Amount of fuel consumed, and
- Amount of oxygen consumed.

Various aspects of NBAF can be evaluated using various models, which included the Consolidated Model of Fire Growth and Smoke Transport (CFAST) code. Other models such as the Fire Dynamics Simulator (FDS) code and the MELCOR computer code, a temperature/time/ventilation model, and others were reviewed for applicability of the facility at the conceptual design stage. In addition, results of modeling at similar facilities were reviewed for applicability. Several general conclusions can be drawn from the body of this work.

- The object of fire modeling is not to determine precise values for fire characteristics but to determine bounding values that keep the areas being evaluated within acceptable limits.
- It is evident from the modeling that a small quantity of fuel that is burning rapidly can produce temperatures above specified room temperature criterion for the various scenarios.
- A large quantity of fuel that is burning at a slower rate may not exceed the same room criterion.
- The arrangement of the fuel and the type of fuel, rather than quantity, determine the rate of burn, and therefore the peak temperatures that can be produced.
- Obviously, peak temperature and duration at peak temperature determine the thermal stress on components such as HEPA filters.

A variety of fuel types and arrangements for fires that were allowed to burn, assuming an infinite supply of oxygen to the fire compartment, and fires for which the oxygen supply was modeled mechanistically and tracked were considered in the qualitative evaluation of the fire scenarios. The construction of the laboratory walls is assumed to provide at least 1 to 2 hours of fire resistance. Walls were considered for their resistance to the free supply of oxygen and for blocking radiant energy transport to other compartments. This is important since moderately elevated temperatures associated with a fire will destroy the viral pathogens.

The outer walls of the NBAF are also considered to be constructed of materials that would provide at a minimum 2 hours of fire resistance. The realistic limiting factor for all fires beyond the trivial is the

availability of oxygen, not the availability of fuel. A robust combustible control program will ensure that the available fuels are limited. Analyses at a variety of laboratory type facilities show that fire propagation between laboratories is not likely, even with open doors.

The laboratory walls and doors (those doors that lead from one compartment or laboratory room to another room, laboratory, or corridor, etc.) provide a mitigative function to prevent the spread of fire and to limit the size of postulated fires. As such, the laboratory walls and doors are broadly credited in the hazards analysis to provide that safety function for any fire in a laboratory room (whether inside a BSC or other enclosure initially). This broad applicability is based on qualitative fire scenarios evaluated in the hazards analysis.

E.3.3.3 Dispersion and Consequence Calculations

Assuming a pathogen release from the NBAF, atmospheric dispersion is estimated using the MACCS2 computer code (MACCS-1) that employs a simple straight-line Gaussian model. MACCS2 is a DOE/NRC-sponsored code that has been widely used in support of probabilistic risk assessments for the nuclear power industry and for consequence analyses for safety documentation throughout the DOE complex. A plume centerline, source-normalized concentration (χ/Q), is calculated for each hourly averaged meteorological data set. These statistics represent the 95th percentile of the set of χ/Q's, regardless of location on or beyond the public boundary, and is taken as representative of public exposure. Therefore, these data are used to represent public exposure from an airborne release and are not expected to be exceeded more than 5% of the time for a randomly initiated accident.

E.3.3.3 Evaluating Consequences

The dose to the receptor outside of the NBAF (animal or human) is represented by the exposure due to inhalation, ingestion, contact, and vector pathways. For the inhalation pathway, the results of the air transport model provide time-integrated normalized air concentrations; therefore, the estimate of the exposure to pathogens in the air is simply the source term (Q) multiplied by the time-integrated normalized air concentration and the breathing rate in units of cubic meters per second.

Once the source term is evaluated from the five-factor formula discussed earlier, an estimate of the potential consequences of an accident scenario can be made based on atmospheric transport. This estimate should be considered an acute exposure and would not consider long-term effects from secondary transport through water sources, biota, other vector transport, or enhanced viability in the ecosphere through other means.

To determine the airborne exposure potential, the downwind normalized concentration term χ/Q is multiplied by the source term (ST) to obtain an estimate of the potential exposure in airborne contaminants. In the case of exposure via the inhalation pathway, the expression for determining the total quantity inhaled by an animal or human is related as follows:

$$\text{Total Exposure} = ST \times \chi/Q \times BR$$

Where:

ST = source term [units of MAR; mass, concentration, etc.]
χ/Q = normalized, time-integrated source concentration [s/m^3]
BR = breathing rate of the receptor [m^3/s]

The expressions for exposure and source term are used in each of the detailed accident analyses to provide a measure of significance and as a means of comparison. The total inhaled quantity (exposure) is compared with the minimum infectious dose, as presented in the Pathogen Safety Data Sheets attached to this appendix, as a measure of the consequence of exposure.

The typical breathing rate for humans is taken to be 3×10^{-4} m^3/s, while the breathing rate for a cow is approximately 6 m^3/hour or 1.6×10^{-3} m^3/s, and a pig is assumed to be approximately the same as a human.

For determining animal exposure from ingestion, both the total time spent grazing and the total quantity of food consumed in a specific time period are important. Calculating exposure from contact or ingestion as well as other indirect mechanisms is considerably more uncertain than estimating exposure from the inhalation pathway. The approach used in this analysis is considered bounding and relied on the quantity deposited on the ground from an atmospheric release. An estimate of the grazing or contact rate was assumed to provide the exposure level. Details are provided in the Spill Accident.

E.3.3.4 Determining Accident Probability

From a risk analysis viewpoint, the risk of a proposed accident can be estimated by combining the consequences of the proposed accident outcome with the frequency of the outcome occurring (what can go wrong, how likely is it, and what are the consequences). The challenge then becomes developing qualitative estimates of frequencies and consequences.

The accident outcome frequencies for the NBAF analysis will be estimated using event trees and knowledge of accident progression and facility operations (both engineered and human). Consequences will be estimated through a parallel path using analysis techniques previously described.

Event tree analysis (ETA) is an analysis technique used for identifying and evaluating the sequence of events in a potential accident scenario following the occurrence of some specific initiating event. The objective of the event tree is to determine whether the initiating event will develop into a serious mishap or if the event is sufficiently controlled by the safety systems and implemented procedures (Ericson 2005). The use of ETA in risk assessment is useful in providing a wide range of risk profiles to support management and design for areas that require additional safety controls.

The ETA process begins by identifying a set of defined accident-initiating events that can lead to an adverse consequence. An initiating event can arise as a result of a system failure or from an event external to the system. The consequence and frequencies of each "scenario" are calculated for each of the individual-initiating events. The event tree is grown based on the number of subsequent events that provide a barrier against the adverse event. For example, the spill accident event tree is depicted in Figure E.4.1.1-1 illustrating the relationship between the initiating event and the subsequent barriers preventing the adverse consequence of a spill.

A proposed accident progression (its sequence), can be constructed using event trees and fault trees. Both are pictorial representations of the accident sequence, and while an event tree depicts the possible *outcomes* of an accident resulting from a single initiating event, the fault tree has its focus on the *cause* of the accident, either resulting from a specific equipment failure or a human error. Fault tree analysis provides added detail to an event tree analysis, and they are often integrated into a single description of a proposed accident and its progression. For the NBAF, event trees will be used without the detail provided by fault trees because the NBAF is a conceptual facility and the detail required for accurate fault tree analysis is not available.

Event trees require knowledge of potential initiating events (equipment failures, system upsets, operator errors, etc.) that could cause potential accidents and knowledge of safety system functions and procedural steps that could mitigate the effects of, or prevent, each initiating event. Estimates of safety system functional reliability and operator performance consistency are used in event tree analysis to determine a qualitative estimate of the likelihood of a particular accident outcome and to suggest an estimate of any mitigative effect on accident outcome likelihood if improvements in equipment reliability or operator performance consistency are made.

The event tree considers the response of engineered safety systems and trained operators to the initiating event when determining the accident's potential outcomes. The result of the event tree analysis is the accident sequence—the set of equipment failures or operator errors that lead to the accident. These results describe the possible outcomes that might result from the successes or failures of these safety functions (engineered or human) in terms of the accident sequence following accident initiation.

Event trees are used to identify various accidents that can occur in complex processes. The accident sequences presented in event tree analyses are logical and combinations of events (they all must occur for the particular outcome to be realized). After the accident sequences are identified, the specific combination of failures leading to the accidents (the causal effect) can be determined using fault tree analysis. Results of these combined analyses are used to identify design and procedural weaknesses and to provide recommendations for preventive or mitigative measures to reduce the likelihood and consequence of the potential accident.

Because of the lack of design and procedural information on the NBAF, however, fault tree analysis was not performed. The event tree analysis in combination with estimates of safety system functional reliability and operator performance consistency are used to determine a qualitative numerical estimate of the likelihood of a particular accident outcome and to suggest an estimate of any mitigative effect on accident outcome likelihood if improvements in equipment reliability or operator performance consistency are made.

E.3.4 Human Health and Safety

This section discusses human health effects from routine NBAF operations for both the workers and the public. This includes the type and rate of injuries and illnesses expected during operation of the NBAF. In addition to handling infectious agents, the NBAF would have identified physical, electrical, and chemical hazards. These hazards are described and analyzed in the context of available information related to the NBAF design and compliance with safety codes.

A virus is a sub-microscopic infectious agent that is unable to grow or reproduce outside a host cell. Each viral particle, or virion, consists of genetic material, DNA or RNA, within a protective protein coat called a capsid. The capsid shape varies from simple helical and icosahedral (polyhedral or near-spherical) forms, to more complex structures with tails or an envelope. Viruses infect cellular life forms and are grouped into animal, plant, and bacterial types, according to the type of host infected.

It has been argued whether viruses are living organisms. Some consider them non-living as they do not meet the criteria of the definition of life. For example, unlike most organisms, viruses do not have cells or independent metabolic capabilities. However, viruses have genes and evolve by natural selection. They have been described as organisms at the edge of life. Viral infections in human and animal hosts usually result in an immune response and may result in disease. Often, a virus is completely eliminated by the immune system. Antibiotics have no effect on viruses, but antiviral drugs have been developed to treat life-threatening infections. Vaccines that produce lifelong immunity can prevent virus infections.

In addition, exposure to viral pathogens can also result from vector-borne transmission such as from the bite of a mosquito (which is the transmission mode for RVF). In this case, the receptor can be an individual or an entire population once the vector carrying the pathogen enters the ecosystem (e.g., West Nile virus). The consideration of potential consequences therefore includes receptor populations both in the vicinity of the proposed NBAF and downwind up to distances of 50 km or more.

The specific operational activities of the NBAF along with the activities of the population outside of the NBAF place site-specific constraints on the potential consequences associated with the inadvertent or intentional release of pathogens from the facility. The importance of change control, management and best practices, laboratory worker training, and limitations on the forms and types of specimens all factor into the

evaluation of potential consequences from operating a biosafety laboratory. Each of the following subsections provides additional details related to specific exposure pathways and routes of transmission.

E.3.4.1 Direct Transmission

Facility operations are designed to minimize opportunities for direct transmission. Direct transmission would first require a worker to be exposed to a communicable infectious agent (autoinoculation accident scenario was modeled). Under proper laboratory procedures, the likelihood of a worker inhaling or otherwise becoming exposed (e.g., through cuts in the skin or ingestion) to an infectious agent should be low. The potential to acquire a laboratory-caused disease is further reduced through the use of effective vaccines or therapeutic measures (CDC & NIH 2007). Every facility worker would be required to be entered into the Human Pathogen Medical Surveillance Program. This medical program, compliant with the immunoprophylaxis policy per the guidance in the BMBL (CDC & NIH 2007), is administered as an administrative control for safety. Workers would receive annual physical examinations and consultation about biological work hazards, and recommended vaccines would be administered by the medical staff. Additionally, an occupational medicine or similar program would be available to workers for injuries or illnesses received during the course of work activities associated with the NBAF.

E.3.4.2 Vector-Borne Transmission

Vector-borne transmission is an indirect transmission mechanism of an infectious agent that occurs when a vector bites or touches a person or in which the infectious agent is transferred to the person by a fomite. Given this discussion, vectors can be separated into two different types of vector transmission: the biological and mechanical. Biological vectors can involve an arthropod (insects such as mosquitoes or arachnids including ticks or spiders) vector in whose body the infecting organism develops or multiplies before becoming infective to the recipient individual. Mechanical vectors can involve an arthropod vector that transmits an infective organism from one host to another but is not essential to the lifecycle of the parasite.

FMDV and Nipah virus are not considered as having a biological vector transmission, while RVFV is transmitted via biological vectors. RVFV is predominantly a vector-borne disease, and mosquitoes are the predominant species for a biological vector. The *Aedes lineatopinnis* mosquito acts as viral reservoir (continuous source) and is depicted in Figure E-9. The virus is dormant in the eggs of the mosquito *Aedes lineatopennis* in dry soil of grassland depressions. With adequate rainfall, the infected mosquitoes develop and infect ruminants. The virus can be spread by many mosquito species. In North America, *Aedes*, *Culex*, and *Anopheles* mosquitoes have been found to be capable vectors. Mechanical vectors such as midges and biting flies play a significant role during major epidemics (uncontrolled release and spread of the disease). The host range is primarily ruminants, with sheep (lambs) being highly susceptible, followed by goats, cattle, camels, several species of rodents, buffaloes, antelope, wildebeest, horses, donkeys, cats, dogs, monkeys, horses, and birds also being affected. In addition, humans are very susceptible to the disease, with the minimum infectious dose being unknown.

Figure E-9 illustrates the mechanisms involved in vector-borne transmission. The illustration indicates how a viral pathogen once in the environment can become part of the ecosystem and cycle through transmission and infection. The concentration of the viral pathogen is continuously replenished in the reservoir leading to additional uptakes and exposures to other receptors such as cows, pigs, and deer.

Because of this potential for continuity in the environment, it is critical that the RVFV is not permitted to get into the environment. Once in the environment, the virus can become established in a mosquito population and remain prevalent as a significant reservoir that can continuously cause re-infection. The figure illustrates methods or techniques for interdicting the viral infection cycle, including vaccines, pest controls (pesticides), inhibiting the uptake of the virus, blocking transmission, and stopping the vectors.

The facility is designed to severely limit the potential for possible vector-borne transmission through insects, rodents, and other mechanisms. It is anticipated that the use of pest control vaccination and other advanced programs would limit the potential for transmission of infectious agents from animals to humans, humans to humans, or from infected animals to insects or rodents and then to humans or animals (Fleming 2006).

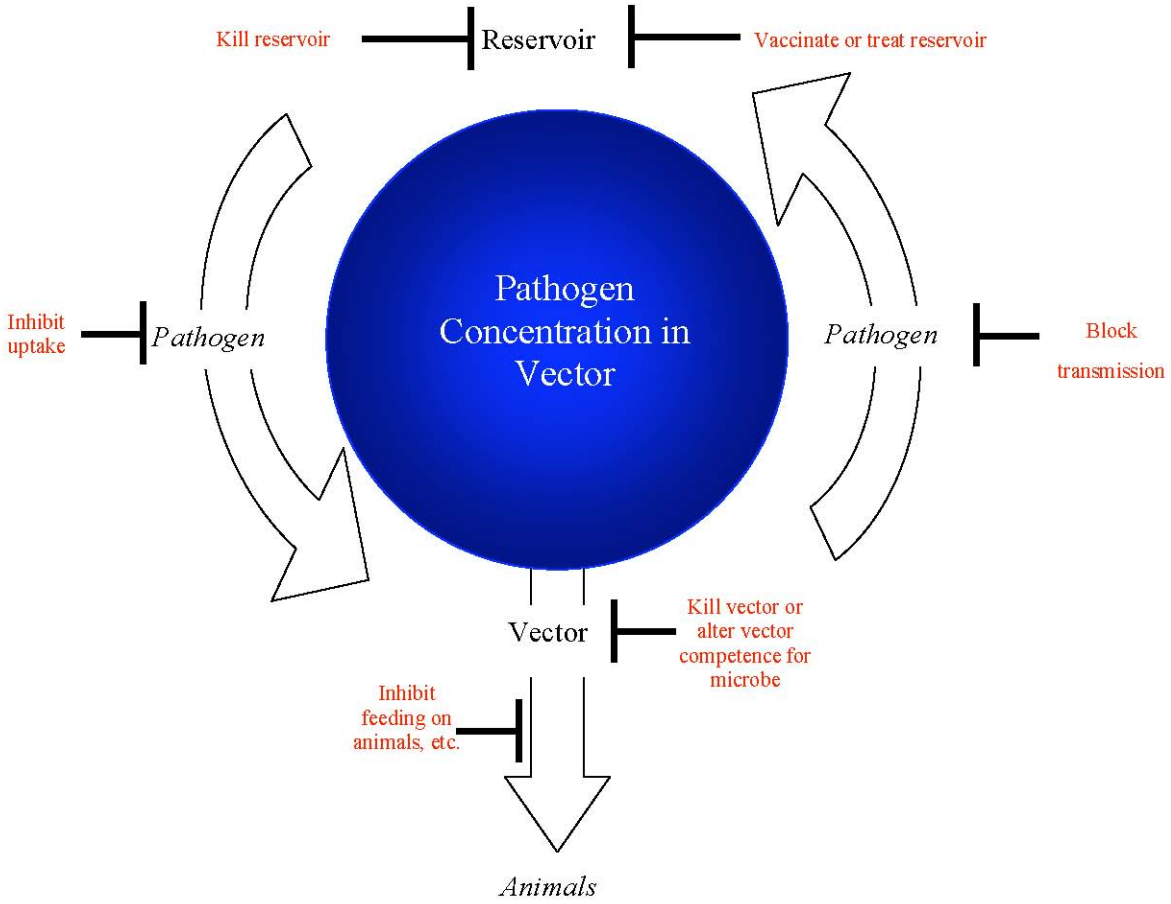


Figure E.3.4.2-1 — Illustration of the Mechanisms Involved in Vector-Borne Transmission

E.3.4.3 Vehicle-Borne Transmission

Mechanical vectors that do not involve the insects or arachnids are often referred to as vehicles and are termed as vehicle-borne transmission. Vehicle-borne transmission refers to a situation in which a person or material (a "vehicle") becomes surface contaminated with an infectious agent. The primary concern for vehicle-borne transmission would be via the workers' clothing, skin, or hair, as all other materials leaving the NBAF must go through a sterilizing autoclave. BMBL guidelines established by the CDC and NIH, which would be followed by the NBAF, are designed to reduce this potential method of transmission. This would substantially reduce any potential for a worker to unknowingly transport biohazardous materials from the facility. This is a significant hazard at the NBAF and was addressed in both the hazards analysis and the accident analysis to provide estimates of potential consequences.

E.3.4.4 Airborne Transmission

In order for airborne transmission to be viable, a virus must survive long enough and in high enough concentrations to infect a target at some downwind location. Two of the biggest contributors to virus' surviving in aerosols are relative humidity and cool temperatures. Humidity greater than 60% and temperatures less than 80ºF have been shown to be the most favorable conditions (Garner 1995). It is conservatively assumed here, unless otherwise stated, that these weather conditions exist at all times to result in maximum concentration of viruses downwind. Realistically, a significantly smaller fraction will survive. Contributing factors to high downstream concentration include low (calm) wind speeds, stable atmospheric conditions, strength of the source released, and relatively flat topography where the release occurs. These latter factors are modeled as part of the plume, which is release following an accident, and are discussed in more detail later in this section.

All air leaving the BSL-3, BSL-3e, BSL-3Ag, and BSL-4 laboratories is directed via the active ventilation system to flow through duct work that is HEPA filtered and exit the facility through stacks on the building roof. All open cultures of the infectious agents in the BSL-2, BSL-3, and BSL-4 laboratories would be handled in a BSC. Each BSC has a ventilation system, and all air emissions from operations in a BSC would pass through a HEPA filter in the BSC and, in the case of the BSL-3 and BSL-4 laboratories, a second HEPA filter in the facility HVAC system (at a minimum) before exiting to the outside air. HEPA filters, at a minimum, remove 99.97% of particulates with a diameter of 0.3 μm.

The U.S. Environmental Protection Agency, DOE, and NRC have specified in various handbooks, guidance, and standards the use of Gaussian Plume models for the modeling of downwind concentrations of hazardous constituents resulting from an accidental release. Atmospheric transport modeling using a standard Gaussian Plume approach was used to address the potential impacts from the inadvertent release of specified biological agents from the facility. The potential impacts from the release of chemicals, radionuclides, and biological agents have been successfully modeled using this approach. This section discusses the methodology, the appropriateness of the application of the atmospheric transport models employed, and the results of the estimated downwind concentrations of a hypothetical biological agent.

Off-site plume dispersion calculations were performed for the facility using the MELCOR Accident Consequence Code System, Version 2 [MACCS2] code (MACCS-1). MACCS2 is a DOE/NRC-sponsored code that has been widely used in support of probabilistic risk assessments for the nuclear power industry and for consequence analyses for safety documentation throughout the DOE complex.

The use of the MACCS2 Gaussian Plume method to model the dispersion of biological agents from a hypothetical release produces a realistic yet reasonably conservative estimate of the downwind concentration of a specified biological agent. The conservative estimate is based on the 95th percentile of the distribution of concentrations at a specified downwind location. This estimate in turn is used to calculate a conservative potential exposure to the Maximally Exposed Off-Site Individual (MEOI). The use of the 95th percentile accounts for variations in both the distance to the site boundary and in meteorological conditions as a function of direction. Furthermore, the method used to derive the 95th percentile is consistent with the statistical treatment of calculated χ/Q (the normalization of the distribution of spores in the air, χ, to the spore source strength, Q) values described in Regulatory Position 3 of NRC Regulatory Guide 1.145, which is used for the modeling of hypothetical radionuclide releases.

NRC Regulatory Guide 1.145 (NRC 1983) provides detailed guidance for performance of dispersion analyses for facilities using the MACCS2 computer codes in order to meet the requirements outlined in DOE-STD-3009-94. This approach has been adopted for performing the atmospheric dispersion calculations supporting the NBAF EIS. Similar evaluations of the transport of viral pathogens have been made using the Gaussian Plum model (Garner 1995; Sorensen 1999).

The MACCS2 code uses the "ATMOS" module to perform all the calculations pertaining to atmospheric transport, dispersion, and deposition. Besides the ATMOS module input file, the only additional input files needed for the MACCS2 calculations are the meteorological data files appropriate for the facility site. The output from the ATMOS module used in the analysis of exposure to specified biological agents is referred to χ/Q, which is the concentration term in normalized units. The χ/Q value obtained from the model is multiplied by the total amount of material containing the biological agents that is estimated to have been released from the hypothetical accident. This quantity of material is referred to as the source term. The product of the source term (ST) and the χ/Q produces the total number of elements (e.g., spores, molecules, cells, etc.) toward which the representative MEOI is exposed. The following sections provide the details of the analysis and the results.

An analysis of a single plume, while having many of the same attributes of a Gaussian plume model, can lead to significantly different results. Qualitatively, a single plume and the Gaussian model both account for dispersion as the combination of downwind transport of particles tougher with diffusion of the plume. Figure E.3.4.4-1 shows these dispersion mechanisms (Till and Meyer 1983). The figure also shows two main particle removal mechanisms: dry deposition and wet deposition (washout).

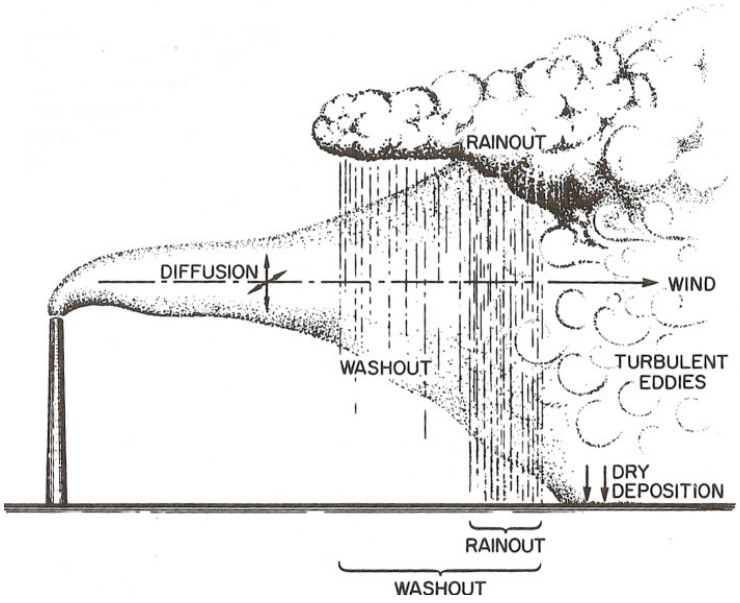


Figure E.3.4.4-1

A Gaussian plume model, such as MACCS2, differs from a single plume in that the weather meteorological data for an entire year can be used to obtain representative values for the time-integrated dispersion factor, χ/Q, for a given location of a release. This is in contrast to a snapshot in time of χ/Q from just one data set. For example, rain may or may not occur during an actual release; therefore, washout may or may not be a factor in the χ/Q for a plume. The Gaussian model, however, can take into account actual rain duration and rain rate over every hour of a year and integrate the results in a cumulative probability distribution function to determine realistically bounding values of χ/Q (i.e., the 95 percentile values) for a given distance from the point of release.

Another way of describing the difference is in terms of the diffusion time. The Gaussian plume model assumes that the concentration of particulates represents a mean value calculated over a given diffusion time. Figure E.3.4.4-2 shows the effects of the plume observed instantaneously and plumes averaged over different time intervals (Till and Meyer 1983). This figure demonstrates that instantaneous plumes are subject to turbulent forces, referred to as eddies, which cause the plume to meander at very short distances from the source. If the time-averaged diagrams of the plume are extended to distances even farther from the source, the

boundaries of these time-smoothed plumes would meander. This is due to the longer length of the plume being influenced by the turbulent forces that are of significant size. Thus, the averaging time used originally would be too short to show a time-averaged picture of these larger fluctuations. If one takes a longer yet time average appropriate for such larger fluctuations, one would find that this is too short of an interval for even greater distances (Till and Meyer 1983). In other words, as the source distance increases, the averaging time must also be increased in order to get a sufficiently smoothed particle distribution. Otherwise, the concentrations observed would not correspond to the concentrations calculated according to Equation 1. Figure E.3.4.4-2 also shows the corresponding cross-plume distribution from the three plumes.

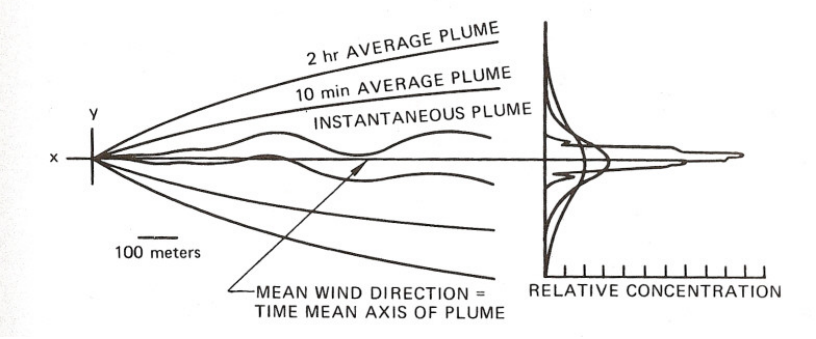


Figure E.3.4.4-2

The Gaussian plume model equation (Equation 1) cannot predict instantaneous values of the particulate concentration in air. Due to the long averaging time for the estimate of routine releases, this does not adversely impact the calculation of time-averaged concentrations downwind of a continuous source. However, during an accidental release, this may be problematic as it is not always possible to make meaningful predictions of short-term particulate concentrations for downwind locations from the source.

If one calculates the instantaneous χ/Q for each wind direction (namely 16 sectors of 22.5° each), a range of χ/Q values for all 360° can be obtained. However, for illustrative purposes of each candidate NBAF site, the time-integrated χ/Q is taken from MACCS2 and plotted in the near field (up to 1000 meters) and the far field (up to 10,000 meters or 10 km) as a contour plot with each radii corresponding to the 95 percentile χ/Q. This is reasonable considering the MACCS2 model was run with 8760 hourly averaged meteorology data sets thereby diminishing the effect of plume meander.

In turbulent flow, the effects of slightly different initial conditions grow with time. As a result, two flows with nominally the same initial conditions eventually become quite different. This dependence on initial conditions has been found to be so sensitive that the initial conditions of a specific realization of a turbulent flow are unlikely to be known well enough to allow its reliable prediction. Thus, in the turbulent dispersion of effluent from a source, the downwind concentration patterns in two realizations of a given event will differ, the variation being more pronounced farther downwind of the source. For this reason, the output of a spatial-average dispersion model is properly interpreted not as a prediction of the dispersion under the specified conditions, but rather as one of a range of possible outcomes under those conditions.

The timely availability of fine-scale wind-field measurements (i.e., with spatial resolution finer than a dispersing plume's local crosswind dimension and temporal resolution finer than the scale of its local time changes) could change this situation. Such data used in a spatial-average dispersion model could substantially reduce the realization-to-realization variability that now accompanies the prediction of the atmospheric dispersion of a short-term release. Currently, such measurements are not feasible except in special circumstances. Radar and Lidar have high potential for enabling such applications in the future, although the

time required to collect and assimilate high-resolution wind field data may continue to limit applicability to immediate emergency response needs.

As Figure E.3.4.4-2 suggests, concentrations at any one point in a given realization can differ substantially from the ensemble average at that point. This further suggests that neither an individual realization nor the ensemble average of realizations is sufficient in general for assessing the detailed, short-term dispersion characteristics of hazardous materials. Both a prediction of the ensemble-average field (interpretable as the most likely outcome) and a measure of the realization-to-realization variations about this average field are needed. Some models (e.g., the Second-order Closure Integrated Puff, or SCIPUFF, model) predict the ensemble-average dispersion plus a measure of the variability of the concentration field from realization to realization (such as the variance or the probability density function).

MACCS2 Dispersion Model Assumptions

The equation for the time integrated dilution factor (χ/Q) for a Gaussian dispersion is given as (Till and Meyer 1983):

$$\frac{\chi}{Q} = \frac{1}{2\pi u \sigma_y \sigma_z} \times \exp\left(-\frac{y^2}{2\sigma_y^2}\right) \times \left[\exp\left(-\frac{(z-H)^2}{2\sigma_z^2}\right) + \exp\left(-\frac{(z+H)^2}{2\sigma_z^2}\right)\right] \qquad \text{Equation 1}$$

Where χ = air pollutant concentration (g/m^3)

Q = pollutant emission rate (g/sec)

u = wind speed at point of release (m/sec)

σ_y = standard deviation of concentration distribution in the crosswind direction at downwind distance x. Also known as the crosswind dispersion coefficient.

σ_z = standard deviation of concentration distribution in the vertical direction at downwind distance x. Also known as the vertical dispersion coefficient.

H = effective height of the centerline of the plume

As discussed above, wind speed, atmospheric stability, strength of the source released, and topography where the release occurs all influence the downstream concentration of a pathogen released as a result of an accident or intentionally. One of the primary outputs of the MACCS2 model is χ/Q, which is concentration normalized by the source strength. Therefore, for the purposes of this discussion, the absolute value of source strength does not matter. The other inputs are discussed below.

Wind Speed – The faster the wind speed, the lower the concentration because more air passes the source of the virus per second. Therefore, slow wind speeds yield greater concentrations. However, the Gaussian plume model assumes that dilution in the direction of the wind is negligible compared to the distribution of particulates as transported with the wind. Therefore, if wind speed is too slow, then the Gaussian plume model breaks down because concentration is inversely proportional to wind speed (Equation 1 above). Hence, as wind speed approaches zero, concentration approaches infinity. To compensate for this, a minimum wind speed is substituted for very calm winds. MACCS2 uses 0.5 m/s as this minimum speed.

Atmospheric Stability – Atmospheric stability depends not only on atmospheric conditions such as wind speed, cloud cover, and level of sunlight but also on other factors such as ground conditions (e.g., temperature, type, roughness) and topography. Six stability classes have been named by Pasquill from A (highly unstable) to F (highly stable) (Pasquill 1962). A method to derive these Pasquill stability classes from available meteorological data is presented in Table E.2.4.4-1 (Till and Meyer 1983). The more stable the atmosphere, the less dispersion in the vertical and horizontal directions and, therefore, the higher the

concentration of particulates. The atmospheric stability class is a direct input into the MACCS2 model in the meteorological data file. MACCS2 uses stability class in determining plume dispersion utilizing the vertical and horizontal dispersion coefficients σ_y and σ_z. This is discussed more in the next section on topography.

Table E.3.4.4-1 — Stability Classes as a Function of Wind Speed, Insolation, and Cloud Cover

Surface wind speed (m/sec) at 10 m	Daytime insolation			Night	
	strong	moderate	slight	thinly overcast or >4/8 cloud	<=3/8 cloud
<2	A	A-B	B	—	—
2-3	A-B	B	C	E	F
3-5	B	B-C	C	D	E
5-6	C	C-D	D	D	D
>6	C	D	D	D	D

Topography – The topography where the site is released is also important because it affects the path of the plume. Namely, rough terrain will tend to increase turbulence resulting in greater dilution. Therefore, sites that are relatively flat will have the converse effect resulting in higher concentrations. With all else being equal, a plume is more likely to be closer to the surface over the sea (New York site) than it is over the land. In addition, stable air is more likely to occur over the sea than land because the sea is affected less than land by diurnal heating and cooling. The topography in MACCS2 is modeled with the use of the vertical and horizontal dispersion coefficients σ_y and σ_z. Selection of appropriate dispersion coefficients is somewhat subjective. Till and Meyer (1983) discusses a series of major tests performed for determining these diffusion coefficients. Each test was conducted using different parameters such as release height, duration, distance, topography roughness, etc. Therefore, each test resulted in different ways to obtain the coefficients, and therefore, the assumptions used in the tests must be validated to be consistent with the object of the specific application of the code. MACCS2 suggest usage of the Tadmor-Gur curve fits for the dispersion coefficients that are useful over flat terrain. These were used for the final MACCS2 runs, although a set utilizing the Karlsruhe-Julich curve fit (useful for more rougher terrain) was also run as part of a sensitivity analysis. MACCS2 allows a scaling factor to be applied to the vertical dispersion coefficient to model rougher terrain. This was used for the Georgia and North Carolina sites.

Wet and Dry Deposition – Particles can also be removed from the plume and deposited on the ground by both gravitational settling (dry deposition) and rain (wet deposition). Dry deposition velocity depends on the size of the particles and is usually taken to be in the range of 0.1 to 1 cm/s. Wet deposition is more complicated as it is a function of the size of the raindrops, wind speed, duration and rate of rain, and how well the particles are captured in the rain. MACCS2 allows both of these parameters to be modeled.

Building Wake Effects – Around buildings, increased diffusion is expected due to a turbulent wake being formed downwind of a given building. Thus, particles released near or at the building will likely be entrained in the wake that increases diffusion. The MACCS2 model allows one to vary the dimensions of a building to simulate the effects of building wake.

Plume Rise – Plume rise due to buoyancy (heat) or stack exit velocity can modify the effective stack release height (H in Equation 1). The net result of a higher effective stack height will be to lower χ/Q near the source and disperse the plume over a longer distance. In other words, for a ground level release, the χ/Q is expected to be highest at the release site; for elevated releases, the highest χ/Q can be at a downstream location. The stack height and sensible heat rate parameters can be modeled with MACCS.

Plume Meander – Large eddies in the downstream path of a plume can cause the plume to meander. This has the effect of widening the horizontal plume dimension or, in other words, increases the horizontal dispersion; thus, concentration is reduced. This parameter was conservatively turned off for all MACCS simulations.

Since the exact location of the NBAF is not determined, initial MACCS model runs were based on one prospective site, Georgia, and modified as necessary for the other sites. The following modeling assumptions were used to select MACCS2 ATMOS module input parameters for the Georgia site. Necessary modifications for other potential NBAF sites are discussed as necessary below.

- MACCS2 requires definition of a radial grid for specification of receptor distances under consideration. Within this grid, the source location is assumed to be the center of the coordinate system (i.e., r=0). For the facility analysis, 17 spatial intervals were defined out to a radius of 10 km to include the farthest distance from the site boundary and to allow smooth interpolation of ground-level air concentration values between the radial grid center points. Ten kilometers downwind was chosen as the farthest point downwind to model because international guidelines recommend an infected zone should extend for at least 10 km (OEI 1992).
- Hourly averaged values for wind speed, wind direction, atmospheric stability, and precipitation rate were provided in year-long weather files compiled specifically for use in MACCS2 at the closest weather station with available data for each site. The weather conditions at the time of an actual release, however, will determine the survival of airborne pathogens and how far they reach. Such actual releases cannot be predicted in advance and instead must be evaluated at the time to determine the level of risk.
- Wet deposition (e.g., precipitation, etc.) was turned on for conservatism at distances near the source (up to 1,000 m). For distances farther from the source (>1,000 m), wet deposition was not modeled (e.g., no precipitation); this allows more of the source term to be deposited at distances farther from the source.
- Stability class for each hour of the year for each site was determined utilizing the Pasquill stability categories.
- Tadmor and Gur analytic correlations to Pasquill-Gifford dispersion coefficient data were applied for plume dispersion and modified with a scaling factor as described in the next bullet. Since the Tadmor and Gur correlations used are generally considered valid to 5 km, the base case was re-run using correlations from Karlsruhe-Julich to show any differences in downwind concentrations.
- An average surface roughness scale factor of $(z/z_0)^{0.2} = (50/3)^{0.2} = 1.75$ was used in accordance with the MACCS2 users guide to correct the smooth-terrain vertical dispersion coefficients that are based on a 3-centimeters (cm) roughness to a local surface roughness of 50 cm. The selection of 50 cm is considered a representative roughness length for the "heavily wooded" areas surrounding the Georgia site (NBAF Feasibility Study). The American Meteorological Society has endorsed this formula as a reasonable modification of available experimental data to site-specific conditions (AMS 1977). No scaling factor was used for the cases with correlations from Karlsruhe-Julich, as these diffusion coefficients are based on terrain with roughness lengths of up to 1 m.
- For the North Carolina site, which is described in the Feasibility Study as having "significant topography" present at the site, the site average surface roughness was assumed to be 100 cm. Therefore, the surface roughness scaling factor of $(100/3)^{0.2} = 2.02$ was used.
- The other sites (Texas, New York, Mississippi, and Kansas) are all described in the Feasibility Study as "flat" sites. Therefore, a surface roughness scaling factor of 1.0 was applied for these sites.
- No credit was taken for additional dilution during plume meander.
- The MACCS2 results of interest to this study are time-integrated air concentrations (i.e., cumulative exposure) as a function of direction and radial distance. For this reason, the exact value specified for release duration is irrelevant. This statement is true for all hypothetical release scenarios.
- MACCS2 meteorological sampling option five (stratified random sampling) with 24 observations per day was used for all dispersion calculations. This choice forces MACCS2 to evaluate every hour of data in a meteorology data file.
- The base case model assumed no plume rise for conservatism. To model energetic releases of various sizes, however, cases were ran modeling 5 MW and 100 MW fires to show the effects on downstream dispersion.

- Building wake effects were minimized by using minimal values for building cross-sectional area dimensions. This minimizes plume dispersion around buildings and increases ground and air concentrations, yielding more conservative results.
- Dry deposition of the specified constituents was allowed with a deposition rate of 0.1 cm/s. This is the suggested value (DOE 2004) for filtered releases into the atmosphere with particles with an aerodynamic equivalent diameter of 0.2 to 0.4 microns, which is on the order of the sizes of the Nipah, RVFV, and FMD virions.

Results of MACCS model runs are for the Georgia site, as described above, are presented in Table E.2.4.4-2.

Table E.3.4.4-2 — Summary of Results for Georgia Site

MEOI Location (Distance From Source) Meters	95th Percentile χ/Q (s/m^3) Base Case - #1	95th Percentile χ/Q (s/m^3) Case #2 - same as base case with 5 MW fire	95th Percentile χ/Q (s/m^3) Case #3 - same as base case with 100 MW fire	95th Percentile χ/Q (s/m^3) Case #4 - same as base case with Karlsruhe-Julich coefficients
50	9.34E-02	5.21E-4	4.33E-6	3.28E-2
200	9.00E-03	4.46E-5	1.06E-6	3.11E-3
400	3.08E-03	2.01E-5	7.07E-7	1.06E-4
600	1.66E-03	1.36E-5	6.94E-7	5.69E-4
800	1.08E-03	1.17E-5	8.55E-7	3.68E-4
1,000	7.69E-04	1.38E-5	7.64E-7	2.63E-4
2,000	9.75E-05	2.09E-5	6.83E-7	4.09E-5
4,000	3.65E-05	1.40E-5	1.28E-6	1.31E-5
6,000	1.43E-05	9.66E-6	2.27E-6	5.62E-6
8,000	1.19E-05	7.33E-6	2.43E-6	3.63E-6
10,000	7.56E-06	5.44E-6	2.27E-6	2.26E-6

These results show that the base case, which is a ground-level release over fairly rough terrain, provides the bounding estimates for evaluating the potential results from an intentional or accidental release. In addition, it is apparent that the concentration falls off significantly with distance from the source. Also:

- Case #4 utilizing Karlsruhe-Julich coefficients are lower, but are on the same order of magnitude, than the same Georgia input file utilizing Tadmor-Gur coefficients with the appropriate scaling factor. Therefore, since the base case #1 using Tadmor-Gur dispersion coefficients are more conservative, these coefficients were used for all sites in the MACCS models.
- Results from the 5-MW fire case are lower the closer to the source but converge on the same values as without a fire at farther distances, as expected. Results from the 100-MW fire case are lower than the 5-MW fire case, as expected. The 100-MW fire results in concentrations of over three orders of magnitude lower than the base case with no fire at distances to 1,000 m but converges at extreme distances. Therefore, to be conservative, the base case (no fire) was used in the final MACCS model for all sites and all accidents. Though it is apparent from the table that if one utilized the values for a large (100 MW) facility fire, then χ/Q and, therefore, exposure is significantly reduced.

Site Comparisons

The tables and sections below describe the ground-level dilution factor (χ/Q in units of s/m^3) and ground concentration (Ci/m^2) for each of the six proposed NBAF sites. For each site, the input assumptions and site characteristics are described. Since four of the sites (Texas, Plum Island, Mississippi, and Kansas) are described in the Feasibility Study as flat sites, all use similar dispersion coefficients and, therefore, have

values of χ/Q that differ as a result of the meteorological data of each site. Since only 1 year of meteorological data was used for each site, sometimes the 95th percentile χ/Q are the same. This is considered acceptable for the purposes of this document for bounding/conservative hypothetical results, which are for illustration purposes only. The results are not intended to model real accident consequences or to be used for epidemiological studies or evacuation response decisions.

Athens, GA

The NBAF feasibility describes the site characteristics as, "A portion of the western side of the site is heavily wooded"; therefore, Tadmor-Gur dispersion coefficients and a vertical scaling factor were used to model the site. The metrological data used were from the closest available location—Athens, GA.

Table E.3.4.4-3 — Athens, GA, χ/Q (s/m^3)

Distance Meters	25th Percentile	50th Percentile	75th Percentile	95th Percentile
50	2.01E-03	3.80E-03	7.83E-03	9.34E-02
200	1.55E-04	2.79E-04	5.99E-04	9.00E-03
400	3.82E-05	7.52E-05	2.04E-04	3.08E-03
600	1.76E-05	3.74E-05	1.10E-04	1.66E-03
800	9.57E-06	2.49E-05	7.15E-05	1.08E-03
1,000	6.46E-06	1.61E-05	5.10E-05	7.69E-04
2,000	1.69E-06	5.44E-06	1.81E-05	9.75E-05
4,000	4.97E-07	1.92E-06	6.35E-06	3.65E-05
6,000	2.67E-07	9.65E-07	3.44E-06	1.43E-05
8,000	1.67E-07	5.70E-07	2.23E-06	1.19E-05
10,000	1.14E-07	3.73E-07	1.28E-06	7.56E-06

Table E.3.4.4-4 — Athens, GA, Ground Concentration (1/m^2)

Distance Meters	50th Percentile	95th Percentile
50	1.24E-05	1.54E-04
200	2.64E-06	2.76E-05
400	1.31E-06	1.12E-05
600	8.81E-07	5.95E-06
800	6.35E-07	3.16E-06
1,000	4.95E-07	2.73E-06
2,000	5.43E-09	1.10E-07
4,000	1.84E-09	3.41E-08
6,000	9.16E-10	1.29E-08
8,000	2.06E-09	9.08E-09
10,000	1.36E-09	5.92E-09

Butner, NC

The NBAF feasibility describes the site characteristics as "significant topography" present on the site; therefore, Tadmor-Gur dispersion coefficients and a vertical scaling factor were used to model the site. The metrological data used were from the closest available location—Raleigh-Durham, NC.

Table E.3.4.4-5 – Butner, NC, χ/Q (s/m^3)

Distance Meters	25th Percentile	50th Percentile	75th Percentile	95th Percentile
50	1.73E-03	2.96E-03	6.79E-03	8.11E-02
200	1.26E-04	2.13E-04	5.19E-04	7.80E-03
400	3.27E-05	6.13E-05	1.77E-04	2.66E-03
600	1.52E-05	3.16E-05	9.56E-05	1.44E-03
800	8.29E-06	2.12E-05	6.19E-05	9.33E-04
1,000	5.60E-06	1.35E-05	4.42E-05	6.66E-04
2,000	1.65E-06	4.91E-06	1.57E-05	1.00E-04
4,000	4.31E-07	1.39E-06	5.50E-06	2.42E-05
6,000	2.40E-07	8.21E-07	2.98E-06	1.46E-05
8,000	1.46E-07	5.20E-07	1.62E-06	8.00E-06
10,000	1.04E-07	3.49E-07	9.98E-07	5.44E-06

Table E.3.4.4-6 — Butner, NC, Ground Concentration (1/m^2)

Distance Meters	50th Percentile	95th Percentile
50	7.73E-06	9.97E-05
200	1.51E-06	1.73E-05
400	7.30E-07	7.35E-04
600	4.76E-07	4.49E-06
800	3.70E-07	2.89E-06
1,000	3.00E-07	2.33E-06
2,000	4.27E-09	8.14E-08
4,000	1.55E-09	2.18E-08
6,000	8.43E-10	1.30E-08
8,000	4.84E-10	8.89E-09
10,000	3.32E-10	5.73E-09

Plum Island, NY

The NBAF feasibility does not describe the site characteristics. However, given that it is an island, it was modeled as a flat site (i.e., water); therefore, Tadmor-Gur dispersion coefficients and no vertical scaling factor were used to model the flat site. The metrological data used were from the closest available location—Islip, NY.

Table E.3.4.4-7 — Plum Island, NY, χ/Q (s/m^3)

Distance Meters	25th Percentile	50th Percentile	75th Percentile	95th Percentile
50	3.46E-03	5.51E-03	3.83E-02	1.61E-01
200	2.73E-04	4.42E-04	1.74E-03	1.57E-02
400	7.87E-05	1.42E-04	3.57E-04	5.38E-03
600	3.33E-05	6.32E-05	1.93E-04	2.91E-03
800	2.10E-05	4.23E-05	1.25E-04	1.88E-03
1,000	1.31E-05	3.33E-05	8.93E-05	1.35E-03
2,000	3.57E-06	1.03E-05	3.18E-05	4.79E-04
4,000	9.91E-07	3.13E-06	1.11E-05	1.67E-04
6,000	4.26E-07	1.35E-06	5.05E-06	9.08E-05
8,000	2.57E-07	1.00E-06	2.82E-06	5.89E-05
10,000	1.74E-07	6.83E-07	1.58E-06	3.01E-05

Table E.3.4.4-8 — Plum Island, NY, Ground Concentration (1/m^2)

Distance Meters	50th Percentile	95th Percentile
50	1.17E-05	2.38E-04
200	2.09E-06	3.19E-05
400	9.95E-07	1.23E-05
600	6.19E-07	6.95E-06
800	4.68E-07	3.78E-06
1,000	3.81E-07	3.00E-06
2,000	9.46E-09	3.27E-07
4,000	3.11E-09	8.49E-08
6,000	1.49E-09	3.14E-08
8,000	9.27E-10	2.84E-08
10,000	7.00E-10	1.91E-08

Flora, MS

The NBAF feasibility describes the site characteristics as "relatively flat"; therefore, Tadmor-Gur dispersion coefficients and no vertical scaling factor were used to model the flat site. The metrological data used were from the closest available location—Jackson, MS.

Table E.3.4.4-9 — Flora, MS, χ/Q (s/m^3)

Distance Meters	25th Percentile	50th Percentile	75th Percentile	95th Percentile
50	3.46E-03	5.79E-03	1.72E-02	1.61E-01
200	2.71E-04	4.46E-04	1.30E-03	1.57E-02
400	6.60E-05	1.32E-04	3.57E-04	5.38E-03
600	3.05E-05	6.18E-05	1.93E-04	2.91E-03
800	1.67E-05	4.07E-05	1.25E-04	1.88E-03
1,000	1.13E-05	3.09E-05	8.93E-05	1.35E-03
2,000	3.37E-06	9.49E-06	3.18E-05	4.79E-04
4,000	8.70E-07	3.05E-06	1.11E-05	1.67E-04
6,000	4.37E-07	1.37E-06	5.05E-06	9.08E-05
8,000	2.90E-07	9.63E-07	2.82E-06	1.95E-05
10,000	1.85E-07	6.51E-07	1.77E-06	1.55E-05

Table E.3.4.4-10 — Flora, MS, Ground Concentration (1/m^2)

Distance Meters	50th Percentile	95th Percentile
50	1.16E-05	2.12E-04
200	1.98E-06	3.03E-05
400	9.49E-07	1.25E-05
600	6.24E-07	6.08E-06
800	4.43E-07	3.41E-06
1,000	3.68E-07	2.89E-06
2,000	9.30E-09	3.27E-07
4,000	3.03E-09	1.00E-07
6,000	1.50E-09	2.73E-08
8,000	9.35E-10	1.64E-08
10,000	6.59E-10	1.16E-08

Manhattan, KS

The NBAF feasibility describes the site characteristics as "relatively flat"; therefore, Tadmor-Gur dispersion coefficients and no vertical scaling factor were used to model the flat site. The metrological data used were from the closest available location—Topeka, KS.

Table E.3.4.4-11 — Manhattan, KS, χ/Q (s/m^3)

Distance Meters	25th Percentile	50th Percentile	75th Percentile	95th Percentile
50	2.93E-03	4.39E-03	9.21E-03	1.61E-01
200	2.39E-04	3.58E-04	7.56E-04	1.57E-02
400	6.60E-05	1.08E-04	2.58E-04	5.38E-03
600	3.05E-05	5.47E-05	1.28E-04	2.91E-03
800	1.67E-05	3.54E-05	7.93E-05	1.88E-03
1,000	1.13E-05	2.58E-05	5.66E-05	1.35E-03
2,000	3.37E-06	8.32E-06	2.01E-05	1.91E-04
4,000	9.91E-07	2.69E-06	7.04E-06	5.21E-05
6,000	4.85E-07	1.33E-06	3.82E+06	2.54E-05
8,000	2.89E-07	8.89E-07	2.21E-06	1.43E-05
10,000	1.74E-07	6.19E-07	1.38E-06	1.18E-05

Table E.3.4.4-12 — Manhattan, KS, Ground Concentration (1/m^2)

Distance Meters	50th Percentile	95th Percentile
50	7.24E-06	1.59E-04
200	1.09E-06	1.92E-05
400	4.89E-07	8.19E-06
600	3.22E-07	3.16E-06
800	2.39E-07	2.73E-06
1,000	1.94E-07	1.93E-06
2,000	8.32E-09	1.43E-07
4,000	2.76E-09	3.68E-08
6,000	1.43E-09	1.66E-08
8,000	9.11E-10	1.13E-08
10,000	6.19E-10	8.22E-09

San Antonio, TX

The NBAF feasibility describes the site characteristics as "relatively flat"; therefore, Tadmor-Gur dispersion coefficients and no vertical scaling factor were used to model the flat site. The metrological data used were from the closest available location—San Antonio, TX.

Table E.3.4.4-13 — San Antonio, TX, χ/Q (s/m^3)

Distance Meters	25th Percentile	50th Percentile	75th Percentile	95th Percentile
50	3.49E-03	6.31E-03	1.36E-02	1.61E-01
200	2.71E-04	4.89E-04	1.30E-03	1.57E-02
400	7.87E-05	1.42E-04	4.43E-04	5.38E-03
600	3.23E-05	6.44E-05	2.39E-04	2.91E-03
800	1.95E-05	4.25E-05	1.55E-04	1.88E-03
1,000	1.21E-05	3.16E-05	1.11E-04	1.35E-03
2,000	3.37E-06	9.90E-06	3.93E-05	2.24E-04
4,000	8.70E-07	3.11E-06	1.37E-05	6.01E-05
6,000	4.26E-07	1.36E-06	6.02E-06	4.02E-05
8,000	2.57E-07	9.76E-07	3.90E-06	1.63E-05
10,000	1.74E-07	6.36E-07	2.34E-06	1.36E-05

Table E.3.4.4-14 — San Antonio, TX, Ground Concentration (1/m^2)

Distance Meters	50th Percentile	95th Percentile
50	1.05E-05	1.64E-04
200	1.59E-06	1.98E-05
400	6.97E-07	8.24E-06
600	4.41E-07	3.86E-06
800	3.35E-07	2.84E-06
1,000	2.63E-07	2.05E-06
2,000	9.49E-09	1.76E-07
4,000	3.05E-09	4.16E-08
6,000	1.51E-09	2.27E-08
8,000	9.30E-10	1.55E-08
10,000	6.30E-10	1.01E-08

ANALYTICAL METHOD

To demonstrate the validity of the above numerical methods (i.e., computer code), one can perform a simplified, conservative hand calculation to determine the bounding χ/Q. These calculations are for illustrative purposes only to demonstrate the values from MACCS make physical sense.

Example 1. If one assumes a ground-level release (H = 0) and receptor (z = 0) at the centerline of the plume (y = 0) at a downwind distance of 1,000 m, as well as conservatively slow wind speed (1.0 m/s) and stable atmospheric conditions (stability class F), one can estimate σ_y and σ_z as power functions (Till and Meyer

1983) as presented below. The wind speed of 1.0 m/s is considerably slow to yield conservative results (i.e., little dispersion); wind speeds on the order of 0.5 m/s and greater are considered sufficient to neglect the effects of diffusion in the direction of the wind versus the transport of material with the wind velocity (Till and Meyer 1983). Also, while stability class F atmospheric conditions are also not representative of everyday conditions, it is not straightforward to determine a generic weather condition for a simple hand calculation; therefore, assuming stability class F conditions for hand calculations does result in less dispersion and more conservative results.

$$\sigma_y = p_y x^q \qquad \text{and} \qquad \sigma_y = p_z x^r,$$

Where:

The variables $p_{y,z}$, q, and r are dependent on the terrain and stability class.

From the input variables for this Georgia case:

$\sigma_y = 0.0722*(1{,}000)^{0.9031} = 36.97$ meters and
$\sigma_z = 0.2*(1{,}000)^{0.602} = 12.79$ meters.

Therefore:

$$\chi/Q = 3.37 \text{ E-4 s/m}^3$$

This value for χ/Q is roughly one order of magnitude higher than the mean value calculated from numerical methods (MACCS) of 8.74E-5 s/m^3.

Example 2. A similar calculation is done for the Flora, MS, site with more realistic wind speed data.

Where:

Annual average wind speed is 7 miles per hour (mph) or 3.13 m/s and was estimated from site-specific data.

$$\chi/Q = 1.07 \text{ E-4 s/m}^3$$

This value for χ/Q is roughly one half the mean value calculated from MACCS of 2.17 E-4 s/m^3.

Example 3. To illustrate the conservative effects of utilizing minimal building wake effects, the following equation is used (Till and Meyer 1983):

$$\frac{\chi}{Q} = \frac{1}{u(\pi\sigma_y\sigma_z + cA)}$$

Where:

A = cross-sectional area of the building normal to the flow. Utilizing the minimum building size as was done in MACCS, A = 0.1×0.1; m = 0.01 m^2.

c = a shape factor that represents the fraction of A over which the plume is dispersed; c is taken to be 0.5 per Till and Meyer.

Therefore, for the values used in Example 1 above. this results in

$$\chi/Q = 6.73 \text{ E-4 } s/m^3$$

or roughly twice the value without building wake effects.

E.3.4.5 Water-Borne Transmission

Facility design features, such as backflow preventers, and uniform plumbing code requirements would minimize the potential for microbes within the NBAF from migrating back through the water supply piping to the public. Also, none of the effluent water from the wastewater plant will contribute directly to any potable water source. Potable water supply wells for each proposed NBAF site are discussed in the specific affected environment section.

Water exiting through the sink drains would be combined and diluted by sanitary waste in the sewer system and would undergo a series of treatment steps at the wastewater facility. These treatment steps consist of aeration, secondary clarification, disinfection, dechlorination (for environmental discharges), water reuse system, effluent holding ponds, and sludge drying beds. It is anticipated that there would be minimal effects from water-borne transmission. Because of the potential hazards associated with this pathway, this scenario was specifically evaluated in the hazards and accident analysis.

Safety controls specifically relied upon to mitigate or prevent the inadvertent release of viable pathogens to the environment includes the following:

- BSL-3 and BSL-4 laboratories floor drains and piping are segregated and isolated from sanitary waste streams;
- Vents for the drains are segregated and isolated and are provided separate HEPA filtration;
- Autoclave(s), chemical, and gas disinfection methods;
- Secondary containment; and
- Facility structure, which is safety-feature designed to current conceptual design requirements.

In addition to equipment and facility systems that serve as primary and secondary barriers to the release of infectious biological materials, administrative controls serve an important support function. Multiple administrative controls and quality assurance measures are also implemented to minimize the potential for degradation of physical barriers and/or to minimize the amounts of infectious biohazardous materials that become involved in an accident with potential exposure to the workers or release to the environment and the public through the water transmission route. Administrative controls include, but are not limited to, the following programs: Quality Assurance, Qualification and Training, Fire Protection, Engineering and Maintenance, Biological Safety, and Conduct of Operations (DOE 2006; CCPS 1992; Bahr 1997; Greenberg 1991).

Potential release through drains/spills was considered in terms of the specific design and operational characteristics of the facility. Sanitary connections are provided to fixtures such as floor or trench drains, lavatories, sinks, showers, and water coolers. The emergency showers/eyewashes are not connected to the wastewater system within the containment areas. There are floor drains associated with the autoclaves, which are tied into the wastewater systems for the containment areas.
Three scenarios were assessed that could result in the contamination of the NBAF plumbing and the wastewater system: 1) a flood initiates, or is associated with, a spill of infectious material that results in infectious liquid entering a floor drain; 2) a viable culture of infectious agent is discharged into a sink without adequate decontamination; or 3) a spill of infectious material enters a facility floor or sink drain. Each of

these scenarios results in the same circumstance, infectious material discharged to the facility plumbing, which has the potential to contaminate the wastewater system.

Infectious biohazardous material in the NBAF plumbing would be rendered inert through addition of chemical decontamination agents using standard operating procedures for decontamination of laboratory effluent. Proper safety controls would also be used if any plumbing work needs to be conducted on potentially contaminated pipes. Workers entering the BSL-3 or BSL-4 laboratory areas would be required to wear the appropriate PPE and would be briefed on potential hazards. Potentially contaminated plumbing would represent one of many scenarios where craft workers would be required to conduct work on potentially contaminated facility systems. Workers that access sewer lines external to the facility are accustomed to treating sewer effluent as potentially infectious, as this wastewater and solid material is often contaminated with various pathogenic agents within the confines of NBAF operations and facility. If infectious material from the facility were to reach the wastewater system, it would present a potential risk to laboratory workers or the operation of the treatment plant system and also poses a risk to potential release to the environment. A lab-scale volume of infectious material, even the amount postulated in the unmitigated release scenario, is a very small fraction of the thousands of gallons of fluid that flows through the plant and resides in treatment plant basins.

Sanitary Sewer Scenarios

Potential release through drains/spills was considered in terms of the specific design and operational characteristics of the facility. Sanitary connections are provided to fixtures such as floor drains, lavatories, sinks, showers, and water coolers. The emergency showers/eyewashes are not connected to the wastewater system. There are floor drains associated with the autoclaves, which are tied into the wastewater system. The autoclaves are not vented and hold the condensate from their process in the after-coolers until the process ends, at which time the sterilized condensate is discharged to the sanitary waste system. The showers in the changing areas are not used for decontamination procedures.

Three scenarios were assessed that could result in the contamination of the NBAF facility plumbing and the wastewater system: 1) a flood initiates, or is associated with, a spill of infectious material that results in infectious liquid entering a floor drain; 2) a viable culture of infectious agent is discharged into a sink without adequate decontamination; or 3) a spill of infectious material enters a facility floor or sink drain. Each of these scenarios results in the same circumstance, infectious material discharged to the facility plumbing that has the potential to contaminate the wastewater system.

E.4 ACCIDENT ANALYSIS

The accidents that follow detail the accident sequences, preventative and mitigative events that can occur, the source term analysis, consequence analysis, and finally a summary of safety barriers and procedural controls. For the purposes of demonstrating failure probabilities on the life of the NBAF (or a yearly frequency, as appropriate), the following quantities were used for the numbers of animals and humans (staff) in the facility:

Type of Space	Large Cows (up to 1,430 Pounds)	Medium Cows (up to 730 Pounds)	Small Cows (up to 440 Pounds)	Swine	Sheep	Staff
BSL-2	—	—	—	—	—	65
BSL-3E	—	—	—	—	—	102
BSL-3E ISO	—	—	—	—	—	25
BLS-3Ag	138	276	414	798	912	316
BSL-4	28	56	84	196	224	61
cGMP	—	—	—	—	—	28
Total	166	332	498	994	1,136	597

Given the number of animals in the facility, one can obtain reasonable upper-bound number of virions for use in accident calculations. For example, from the Feasibility Study, the NABF facility will utilize a standard pen size designed around the use of large animals at a nominal 144 ft^2 for flexibility. The standardization to one size will allow the facility to accommodate more animals at lower weight ranges as long as the weight of one individual does not exceed the minimum required by the NRC guide.

BSL-3Ag: The Feasibility Study Section 4.1 provides the size of each holding room to accommodate 138 large cows (up to 1,430 pounds [lb] each).

BSL-4: From Section 4.4 page 3, the total area for animal space (not including necropsy) requires approximately 4,040 ft^2 or roughly 28 additional large cows.

Total = 166 large cows or:

	Large Cows (up to 1,430 Pounds)	Medium Cows (up to 730 Pounds)	Small Cows (up to 440 Pounds)	Swine	Sheep
BLS-3Ag	138	276	414	798	912
BSL-4	28	56	84	196	224
Total	166	332	498	994	1,136

Therefore, taking only the case of cattle and ignoring swine and sheep and assuming a single cow can respire 1 infectious unit (IU or dose) of FMDV, cattle may excrete up to 180,000 IU/day or, assuming 10 virions is required for an infection, roughly 2.52×10^6 virions/day. Assuming the "average" cow size is medium cows, which the facility can hold 332, then approximately 8.3×10^8 virions are expired by cattle alone in a given day. The accident for a lost animal that follows assumes a MAR value of 1×10^{10} virions, which is a credible upper-bound estimate given this semiquantitative analysis.

Similarly, one can estimate the number of employees in the facility from the Feasibility Study as follows:

BSL-3Ag – from Section 4.1, page 16, if one excludes maintenance staff because they do not directly handle pathogens, there are 316 employees maximum.

Other BSLs – area based on square footage that there are four employees per 1,000 ft^2. This is nearly the same number of employees for the BSL-3Ag if one takes 316 employees divided by the total area of BSL-3Ag space from Section 1.1, page 4 (83,300 ft^2).

Therefore:

BSL-2 labs (Section 4.3, page 2) = 9,570 ft^2 plus 6,710 ft^2 for support = 65 employees

BSL-3E (Section 4.3, page 8) = 28,160 ft^2. However, because employees will not handle pathogens as readily or in very dispersible forms in this area, the value is following subtracted from the total:

990 ft^2 for break room

1,320 for freezer storage room

330 for change rooms

for a total BSL-3E = 25,520 ft^2 = 102 employees

BSL-3E ISO (Section 4.3, page 18)= 7,920 ft^2 minus 1,760 for autoclave space = 6,160 ft^2 = 25 employees

BSL-4 (Section 1.1, page 4) – (Note: there is little information available on this space except for that represented by the figure in Section 4.4, page 3, so the 15,290 ft^2 = 61 employees was used.)

cGMP = 7,080 ft^2 = 28

TOTAL = 597

Thus, given roughly 600 employees handling pathogens in a facility operating a nominal 2,000 hours per year (50 weeks per year at 40 hours per week) and assuming that there are on the order of hundreds of opportunities to mishandle pathogens in a given year per person, this yields on the order of 6×10^5 opportunities per employee-year. Controls such as proper training, qualification, procedure use, PPE use, and quality assurance, to name just a few, significantly mitigate (reduce the frequency of human errors) the number accidents that actually happen given this high number of opportunities that exists.

E.4.1 Operational Accidents

E.4.1.1 Spill or Uncontrolled Release of Pathogens

The presentation of this accident scenario includes additional details to illustrate the methodology. The essential details of the other accidents are provided in Appendix E. This scenario considers the release of pathogens from a small to medium spill. For the purposes of developing a reasonably credible scenario, this accident is considered to be caused by a storage container–handling accident, specifically a dropped container or a type of equipment failure that results in spilled or sprayed contents and aerosol production. This scenario effectively bounds the small- and medium-level spill accidents. This accident was selected for analysis because of the potential hazard associated with aerosol production as evaluated in the hazards analysis and accident selection. In addition, this type of spill event was evaluated to potentially occur with a relatively high frequency and can be used to bound the consequence of aerosol release outside of qualified BSCs or other engineered enclosures.

Spills and releases can occur from degraded containers; improper packaging of containers or materials; mechanical impact; dropped containers; equipment malfunction due to improper use or inadequate maintenance; procedure violation from packaging, handling, operation, etc.; or a combination of the set. Because pathogens are packaged or processed in various configurations, the configuration most susceptible to becoming an aerosol is examined as a bounding scenario.

Several types of aerosol-producing scenarios can be envisioned to occur to packages containing pathogens as they are handled prior to transport or during actual process operations outside of BSCs or other engineered enclosures, including the following:

- Drops during container packaging activities prior to or during transport,
- Spills or drops during handling and movement,

- Equipment malfunction from procedural error, and
- Equipment malfunction from inadequate maintenance.

The bounding scenario is taken to be a spill from the fall and breaking of a package from the top shelf of a storage unit or the failure of equipment (centrifuge, blender, grinder, etc.) causing the contents of the package or equipment to be released and aerosolized. In all of these postulated accident scenarios, significant aerosol production is realized causing personnel exposure, laboratory and facility contamination, and a potential release from the facility.

Accident Sequence

A storage package is dropped and breaks, or process equipment (centrifuge, blender, grinder, etc.) fails, releasing pathogen-containing contents in the form of an aerosol. The formation of the aerosol is considered to occur as a result of the energy applied to the contents either as a result of a drop or from an equipment failure. The total amount of energy applied to the contents depends on the equipment (e.g., a centrifuge) failure or the height from which a container is dropped. In either case, the accident is postulated to result in a sequence composed of a number of independent events in series that have a qualitatively determined failure rates derived from hazard rates and demand failure probabilities (McCormick 1981; Fullwood 1988; Gertman 1994). A hazard rate can be interpreted as the number of times that a particular component, system, or piece of equipment fails in some specified time frame. The units of hazard rates are typically in units of time. For equipment that is needed on a continuous basis, the hazard rate is often determined in units of number of failures per hour. When a system needs to respond only in certain situations, the hazard rate is presented in number of failures per demand. These events are shown on event trees, an example of that appears in Figure E.4.1.1-1.

The following preventive and mitigative features form the basis of this accident to determine the accident probabilities.

Preventive Features

- Packaging intact and appropriate for the material
- Container handled properly and not dropped or impacted
- PPE appropriate and used appropriately
- Proper handling and use of equipment
- Equipment is properly maintained
- Procedures in effect and followed

Mitigative Features

- Active exhaust ventilation system operates
- Passive containment intact and functional
- Other biosafety systems or barriers in place and maintained

Accidents leading to the release of biological material are considered to occur if all the protective features in the prescribed sequence are compromised or fail. Should any one event succeed, the accident is prevented or mitigated to varying degrees, depending on precisely what features fail and what continue to function (the effectiveness of the control is also evaluated in terms of mitigated and unmitigated accident frequencies as previously described).

Accidents leading to the release of biological material are considered to occur if all the protective features in the prescribed sequence are compromised or fail. Should any one event succeed, the accident is prevented or mitigated to varying degrees, depending on precisely what features fail and what continue to function as intended. The accident sequence for spills is illustrated in Figure E.4.1.1-1 as an event tree. The overall

accident frequency was identified in the hazards analysis as a frequency category II (FC II), indicating that a small to medium spill could occur occasionally over the life of the facility. The event tree is used to illustrate the specific probability of an accident based on the specified initiating event. In addition, based on the number of opportunities for the initiating event and the individual accident sequence events, the overall accident frequency is estimated for the life of the facility, which is assumed to be on the order of 50 years. Each accident is assigned to a qualitative frequency category based on the estimated frequency of the initiating event and the conditional probability of the accident per individual demand for each event in the accident sequence. Weighting or averaging over the individual events determines the overall accident frequency. The estimates of the overall accident frequencies are based on the specific failure rates (probability of failure per demand or unit time) for both unmitigated and mitigated sequences.

The basis for these assignments of frequency and probability is derived from historical experience of failures in similar facilities and generic industrial data sources for equipment failure, together with well-established estimates of human error probabilities. A review of mechanical systems such as pumps, motors, and fans shows that failures can be represented in terms of failure to start and/or failure to run. For other types of mechanical systems, the overall failure can be represented by the failure to operate as expected or failure to perform to a specific level. In these cases, the failure probability could be represented as a failure per demand, for pumps or motors, or even as a failure probability per unit time, for fans or pumps, that are required to run continuously. In the case of HEPA filters, failures can result from being plugged (consequence is high pressure drop across filter), bypassing (characterized by a drop in pressure across the filter housing), or degraded efficiency (higher than expected particulates emerging through the filter). The failure probability for these situations may be represented as a single probability per demand.

Modeling system behavior of individual components within the various safety systems was found to be unnecessary for providing upper-bound estimates on the probability of failure for mechanical systems. Data for air handling units, as might be found in a typical HVAC system, show that failure probabilities range from a low of 4×10^{-5} to a high of 2×10^{-2} depending on the application and demand (NRC 2007). Other components including pumps valves, water filters, and fans were found to exhibit failure probabilities that range from as low as 4×10^{-9} to high values of 2×10^{-2} again depending on the demand and application. Because failure of an entire system, as envisioned in the event tree depicted in Figure 3.14.3.1-1, is dependent on a variety of individual component interactions that each have small failure probabilities, it is credible and bounding to assign the failure probabilities to the events in the tree as follows. For this analysis, failure probabilities for mechanical systems and human error (reliability) were derived from generic data for various mechanical systems and different types of human activity. The failure probabilities for human error are assigned the values of 0.1 for unmitigated and 0.01 for mitigated accidents scenarios. Failure probabilities for mechanical systems are assigned the values of 0.01 for unmitigated and 0.001 for mitigated accident scenarios. Failure probability data for components of systems that would be expected in the NBAF were estimated from values related to the nuclear and chemical industries. The range of failure probability for critical safety systems was collected over a long period of time from numerous sources, providing a defensible basis for the assigned values used in this analysis (Gertman 1994; McCormick 1981; Fullwood 1988).

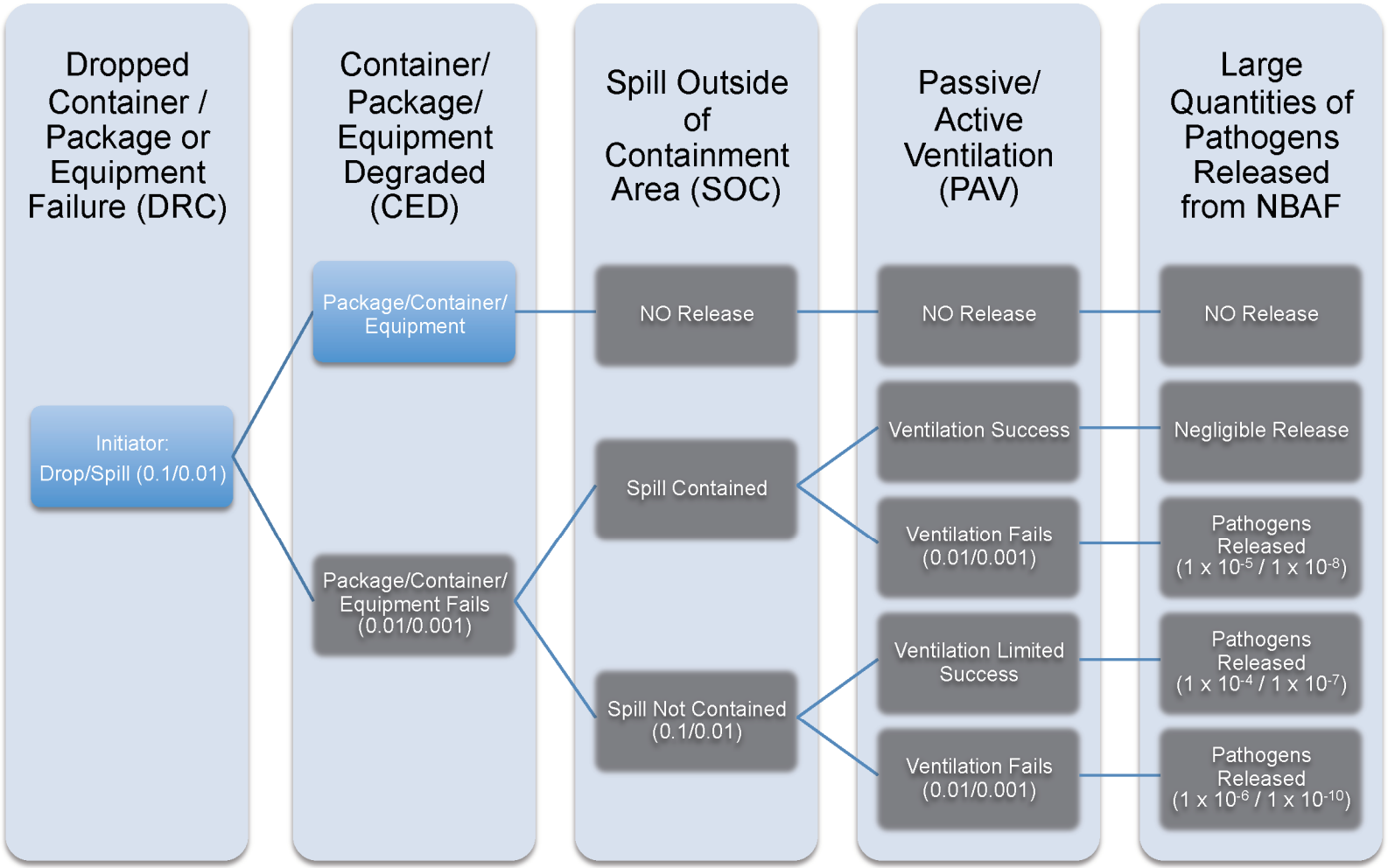
The basic events in the overall sequence include the initiating event, which is either a dropped container (package) or equipment failure. The second event in the sequence is that the contents leak from the container or equipment because of container degradation or improper maintenance. The third event is to evaluate the location of the event as inside or outside of containment area. The fourth is evaluating the ability for the released materials to be contained by equipment or location within the facility in order to mitigate or prevent the release from the facility. This last event is referred to as active/passive ventilation. This event addresses the "leak tightness" of the facility by maintaining proper filtration and pressure gradients (negative pressure in the location of the release directing airflow to the HEPA filters prior to exhausting through the vents). Should all of these protective features fail, then a release of pathogens to the environment would result. Each of these events is discussed and evaluated in detail in the following sections. The analysis of the accident in some detail provides insight into the likelihood (probability) that there is a release given the initiating event. The

overall frequency of the accident (unmitigated/mitigated) in a given year, and over the life of the facility, is dependent on the number of demands made for specific event. The accident frequency over the life of the facility, along with the supporting analysis, is used to designate the unmitigated and mitigated risk rank.

The spill accident sequence is represented in the form of an event tree (Figure E.4.1.1-1) depicting several protective features. Failure of all of these protective features will produce a release of pathogens. The individual events in the accident sequence are related to safety barriers that are modeled as either administrative or engineered controls. The representation of the overall accident frequency in terms of operational years or facility life is determined by the product of the individual event demand probabilities and the total number of demands (or opportunities) for the accident to occur in a year or over the life of the facility. For this accident, the initiating event is presented in terms of a single human error without specific regard to the total number of opportunities. For this reason, the resulting accident probability is in terms of a single demand from the initiating event. To convert this initiating probability to a frequency requires knowledge of the number of handling events per year, which can be determined from knowledge of the expected operations in NBAF. The initiating event frequency is then the product of the initiating event probability and the number of handling operations per year. The number of handling operations in any given period of time is dependent on the operating characteristics of the NBAF. These characteristics include the number of technicians or animals, the number of containers or unit operations in a given period of time, the number of days or hours per year that the safety systems are expected to be in service, and even the type and amount of specific mission research work that is ongoing. Research facilities have tendencies to fluctuate in types and amount of operations depending on mission objectives.

The event tree with the sequence of events leading to a release of pathogens as a result of a spill is presented in Figure E.4.1.1-1. The event tree focuses on those events that have a potential to result in a release of pathogens from the NBAF. Each of the discussions that follow provides the rationale for assigning the branch event failure probabilities.

Container/Package Dropped – Equipment Failure – This is considered the initiating event, labeled Dropped-Container (DRC), and is assumed to be the result of a human error. Given the size of the NBAF, the number of laboratories (BSL-3 and BSL-4), animal holding areas, and the expected number of laboratory workers, a dropped container/package or equipment malfunction leading to a spill is considered both reasonable and credible. This accident scenario was developed because a dropped container does not automatically result in a release of pathogens. This initiating event is assigned a demand failure probability, associated with a human error, of 0.1 per demand. Since it is likely that many such opportunities for a container drop are expected to occur in a given year of operation, the overall frequency of this initiating event is much greater than one per year. The total number of drops or equipment failures expected in a year is qualitatively estimated based on facility operations.



The three-letter code in the event title represents the event in the sequence. The branch failure probability value is provided in parentheses for each event. For example '(0.1/0.01)' for the initiating event represents the unmitigated/mitigated failure probability for that event. The unmitigated event tree represents the situation where there are minimal procedures, training, maintenance, and reliability of systems and personnel. The mitigate event tree represents a robust management, formality of operations, well-maintained and effective equipment, and rigorous implementation of procedures and controls. The final likelihood (probability) estimates for the sequence are calculated by multiplying each branch (e.g., the largest release is sequence DRC-CED-SOC-PAV), which is an unmitigated likelihood of 1×10^{-6} = 0.1 x 0.01 x 0.1 x 0.01 per drop event.

Figure E.4.1.1-1 — Small to Medium Spill and Aerosol Release Accident Scenario

Container/Package/Equipment Degraded Leading to a Spill of Contents – This is the first event in the accident sequence after the initiating event and is labeled Container-Equipment-Degradation (CED) in Figure E.4.1.1-1. It is assumed that a storage container is dropped or some piece of process equipment fails. The event tree quantification, and the subsequent representation of the risk based on the accident probability (per year of over the life of the facility) and the potential consequences, does not explicitly take into account that there is a wide range of potential outcomes resulting from a degraded container or package. These outcomes vary from small leaks to complete, instantaneous release of the contents. Conservatively, this accident is considered to result in the release of the entire contents of the package. In addition, it is reasonable to consider that the spilled material could be aerosolized as a result of the impact (see below for a discussion of the fraction aerosolized). The failure probability for this event is primarily based on mechanical failure or wear, and tear leading to degradation is assigned a value of 0.01 per demand (per package or container or equipment being called on into service) for the unmitigated case conditional on the occurrence of the drop, as is explained in Appendix E, and a value of 0.001 for the mitigated case. While human error is also an element, because of the potential for improper maintenance of equipment or improper packaging, the failure probability is assumed to be entirely the result of mechanical failure.

Because the NBAF is a new facility, it is assumed that the packages and equipment in use would be new and degradation would not initially be a significant contributor to the failure probability. Procedures and training would be current, and attention-to-detail is expected to be high. The likelihood of encountering degraded transport packages or process equipment may increase with operating history and could be further enhanced by personnel complacency. A robust management system with attention to formality of operations, configuration management, quality assurance, and training in place is expected to significantly reduce the likelihood of human error and mechanical failure.

Spill Outside of Containment Areas – This is the second event in the accident sequence after the initiating event and is labeled Spill-Outside-Containment (SOC) in Figure E.4.1.1-1. The evaluation of whether a spill is inside or outside containment areas alters the manner in which the spill can be contained. In addition, this event allows consideration of the fact that laboratory rooms where pathogens are present are separated from the non-containment areas or areas with less stringent safety controls (e.g., BSL-2 laboratories, offices, and maintenance areas as opposed to BSL-3 or BSL-4 areas). The plumbing and ventilation are also separated based on the types of work and hazards that are expected. The unmitigated probability of failure for the dropped container (and subsequently the spill) to occur outside of containment was assigned a value of 0.1 for the unmitigated case and a value of 0.01 for the mitigated case because this event, dropping of a package containing pathogens, outside of the appropriate containment area is primarily dependent on human error as opposed to mechanical failure. The procedures for the handling of packages or equipment differ based on the types of hazardous materials contained in the package. The effectiveness of safety controls in preventing the handling of packages in areas where it is not appropriate provides a means for reducing the likelihood of the release. The overall frequency of package handling in an area where the containment protection is less than what is needed for the package contents is determined based on the operational practices (demands) of the various laboratory activities.

Passive/Active Ventilation Operates – This is the last event depicted in the accident sequence. This event is labeled Passive-Active-Ventilation (PAV) in Figure E.4.1.1-1. Once material has escaped from the breached container or failed equipment, it becomes airborne in a specific area of the facility. Taking into consideration that ventilation is expected to be operating at the time of the release, the aerosol is carried to HEPA filters where it becomes trapped with a specified efficiency of 99.97% per filter (potentially multiple filters in series). The likelihood that ventilation is operating in the critical period after a container drop is based qualitatively on an unanticipated electrical outage or a random mechanical failure. Unanticipated electrical outages are infrequent, and normal operations in the facility are suspended during planned outages. Historically, outages at similar types of biological facilities have occurred approximately four times per year and have lasted less than 2 hours. Considering the number of 2-hour periods in a year, the implication is that power could be interrupted in a given 2-hour period at the rate of 1×10^{-3}. Assuming the critical period for

dispersal after the release is less than 2 hours, the probability that ventilation would shut off during the critical period of the event is on the order of 1×10^{-3} (this failure probability estimate conservatively neglects the capability of on-site back-up power to make up for the loss of off-site power during this critical time). In addition, there are other features of the active/passive ventilation system that would have to fail in order for pathogens to escape the facility in large quantities. These include the HEPA filter failure, "leak tightness" of the facility is compromised, or there is airflow from containment areas to non-containment areas. Each of these features needs to be factored into the determination of the failure probability for the PAV event; however, because this event is essentially a mechanical system, the failure probability assigned is 0.01 for unmitigated case and 0.001 for the mitigated case.

Evaluation of the various accident sequences illustrated in this tree shows that three discrete accident sequences (combined event failures) can result in a potential release of a large number of virions. These sequences are as follows:

- DRC-CED-SOC-PAV
- DRC-CED-PAV
- DRC-CED-SOC

The first sequence represents the accident scenario where all of the safety controls fail (each branch in the event tree fails). This sequence is the least likely to occur and has a per demand probability (per handling operation) of 1×10^{-6} for the unmitigated case and 1×10^{-10} demand failure probability for the mitigated case. The second sequence represents the situation where the spill occurs in the appropriate area of the facility, but the passive/active ventilation controls fail, resulting in a release of pathogens with a per demand probability of 1×10^{-5} for the unmitigated case and 1×10^{-8} for the mitigated case. The essential difference between these two sequences is the human error associated with the handling of the package has been removed (event success where the location of the spill is either inside or outside a contained area). The third sequence involves the situation where the package is not in the appropriate area of the facility, but the passive/active ventilation control operates. This sequence still leads to a release because the filtration and "leak tightness" of the facility is less stringent in these areas for the pathogens involved. The individual per demand failure probability is estimated at 1×10^{-4} for the unmitigated case and 1×10^{-7} for the mitigated case. This last sequence has the highest failure probability because the entire accident is dependent on two human error events and a single mechanical failure. The evaluation of these sequences indicates the value of the engineered safety controls in contrast to those dependent on operator actions. In addition, the likelihood of the release is reduced when there are a greater number of barriers or controls that must fail before a release is possible.

The accident sequence DRC-CED is one in which the drop and spill occurs, in an appropriate area of the facility, with all subsequent protective features working. Because this accident sequence is in an area where the pressure differential is towards the region of higher containment and the HEPA filtration is more stringent, there is a negligible release.

For purposes of evaluating this accident in the context of all of the remaining accidents to arrive at an overall risk ranking for the facility, it is necessary to convert these individual accident sequences into an overall spill accident frequency. This is accomplished in a qualitative fashion by considering the operational characteristics of the NBAF. Information obtained from the Feasibility Study for the NBAF included details of the mission, numbers and types of animals expected, and laboratory space and projected staff, including maintenance (DHS 2007). From these data, qualitative assessment was made to estimate the total number of potential opportunities (e.g., handling operations) that there are for the initiating event to occur. The assessment also included consideration of the operating time and an expected total operating life of the facility on the order of 50 years (the operational life of the facility is based on the fact that many of the missions the NBAF will replace are currently or have been performed in facilities that are approximately 40 to 50 years old).

Taking these factors into consideration, this accident is assigned a qualitative frequency of $\geq 1\times10^{-1}$ (less than 1 accident, resulting in a release, per year) for the unmitigated case, corresponding to a FC II and 1×10^{-5} per year for the mitigated case, corresponding to an FC IV. Since the range of the accident sequence probabilities (individual demand) was 1×10^{-4} to 1×10^{-10}, the impact of mission objectives, facility operating time, and the total number of workers and packages were sufficient to increase the frequency of a spill accident resulting in a release of pathogens to be less than 1 accident in more than 10,000 operating years of the facility for the mitigated case.

As shown in the above discussion, a completely unmitigated (assumes marginal functioning of the safety controls and high human error rates) release of material is therefore assigned to FC II (occasional). Taking into account the engineered and administrative controls that can reduce the frequency of the accident, the mitigated accident frequency is assigned FC IV, indicating that a spill leading to a release from the NBAF is improbable (unlikely to occur during the life of the facility) when the protective safety features have a high reliability.

To determine the unmitigated risk rank for this accident scenario, the source term is calculated.

Source Term Analysis

The source term is the product of the MAR, ARF, RF, DR, and LPF as discussed in Section E.3.3.1. In this accident scenario, the unmitigated source term was calculated using conservative values. The specific values for each of these five factors are discussed below and presented in Table E.4.1.1-1.

MAR – Based on the mission objectives and regulatory requirements, a particular package of biological material could contain approximately 100 mL of culture containing viable pathogens. While there are differences between pathogens in relation to the number of particles in a solution or gel media, it is reasonable to assume that approximately 1×10^{8} viable virions could be present in a single milliliter of culture media. This would yield a total inventory of approximately 1×10^{10} viable virions in a single package containing 100 mL of culture. The biological materials consist of various forms, but the most sensitive are those able to be easily aerosolized upon impact, such as solutions or powders. The MAR for this scenario is then taken to be 1×10^{10} virions of a specific pathogen. For purposes of evaluating the consequences, the MAR represents each of the viruses, FMD, RVF, and Nipah.

DR – For the unmitigated analysis, the DR is conservatively set at unity (1.0). In even the worst-case spill, however, it is unlikely that all of the biological material would escape the container, and the DR would more likely to be much less than 1. Therefore, using a value of DR = 1.0 for this consequence estimate is extremely conservative.

ARF and RF – Results of studies with powdered materials, liquids splashing, and solids being crushed on impact provide bounds on the total quantity of inventory that can become airborne as a result of a drop or a spill. As discussed in Section E.3.3.1, the ARF is assigned a value of 1×10^{-4} and the RF is conservatively taken to be 1.0 (meaning that all of the aerosol is at the respirable size).

LPF – For the unmitigated analysis in which the aerosolized material escapes the facility without being filtered or otherwise mitigated by the building containment system, the LPF is set to 1.0. For the mitigated analysis the LPF is determined by taking into account the containment system (ventilation, HEPA filtration, and facility structure). The LPF for the active/passive HEPA filtered system is conservatively estimated to be 1×10^{-5} for the mitigated accident scenario.

Table E.4.1.1-1 — Small to Medium Aerosol Release Source Term Parameters

Scenario	MAR	DR	ARF	RF	LPF
Unmitigated (No credit for HEPAs, maintenance, or procedures)	1×10^{10} virions	1	1×10^{-4}	1	1
Mitigated (Active/passive ventilation, procedures, maintenance, etc.)	1×10^{10} virions	1	1×10^{-4}	1	1×10^{-5}

Unmitigated Source Term
The unmitigated source term (only considers the physical properties of the pathogens and the culture media; no credit is taken for safety systems) for the small to medium spill accident is given by:

$Q = 1\times10^{10}$ virions $\times$ 1 $\times$ 1×10^{-4} $\times$ 1 $\times$ 1 = 1×10^{6} virions

Where:

Q = Quantity of viable pathogens released from the NBAF following the spill.

Mitigated Source Term
The LPF for the NBAF, as presented in Section E.3.1 and Table E.4.1.1-1 above, is used to calculate the mitigated source term (considers the efficiency of the HEPA filtration and the leakage of the facility; no credit is afforded the container as a conservative estimate) is given by:

$Q = 1\times10^{10}$ virions $\times$ 1 $\times$ 1×10^{-4} $\times$ 1 $\times$ 1×10^{-5} = 1×10^{1} or 10 virions for the active/passive ventilated safety system, proper maintenance, and high HEPA efficiency.

Consequence Analysis
The dose to the receptor outside of the NBAF (animal or human) is represented by the exposure due to inhalation, ingestion, contact, and vector pathways. For the inhalation pathway, the results of the air transport model provide time-integrated normalized air concentrations; therefore, the estimate of the exposure to pathogens in the air is simply the source term (Q) multiplied by the time-integrated normalized air concentration and the breathing rate in units of cubic meters per second.

The inhalation exposure to air containing transported viral particles is calculated by:

$Exposure = Q \times BR \times \chi/Q$

Where:

Q = the source term (mitigated or unmitigated) [virons]
BR = is the breathing rate [m^3/s]
χ/Q = the 95th percentile normalized distribution of pathogen in the air at the receptor location [s/m^3]

The typical breathing rate for humans is taken to be 3×10^{-4} m^3/s, while the breathing rate for a cow is approximately 6 m^3/hour or 1.6×10^{-3} m^3/s, and a pig is assumed to be approximately the same as a human.

For determining animal exposure from ingestion, both the total time spent grazing and the total quantity of food consumed in a specific time period are important. The estimate of the amount of grass or feed an animal consumes is approximately 100 lb/day for a cow. The amount is expected to vary greatly depending on the species of animal such as pigs, deer, elk, etc. Because the data obtained for the livestock in the vicinity of each proposed site are taken to be cattle, the estimate of 100 lb/day is sufficiently representative for purposes

of estimating risk. The results of the atmospheric modeling also provide estimates of the quantity of virions deposited on the ground as a function of distance from the site. Therefore, in order to assess the potential risk to cattle grazing on grass where viral pathogens have been deposited, an estimate of the total area covered by the animal grazing is necessary. Knowing the total amount of food consumed by an animal in a given period of time and the quantity of food produced per area will provide the basis for estimating the total exposure to pathogens while grazing. Estimates of grass production per unit vary somewhat depending on the species of grass, the type of soil, and available moisture, etc. A conservative estimate for the yield for typical pasture grass is on the order of 3.5 lb/m^2. As an example, if one were to assume that a cow eats nearly 100 lb of feed per day (8 lb/hour assuming that cows eat 12 hours out of 24) and that there is approximately 3.5 lbs/m^2, then a cow would need to cover nearly 30 m^2/day at a average rate of 2.5 m^2/hour to ingest 100 lb of food.

The calculation of unmitigated and mitigated consequences uses these same relationships to provide estimates of exposure. The difference is in the magnitude of the source term (how many virions are available) for inhalation and ingestion.

Unmitigated Off-Site Consequences – Calculation of site-specific exposure values are provided in Section E.4.4. The calculated χ/Q is site specific and varies with distance from the point of release. A typical χ/Q value at a distance of 250 m (approximate NBAF fence line) is on the order of 1×10^{-2} s/m^3. Using this value to determine the unmitigated exposure results in an inhalation dose of approximately 10,000 virions or about 1,000 times the MID for FMDV. Because 10 virions is also taken to be the MID for both RVFV and Nipah virus, these results are applicable to all three representative viruses for the inhalation pathway. Similarly, the exposure due to ingestion at the site boundary, for which the typical ground concentrations is approximately 20 virions/m^2 resulting in a total dose nearly 60 times the MID, is also greater than the minimum necessary to cause infection. Given that the unmitigated consequences at the site boundary are significantly higher than the MID, the identification of robust safety controls to prevent the accident or mitigate the consequences is necessary.

Mitigated Off-Site Consequences – Mitigated accident consequences, in a similar manner as the mitigated accident frequency, are estimated by evaluating the reduction in material released in an accident through the improvement of effectiveness of various controls. In the mitigated consequence analysis, as discussed above, the passive and active ventilation system is credited for reducing the LPF (amount of material that escapes from the facility through leaks and filters) to a fraction of that considered for the unmitigated case. Because the mitigated release is much smaller than the unmitigated case, there is little chance for significant downwind transport of the pathogens in a concentration that would result in an exposure. Because of the active/passive LPF mitigation effects, the mitigated exposure levels would be 100,000 times smaller than those described for the unmitigated release. The resultant dose at the site boundary would be 1×10^{-1} or 0.1 virions (less than the MID of 10 virions). These results illustrate that focusing resources and attention on the ability for the NBAF to contain pathogens in the event of an accident (in this case a small- to medium-size spill) provides a large reduction in the risk.

Risk Ranking

Based on the evaluation of the likelihood of a specific accident (as described in the evaluation of the event tree) and the consequences (as described by estimating exposure through inhalation and ingestion) associated with this accident, specific risk ranks can be assigned for the unmitigated and mitigated spill accident.

Unmitigated Risk Rank

The unmitigated risk rank is the combination of the accident likelihood (probability) and the bounding consequences through all pathways.

The spill accident has a per drop probability, from the event tree analysis for all three large release sequences, in the range of 1×10^{-4} to 1×10^{-6}. Considering the total opportunities for a drop to occur during the life of the facility, the unmitigated frequency for this spill accident has a range of 1×10^{-2} to 1×10^{0} or FC II (occasional) from Table E.3-3.

The spill accident consequences were shown to be greater than the MID, at the site boundary, indicating an unmitigated consequence severity category of B for the worker (long-term health effects) and A for the public/environment (exceeds the MID by more than a factor of 10 at the site boundary).

Using Table E.3-4, Public/Worker Risk Ranking, the combination of the accident likelihood of FC II and consequence severity of A/B (public/worker), the assigned risk rank is 1 indicating that robust safety controls are required to prevent or mitigate the accident and reduce the risk. Given that the unmitigated consequences at the site boundary are significantly higher than the MID, the identification of safety controls to prevent an accident or to mitigate the consequences is essential. The following table presents the safety controls or barriers relied upon to reduce or prevent a release. The safety controls considered appropriate for reducing the risk for this accident are summarized below.

Table E.4.1.1-2 — Summary of Safety Barriers and Procedural Controls

Control	Description
Safety Barriers	Active ventilation, which maintains a pressure drop across critical areas and rooms. Passive ventilation system, which includes the leak-tight facility structure, the efficiency of HEPA filters (in series at 99.97% efficient or better), and plenum to trap the spilled pathogen materials. Engineered containment systems within laboratories to provide containment during process operations. Robust containers and packaging that meet DOT requirements. Specialized process equipment for biomaterial processing, packaging, handling, movement, storage, etc. Properly maintained equipment. PPE available and used appropriately.
Procedural Controls	Conduct of engineering and operations consider maintenance, contamination control, PPE use, training, specialized operational procedures, monitoring and inspections, quality assurance, etc.

After taking into consideration the safety controls in the context of the spill accident, the mitigated risk rank is assigned. Determining the mitigated consequences depends on whether the accident is prevented. If the accident is totally prevented, for example, by robust packaging as well as procedures, maintenance, etc., then the spill and subsequent release are prevented or mitigated. In the case where the accident is prevented, then there is no release and therefore no consequences to the public or worker. Should the accident occur, but with lower frequency, and the safety systems function as expected, the consequences are significantly reduced as presented above. In either case, the risk is significantly reduced.

Mitigated Risk Rank

The mitigated risk rank, like the unmitigated evaluation above, is the combination of the accident likelihood (probability) and the bounding consequences through all pathways for the mitigated accident.

Through improvements in procedures, training, and quality assurance, the mitigated spill accident has a per drop probability, from the event tree analysis for all three large release sequences, in the range of 1×10^{-7} to 1×10^{-10}. In the same manner as for the unmitigated accident frequency, taking into account the total opportunities for a drop to occur during the life of the facility, the mitigated frequency for this spill accident has a range of 1×10^{-4} to 1×10^{-6} or FC IV (improbable) from Table E.3.3.

The spill mitigated accident consequences were shown to be much less than the MID at all distances from the point of release, indicating a mitigated consequence severity category of C for the worker (lost time injury or exposure – no health effects due to proper PPE use) and D for the public/environment (negligible off-site consequences much less than infectious dose).

Using Table E.3.4, Public/Worker Risk Ranking, the combination of the accident likelihood of FC IV and consequence severity of D/C (public/worker), the assigned risk rank is 4 indicating that the robust safety controls considered are sufficient to prevent or mitigate the accident and greatly reduce the risk. The overall risk summary is presented in the following table.

Table E.4.1.1-3 — Risk Rank Summary - Spill Accident

Scenario	Risk Rank	Accident Frequency	Consequence Severity
Unmitigated (No credit for HEPAs, maintenance, or procedures)	1	FC II (1×10^{-2} to 1×10^{0}) Occasional	A/B (Public/Worker) Exceeds the MID
Mitigated (Active/passive ventilation, procedures, maintenance)	4	FC IV (1×10^{-4} to 1×10^{-6}) Improbable	D/C (Public/Worker) Negligible off-site consequences

E.4.1.2 LAI

This scenario considers a type of release that is only a local accident where a laboratory worker through a variety of personnel errors results in an autoinoculation, ingestion, or contamination event serious enough to result in a personal infection. This scenario specifically addresses the consequences of an LAI.

In spite of the programs that are expected to be in place to identify and mitigate the effects and consequences of LAI, these do not explicitly prevent the occurrence. For this reason, this accident scenario was developed to address those accidents that occur as a result of personnel error. Several types of errors can lead to an LAI and include use of equipment that was not properly disinfected or failure to follow essential procedures for the use of equipment and disinfecting equipment. In addition, there is the potential for human error that leads to a cut or puncture, the splashing of pathogen-containing solutions into mucous membranes, or the inadvertent contamination incident serious enough to result in a personal infection. The failure to wear proper PPE is also a significant contributor to the occurrence of an LAI. The bounding scenario is taken to be an LAI as a result of personnel error. Mechanical failures can also lead to LAIs; however, the spill accident scenario bounds these events.

Based on the mission of the NBAF, it is considered a given that laboratory workers will be in contact with sufficient numbers of viable pathogens and that an infection could result from an exposure. For this particular accident scenario, the form of the pathogen is less significant than the exposure pathway and the occurrence of the LAI itself. This accident scenario is essentially only applicable to RVFV. FMDV is not considered to be available as an LAI, and humans are not considered susceptible to the disease. While humans can be infected with Nipah virus, there are no documented cases of acquiring the disease through an LAI.

Accident Sequence

The scenario is defined as several types of errors leading to an LAI and include use of equipment that was not properly disinfected, failure to follow essential procedures for the use of equipment, and disinfecting equipment. The significant features found to be relevant in preventing or mitigating the accident are as follows.

Preventive Features

- Equipment properly disinfected
- Proper handling, use, and maintenance of equipment
- Proper use of procedures
- Proper PPE and use of PPE
- Proper vaccinations

Mitigative Features

- Immediate reporting of potential mishaps and operational upsets
- Immediate reporting of symptoms that could be due to an LAI
- Proper health care post-exposure

An accident leading to an LAI is considered to occur if all the events in the prescribed sequence are compromised or fail. Should any one preventive or mitigative event succeed, then the accident is prevented or mitigated. This is illustrated in Figure E.4.1.2-1 event tree.

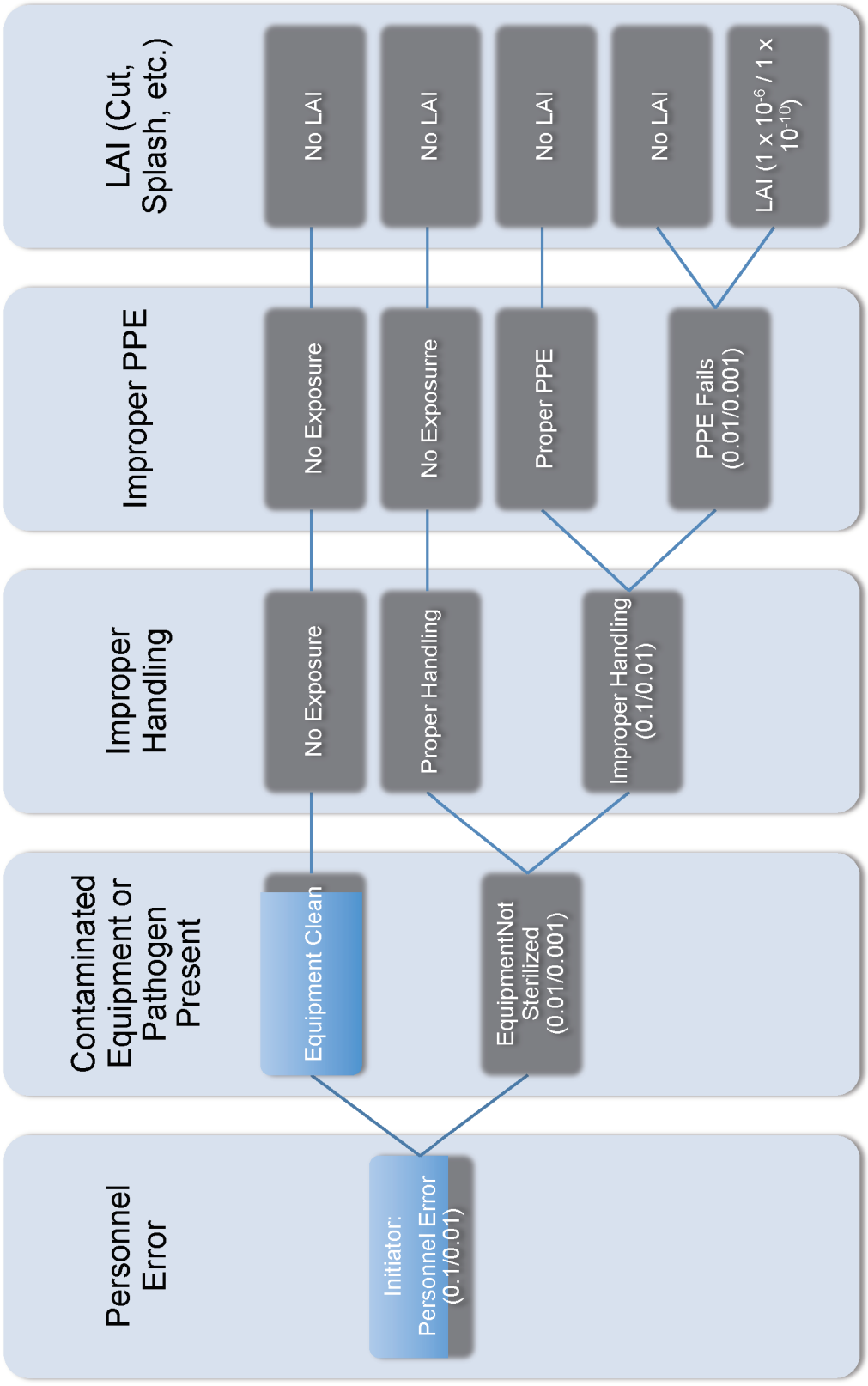


Figure E.4.1.2-1 — Laboratory Acquired Infection (LAI) / Consequence Scenario

Improperly Disinfected Equipment – It is assumed that contaminated equipment or its improper disinfection as a result of working with the specific pathogens is the initiating event in the accident sequence. Working with pathogens creates contaminated equipment and is the reason for the existence of contamination controls; PPE and procedures being the important ones in this instance. Whether the personnel error occurs while working with improperly disinfected equipment or whether the contamination is the direct result of working with the pathogens, the first event in the accident scenario is the presence of the pathogen on equipment and in a setting that lends itself to a potential infection event. For the purposes of these accidents, unmitigated human error failure probability is estimated as 0.1 per demand, and unmitigated equipment failure probability is estimated as 0.01 per demand. Since human error is an order of magnitude larger than equipment failure probability, the unmitigated failure probability is taken as 0.1 per demand.

Because the NBAF is a new facility, it is assumed that the workers are well trained and equipment is in good working order (easily disinfected, cleaned, etc.), and there is a relatively low initial probability of an LAI occurring. The probability of encountering improperly disinfected equipment in the future could likely increase with operating history and will be further exacerbated by personnel complacency unless there are disciplined operations in place to include (as examples) continuous personnel training, lessons learned experiences, management commitment, robust configuration management programs, and quality assurance and control programs in place.

Equipment Improperly Handled – Because of the nature and variety of work encountered in the NBAF, it is considered likely that once pathogens are present and the equipment is contaminated, it is assumed that it is available for exposure to the laboratory worker. The next significant event in this accident scenario is the improper handling of the contaminated equipment (glassware, sharps, centrifuge, work space, sink, BSC, etc.). Because of the large number of possible combinations of situations that can result in the improper use of equipment combined with the number of laboratory workers involved in similar activities, the unmitigated probability of improperly handling equipment in a manner that results in an LAI is conservatively estimated as 0.1 per demand for the unmitigated and 0.01 for the mitigated conditions.

Improper Use of, or Insufficient or Inadequate, PPE – The proper use of PPE can effectively eliminate a variety of potential exposure events; however; if the types of PPE available are not capable of preventing all types of cuts, punctures, splashes, scrapes, etc., that can lead to an LAI, then the frequency of an occurrence increases and approaches the unmitigated failure probability of 0.1 per demand (human error failure probability for following procedures) or 0.01 for the mitigated. For this event in the sequence to be successful in preventing or mitigating the accident, it is necessary that both the proper PPE is used and that the PPE is used properly.

Laboratory Worker Suffers a Puncture, Splash, Cut, etc. – During the variety of process steps that are likely to be encountered in routine operations at the NBAF, along with the number of laboratory workers, the potential for a worker suffering a cut, puncture, or splash is non-trivial. Evaluation of the range of accident sequences that can result from the failure or success of each event shows that the most likely accident sequence is when a laboratory worker suffers a cut or splash, etc., while working with equipment and animals. This accident sequence relies almost entirely on worker proficiency; therefore, the unmitigated failure probability is taken as 0.1 per demand (0.01 for mitigated).

Laboratory Worker Diagnosed with an Infection (LAI) – The consequence from this accident scenario is that the laboratory worker was exposed to a pathogen and ultimately acquires an infection as a result of a breakdown in procedure compliance. In this instance, the wound occurs, but the individual either does not recognize the incident as a wound or simply does not report it properly and enters the general population both inside the NBAF and outside the facility.

Source Term Analysis

As previously discussed in developing the LAI hazard scenarios, a completely unmitigated LAI would be a frequent event (one or more occurrences per year). This assignment of frequency is credible given the total number of laboratory technicians expected to be working in the laboratories during any particular year. However unlikely this seems, this occurrence is considered unmitigated since there is little or no credit taken for safety controls in place (no PPE, no training, no skilled personnel, etc.). The evaluation of the deterministic consequences is presented in the following analysis. This is done to determine the effect of the existing controls on preventing or mitigating both the accident occurrence (likelihood) and the consequences that result. This analysis helps to determine whether the control set is adequate and sufficient to prevent or mitigate the outcome of the accident to an acceptable level (is the risk acceptable).

MAR – Based on the mission of the NBAF, is it considered that laboratory workers will be in contact with sufficient numbers of viable virions and that an infection could result from an exposure. For this particular accident scenario, the form of the pathogen is less significant than the exposure pathway and the occurrence of the LAI itself. For the accidents considered in this analysis, pathogen concentration is nominally 10^8 virons/mL. In the course of an LAI, the volume of solution exposed to an individual might be on the order of 0.01 μL to 1 μL, which translates into 10^3 to 10^5 virons during an LAI exposure—assumed to be an infectious dose for those diseases that can be transmitted to humans.

The following parameters are a part of the normal consequence analysis as described in the accident analysis methodology but are generally reserved for discussions around airborne transport of aerosols.

- *DR* – The DR is the amount of MAR available for transport after acted on by the accident initiator (the energy of the spill, the fire, the drop, the splash, etc.). This term has no meaning in this LAI scenario and will be taken as 1.0 for calculation purposes.
- *ARF and RF* – These terms also do not share their conventional meaning in this scenario, as the ARF is the fraction of the MAR×DR that becomes airborne after acted on by the accident, and the RF is the RF of the MAR×DR. For this LAI example, these values will also be taken as 1.0. Recall that the product of DR×ARF×RF is the amount of airborne respirable MAR that a receptor would be exposed to during an accident scenario.
- *LPF* – For this particular accident, the traditional definition of LPF also has no meaning. This factor is a measure of the facility's ability to mitigate or prevent the release of aerosol generated during the accident conditions. This LAI accident may generate aerosol, but the focus of the accident is on the exposed individual—not on the facility's ability to contain an aerosol release. For this case, there is no additional facility release considered, as those scenarios will be addressed in subsequent evaluations. The LPF value for these calculation purposes is 1.0.

The worker in this scenario exposes himself to pathogen through an LAI inflicted by an autoinoculation event, a cut, puncture, aerosol ingestion, splash into mucous membranes, scratch on a contaminated piece of glassware, contamination of a pre-existing open wound, etc. No other release is considered in this event.

Table E.4.1.2-1 — LAI Accident Source Term Calculation Parameters

Scenario	MAR	DR	ARF	RF	LPF
Unmitigated	Viable pathogens are present	1	1	1	0

Unmitigated Source Term

The unmitigated respirable source term from this accident is

$Q = 1\times10^5 \times 1 \times 1 \times 1 \times 1 \times 1 = 1\times10^5$ potential pathogens released from the facility through the infected worker, who takes no precaution to alert others of the accident because the contact was either not noticed or not considered significant.

Consequence Analysis

Unmitigated Off-Site Consequences – The exposure to the laboratory worker results in an infection. The worker takes no steps to alert medical personnel because the contact was either not noticed or not considered significant, and he/she proceeds to enter the NBAF population and the general population outside of the NBAF, which could lead to secondary infections to the public.

Mitigated Off-Site Consequences – There are no off-site consequences associated with this accident scenario providing the worker follows protocol and contacts medical personnel in the event of any LAI concern. The mitigative controls in place include recognizing and reporting the event, followed by prompt medical attention to prevent infection and later public contact.

Table E.4.1.2-2 — Summary of Safety Barriers and Procedural Controls

Control	Description
Safety Barriers	Properly maintained equipment Appropriate PPE available
Procedural Controls	• Sharps procedures developed and implemented • Training against procedures • Conduct of engineering and operations consider maintenance, contamination control, PPE use, training, specialized operational procedures, etc.

Table E.4.1.2-3 — Risk Rank Summary – LAI

Scenario	Risk Rank	Accident Frequency	Consequence Severity
Unmitigated (no credit for PPE maintenance, or procedures)	1	FC I ($\geq1\times10^0$) Frequent	B (Primarily a worker with potential subsequent infections in the public or transfer to animals) LAI long-term health effects
Mitigated (PPE, procedures, maintenance)	4	FC III (1×10^{-2} to 1×10^{-4}) Probable	E (Worker) No measurable consequences

E.4.1.3 Loss of Infected Animal/Insect

This scenario considers the release of pathogens resulting from the loss or escape of an animal from containment in any of the BSL-Ag facilities or the insectary. This includes potential hosts from the outside environment accessing the BSL-3E, BSL-3Ag, or BSL-4 facilities; becoming infected; and returning to the outside environment. This accident was selected for analysis because of the hazard associated with loss of containment as evaluated in the hazards analysis. In addition, this type of loss of containment can have a

unique impact on the surrounding ecosystem. The potential for viral pathogens such as RVFV and FMDV to become established in the environment has far reaching consequences. The release of a pathogen as a result of loss of containment of a vector is a credible scenario and appropriate for detailed analysis.

The likelihood of the loss of an infected animal is dependent in part on the number of infected animals in the facility, as well as on the size of the animal. Containment is much easier for a large animal than for a smaller animal, and the safety systems expected to be in place will significantly reduce the likelihood that an infected animal is released. Because much of the high-containment work will occur with large animals, and not with insects, the focus of this accident is on the inadvertent release of animals from the BSL-3Ag areas of the NBAF. The safety controls identified for this accident scenario are expected to provide effective measures against the loss of containment for other types of animals or insects within the facility.

A loss of containment of an animal can occur as a result of inattentive laboratory workers coupled with a series of mechanical failures including the failure of isolation doors, interlocks, alarms, and detection devices. In this accident scenario, it is assumed that an infected animal contains sufficient viable pathogens to be considered a source of infection in the environment. The bounding scenario is taken to be an infected animal escaping to the environment outside of the NBAF.

Accident Sequence

The accident is defined as the loss of an infected animal from the NBAF. The following preventive and mitigation features or controls are identified that if effectively implemented, then it will mitigate the accident consequences or prevent the accident entirely.

Preventive Features

- Robust containment areas
- Multiple doors prohibiting access to environment
- Interlocks on access and egress points
- Proper handling of infected animals
- Procedural controls in effect and followed

Mitigation Features

- Alarms and detection equipment in place and maintained
- Procedures for emergency response

The accident sequence includes 1) improper handling of animals (procedures), 2) malfunction of containment systems (doors, seals, interlocks, etc.), 3) detection and alarm systems, and 4) emergency response and recovery. The event tree for the release of an infected animal is presented in Figure E.4.1.3-1.

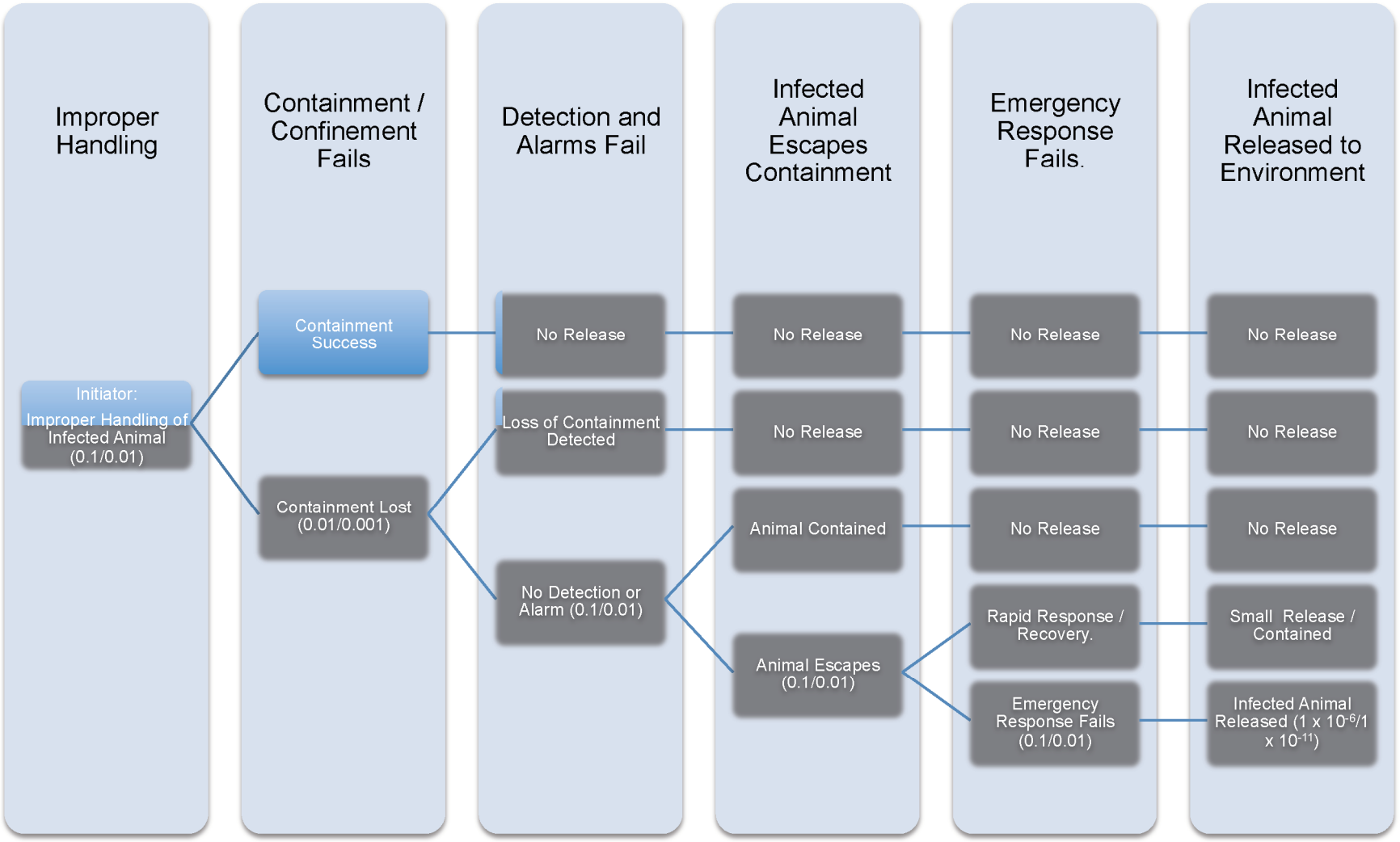


Figure E.4.1.3-1 — Loss of Containment or Confinement and Release of Infected Animal Consequence Scenario

Improper Handling of Animals – This is considered the initiating event, labeled Improper Handling of Animals (IHA), and is assumed to be primarily the result of a human error. Given the size of the NBAF, the number of holding pens for animals in the BSL-3Ag protective level areas and the expected number of laboratory workers, the initiating event of improper handling of animals leading to an animal release is both reasonable and credible. This accident scenario was developed because improper handling of an animal does not automatically result in a release of the animal and hence pathogens (FMDV, RVFV, and Nipah virus) becoming established in the environment. This initiating event is assigned a demand failure probability, associated with a human error, of 0.1 per demand. Since it is likely that many such opportunities for improper handling of infected animal are expected to occur in a given year of operation, the overall frequency of this initiating event can be greater than 1 per year. The total number of opportunities for an animal to be improperly handled expected in a year is qualitatively estimated based on facility operations and the total number of animals in the facility at any given time. The NBAF Feasibility Study Report presents information related to the total area of the facility that could contain animals. This area was used as the basis for estimating the upper-bound estimates for determining the accident frequency over the life of the facility. In a similar fashion, the mitigated frequency for this initiating event is assigned a failure probability of 0.01 indicating improvement in the management, training, and use of procedures, etc.

Containment Systems Fail – The likelihood of the containment systems failing is dependent on both mechanical reliability and human reliability for proper operations and maintenance. The containment systems in the NBAF are segmented with separate entrances from areas where there are no animals. These segmented areas are controlled with isolation doors, alarms, and interlocks as appropriate. Because the overall containment systems are primarily mechanical, the combined unmitigated likelihood of these systems failing is qualitatively assigned a value of 0.01. The mitigated failure probability for this event is assigned a value of 0.001 for the bounding assessment of accident frequency.

Detection System and Alarms Fail – The failure of the detection system to recognize and alarm if an animal has escaped containment is dependent on the reliability of the monitoring systems and on the reliability of the laboratory workers in being able to assess that an animal has in fact escaped containment. The most important aspect of the detection and alarm systems are those associated with the assessment of the monitoring. For example, if an alarm/monitor is activated indicating that animal containment has failed, the assessment of the significance of the alarm (the validity of the alarm, whether to act immediately, the location of the alarm, or the type of infected animal) are basically activities that rely on human interpretation. For this reason, the probability of failure of the detection system is characterized as a human error and is assigned a value of 0.1 for the unmitigated accident frequency and a value of 0.01 for the mitigated accident frequency.

Animal Escapes Containment – Based on the variety of infected animals expected to be in the NBAF and the variety of mechanisms used to contain the animals, the unmitigated likelihood that animal escapes containment, which is a mechanical-based failure, is assigned a value of 0.01 for the unmitigated and 0.001 for the mitigated accident frequency.

Emergency Response Initiated – The final barrier against the release of animals to the environment is the response to an emergency alarm condition. The likelihood of failure for emergency response to recover the animal and prohibit release to the outside of the facility is dependent on the response of laboratory personnel in a timely manner after detection has occurred. Because success here is totally dependent on the reliability of humans to recover the animal in a short time period, the unmitigated frequency is assigned a value of 0.1 for the unmitigated and 0.01 for the mitigated accident frequency.

Based on the overall accident scenario and the various sequence paths, the unmitigated frequency for this accident, over the life of the facility based on numerous opportunities for improper handling, is assigned a FC II or occasional (1×10^{-2} to 1×10^{0}).

Source Term Analysis

MAR – For discussing this scenario, the infected animal contains an inventory of approximately 1×10^{10} viable virions. As an example, viable pathogens are found in blood, saliva, and respired air of the infected animal and in large quantities. Should an infected animal get out of the NBAF undetected, the animal could act as a reservoir for a specific pathogen over a long period of time. The animal would in effect be a source term for direct atmospheric transport, as well as gross environmental contamination.
Because the source of pathogens is inside the infected animal, the unmitigated source term for this accident is related to the animal respiration rate contributing to air transport and other factors contributing to environmental contamination (external contamination on the animal, breathing, perspiration, sneezing, drooling, waste excretion, etc.). In addition, the animal could act as a potential vector host to various secondary arthropod vectors (mosquitoes, ticks, flies, etc.). The efficiency of the released animal act as a source is related to the time the animal is in the environment.

For the unmitigated accident conditions, it is assumed that more than sufficient virions could be released as an aerosol time for transport downwind. Accident consequences are described on a potential NBAF site-specific basis in Section 3.14.4.

DR – For this scenario, assume the DR is conservatively set at 1.0. This situation is actually more complicated than simply relating the contained MAR before the accident to the fraction of that MAR released by the accident. The infected animal in the environment is a source of pathogen releasing it at a rate described in the overall source term (above, in the MAR description).

ARF – Results of studies with powdered materials, liquids splashing, and solids being crushed on impact provide bounds on the total quantity of inventory that can become airborne as a result of a drop or a spill. As discussed previously, the ARF is often considered to be 1×10^{-4}, and the RF is conservatively taken to be 1.0. For this scenario, however, this is not the situation. In this case, the infectious pathogen available for release is in the form of an aerosol due to respiration directly from the infected animal, as well as a source of direct environmental contamination and via vector transmission through insects in the case of RVFV and close contact with FMD and Nipah viruses. In this case, the ARF value and RF value are very conservatively assumed to each be 1.0.

LPF – For this situation, the traditional definition of LPF as discussed earlier is not appropriate. LPF is a characteristic of the facility and is accident specific. It is a measure of the facility's efficiency for confining airborne aerosol generated in the course of an accident and is dependent on the facility configuration at the time of the accident. For this particular scenario, the infected animal is either confined inside the facility (LPF = 0), or the animal is outside the confines of the facility (LPF = 1.0).

Unmitigated Source Term
Because the source of pathogens is inside the infected animal, the unmitigated respirable source term from this accident is related to animal respiration rate and other factors (external contamination, breathing, perspiration, sneezing, drooling, waste excretion, etc,), as well as the suitability of the host animal to act as a vector host to insects. The total infectivity of the released animal is related to the time the animal is in the environment. Conservatively, the unmitigated source term is represented by:

$$Q = \geq 1\times10^{10} \text{ virions} \times 1 \times 1\times1 \times 1 \times 1 = \geq 1\times10^{10} \text{ virions}$$

Clearly, this estimate of the virions released for transport is an upper-bound value and is therefore a very conservative representation of the unmitigated source term. Since the animal is a constantly generating pathogens as a function of its level of morbidity (time dependent), as well as contaminating the environment as a function of time via respiration, direct contamination, and secondary vectors, the total unmitigated source term is a function of the total time the animal has uncontrolled access to the environment.

Mitigated Source Term

As described above in the LPF description, if the animal remains confined to the facility, then the LPF is zero and no pathogen release occurs. This is the situation where the NBAF design, its safety systems, barriers, detection systems, and alarms effectively work to prevent pathogen release during normal operations. If an animal does escape, mitigation of the source term can only occur through minimizing the amount of time the infected animal is in the environment.

Consequence Analysis

Unmitigated Off-Site Consequences – The dose to the receptor outside of the NBAF (animal or human) is represented by the exposure due to inhalation, ingestion, direct contact, and vector pathways. Since the results of the air transport model provide time-integrated normalized air concentrations, the estimate of the exposure to pathogens in the air is simply the source term (Q) multiplied by the time-integrated normalized air concentration and the breathing rate.

$$\text{Exposure} = Q \times BR \times \chi/Q$$

Where:

Q = the source term (mitigated or unmitigated) [virons]

BR = the breathing rate [m^3/s]

χ/Q = the 95th percentile normalized distribution of pathogen in the air at the receptor location [s/m^3]

For the unmitigated case, sufficient infectious concentrations of pathogen would be released for transport downwind. The concentration is reduced as a result of dilution effects, and the farther downwind the receptor is located, the less likely that sufficient concentration of viral pathogens will result in exposure and infection. The highest χ/Q value for any site at a distance of 250 m (approximate NBAF fence line) is on the order of 1×10^{-2} s/m^3 is 1.61×10^{-1} s/m^3 . Using these values, it is clear that loss of an infected animal from the NBAF would result in infectious concentrations of pathogen outside of the containment bounds of the NBAF.

Mitigated Off-Site Consequences – As described above, mitigation of this accident occurs through minimizing (to $t = 0$) the amount of time the animal is outside the confines of the facility.

Mitigated Risk Rank

FC III (probable), meaning that it is unlikely but possible to occur during the life of the facility.

Worker consequence category is C (lost time injury or exposure; no health effects due to proper PPE use).

Public/environment consequence category is D (negligible off-site consequences much less than infectious dose).

Risk rank is 3 (consider additional safety controls to prevent or mitigate the accident).

Table E.4.1.3-1 — Summary of Safety Barriers and Procedural Controls

Control	Description
Safety Barriers	Passive and active ventilation systems, redundant HEPA filtration to confine material during normal operations. Detection systems, alarms, door interlocks, redundant doors. Animal locator systems to minimize time in the environment in the event of an escape.
Procedural Controls	Conduct of engineering and operations consider maintenance, contamination control, PPE use, training, specialized procedures.

Table E.4.1.3-2 — Risk Rank Summary — Animal Release Accident

Scenario	Risk Rank	Accident Frequency	Consequence Severity
Unmitigated (no credit for containment, monitoring, or procedures)	1	FC II (1×10^{-2} to 1×10^{0}) Occasional	A/B (Public/Worker) Exceeds the MID potential to spread disease
Mitigated (containment, procedures, monitoring, response)	3	FC III (1×10^{-2} to 1×10^{-4}) Probable	D/C (Public/Worker) Negligible off-site consequences

E.4.1.4 Improper Sterilization/Disinfection of Solid or Liquid Waste

This scenario considers the release of pathogens caused by improper or incomplete sterilization or disinfection of solid or liquid waste with the final outcome consisting of pathogens released to the environment. The pathways of concern are vehicle-borne and water-borne transmission of pathogens. Because the viral agents considered in this hazard and accident analyses include those pathogens that are resistant to environmental factors for extended periods of time, these two pathways are particularly significant. The hazards evaluation identified a number of scenarios for which incomplete or inadequate sterilization could result in high consequences to receptors outside of the NBAF.

The release of biological materials that are incompletely sterilized can occur for a variety of reasons including the following:

- The equipment used to perform disinfections or sterilization fails to perform properly;
- Monitors and testing of post-sterilized material is not performed, or is not adequate, prior to the release of the waste to sanitary or other waste handling units;
- The time period for sterilization is too short as a result of human error or equipment malfunction;
- There are leaks in systems designed to contain the infectious materials; and
- Containers, mechanical systems, and facility structures (piping and drains, etc.) are not properly maintained and/or are degraded.

Several different types of accidents involving contaminated liquid or solid waste materials could occur as they are handled or processed that include the following:

- Inappropriate disposal of biological waste materials;
- Failure to completely sterilize the waste materials prior to disposition; and
- A malfunction of systems designed to handle infectious wastes.

Several decontamination and sterilization technologies were initially reviewed in the NBAF Feasibility Study including chemical, incineration, rendering, autoclave processing, and digestion. The bounding scenario is taken to be a release of an improperly sterilized solid or liquid waste containing significant quantities of viable pathogens into either the commercial solid or liquid waste handling systems.

Accident Sequence

The accident is defined as a failure to completely sterilize solid or liquid waste intended to leave the facility and the introduction of the incompletely sterilized material into commercial systems or repositories where viable pathogens may contaminate and propagate into the environment. The significant features found to be relevant in preventing or mitigating the accidents are as follows.

Preventive Features

- Sterilization equipment and systems
- Containment structure and support systems
- Interlocks and alarms
- Robust configuration management and maintenance programs
- Post sterilization quality assurance and testing protocol

Mitigative Features

- Formality of operations including procedures and training
- Facility and process confinement intact and functional
- Separate systems for biowaste and non-biowaste handling and treatment

An accident leading to the release of biological material is considered to occur if all the events in the prescribed sequence are compromised or fail. Should any one event succeed, then the accident is prevented or mitigated to varying degrees depending on precisely which features fail and which continue to function. The effectiveness of each control is also evaluated in terms of mitigated and unmitigated accident frequencies as described in the introduction to this appendix. The accident sequence for spills is illustrated in Figure E.4.1.4-1 as an event tree.

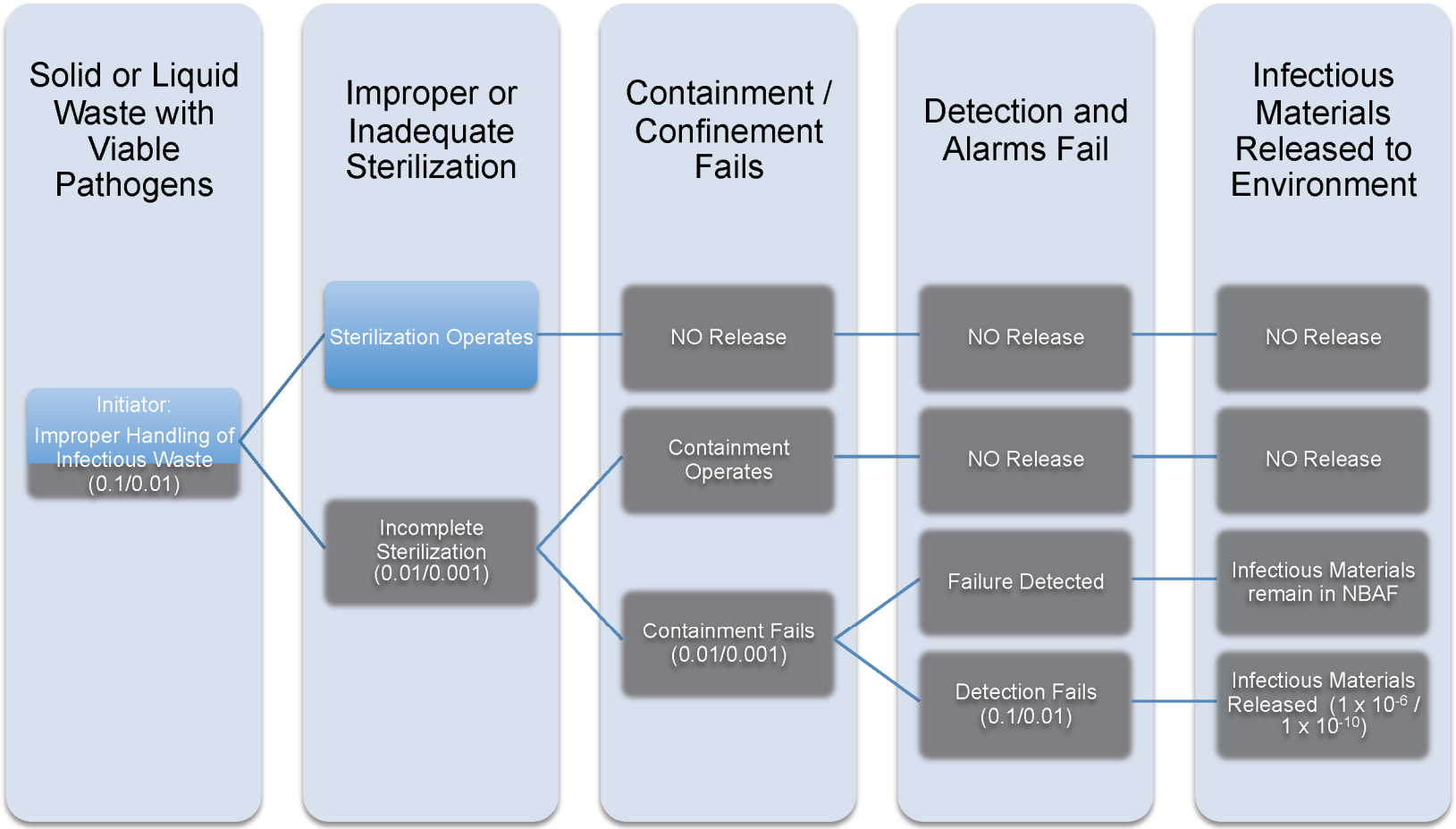


Figure E.4.1.4-1 — Improper Sterilization/Disinfection of Solid or Liquid Waste Scenario

Incomplete Sterilization – The initiating event in this accident scenario is the equipment malfunction or the operator error resulting in an incomplete sterilization of liquid or solid waste containing enough pathogens to pose a danger to the environment if allowed to exit undetected and untreated. Most sterilization operations are batch processes where consistency in performance is due to repetition and replication of a sterilization cycle. Equipment malfunction could occur through a loss of electronic control of vital parameters during a sterilization cycle (temperature, time, operating pressure, etc.). This particular type of equipment failure probability is taken as 0.01 per demand (unmitigated). For operator error leading to a similar outcome, the operator could mistakenly enter incorrect set points into a control consol or could fail to adequately distribute solid waste in a manner that would eliminate potential areas where the sterilization was not effective. These areas are referred to as "hot spots" that would not be effectively sterilized in a standard operation. Similarly, in liquid streams, ineffective sterilization could result from inadequate mixing or inadequate residence times in the mixer, through improper reagent concentrations, or from the presence of unintended solid precipitates in the waste stream. For this type of human error, the failure probability is taken as 0.1 per demand (unmitigated).

Based on the large number of operations expected to take place in the NBAF on a given day and throughout the year, the generation of biological wastes is considered to be continuous. The various sterilization operations that are expected in the facility are dependent on both mechanical and human reliability, along with the inherent uncertainty associated with a batch sterilization process. Given that human error is on the order of 0.1 per demand and that mechanical failure can be as high as 0.01 per demand, the combined unmitigated probability for inadequate sterilization is taken to be on the order of 0.1 per demand.

Containment Systems Fail to Operate – Once some amount of biological material has left the sterilization units still containing viable pathogens, it enters the separate systems designed to handle non-infectious waste materials. Given that the facility will be new, the probability of degraded containment systems (piping, valves, etc.) is relatively low. The probability that these secondary waste treatment processes will fail is small and will increase over time unless robust configuration management and maintenance programs are in place. The unmitigated failure probability for the containment systems for the biological wastes is estimated to be on the order of 0.01 per year.

Monitoring, Detection, and Alarm Systems Fail – Biological materials exiting the sterilization processes or residing in the solid and liquid waste systems leaving the NBAF are expected to be monitored to ensure that proper disinfection has occurred. Because of the difficulties and uncertainties associated with effectively monitoring biological wastes, the overall potential of detecting biological materials that were inadequately or incompletely sterilized is relatively low. In addition, the systems necessary to confirm with a high degree of certainty that no viable pathogens exist in the biological wastes is limited by human error, time for analysis, the equipment used to analyze the samples, and the design of the sampling or limited by the quality assurance program, etc. The likelihood of workers failing to follow administrative procedure is taken to be 0.1 based on a nominal human error probability associated with failure to follow administrative safety controls. Coincident with failing to follow procedures is the technological uncertainty in detecting trace levels of pathogens in the sterilized waste materials. The overall unmitigated probability of failure to detect and alarm prior to release of the biological materials is considered to be on the order of 0.5 per demand.

Accident Sequence Results – Evaluation of the range of accident sequences that can result from the failure or success of each event shows that the accident sequence of most concern is when a there is incomplete or inadequate sterilization. Once this occurs, the likelihood that viable pathogens will be released to the environment is high. The bounding unmitigated accident sequence has a combined failure probability of 2.5×10^{-4} per year and an FC III (probable; from Table E.3-3; also see Figure E.4.1.4-1).

Source Term Analysis

As shown in the previous section, a completely unmitigated release of material is considered to produce a significant release of infectious materials to the environment if the outcome is realized. It is possible that the mitigative features intended to minimize the potential for the material to escape the facility will perform as designed or that the preventive features will be in place and operational performing their safety function. The source term for this type of accident can have a wide range. For this analysis, the source term is based on a conservative estimate for the MAR.

MAR – Based on the mission objectives and the number of potential operations ongoing in the NBAF, the amount of biological materials that remains in a particular sterilizer batch after an inadequate or incomplete operation is estimated to contain a nominal volume of 10 mL solution containing viable pathogens (1×10^9 virions). This is based on an assumption of approximately 1×10^8 viable virions/mL. The biological materials consist in various forms, but the most sensitive are those able to be easily aerosolized or transported in the environment upon release.

DR – For the unmitigated analysis, the DR is conservatively set at 1.0, which is representative of the entire MAR being released as postulated in the scenario.

ARF and RF – Results of studies with powdered materials, liquids splashing, and solids being crushed on impact provide bounds on the total quantity of inventory that can become airborne as a result of a drop or a spill. As discussed in Section 3.14.2.4, the ARF is considered to be 1×10^{-4} and the RF is conservatively taken to be 1.0 to address the mix of solids, liquids, and aerosol particles.

LPF – For the solid and liquid wastes that are incompletely sterilized, the traditional definition of LPF as discussed previously in Section 3.14.2.4 is not appropriate. LPF is a characteristic of the facility and is a measure of the facility's efficiency for confining airborne aerosol generated in the course of an accident. LPF is accident specific and dependent on the facility configuration at the time of the accident. For this particular scenario, either the waste is completely sterilized (or detected before leaving the facility) and the LPF = 0, or the waste leaves the facility and enters the environment, in which case LPF = 1.0. For the accident, the assumption is that no aerosol is generated (facility filtration plays no role in mitigating a release), and the unmitigated LPF is 1.0 for any incompletely sterilized waste leaving the facility; either solid or liquid.

Table E.4.1.4-1 – Incomplete Sterilization of Solid or Liquid Waste Source Term Calculation Parameters

Scenario	MAR	DR	ARF	RF	LPF
Unmitigated (incompletely sterilized waste released)	1×10^9 virions	1	1×10^{-4}	1	1
Mitigated (passive and active ventilation)	1×10^9 virions	1	1×10^{-4}	1	0

Unmitigated Source Term

The unmitigated respirable source term from this accident is difficult to estimate. The liquid or solid waste has undergone some aspect of sterilization and has been transferred out of the facility containing an amount of viable pathogen. None, however, have been aerosolized. Conservatively, if the entire source term were aerosolized by impacts, spray, or other energy being applied to the waste materials, then the unmitigated scenario could be represented by the following:

$$\overline{Q} = 1\times10^{9} \text{ virions} \times 1 \times 1\times10^{-4} \times 1 \times 1 = 1\times10^{5} \text{ virions}$$

Mitigated Source Term

As described above in the LPF description, if the incompletely sterilized waste remains confined to the facility or is never generated in the first place, then the LPF is zero and no release occurs. This is the situation where the NBAF design, safety systems, barriers, and disciplined operations like quality assurance and testing protocol work to ensure sterilizer effectiveness and consistency to prevent pathogen leakage during normal operations. If the waste does leave the facility, mitigation of the source term can only occur through minimizing the amount of time the infectious waste is in the environment prior to detection and retrieval.

Consequence Analysis

Unmitigated Off-Site Consequences – The dose to a receptor outside of the NBAF (animal or human) is represented by the exposure due to pathways. Because of the viability of various pathogens in the environment and on shoes, tools, and in soils and water, the exposure time is considered to range from as little as 1 hour to as long as several weeks. Various transmission routes including inhalation and direct contamination while foraging can infect animals. Total exposure under these circumstances can be modeled as direct inhalation using the assumed air concentration (aerosolized particles, resuspension of contaminated dusts, etc.) and the breathing rate. If the contamination is associated with solid materials, the environmental contamination may take longer to materialize due to packaging and transportation constraints. If solid materials are overpacked into 55-gal drums, for instance, and transported to a landfill for burial, then uncontrolled release of the pathogen might be prevented or mitigated even outside the NBAF. Conservatively, however, this outcome will not be considered, and it is assumed the solid materials are available for resuspension and aerosol production for conventional air transport according to the traditional model.

$\text{Exposure} = Q \times BR \times \chi/Q$

Where:

- Q = the source term (mitigated or unmitigated) [virions]
- BR = the breathing rate [m^3/s]
- χ/Q = the 95th percentile normalized distribution of pathogen in the air at the receptor location [s/m^3]

If the release pathway is through the discharge of a contaminated liquid effluent, the impact on the environment could be more rapid. The pathogen distribution would be slower that via aerosol production but would be just as uncontrolled. For these purposes, the unmitigated consequence will be conservatively estimated as though it were an aerosol fully available for air transport. In this case, sufficient infectious concentrations of pathogen would be released for transport downwind. The concentration is reduced as a result of dilution effects, and the further downwind the receptor is located, the less likely that sufficient pathogen concentration would exist for exposure and infection. The highest χ/Q value for any site at a distance of 250 m (approximate NBAF fence line) is on the order of 1×10^{-2} s/m^3. Using these values, it is clear that the aerosolized source term from contaminated waste result in infectious concentrations of pathogen outside of the containment bounds of the NBAF.

Mitigated Off-Site Consequences – Because of the nature of the accident and the subsequent release, there is little that can be done to mitigate the accident once the infectious material is outside of the NBAF other than detection of active pathogens and retrieval of contaminated waste (if feasible). One feature that is useful is that the facility has a land buffer that can be controlled to inhibit receptors from gaining access to potentially contaminated areas. However, the accident is prevented if the equipment is properly sterilized and there is no release.

Mitigated Risk Rank

FC III (probable), meaning that it is unlikely but possible to occur during the life of the facility.
Worker consequence category is C (lost time injury or exposure; no health effects due to proper PPE use).
Public/environment consequence category is D (negligible off-site consequences much less than infectious dose).

Risk rank is 3 (consider additional safety controls to prevent or mitigate the accident).

Table E.4.1.4-2 — Summary of Safety Barriers and Procedural Controls

Control	Description
Safety Barriers	Disinfection and sterilization equipment; possibly redundant processing protocol. Containment systems for liquid and solid waste used as surge awaiting quality assurance approval prior to discharge to the environment. Detection and alarm systems. Active and passive ventilation system, which includes the leak-tight facility and the efficiency of the HEPA filters to trap the biological material resulting from a release inside the NBAF.
Procedural Controls	• Conduct of engineering and operations consider maintenance, contamination control, PPE use, training, specialized operational procedures, etc. • Waste sterilization quality assurance and testing to ensure complete sterilization of infectious waste prior to discharge from facility.

Table E.4.1.4-3 — Risk Rank Summary – Improper Sterilization of Solid or Liquid Waste

Scenario	Risk Rank	Accident Frequency	Consequence Severity
Unmitigated (no credit for containment, monitoring, or procedures)	1	FC II (1×10^{-2} to 1×10^{0}) Occasional	A/B (Public/Worker) Exceeds the MID potential to spread disease
Mitigated (containment, procedures, monitoring, response)	3	FC IIII (1×10^{-2} to 1×10^{-4}) Probable	D/C (Public /Worker) Negligible off-site consequences

E.4.1.5 Large Room or Facility Fire

Fires in the NBAF were evaluated in the hazards analysis and were found to produce significant consequences to the laboratory workers (involved and non-involved) and the public. In addition, a subsequent release of

pathogens would also pose a significant risk to the environment. For these reasons, fire accidents were evaluated in detail as part of the accident analysis.

Facility-wide or room fires can result from mechanical failures, flammable materials, and as a result of exothermic reactions. Because the initial hazards identification identified one or more specific fire initiators, this fire accident analysis was developed to reasonably bound the potential consequences associated with this hazard. The accident scenario involves a series of individual and separate events that ultimately lead to the potential for release of one or more pathogens. The events include both human error (e.g., failure to follow procedures, mixing incompatible chemicals, etc.) and mechanical failures (e.g., fire detection and alarm system failure, failure of fire protection system, etc.) that could ultimately lead to the release of pathogens. It is noted that in areas where the heat is significant, there is destruction of pathogen source term and a reduction of the total quantity that is available for release.

Operations and processes that may be encountered in the NBAF could include the use of volatile or flammable chemicals, as well as energy sources, along with sufficient combustible materials being co-located such that a resulting fire is not precluded from consideration. The sequence of events that could occur as a result of a fire being initiated is addressed below.

The assumed accident progression begins when a laboratory worker is engaged in cleaning, processing, or another type of routine activity and encounters a situation where there is a combination of fuel, heat, ignition source, and oxygen and a fire results. This situation can occur inside a BSC, in a laboratory room, or in any location in the NBAF. In a normal operational mode, this is considered an improbable event but is evaluated here for completeness. Once a fire is initiated in a location within the NBAF, a number of events must occur for the fire to become sufficiently large that spreading to other areas is possible.

Accident Sequence

The accident outcome is defined as the release of pathogen from the facility that results from a fire occurring during routine processing or maintenance activities. In this accident scenario, the flammable materials are assumed to be available in sufficient quantities to ignite from some source, the protective fire systems do not respond in time, and there is the subsequent involvement of pathogen (a failed BSC, storage cabinet, process equipment, process operation, etc). This accident sequence consists of independent events in series that have a qualitatively determined failure rate. For human error failures, the unmitigated failure probability is taken as 0.1 per demand; and for equipment failures, the failure probability is assumed to be 0.01 per demand. Theses significant accident events were found to be either preventive or mitigative in nature.

Preventive Features

- Flammable and combustible material inventories are limited
- Storage containers (BSCs, containers, cabinets, etc.) are fire resistant
- Biological materials stored in a form or in a package that is resistant to spread by fire

Mitigative Features

- Fire detection and alarm systems identify fire early and fire protection (suppression) system activates in time to extinguish or mitigate the fire
- NBAF confinement intact and functional

An accident leading to the release of biological material is considered to occur if all the events in the prescribed sequence are compromised or fail. Should any one event succeed, the accident is prevented or mitigated (see Figure E.4.1.5.1 for the event tree describing this scenario).

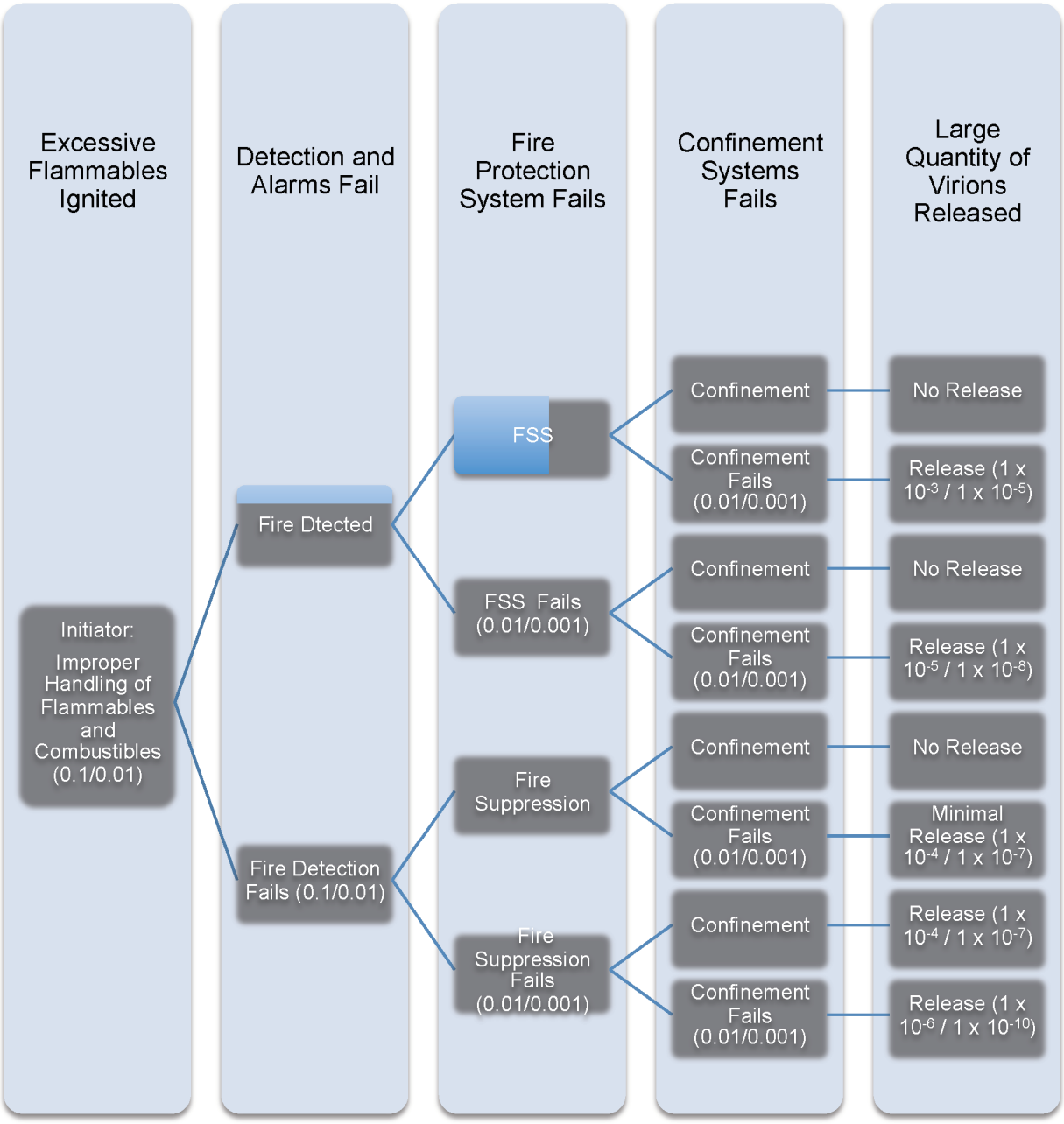


Figure E.4.1.5-1 — Facility of Room Fire with Subsequent Release of Pathogens

Excessive Flammable and Combustible Materials Ignite and Cause Uncontrolled Fire – Typical operations would necessarily restrict the accumulation of excessive combustible materials; however, certain flammable materials are likely to be unavoidable. In the event of poor housekeeping (lack of operational formality), excessive combustible materials accumulate. Combine this with another operator error, which might be the accumulation of excessive combustible liquids, and add an ignition source or ignition situation, and a fire results. For the postulated scenario to occur, a laboratory worker would have to make at least two procedural errors. The first error would be attempting to perform activities when there were excessive combustible and flammable materials present. The second error—also in direct violation of procedure—would be to engage in operations while involving an ignition source. The likelihood of workers failing to follow multiple administrative procedures is conservatively taken to be 0.1.

In this unmitigated scenario, two errors are made by the worker, but a single failure probability is required for the event tree. This value is conservatively estimated as the product of the two operator error failure probabilities, giving a failure probability for the event occurring of 0.01 per demand. Conservatively assuming at least 10 operations per year (demands), and not taking credit for ongoing evaluations and assessments identifying hazardous situations, the likelihood of excessive flammable or combustible materials being accumulated and ignited, causing a fire is less than 0.1/year.

Fire Detection and Alarm Systems Fail to Operate – The fire detection system would likely respond to a fire that was initiated in a laboratory room. The time delay for detection is dependent on the locations of the detectors (heat and/or smoke) and where the fire starts. A fire that starts inside a BSC (without its own fire sensor) could grow in size (with ventilation on) for a significant time period before room detectors respond. Once a fire is started, the time frame between detection, alarm, and response is critical in controlling the size of the fire. For the purposes of this accident scenario, it is assumed that if the detection system detects the fire, then the fire protection system can be initiated (automatically) to either extinguish the fire or to prevent the fire from growing in size. The probability of failure of the fire detection system is conservatively estimated at 1/100 or 0.01 per demand. This value is consistent with other equipment failure probabilities used throughout this accident analysis.

Fire Protection System Fails to Respond – Once the fire is detected, the fire suppression system would be actuated. At this point, the type of system (dry, wet, or otherwise) does not factor into the analysis. The potential for failure of a fire suppression system is dependent on at least one of three main elements being inadequate or inoperable. These elements include 1) a sufficient source of fire suppression material available (usually water), 2) an unobstructed flow path from the source of fire suppressant to the location of the fire, and 3) sufficient energy to move the fire suppressant from the source to the fire. This can be accomplished with fire pumps or by gravity feed. The failure probability of the fire suppression system to respond is then determined by the cumulative probability of failure of the individual components. The unmitigated failure probability for the fire suppression system consisting of these three elements is estimated to be on the order of 0.01 per demand, assuming appropriate design, procurement, installation, and maintenance.

Facility Confinement System Fails to Remain Intact and Functional – The confinement system consists of the intake and exhaust HEPA filters and plenums, the duct work from the plenums to the structure, and the NBAF structural shell (including doors). The confinement system is essential in preventing a release from the NBAF, thereby maintaining the confinement boundary. Failure of the confinement system to function would be caused by the facility doors (especially exterior doors) not being closed or the ventilation system's HEPA filters not able to perform their function. Confinement system integrity is considered to be maintained by means of administrative procedure and verified through regular surveillance. The likelihood of workers failing to follow administrative procedure is taken to be 0.1 based on a nominal human error probability associated with failure to follow safety administrative controls.

Conservatively assuming that components of the confinement system (door closures, HEPA filters, etc.) need to be regularly inspected to be functional, but realizing that multiple doors would need to fail open or that

multiple banks of HEPA filters would need to be dysfunctional for the confinement system not to function, the frequency of confinement system failure is based primarily on the failure of the ventilation and HEPA filtration system and is estimated at ~1E-4 per demand. Considering additionally that certain accidents in the NBAF could lead to workers evacuating the building (perhaps hurriedly) and conceivably propping open the doors that would normally close on their own, a conservative frequency of confinement system failure is taken generically (independent of accident scenario) to be 1E-3 per demand.

Accident Sequence Results – Evaluation of the range of accident sequences that can result from the failure or success of each event shows that the most likely accident sequence for a fire in a laboratory room or BSC is when the fire detection and suppression systems, the active and passive ventilation systems, and the confinement systems are robust, intact, and functional. The unmitigated accident sequence has a combined failure probability falling within FC III (probable; Table 3.14.2-3). The mitigated frequency estimated to be in FC V (remote).

Source Term Analysis

The possibility exists that enough flammable or combustible materials could be accumulated that a fire would start and, without interdiction, would engage more than a single laboratory room. A fire of sufficient energy to expand beyond a single laboratory room or area presents a significant potential for release of pathogen from the NBAF. The energy associated with a fire is more than the local heat from the fire and also includes the build-up of pressures and the generation of soot. These additional factors may overload the HEPA filtration system and cause them to fail by any of several ways: hot gases could burn through the filter media, the filters could plug with soot and fail due to excessive pressure drop, or the filters could plug with soot and the fans shutdown due to excessive pressure drop, allowing the fire to pressurize the fire room and reverse the air flow and bypass the filtration system. The fire itself does several things; it may compromise the facility and produce a communication path to the outside, it provides energy necessary aerosolize the pathogen into a form that is easily dispersible, and it provides the mechanism for dispersing the aerosol to the environment. In addition, this analysis assumes that heat from the fire destroys 99% of the available pathogen source term.

MAR – The MAR for this scenario involves multiple laboratory rooms or areas and is assumed to involve 30 L volume of material from the cGMP laboratory and comprises an amount of pathogens on the order of 1×10^{13} virions.

DR – The DR is the fraction of MAR affected during the accident. The MAR value is assumed to be reduced by 99% as a result of exposure to the heat of the fire. This translates into a DR of 0.01 and a reduction in the involved MAR to 1×10^{11} virions.

ARF – The ARF for dynamic stress on MAR caused by aerodynamic shock and pressure rise from burning materials is higher than that estimated for a simple spilled container. For this reason, the ARF is taken to be 1×10^{-2}. In addition, the RF of the release fraction is taken as 1.0 for both the unmitigated and mitigated accident cases.

LPF – For the unmitigated analysis in which the aerosolized material escapes the NBAF without being filtered or otherwise mitigated by the building confinement system, the LPF is set to 1.0. For the mitigated analysis, the LPF is determined by taking into account the facility confinement system, which includes the fans, the plenum structures, the redundant HEPA filters, the facility structural shell, the entry and exit doors, etc. For a robust facility with good disciplined operations, procedures, and training; the mitigated LPF can be taken as 1×10^{-5}.

The parameters of the source term formula are summarized in Table E.4.1.5-1. The mitigated LPF calculation includes the NBAF confinement system as a credited safety barrier.

Table E.4.1.5-1 — Source Term Calculation Parameters for Multiple Room Area Fire

Scenario	Source	MAR	DR	ARF	RF	LPF
Unmitigated	Pathogen aerosol	1×10^{13}	0.01	0.01	1	1
Mitigated	Pathogen aerosol	1×10^{13}	0.01	0.01	1	1×10^{-5}

Unmitigated Source Term

The unmitigated respirable source term from this accident is:

$Q = 1\times10^{13}$ viable pathogens $\times$ 0.01 $\times$ 0.01 $\times$ 1$\times$ 1 = 1×10^{9} virions

It is clear that this level of release from the NBAF would cause considerable environmental damage.

Mitigated Source Term

The appropriate LPF for this scenario is given as LPF = 1×10^{-5} for a robust and well-maintained facility confinement system. With these values, the mitigated respirable source term is:

$Q = 1\times10^{13}$ viable pathogens $\times$ 0.01 $\times$ 0.01$\times$ 1 $\times$ 0.00001 = 1×10^{4} virions

This level of release from the NBAF would also cause considerable environmental damage but in a range closer to the facility.

Consequence Analysis

Unmitigated Off-Site Consequences – The dose to the receptor outside of the NBAF (animal or human) is represented by the exposure due to inhalation, ingestion, direct contact, and vector pathways. Since the results of the air transport model provide time-integrated normalized air concentrations, the estimate of the exposure to pathogens in the air is simply the source term (Q) multiplied by the time-integrated normalized air concentration and the breathing rate.

$$\text{Exposure} = Q \times BR \times \chi/Q \times ET$$

Where:

Q = the source term (mitigated or unmitigated) [virions]

BR = the breathing rate [m^3/s]

χ/Q = the 95th percentile normalized distribution of pathogen in the air at the receptor location [s/m^3]

The calculated χ/Q is site specific and varies with distance from the facility. Because the unmitigated release is large, there is a greater chance for significant downwind transport of the pathogens at a concentration that would result in an exposure. Base-case χ/Q values (no fire) are very conservative and the results assuming a 100-MW fire are up to 3 orders of magnitude lower, depending on distance from site. The highest χ/Q value for any site at a distance of 50 m is 1.61×10^{-1} s/m^3 and is approximately 3×10^{-5} s/m^3 at a distance of 10 km. By inspection, the use of these values to estimate downwind exposure produce high values close to the facility release point and much lower values as pathogen transport is diluted by distance.

Mitigated Off-Site Consequences – Because of the contribution of the facility structure and its engineered safety barriers in mitigating the initial release, the mitigated exposure levels are 100,000 times lower than the unmitigated release.

Mitigated Risk Rank

FC IV is (improbable) unlikely to occur during the life of the facility.

Worker consequence category is C (lost time injury or exposure; no health effects due to proper PPE use).

Public/environment consequence category is D (negligible off-site consequences much less than infectious dose).

Risk rank is 4 (no additional safety controls to prevent or mitigate the accident).

Table E.4.1.5-2 — Summary of Safety Barriers and Procedural Controls

Control	Description
Safety Barriers	The NBAF confinement system, including the NBAF structure, intake and exhaust HEPA filters, and duct work between the plenums and the structure, provides a barrier against pathogen release to the environment. Fire detection and protection systems. Additional safety barriers to provide redundant containment in the event of a large release accident to include BSC, MAR containers, and compartmentalization philosophies.
Procedural Controls	Conduct of engineering and operations consider maintenance, contamination control, PPE use, training, specialized operational procedures, etc. Operational MAR limit (use of small quantities of pathogen in the BSCs).

Table E.4.1.5-3 — Risk Rank Summary — Large Fire Accident

Scenario	Risk Rank	Accident Frequency	Consequence Severity
Unmitigated (no credit for fire suppression, ventilation, HEPA filtration, maintenance, or procedures)	2	FC III (1×10^{-2} to 1×10^{-4}) Probable	A/A (Public/Worker) Exceeds the MID potential to spread disease
Mitigated (facility confinement, active and passive ventilation, fire suppression, procedures)	4	FC IV (1×10^{-4} to 1×10^{-6}) Improbable	D/C (Public/Worker) Negligible off-site consequences

E.4.1.6 Overpressure Event from a Deflagration

Operations and processes that may be encountered in the NBAF could include the use of chemicals (gas or liquid) that are volatile or flammable. The NBAF Feasibility Study indicates that natural gas is supplied to the facility for use in laboratory rooms. In addition, the disinfectant gases formaldehyde and ethylene oxide are also flammable and are potential agents for use in large-volume disinfection operations in the NBAF. Because of the potential for flammable or combustible chemicals and natural gas to be routinely used in the facility, an accident scenario involving a deflagration was postulated.

The assumed accident progression begins when a laboratory worker is engaged in cleaning, processing, or another type of activity that requires natural gas or a flammable chemical. A situation develops where there is a build-up of gas inside a BSC or another enclosed area that reaches the lower flammable limit (LFL). During normal operations this would be considered an improbable event but is evaluated here for completeness.

The free volume of a BSC is approximately 4,700 L, thereby providing a sufficiently small confined space to support reaching the LFL. This means under certain conditions (loss of ventilation coupled with flammable chemical or natural gas use) a flammable mixture in the BSC is possible and must be controlled. In this scenario development, the existence of a heat or ignition source is also assumed to be available, and in order to examine the bounding potential release that could affect the public, it is further assumed that an inventory of pathogens exists in the BSC and that a deflagration occurs. Because the specific chemicals are not identified, the deflagration is the result of the build-up of natural gas (recognizing that natural gas is not piped to the BSCs).

The most significant aspect of the deflagration is the resulting pressure wave that could provide sufficient energy to breach the BSC and release biological materials in aerosol form. This scenario also assumes that the viable pathogens are not destroyed by the heat associated with the deflagration and that they survive the shock wave as well.

Accident Sequence

In this accident scenario, the flammable gases are assumed to be available in sufficient quantities to ignite from some source; the BSC fails and releases biological material. This accident sequence consists of independent events in series that have a qualitatively determined failure rate. The significant accident events were found to be preventive and mitigative.

Preventive Features

- Generation and availability of flammable gases is limited
- BSC exhaust ventilation system operates to prevent flammable gas build-up
- During large room disinfection operations, parameters to increase LFL and prevent a deflagration are rigorously controlled (humidity, concentration)
- Ignition sources controlled during gas use or gas generation

Mitigative Features

- NBAF ventilation system operates, including HEPA filtration
- NBAF confinement intact and functional
- Flammable gas detection system in BSCs or other routine-use areas

An accident leading to the release of biological material is considered to occur if all the events in the prescribed sequence are compromised or fail. Should any one event succeed, then the accident is prevented or mitigated (see Figure E.4.1.6.1 for the event tree describing this scenario). The following sections describe the qualitative failure frequency.

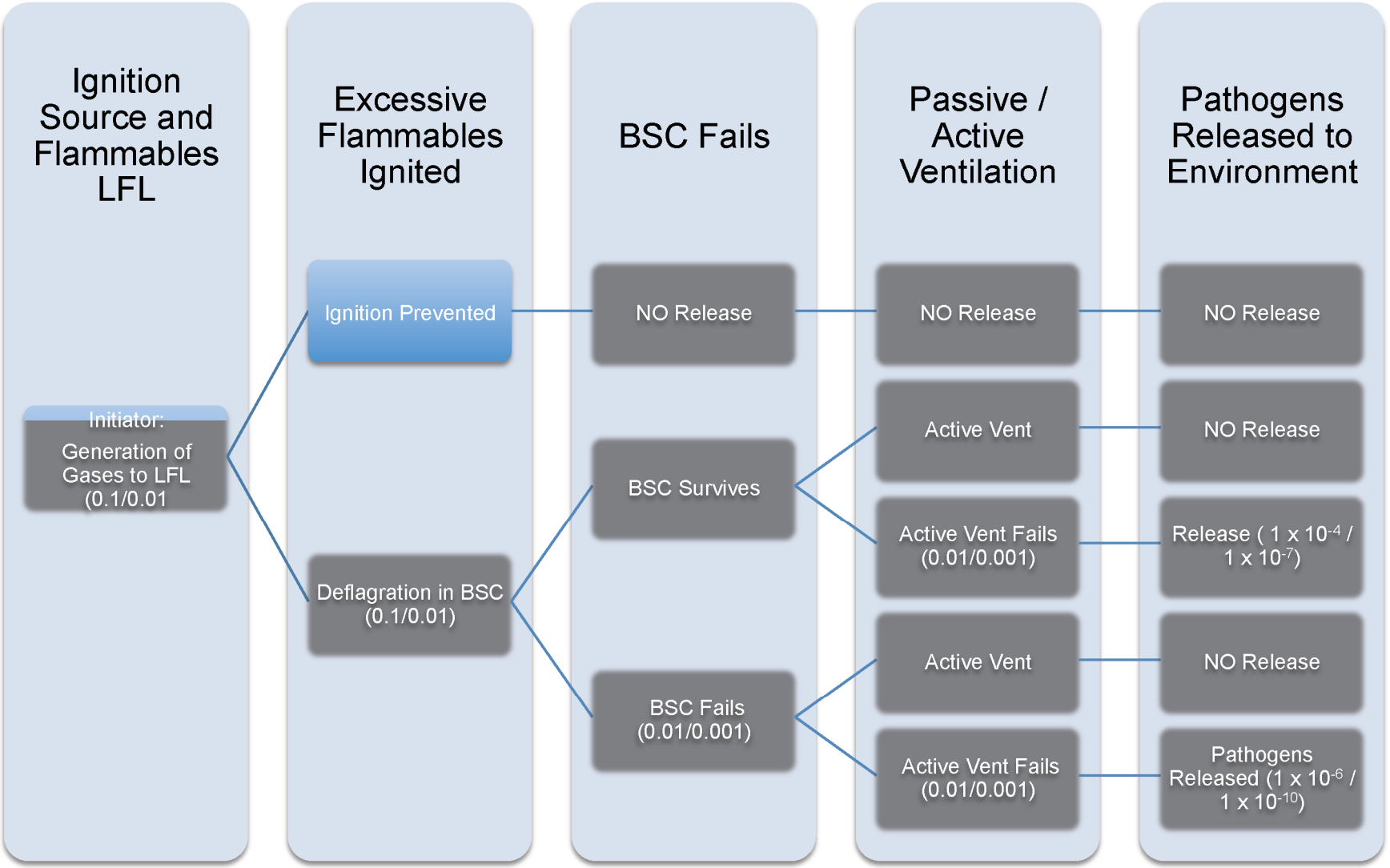


Figure E.4.1.6-1 — Deflagration with Subsequent Release of Pathogens Consequence Scenario

Excessive Flammable Gases Accumulate and Ignite Causing BSC to Fail – This particular occurrence in the event tree is a result of operator error. For the postulated scenario to occur, a laboratory worker would have to make more than a single error. The first error would be to perform activities in an environment where significant flammable gases are present (procedure violation). The second error—also in direct violation of procedure—would be the failure to ensure that safety systems and equipment were operating appropriately. In this case, failure to respond to the flammable gas detectors, failure to verify operation of the negative-pressure ventilation system in the BSC, or failure to adequately secure ignition sources would be candidates for procedure violation. The likelihood of workers failing to follow procedural controls is taken to be 0.1.

In this unmitigated scenario, two errors are made by the worker, but a single failure probability is required for the event tree. This value is conservatively estimated as the product of the two operator error failure probabilities, giving a failure probability for the event occurring of 0.01 per demand. Conservatively assuming 10 operations per year (demands) and not taking credit for the vacuum system or normal BSC ventilation to purge flammable gases, the likelihood of excessive flammable gases being generated and ignited thereby causing a BSC to fail is less than 0.1/year.

Ventilation System Operation – Once biological material escapes the BSC after a deflagration, it is assumed that it becomes airborne in the NBAF. If the ventilation is operating at the time of the release, the aerosol is carried to HEPA filters where it is collected. The probability that ventilation is operating after the event is difficult to quantify, but assuming a site electrical outage to be the most likely cause of ventilation being interrupted, a value can be assigned. Unanticipated electrical outages are infrequent, and normal operations in the facility are suspended during planned outages. Historically, outages at similar types of facilities have occurred fewer than 4 times/year and have lasted less than 2 hours per event. Given that there are 4,380 2-hour periods in a year, four periods of failure per year implies a likelihood that power will be interrupted in any given 2-hour period of 1E-3. Assuming the critical period for dispersal after the release is less than 2-hours, the frequency for ventilation shutting off during the critical period of the event is 1E-3. (Note that this frequency conservatively neglects the capability of the back-up generators to make up for the loss of off-site power.)

Confinement System Intact and Functional – The confinement system consists of the intake and exhaust HEPA filters and plenums, the duct work from the plenums to the structure, and the NBAF structural shell (including doors). The confinement system and ventilation is essential in preventing a release from the NBAF, thereby maintaining the confinement boundary.

Failure of the confinement system to function could be caused by the facility doors (especially exterior doors) not being closed or the ventilation system's HEPA filters not able to perform their function. Confinement system integrity is considered to be maintained by means of administrative procedure and verified through regular surveillance and maintenance. The unmitigated likelihood of workers failing to follow procedural controls is taken to be 0.1 based on a nominal human error probability associated with failure to follow administrative safety controls.

Conservatively assuming that components of the confinement system (door closures, HEPA filters, etc.) need to be regularly inspected to be functional, but realizing that multiple doors would need to fail open or that multiple banks of HEPA filters would need to be dysfunctional for the confinement system not to function, the frequency of confinement system failure is based primarily on the failure of the ventilation and HEPA filtration system and is estimated at ~1E-4 per demand. Considering additionally that certain accidents in the NBAF could lead to workers evacuating the building (perhaps hurriedly) and conceivably propping open the doors that would normally close on their own, a conservative frequency of confinement system failure is taken generically (independent of accident scenario) to be 1E-3 per demand.

Accident Sequence Results – Evaluation of the range of accident sequences that can result from the failure or success of each event shows that the most likely accident sequence for a flammable gas deflagration is when

the ventilation system operates and the confinement system is intact and functional. There are two unmitigated accident sequences that have a combined failure frequency falling within FC IV (improbable; Table E.2-3).

Source Term Analysis

The possibility exists that enough flammable gas could be generated at one time and be ignited inside an enclosed area or a BSC to cause a high-energy deflagration (but no sustained fire) that results in a release of biological material into the laboratory. Once present in the laboratory, the pathogens are assumed to be released from the facility as a result of collateral damage effects produced by the initial deflagration on some of the remaining facility systems. The deflagration itself may do damage to the facility in several ways; it may compromise the facility and produce a communication path to the outside, it provides energy necessary aerosolize the pathogen into a form that is easily dispersible, and it provides the mechanism for dispersing the aerosol to the environment through the deflagration pressure pulse and resulting gas transport. In addition, this analysis assumes that flash-heat from the deflagration destroys 90% of the available pathogen source term.

MAR – The MAR for this scenario involves one laboratory room and a BSC. It is assumed to also involve a 30-L volume of material from the cGMP laboratory that comprises an amount of pathogens on the order of 3×10^{12} virions.

DR – The DR is the fraction of material affected during the accident. The MAR value is assumed to be reduced by 90% as a result of exposure to the flash-heat of the deflagration. This translates into a DR of 0.1 and a reduction in the involved MAR to 3×10^{12} virions.

ARF – The ARF for dynamic stress caused by aerodynamic shock may be considerably higher than that estimated for a simple spilled container. For this reason, the ARF is taken to be 1×10^{-1} or 0.1. In addition, the RF of release fraction is taken as 1.0 for both the unmitigated and mitigated accident cases.

LPF – For the unmitigated analysis in which the aerosolized material escapes the NBAF without being filtered or otherwise mitigated by the building confinement system, the LPF is set to 1.0. For the mitigated analysis, the LPF is determined by taking into account the facility confinement system, which includes the fans, the plenum structures, the redundant HEPA filters, the facility structural shell, the entry and exit doors, etc. For a robust facility with good disciplined operations, procedures, and training; the mitigated LPF can be taken as 1×10^{-5}.

The parameters of the source term formula are summarized in Table E.4.1.6-1. The mitigated LPF calculation includes the NBAF confinement system as a credited safety barrier.

Table E.4.1.6-1 — Deflagration of Flammable Gas Event Source Term Calculation Parameters

Scenario	Source	MAR	DR	ARF	RF	LPF
Unmitigated	Pathogen aerosol	3×10^{12}	0.1	0.1	1	1
Mitigated	Pathogen aerosol	3×10^{12}	0.1	0.1	1	1×10^{-5}

Unmitigated Source Term

The unmitigated respirable source term from this accident is:

$\overline{Q} = 3\times10^{12}$ viable pathogens × 0.1 × 0.1 × 1 × 1 = 3×10^{10} virions

It is clear that this level of release from the NBAF would cause considerable environmental damage.

Mitigated Source Term

The appropriate LPF for this scenario is given as LPF = E-5 for a robust and well-maintained facility confinement system. With these values, the mitigated respirable source term is:

$\overline{Q} = 3\times10^{12}$ viable pathogens × 0.1 × 0.1× 1 × 0.00001 = 3×10^{5} virions

This level of release from the NBAF would also cause considerable environmental damage but in a range closer to the facility.

Consequence Analysis

Unmitigated Off-Site Consequences – The dose to the receptor outside of the NBAF (animal or human) is represented by the exposure due to inhalation, ingestion, direct contact, and vector pathways. Since the results of the air transport model provide time-integrated normalized air concentrations, the estimate of the exposure to pathogens in the air is simply the source term (Q) multiplied by the time-integrated normalized air concentration and the breathing rate.

Exposure = Q × BR × χ/Q × ET

Where:

Q = the source term (mitigated or unmitigated) [virions]
BR = the breathing rate [m^3/s]
χ/Q = the 95th percentile normalized distribution of pathogen in the air at the receptor location [s/m^3]

The calculated χ/Q is site specific and varies with distance from the facility. Because the unmitigated release is large, there is a greater chance for significant downwind transport of the pathogens at a concentration that would result in an exposure. The highest χ/Q value for any site at a distance of 50 m is 1.61×10^{-1} s/m^3 and is approximately 3×10^{-5} s/m^3 at a distance of 10 km. By inspection, the use of these values to estimate downwind exposure produce high values close to the facility release point and much lower values as pathogen transport is diluted by distance.

Mitigated Off-Site Consequences – Because of the contribution of the facility structure and its engineered safety barriers in mitigating the initial release, the mitigated exposure levels are 100,000 times lower than the unmitigated release.

Mitigated Risk Rank
FC IV (improbable), meaning that it is unlikely to occur during the life of the facility.

Worker consequence category is C (lost time injury or exposure; no health effects due to proper PPE use).

Public/environment consequence category is D (negligible off-site consequences much less than infectious dose).

Risk rank is 4 (no additional safety controls to prevent or mitigate the accident).

Table E.4.1.6-2 — Summary of Safety Barriers and Procedural Controls

Control	Description
Safety Barriers	The NBAF confinement system, including the NBAF structure, intake and exhaust HEPA filters, and duct work between the plenums and the structure, provides a barrier against pathogen release to the environment. Flammable gas monitors. Additional safety barriers to provide redundant containment in the event of a large release accident to include BSC, MAR containers, and compartmentalization philosophies.
Procedural Controls	• Conduct of engineering and operations consider maintenance, contamination control, PPE use, training, specialized operational procedures, etc. • Operational MAR limit (use of small quantities of pathogen in the BSCs).

Table E.4.1.6-3 — Risk Rank Summary — Overpressure from Deflagration

Scenario	Risk Rank	Accident Frequency	Consequence Severity
Unmitigated (no credit for fire suppression, flammable gas monitoring, ventilation, HEPA filtration, maintenance, or procedures)	2	FC III (1×10^{-2} to 1×10^{-4}) Probable	A/A (Public/Worker) Exceeds the MID potential to spread disease
Mitigated (facility confinement, HEPA filtration, fire suppression, flammable gas monitoring, procedures)	4	FC IV (1×10^{-4} to 1×10^{-6}) Improbable	D/D (Public/Worker) Negligible off-site consequences

E.4.2 Natural Phenomena Accidents

E.4.2.1 Earthquake

Results from the evaluation of the geology of each proposed NBAF site indicate that there are geologic formations in the vicinity of each candidate site such that seismic activity cannot be considered negligible (USGS 2008). The site-specific geologic information was considered in estimating both the likelihood of and the potential magnitude of a potential seismic event on the NBAF.

If an earthquake of sufficient magnitude did cause a breach in the facility and the HVAC and BSC systems continued to operate, much of the air in the BSL-3 and BSL-4 laboratories may continue to be exhausted

through the HEPA filters (depending on the extent of the breach). This is a result of the facility design that ensures a negative air pressure within the BSL-3 and BSL-4 laboratories compared with the other facility sections and the outside environment. Consequently, most particulate matter in the air, including microorganisms, would continue to be captured by the filters. In addition, some of the bacterial biological material is adherent to the surface of nutrient agar media necessary to keep the organisms viable. Viral cultures employ liquid nutrient media, and leakage of infectious liquid is possible. Therefore, there would be some minimal aerosol generated. After a period of time, however, laboratory staff would be able to return in appropriate PPE to decontaminate any spilled material. Similarly, a partial or complete building collapse resulting in HVAC or BSC failure such as could occur with an earthquake with a magnitude 6 or greater (annual probability of occurrence of once every 4,000 years [see Section 3.3.5]). This would have a greater potential for significant impact to the public because of the greater opportunity for animals and insects to escape and pathogens to be transported to the environment. Biological agent vulnerability to environmental conditions through bacteria death or virus inactivation, although more of an issue for spores and certain bacteria, would further reduce the potential of public exposure. An earthquake coupled with extreme environmental conditions, such as high winds, could potentially affect transport and cause more dispersal. However, these conditions would also result in substantial dilution of the biological agent.

Natural Phenomenon Accident #7 – Large, Multi-Laboratory Spill as a Result of Seismic or High Wind Natural Phenomena

This section addresses accident scenarios associated with weather-related initiating events such as floods, high winds, lightning, earthquakes, tornadoes, and hurricanes. For the purposes of this accident analysis, the effects from natural phenomena events are combined into a single bounding analysis. The current design of the NBAF defines the seismic capacity of the facility to meet a 0.19-g seismic event and a 119 mph wind (156 mph for Plum Island). While the proposed NBAF sites show a relatively low probability of a significant seismic event with a return period on the order of 50 years, Executive Order 12699 (EX Order 1990) issued in January 1990 requires high-hazard government facilities to be designed to meet or exceed seismic events with return periods of 2,500 years. All of the proposed NBAF sites fall within regions where a seismic event with a return period of 2,500 years is on the order of 0.3-g peak ground motion.

The basis for establishing the anticipated wind speeds were the International Building Code, ASCE 7 and the local jurisdictions. Because of code specified building importance modification factors and normal factors of safety incorporated into the structural design, the facility would withstand wind speeds of 119 mph at all of the sites except for Plum Island, which would withstand winds of 156 mph.

Because of the critical nature of this facility and the toxic substances contained within, building codes require this building be classified as a Category IV facility. This classification groups this facility with hospitals, fire, rescue, ambulance, police and other designated critical emergency facilities. Because of this classification, the building code specifies an Importance Factor be applied to the base wind design pressure condition. The Importance Factor is a factor (> 1.0) applied to the code specified base design wind pressures to account for the potential degree of hazard to human life and damage to property that could occur as a result of structural failure of a facility under the base design wind loading condition. For this facility the code specified Importance Factor is 1.1. The application of this factor has the effect of increasing the mean recurrence interval of the design wind speed from 50-year to 100-year.

As an additional factor of safety, to account for deviations of the actual load from the nominal load, uncertainties in the analysis that transforms the load into the forces and deformations produced in structural members by the applied loads, and for the probability that more than one extreme load will occur simultaneously, the building code specifies a Load Factor be applied to the base wind design pressures. A Load Factor of 1.6 is applied to the code specified base design wind pressures for wind loads.

Because of incorporation of the Importance Factor and Load Factor into the design, this facility will be capable of resisting 170% of the wind pressures that are expected to occur on the average only once every 50-years. In other words, the facility will be designed to resist wind loads that could be expected to occur on the average only once every 500 years.

Similar facilities such as the Centers for Disease Control and Prevention, Building 18, were designed and constructed under the same building code criteria.

> "…Section 1. Requirements for Earthquake Safety of New Federal Buildings.
> The purposes of these requirements are to reduce risks to the lives of occupants of buildings owned by the Federal Government and to persons who would be affected by the failures of Federal buildings in earthquakes, to improve the capability of essential Federal buildings to function during or after an earthquake, and to reduce earthquake losses of public buildings, all in a cost-effective manner. A building means any structure, fully or partially enclosed, used or intended for sheltering persons or property.
>
> Each Federal agency responsible for the design and construction of each new Federal building shall ensure that the building is designed and constructed in accord with appropriate seismic design and construction standards. This requirement pertains to all building projects for which development of detailed plans and specifications initiated subsequent to the issuance of the order. Seismic design and construction standards shall be adopted for agency use in accord with sections 3(a) and 4(a) of this order…"

Design and evaluation criteria for of essential facilities (e.g., hospitals, fire and police stations, centers for emergency operations) are considered as Seismic Use Group III of IBC 2000. Critical safety controls or barriers are those for which failure to perform their intended safety function poses a significant potential hazard to public health, safety, and the environment because biological materials are present and could be released from the facility as a result of that failure. In the case of the NBAF, the critical safety equipment is required to prevent or mitigate events with the potential to release significant quantities of viral pathogens outside the facility. Design considerations for these critical safety barriers are to limit facility damage as a result of design basis natural phenomena events so that hazardous materials can be controlled and confined, occupants are protected, and the functioning of the facility is not interrupted. Because the safety analyses determined that high-containment biological materials are required for worker safety, a higher design requirement designation is appropriate for the safety equipment necessary to prevent a release. Given the risks posed by the potential seismic and other natural phenomena accidents, provisions for design consideration of the facility structure and critical safety equipment should be consistent with those used for facilities designed to standards above that for the model building code requirements for essential facilities (DOE 2000; DOE 1996).

In addition, all of the proposed NBAF sites are located within regions that experience severe weather where wind speeds could exceed the 119 mph (156 mph for Plum Island) criteria specified in the Feasibility Study for the NBAF. Tornado and hurricane events are a significant potential at the proposed sites and can occur with wind speeds in excess of 150 mph (Pasquill 1983; Panofsky 1984).

In addition, other natural phenomena events have a significant potential for adversely impacting the NBAF and operations. These include lightning strikes that can result in facility fires (previously analyzed) or widespread equipment failures including loss of the active containment systems. Floods also have the potential to adversely impact the operations of the NBAF. A significant flood could produce a loss of power and result in floodwater infiltration of waste containment systems subsequently releasing pathogens to the environment.

For the purposes of this accident analysis, the seismic event was considered as the potentially bounding natural phenomena accident because the dispersion and dilution of pathogens would be much greater in a high-wind event; floods, while a potential threat, would likely result in localized consequences.

The high wind and seismic event accident analysis was developed without considering a subsequent fire in the NBAF. Facility fire was previously evaluated both in the hazards analysis and as an accident and was determined to result in significant consequences to the laboratory workers (involved and non-involved), as well as the public and the environment.

The central difference between the natural phenomena events and other accidents is that the natural phenomena events have a greater potential to impact the entire facility. Internally initiated fires require time and combustible materials to grow to a facility-wide event. A storm (tornado, hurricane, or high straight line winds) and a seismic event will act on the entire facility simultaneously. Because of the extent of the impact, the amount of infectious biological material (and chemicals or radioactive substances) available for release is greater.

The assumed accident progression begins when the NBAF experiences a significant natural phenomena event. In the situation of a major storm, there is the potential that actions can be taken in advance to containerize infectious materials prior to the storm occurring. This is not possible with a seismic event where there is no warning system available. For purposes of estimating potential consequences, either event is conservatively assumed to occur when the facility is in normal operational mode.

The biological material (MAR) considered in this accident scenario was on the order of 1×10^{15} virions considering the entire NBAF is at risk with maximum volumes of viable pathogens in all available areas. The single maximum volume considered is the 30 L cGMP. The release fraction is taken to be 1×10^{-1}, and the unmitigated source term is estimated at 1×10^{11} virions released from the facility.

Unmitigated Risk Rank

For the unmitigated accident conditions, it is assumed that more than sufficient viral pathogens could be released for transport in the environment. Based on the overall accident scenario and the various sequences, the unmitigated frequency for this accident is assigned a FC IV improbable.

Public/environment consequence category is A (high likelihood for environmental life-threatening effects); off-site consequences are much greater than minimum infectious dose.

Risk Rank is 2 (additional safety controls required to prevent or mitigate the accident).

Mitigated Risk Rank

FC V (remote) should not occur during the life of the facility.

Worker consequences category is D (lost time injury or exposure; no health effects due to proper PPE use).

Public/environment consequence category is E (negligible off-site consequences much less than infectious dose).

Risk Rank is 4 (no additional safety controls to prevent or mitigate the accident).

Using Table E.3-4, Public/Worker Risk Ranking, the combination of the accident likelihood of FC IV and consequence severity of D/C (public/worker), the assigned risk rank is 4 indicating that the robust safety

controls considered are sufficient to prevent or mitigate the accident and greatly reduce the risk. The overall risk summary is presented in the following table.

Table E.4.2.1-1 — Risk Rank Summary – NPH Event (Seismic)

Scenario	Risk Rank	Accident Frequency	Consequence Severity
Unmitigated (No credit for NBAF structure, ventilation HEPAs)	2	FC IV (1×10-4 to 1×10-6) Occasional	A/A (Public/Worker) Exceeds the MID
Mitigated (NBAF structure, ventilation HEPAs)	4	FC V (≤1×10-6) Remote	E/D (Public/Worker) Negligible off-site consequences

The NBAF designed to earthquake criteria of 0.19-g would be expected to catastrophically fail in a 0.3-g magnitude earthquake.

In addition, all of the proposed NBAF sites are located within regions that experience high winds greater than 119 mph. Tornado or hurricane events are a significant potential at the proposed sites and occur with wind speeds in excess of 150 mph. Under these conditions, the currently proposed NBAF would catastrophically fail if designed to the proposed criteria of 119 mph except for Plum Island, which would withstand winds of 156 mph.

In addition, other natural phenomena events have a significant potential for adversely impacting the NBAF and operations. These include lightning strikes that can result in facility fires (previously analyzed) or widespread equipment failures including loss of the active confinement systems. Floods also have the potential to adversely impact the operations of the NBAF. A significant flood could produce a loss of power and result in floodwater infiltration of waste containment systems subsequently releasing pathogens to the environment.

For the purposes of this accident analysis, the combined high-wind or seismic event was considered as the potentially bounding natural phenomena accident.

Large, multi-laboratory spill as the result of a seismic or high-wind event without an accompanying fire

The high-wind and seismic event accident analysis was developed without considering a subsequent fire in the NBAF. Facility fire was previously evaluated both in the hazards analysis and as an accident and was determined to result in significant consequences to the laboratory workers (involved and non-involved), as well as the public and the environment.

The central difference between the natural phenomena events and other accidents is that the natural phenomena events have a greater potential to impact the entire facility. Internally initiated fires require time and combustible materials to grow to a facility-wide event. A storm (tornado, hurricane, or high straight line winds) and a seismic event will act on the entire facility simultaneously. Because of the extent of the impact, the amount of infectious biological material (and chemicals or radioactive substances) available for release is greater.

The assumed accident progression begins when the NBAF experiences a significant natural phenomena event. In the situation of a major storm, there is the potential that actions can be taken in advance to containerize infectious materials prior to the storm occurring. This is not possible with a seismic event where there is no warning system available. For purposes of estimating potential consequences, either event is conservatively assumed to occur when the facility is in normal operational mode.

Accident Sequence

The accident is defined as the NBAF experiencing a significant seismic (with a peak ground acceleration in excess of 0.3 g) or weather (high winds in excess of 150 mph) event with the subsequent release of biological material from occurring. The seismic event has substantial energy to affect the facility structure and systems or components inside. There is, however, little energy to provide a mechanism for transport of pathogens outside of the facility. In the case of a high-wind event, there is energy to both affect the facility structure and to provide the mechanism to transport the pathogen into the environment. In both cases, the total amount of infectious agents released into the environment would be significant.

In this accident scenario, the operability of the protective systems available to mitigate or prevent a release is dependent on the design and construction of the facility. For this accident scenario, the base case is the conceptual design provided in the Feasibility Study. For the unmitigated case, the structure and safety systems are assumed to fail catastrophically in either the high-wind or the seismic event.

Preventive Features (preventing the release, not the accident)

- Robust storage containers (BSCs, containers, cabinets, etc.) seismically anchored and resistant to mechanical insults

Mitigative Features

- Facility structure
- Ventilation and confinement systems
- Working inventory is minimized

An accident leading to the release of biological material is considered to occur if all the events in the prescribed sequence are compromised or fail. Should any one event succeed, the accident is prevented or mitigated. The following sections describe the qualitative failure frequency.

Seismic or Wind Event Occurs – Because the initiating event is a natural phenomena event, the occurrence frequency is taken to be 1.0 for purposes of the accident scenario development. In reality, the likelihood of a significant seismic or high-wind event directly impacting the facility is relatively low over the life of the facility.

Facility Structure Resists Seismic or High-Wind Event – Given the current design specification for the NBAF, the likelihood that the structure would resist the event is low. A 0.3-g seismic event (required to be evaluated for high hazard facilities) would catastrophically impact the facility, and a seismic event at 0.24-g seismic event (required to be analyzed for moderate hazard facilities) would suffer significant degradation with large cracks with significant spalling and likely loss of most of the safety systems inside the facility.

Active Ventilation Operates – Because the structure would not survive the forces associated with either the high-wind or the seismic event, it is extremely unlikely ($<1\times10^{-5}$) that power would be maintained and the fans would continue to ensure a pressure difference across the confinement barriers.

Passive Confinement System Intact and Functional – The confinement system consists of the intake and exhaust HEPA filters and plenums, the duct work from the plenums to the structure, and the NBAF structural shell (including doors). The confinement system and ventilation is essential in preventing a release from the NBAF, thereby maintaining the confinement boundary. However, under the stresses imposed from the postulated accident, there is little chance that the duct work would survive and the integrity of the confinement seals would not be maintained.

Accident Sequence Results – Evaluation of the range of accident sequences that can result from the failure or success of each event shows that the most likely accident sequence for a release of pathogens from a natural phenomena event ranges on the low side of no release (for a high-wind ≤90 mph or a seismic event with a peak ground acceleration <0.2 g) to catastrophic failure and a total release of pathogens for a significant seismic or high-wind event.

Source Term Analysis

The possibility exists that either a high-wind or significant seismic event could occur resulting in the release of pathogen from the facility.

MAR – The MAR is the same for this scenario is assumed to be a significant number of viable pathogens on the order of 1×10^{20} (or greater) that could be available for release in either of the proposed natural phenomena events.

The source of pathogen would include the cGMP facility considered for operation in the NBAF that is capable of processing tens of liters of pathogen-rich solution. In addition, the NBAF also houses the inventory of infected animals as discussed in previous accident scenarios.

DR – The DR is the fraction of material affected during the accident. All of the MAR in the facility is affected by the natural phenomena event, so the DR is set equal to 1.0.

ARF – The ARF for dynamic stress caused by shock associated with a seismic event is far less significant that the forces associated with a high-wind event when considering release and transport of the pathogens. The ARF for the seismic event may be equivalent to than that estimated for a spill or 1×10^{-4}. The ARF for the high-wind event is estimated to 1.0, which is the ARF for material in the form of an aerosol. The RF of the ARF is taken as 1.0 for both the unmitigated and mitigated accident cases.

LPF – For the unmitigated analysis in which the aerosolized material escapes the NBAF without being filtered or otherwise mitigated by the building confinement system, the LPF is set to 1.0. For the mitigated analysis, the LPF is also set to unity based on the current conceptual design specifications.

The parameters of the source term formula are summarized in Table 3.14.3.2-1. The unmitigated consequence calculation shows the need for improved safety controls over what was identified in the Feasibility Study. The mitigated LPF calculation includes the NBAF confinement system as a credited safety control. This includes the NBAF structure, intake and exhaust HEPA filters, and duct work between the plenums and the structure.

Table E.4.2.1-2 — Seismic or High-Wind Natural Phenomena Events Source Term Calculation Parameters

Scenario	Source	MAR	DR	ARF	RF	LPF
Unmitigated – Seismic	Solutions of biological materials	1×10^{20}	1	1×10^{-4}	1	1
Unmitigated – High Wind	Solutions of biological materials	1×10^{20}	1	1	1	1
Mitigated – Seismic	Solutions of biological materials	1×10^{20}	1	1×10^{-4}	1	1
Mitigated – High Wind	Solutions of biological materials	1×10^{20}	1	1	1	1

Unmitigated Source Term

Therefore, the unmitigated respirable source terms from this accidents are:

$\overline{Q}$ = 1×10^{20} viable pathogens × 1 × 1×10^{-4} × 1 = 1×10^{16} virions (seismic)

$\overline{Q}$ = 1×10^{20} viable pathogens × 1 × 1 × 1 = 1×10^{20} virions (high wind)

It is clear that this level of release from the NBAF would cause considerable environmental damage.

Mitigated Source Term

The facility structure and safety systems are not adequate to prevent or mitigate the release of either of these postulated accidents.

Consequence Analysis

Unmitigated Off-Site Consequences – The dose to a receptor outside of the NBAF (animal or human) is represented by the exposure due to inhalation pathway. Once the pathogens are in the environment, however, all pathways are available for transmission. The exposure time is considered to be approximately 1 hour (3,600 seconds) for situations where there is a release of biological materials to the environment, and the typical breathing rate for humans is taken to be 3×10^{-4} m^3/s (the breathing rate for pigs or cows is significantly different, where cows breathing rate is approximately 6 m^3/hour or 1.6×10^{-3} m^3/s and a pig would be approximately the same as a human).

$$\text{Exposure} = Q \times BR \times \chi/Q \times ET$$

Where:

Q = source term calculated from the five-factor formula (mitigated or unmitigated) [virions]
BR = breathing rate [m^3/s]
χ/Q = the 95th percentile normalized distribution of pathogen in the air at the receptor location [s/m^3]

The calculated χ/Q is site specific and varies with distance from the facility. Because the unmitigated release is large, there is a greater chance for significant downwind transport of the pathogens in a concentration that would result in an exposure. The highest χ/Q value for any site at a distance of 50 m (approximate NBAF fence line) is 1.61×10^{-1} s/m^3 and is approximately 3×10^{-5} s/m^3 at a distance of 10 km. Using these values to

determine exposure results in a total inhalation of approximately 2×10^{15} virions/m^3 at 50 m and 3×10^{11} virions/m^3 at 10 km for the seismic event, the high-wind event will result in 1×10^4 more virions. At these exposure levels there is significant potential for widespread infection in the environment.

Mitigated Off-Site Consequences – Under these proposed conditions, there is no mitigated consequence estimates.

Comparison to MID of 10 Virions – The unmitigated and mitigated consequence or dose to the receptor was conservatively based on a loss of function of the current design of the facility structure and the confinement and containment systems. This mitigated accident is not able to mitigate or prevent the release and exposure of pathogen to the environment.

Table E.4.2.1-3 — Summary of Safety Barriers and Procedural Controls

Control	Description
Safety Barriers	The NBAF confinement system, including the NBAF structure, intake and exhaust HEPA filters, and duct work between the plenums and the structure, provides a barrier against pathogen release to the environment. Additional safety barriers to provide redundant containment in the event of a large release accident to include BSC, MAR containers, compartmentalization philosophies.
Procedural Controls	Conduct of engineering and operations consider maintenance, contamination control, PPE use, training, specialized operational procedures, etc. Operational MAR limit (use of small quantities of pathogen in all operations).

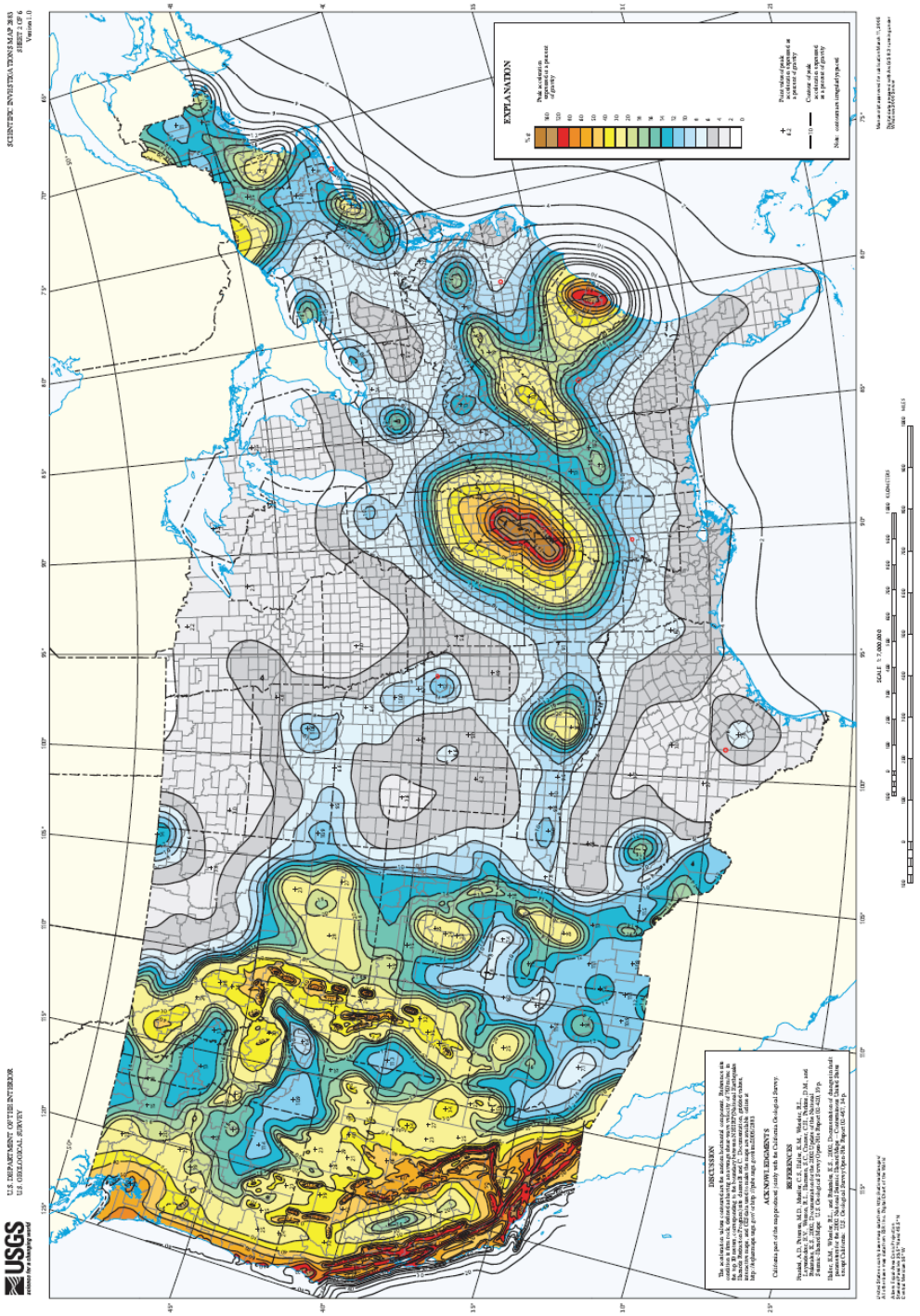


Figure E.4.2.1-1 — USGS Seismic Hazard Curves for Lower 48 States

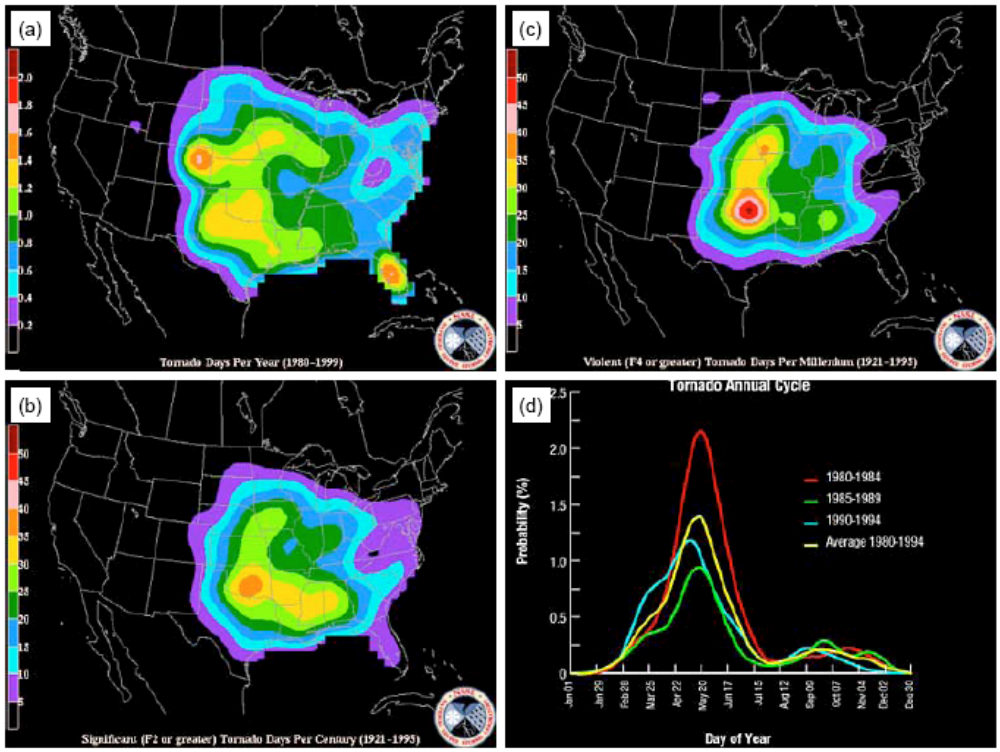
Seismic Events

The USGS provides *Seismic-Hazard Maps for the Conterminous United States* showing peak ground acceleration with 2% probability of exceedance in 50 years. The locations of the proposed NBAF sites correspond to peak ground accelerations between 0.08 g and 0.14 g based on the USGS seismic hazard maps. All of the sites fall within regions where there is a small probability ($<1\times10^{-4}$) that seismic events with peak ground accelerations can exceed 0.2 g. Based on the USGS maps, the likelihood of a seismic event that could catastrophically fail the NBAF, for the unmitigated conditions, was assigned to the FC IV (improbable with a range of 1×10^{-4} to 1×10^{-6}). With appropriate design, the NBAF could be made to withstand the less likely, yet much higher ground accelerations associated with, large-magnitude earthquakes. The mitigated frequency considered the reduction in seismic event frequency for larger earthquakes and assigned a value of FC V or remote ($<1\times10^{-6}$).

Tornados and high-wind events can produce great damage to facilities. An F-3 tornado (Fujita scale) can have fastest quarter-mile wind speeds in the range of 158 to 207 mph and 3-s gusts in the range of 162 to 209 mph (NOAA). An F-3 tornado on this scale can have fastest quarter-mile wind speeds in the range of 158 to 207 mph and 3-s gusts in the range of 162 to 209 mph (NOAA). Since the conceptual design of the NBAF is currently identified for 119 mph winds (156 mph for Plum Island), it is credible to estimate unmitigated consequences associated with catastrophic failure of the NBAF structure. Data obtained from the National Oceanic and Atmospheric Administration's Web site provided information on the likelihood of tornados in the region of the proposed NBAF sites (http://www.nssl.noaa.gov/primer/tornado/tor_hazardgraph.html).

Understanding the Threat Posed by Tornadoes

A recent NSSL study, using data from 1921 to 1995, estimated the daily climatological probability of an F2 or greater tornado occurring near any location in the U.S. For this work developing highly accurate and accessible estimates of the long-term threat from thunderstorms, winds, and large hail as well as tornadoes, an NSSL scientist was awarded a Department of Commerce Silver Medal.



a. **Probability of Any Tornado**:
The map shows the average number of days per year any tornado, no matter how strong or weak, might occur within 25 miles of a point. The highest numbers indicate where at least one tornado might occur somewhere within 25 miles as often as on 1.5 days per year.

b. **Significant Tornado (F2 or greater)**:
Now we're looking at days per century. In other words, central Oklahomans can expect an F2 or greater tornado within 25 miles about every 3 years.

c. **Violent Tornado (F4 or greater):**
Now the scale is days per millennium, meaning that southcentral Oklahoma may have a violent tornado within 25 miles about once every 20 years.

d. **Annual Cycle:**
Residents of Norman, OK experience a distinct tornado season, beginning late February and peaking late May. Even though we are in the heart of tornado alley and can expect one- to one-and one-half tornado days per year, our chances on any particular day peak at only about two percent.

Figure E.4.2.1-2 — Maps of Tornado Probability in the U.S.

Wind-Generated Missiles

Representing possible missiles that could be borne to the site by tornado or high-wind, wind-generated missiles were assumed to be the following:

A light-weight, high-velocity missile (wood plank, 2 inches thick by 12 inches wide by 12 feet long, weighing 80 lb) was selected for its penetrating effect. This missile was assumed to travel end on, hitting a wall at any elevation with a speed of 155 mph or greater, or hitting a roof with a speed of 103 mph.

A massive, low-velocity missile (compact passenger auto weighing 2,000 lb) was selected for crushing effect. This missile was assumed to travel at 75 mph, impacting more than 15 ft^2 on any wall at an elevation not higher than 25 feet above grade.

These missiles were selected according to the size of a potential tornado. Based on formulae for vertical wind velocity and drag forces on objects, the 2-inch-thick plank must be injected to an altitude of ~25 feet before this will happen. Injection can be the result of the explosion of an unvented structure or by a high rebound of the plank tumbling along the ground. By either method, 25 feet would be a realistic approximation of the obtainable injection height. On this basis, the 2-inch-thick plank was selected as one of the missiles to be considered. If a heavier plank (such as 4 inch by 12 inch by 12 feet long) was considered, the required injection height would be ~65 feet. It was judged very unlikely that the heavier plank could become airborne to an elevation in which it would be subjected to the higher velocity winds.
Likewise, it was judged that the 2,000-lb compact auto could never be injected to a sufficient height for the vertical wind currents to carry it aloft into the higher velocity winds. Instead, the compact auto will tumble along the ground surface subjected to comparatively low-wind velocities. For missile analysis, a conservative approximation of ground-level wind velocities is two-thirds the maximum wind velocities. In calculating missile velocity, the following assumptions were made:

Radial wind velocity was assumed to be defined by the following formula:

$$V_r = \left[\frac{r_{75} - r}{r_{75} - R}\right] r$$

Where:

Vr = Radial wind velocity
r_{75} = Radius to 75-mph tangential wind
r = Radius to point of consideration
R = Radius to maximum tangential wind

The 2-inch-thick plank was assumed to have been aerodynamically lifted into the wind field and remained lifted until ejected. The 2,000-lb compact auto was assumed to have tumbled at ground level and to have been subjected to two-thirds the maximum wind velocities until ejected. Random tumbling was assumed with equal angular speeds about the orthogonal axis. The drag force was calculated as follows:

$Fd = 6\times10^{-4}\ (WV^2)\ (h + d)$ (for parallel piped)

Fd = 3.6 • 10–4 (DV2) (h – 0.66D) (for right circular cylinder)

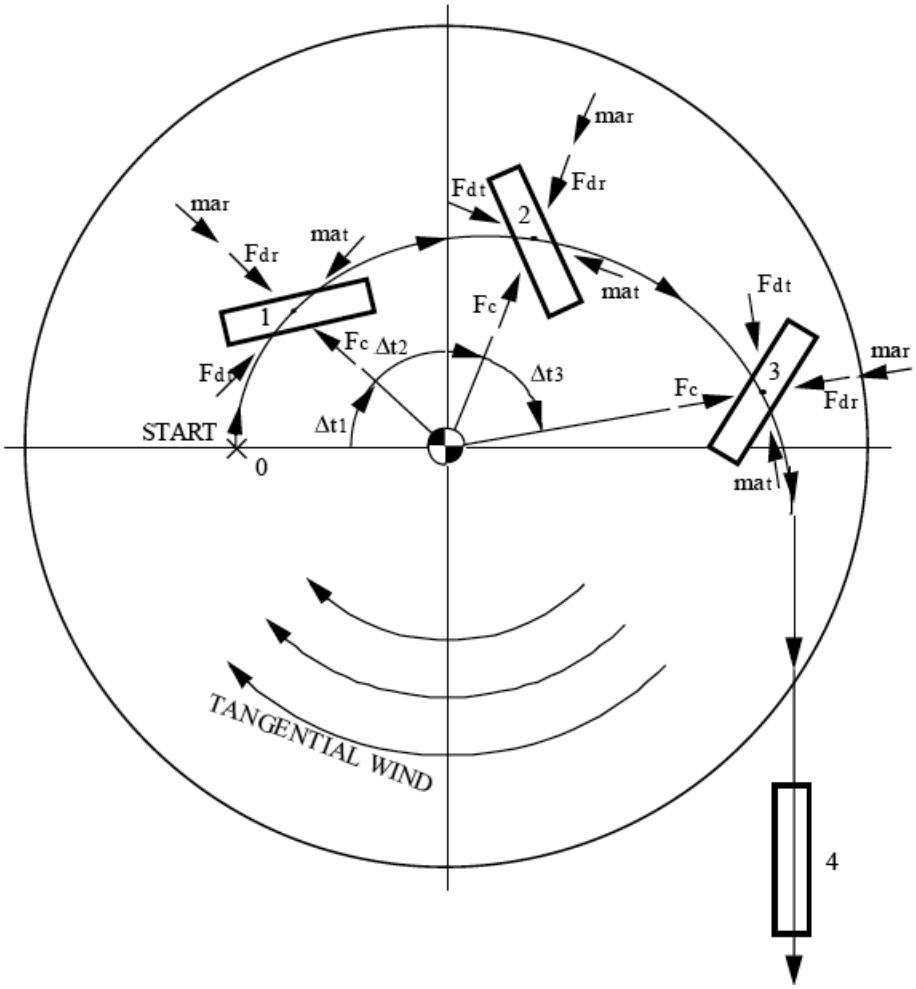
Where:

Fd = Drag force in pound(s)
W = Width in feet
h = Length in feet

d = Depth in feet
D = Diameter in feet
V = Velocity in feet per second

The method used to calculate missile velocity follows.

With reference to the illustration below, the forces acting on the object in the horizontal plane were:
Fdt = Tangential wind drag force
Fdr = Radial wind drag force
Fc = Centrifugal force
ma = Force resisting velocity change



The missile was assumed to have started from some point within the wind at a 30-feet radius. Wind drag forces were calculated on the missile based on the wind velocities at this location. Then, for a small time increment (0.2 s), the missile was allowed to accelerate and the new missile position and velocity were calculated. New drag forces were then calculated that considered the new missile position and velocity. The missile was assumed to have accelerated for another small time increment and the next missile position and velocity was calculated. This procedure was repeated many times, allowing the missile to gain speed and follow a somewhat spiral path within the wind. The missile was assumed to have left the wind when it reached a maximum speed that equaled or exceeded the wind velocity associated with the missile's position.

The 30-mph wind-translation speed was then added directly to the calculated missile speed at the instant it left the wind. The missile then traveled to its impact point without drag forces or lost velocity.

In the design for missile impact, minor damage to the structure such as inner face scabbing or cracking of the concrete was considered acceptable, provided that secondary missiles generated within the structure were not damaging equipment or otherwise endangering the facility, and the ability to contain radioactive materials within the facility was not impaired. The modified Petry impact formula was used to determine the penetration depth of the missile impact because it produced the most conservative design. It was used to determine the minimum concrete thickness to prevent high-velocity missile penetration. The impact formula used was as follows:

$$D = K * Ap * V'$$

Where:

D = Depth of penetration in concrete slab of thickness 3D or greater
K = Coefficient for penetration obtained by experiment to be 0.0051 for 3,000 psi concrete and 0.0039 for 4,000 psi concrete
A_p = Sectional pressure obtained by dividing missile weight by contact area V' = where V is the terminal velocity (ft/s)
$V' = \text{Log}_{10}[1 - V^2 / 215{,}000]$

The minimum thickness to eliminate complete penetration was taken as 2D. The minimum thickness to eliminate scabbing was taken as 3D.

The thickness of the wall and roof sections was determined by dynamic shear loading from the missile impact rather than the resistance to missile penetration. The calculated wall thickness needed to resist penetration of the 2-inch by 12-inch by 12-feet plank was 6 inches. However, the calculated wall thickness needed to resist a shear failure caused by a missile impact close to the wall panel support was much more. The required wall thickness needed to resist this loading was determined using elastic design indices as presented in the Department of the Army Technical Manual TM5-855-1, *Fundamentals of Protective Design* (ref. 5) for the appropriate damage levels.

The load impulse for the determination of dynamic moment and shear in the walls and roof was calculated by the energy method as follows:

The kinetic energy of the missile:

$$E = 1/2(mV^2)$$

The effective dynamic force:

$$F = E/D$$

The duration of the impact load:

$$t = 2D/V$$

Where:

m = mass of the missile ($lb/ft/s^2$)
V = missile impact velocity (ft/s)
D = missile stopping distance (ft)

The high-velocity missile (2-inch by 12-inch by 12-feet plank) was selected for its penetrating effect and was conservatively assumed to be non-deforming. Therefore, when considering this missile, the distance D in the above formulae (3 and 4) corresponded to the concrete penetration as determined by the modified Petry formula. The massive, low-velocity missile was selected for its crushing effect on the structure. The missile itself was assumed to deform on impact. The amount of assumed deformation corresponded to the distance D. The assumed deformation was based on a conservative estimate of automobile shortening or crushing on impact at 60 to 70 mph. This deformation was assumed to be 3 feet. This estimate was based on research work involving auto-to-barrier crashes at 30 mph. Based on these results, the proposed NBAF conceptual design is not expected to resist the effects of wind-blown missiles.

E.4.3 External Accidents

The potential adverse effects to the NBAF from external events such as transportation accidents, aircraft crash incidents, wildfires, or other occurrences other than natural phenomena can range from almost no effect to possible catastrophic results. A wide range of external events was considered in the hazards evaluation, and the aircraft crash was selected as the bounding scenario for which to perform detailed calculations of likelihood and consequences.

E.4.3.1 Aircraft Crash Accident

In addition to the operational scenarios evaluated to assess the potential for inadvertent release of biological material into the environment, a scenario involving an aircraft crash into the facility was also considered. The scenario involves the potential for material release given that a small aircraft crashes into the facility. Penetration of the engine into one of the main laboratory areas occurs and the ventilation system is compromised. Any material outside of secure storage (e.g., freezer, transport packaging) is considered susceptible to the impact and available for release. Incubators provide a small measure of protection; however, the biological materials in incubators are maintained in an active growth state through the presence of nutrient media and the temperature-controlled atmosphere. Major damage to the incubators could result in a release; however, if a fire were to ensue, viability of the organisms would likely decrease. Aircraft crash scenarios are based on a jet aircraft of the size and configuration as those that commonly take off and land at smaller airports in the vicinity of the proposed NBAF sites. Although these accidents would likely result in penetration of the facility, the most serious hazard is the potential for a significant release of viable pathogens to the environment. The aircraft crash with a coincident fuel fire may result in a smaller quantity of pathogens released as a result of the significant heat associated with the fire destroying a portion of the pathogen source term. A crash into the facility without a subsequent fire would result in a potential release of biological material on the order of that modeled for large operational spills. The aircraft crash accident scenario was specifically modeled for the proposed NBAF.

Fundamentals of Determining Aircraft Crash Frequency

The aircraft crash impact frequency for the NBAF was estimated using the four-factor formula described in U.S. DOE Standard (STD) 3014-96 (DOE 2006a). This formula considers: 1) the number of aircraft operations; 2) the probability that an aircraft will crash; 3) the probability that, given a crash, the aircraft crashes into an one-square-mile area where the facility of interest is located; and 4) the size of the facility. The formula from DOE-STD-3014-96 is:

$$F = \sum_{i,j,k} N_{ijk} \cdot P_{ijk} \cdot f_{ijk}(x, y) \cdot A_{ij}$$

Where:

F = estimated annual aircraft crash impact frequency for the facility of interest (number/year)

N_{ijk} = annual number of site-specific airport operations (i.e., takeoffs, landings, in flights) for each applicable summation parameter (number/year)

P_{ijk} = aircraft crash rate per takeoff or landing for near-airport phases and per flight for the in-flight (non-airport) phase of operation for each applicable summation parameter

f_{ijk} (x,y) = aircraft crash location conditional probability (per square mile) given a crash evaluated at the facility location for each applicable summation parameter

A_{ij} = site-specific effective area for the facility of interest that includes skid and fly-in effective areas (square miles) for each applicable summation parameter, aircraft category or subcategory, and flight phase for military aviation

i = (index for flight phases): i = 1, 2, and 3 (takeoff, in flight, and landing)

j = (index for aircraft category or subcategory): j = 1, 2,…, 11

k = (index for flight source): k = 1, 2,…, k (there could be multiple runways and non-airport operations)

$\Sigma = \Sigma_i \Sigma_j \Sigma_k$

ijk = site-specific summation over flight phase: i; aircraft category or subcategory: j; and flight source: k

The NBAF is modeled as a single structure, although the facility consists of an irregular shaped building. The overall rectangular area in which the building's footprint resides determined the facility dimensions used in this evaluation. The dimensions used are 1,000 feet by 500 feet by 30 feet high. The height of the facility is assumed based on the information provided in the Feasibility Study Report and does not consider the height of the mechanical areas. The results of the aircraft crash frequency analysis and a discussion of how the four-factor formula was applied to the NBAF follow.

Potential Aircraft Crash Frequencies

Table E.4.3.1-1 presents an estimate of the annual aircraft impact frequency for airport and non-airport operations, along with the aircraft crash probability for the NBAF. These frequencies are calculated in Table E.4.3.1-3 for airport operations using the four-factor formula discussed above and in Table E.4.3.1-4 for non-airport operations. The frequency of potential aircraft crashes for this representative site indicates the need to perform penetration analyses and was therefore the basis for including the aircraft accident in the risk assessment.

Table E.4.3.1-1 — Estimated Annual Aircraft Impact Frequency for Proposed NBAF

Type of Crash	Aircraft Operation	Aircraft Crash Frequency (per year)
Airport (take-offs and landings)	Commercial aviation (air taxi), general aviation, and helicopter	1.8×10^{-4}
Non-airport (over-flights)	Commercial aviation (air carrier and taxi), general aviation, and military aviation (large and small aircraft)	1.7×10^{-4}
Total Aircraft Crash Frequency		**3.5×10^{-4}**

Impact Frequency from Airport Operations

This section describes how the annual aircraft impact frequency during takeoff and landing operations at a typical small airport close the proposed NBAF would be calculated due to airport operations (i.e., takeoffs and landings). Because there are numerous airports within 50 km to each of the proposed NBAF sites, this calculation was developed to represent the nominal aircraft crash probability independent of the selected site. The DOE standard considers both local and iterant operations as stated below:

> "…Local airport operations are flights in which the aircraft flies to a nearby airport or performs simulated approaches to the airport. Also classified as local operations are those which include aircraft that (1) operate in the local traffic pattern or within sight of the airport, (2) are known to be departing for or arriving from practice areas located within a 22-mile radius of the airport, or (3) execute simulated instrument approaches or low passes at the airport. All other airport operations are classified as itinerant operations. Itinerant operations are basically flights which land at the airport after a trip from somewhere else, or take off from the airport for a trip elsewhere. For both itinerant and local airport operations, each takeoff, landing, or approach without landing is an operation…"

The aircraft crash frequency analysis also includes helicopter flights in its scope. According to DOE-STD-3014-96, helicopters flying over a facility pose a hazard to the facility that must be considered when applicable. Helicopter operations occur at the representative airport were therefore considered in this analysis.

Impact Frequency

The aircraft impact frequency per year for airport operations is determined by multiplying the number of operations, the conditional crash probability, the crash probability, and the effective area of the facility as described in the four-factor formula presented previously. How the four input parameters are determined are discussed below.

Annual Number of Site-Specific Airport Operations

Data for numbers of aircraft operations at several airports were obtained from the U.S. Department of Transportation Federal Aviation Administration's Airport Master Record for the airports close to the proposed NBAF sites. The representative airport chosen for estimating aircraft crash frequencies was the Manhattan Regional Airport near Manhattan, Kansas. This airport is nearly 10 km (6.2 miles) from the site of the proposed NBAF. The latest traffic information for commercial air taxis cites 4,208 total takeoffs and landings per year. General aviation traffic consists of a total of 9,011 takeoffs and landings per year (i.e.,

9,011 takeoffs and 9,011 landings). Finally, helicopter traffic involves 100 operations per year. Airport information provided by GCR & Associates, Inc. is accessible via their Web site at http://gcr1.com/5010web/. The effective date for the data used was December 31, 2006.

Aircraft Crash Rate per Takeoff or Landing

The takeoff and landing crash rates for each type of aircraft listed in Table E.4.3.1-3 are taken from Table B-1 of DOE-STD-3014-96. This table lists the probability that a given type of aircraft will crash upon takeoff or landing.

Table E.4.3.1-4 provides a summary of the aircraft crash frequency for the facility for each type of aircraft operation. The table is further broken down into airport type crashes (i.e., crashes during takeoff or landing operations) and non-airport type crashes (i.e., aircraft crashes associated with over-flights). The bottom of the summary table sums the aircraft crash frequency for each type of aircraft to give an overall aircraft impact frequency for the NBAF.

Aircraft Crash Location Conditional Probability

Table E.4.3.1-3 lists the orthonormal distance (Cartesian distance in miles, both x and y coordinates) from the airport runway to the NBAF. The origin of the coordinate system is at the center of the runway. The x-axis coincides with the extended runway centerline; the positive direction is the direction of flight. The y-axis is perpendicular to the x-axis with the positive direction created by a 90-degree counterclockwise rotation of the positive x-axis. The orthonormal distances are estimated using the map and distance features in Google Earth Pro for the distance to the NBAF.

Airplanes

From the orthonormal distance, the generic aircraft crash location probability was determined using Tables B-2 through B-13 in DOE-STD-3014-96. These tables list the probability that, given a crash upon takeoff or landing of a specific type of aircraft, the crash will occur in the 1 square-mile area where the facility of interest is located.

Helicopters

For helicopters, DOE-STD-3014-96 defines the impact frequency as:

$$F_H = N_H \cdot P_H \cdot \frac{2}{L_H} \cdot A_H$$

The term F_H is the helicopter impact frequency, N_H the expected number of local helicopter over-flights per year, P_H the probability of a helicopter crash per flight, and A_H the effective area. Note that f(x,y) is replaced with $2/L_H$ where L_H is the average length, in miles, of a helicopter flight. For this calculation, the lateral variations in crash locations for a helicopter are assumed to be one-quarter of a mile from the centerline of its flight path. Since the crash frequency increases or decreases dramatically with a change in flight length, to be conservative, the length of flight is set at one-quarter of a mile less than the distance from the airport to the NBAF. This is the most conservative length of flight that is still considered to have the ability to impact the facility.

Site-Specific Effective Area

Table E.4.3.1-2 lists the effective area for the facility of interest used in the four-factor formula to determine the impact frequency of aircraft. In calculating the effective area, the following assumptions were made: 1) an aircraft can crash into the facility either by skidding or by flying directly into it and 2) an aircraft skids or flies into the facility in the direction that produces the largest area, i.e., the crash occurs in a direction perpendicular to the largest diagonal of the facility. The effective area of the facility, therefore, depends on the type of aircraft and the actual dimensions of the facility.

Aircraft Characteristics: The facility's effective area depends on multiple factors. Among these factors, aircraft characteristics play a very important role. The wingspan dictates how close the aircraft can come to the facility and still impact it. The angle of an impact is also specific to the type of aircraft is involved in the accident. In this analysis, the cotangent of the impact angle is used in the calculation. The skid-distance is also specific to the type of aircraft involved, as well as the airspeed of the aircraft. Values that characterize the types of aircraft examined are given in Appendix B to DOE-STD-3014-96 (Tables B-16, B-17, and B-18). These values are used in Table E.4.3.1-2 to determine the effective area for the NBAF.

Facility Dimensions: Another important factor that affects the size of an effective area of the facility is the facility's actual external dimensions. The facility's dimensions, i.e., the height, width, and length, are input into Table E.4.3.1-2. The length and width are used to calculate the length of the diagonal of the facility:

$$R = \sqrt{L^2 + W^2}$$

Where:

R = diagonal length of facility

L = length of facility, facility specific

W = width of facility, facility specific

Each of these parameters is then used to calculate the effective fly-in area (A_f) and the effective skid area (A_s) for the facility according to the following formulas from Appendix B to DOE-STD-3014-96:

$$A_f = (WS + R) \cdot H \cot\phi + \frac{2 \cdot L \cdot W \cdot WS}{R} + L \cdot W$$

and

$$A_s = (WS + R) \cdot S$$

Where:

WS = aircraft wingspan (provided in Table B-16 of DOE-STD-3014-96)

H = facility height, facility specific

$\cot\phi$ = mean of the cotangent of the aircraft impact angle (Table B-17)

S = aircraft skid distance (mean value) (Table B-18)

These two areas are then summed to determine the effective area of the facility (A_{eff}):

$$A_{eff} = A_f + A_s$$

Impact Frequency From Non-Airport Operations

Although typically small, the impact frequency contribution from non-airport operations cannot be overlooked when following the DOE-STD-3014-96 methodology. Impact frequency calculations for non-airport operations are performed based on the same four-factor formula used for airport operations except that the first three terms are lumped together, i.e., NPf(x,y), the expected number of crashes per square mile per year. NPf(x,y) values are given in Tables B-14 and B-15 in Appendix B of DOE-STD-3014-96. Table B-14 provides values of NPf(x,y) for general aviation applicable to selected DOE sites. Table B-15 presents selected DOE site values of NPf(x,y) for commercial and military aviation. For this calculation, the values from the DOE STD were chosen for sites closest to the proposed NBAF sites. The best fit for purposes of calculating the impact frequency is Kansas City, with a value of 6×10^{-4}.

Table E.4.3.1-2 — Effective Area Data and Calculations for NBAF

Variable	Commercial Air Carrier	Commercial Air Taxi	General Aviation	Military Large (Takeoff)	Military Small (Takeoff)	Helicopter
WS (ft)[a]	98	59	50	223	110	55
L (ft)	1,000	1,000	1,000	1,000	1,000	1,000
W (ft)	500	500	500	500	500	500
H (ft)	30	30	30	30	30	30
R (ft)	1,180	1,180	1,180	1,180	1,180	1,180
cot (Φ) [a]	10.2	10.2	8.2	7.4	8.4	0.58
S (ft) [a]	1,440	1,440	60	780	246	0
A_f (mi^2)	3.49E-02	3.33E-02	3.03E-02	3.59E-02	3.29E-02	2.04E-02
A_s (mi^2)	6.60E-02	6.39E-02	2.65E-03	3.92E-02	1.14E-02	0
A_{eff} (mi^2)	**1.01E-01**	**9.73E-02**	**3.29E-02**	**7.51E-02**	**4.43E-02**	**2.04E-02**

[a]WS, cotΦ, and S values are taken from Tables B-16, B-17, and B-18, respectively, in Appendix B of DOE-STD-3014-96.

Table E.4.3.1-3 — Aircraft Crash Frequency Calculation for Airport Operations

Aircraft Operation	ΣN_{ijk} Number of Operations (per year)[a]	P Crash Rate[b]	X Distance	Y Distance	f(x,y) Aircraft Crash Location Probability[c]	A_{eff} Effective Area (square mile)[d]	F Impact Frequency (per year)
Commercial Aviation - Air Taxi (Takeoff)	4,208	1.00E-06	6.28	0	1.5E-03	9.7E-02	6.1E-07
Commercial Aviation - Air Taxi (Landing)	4,208	2.30E-06	-6.28	0	8.6E-03	9.7E-02	8.1E-06
General Aviation (Takeoff)	9,011	1.10E-05	6.28	0	1.5E-03	3.3E-02	4.9E-06
General Aviation (Landing)	9,011	2.00E-05	-6.28	0	2.9E-03	3.3E-02	1.7E-05
Helicopter[f]	100	2.50E-05	6.28 miles (from NBAF to origin on runway)		3[e]	2.0E-04	1.5E-04
Total Aircraft Crash Frequency (per year)							**1.8E-04**

[a] U.S. Department of Transportation Federal Aviation Administration
[b] Table B-1 in Appendix B to DOE-STD-3014-96.
[c] Tables B-2 through B-13 in Appendix B to DOE-STD-3014-96.
[d] Taken from Table XXX.
[e] In place of f(x,y), $2/L_H$ is used. L_H is the distance from the center of the airport runway to the NBAF less 1/4 mile.
[f] Estimated

Table E.4.3.1-4 — Summary: Aircraft Crash Frequencies Calculated for NBAF

Type of Crash	Aircraft Operations	Aircraft Crash Frequency (per year)
Airport	Commercial Aviation - Air Taxi (takeoff)	6.1E-07
	Commercial Aviation - Air Taxi (landing)	8.1E-06
	General Aviation (takeoff)	4.9E-06
	General Aviation (landing)	1.7E-05
	Helicopter	1.5E-04
Total of Airport Operations Aircraft Crash Frequency		**1.8E-04**
Non-airport	Commercial Aviation - Air Carrier	5.84E-05
	Commercial Aviation - Air Taxi	5.84E-05
	General Aviation	1.98E-05
	Military Aviation - Large Aircraft	1.98E-05
	Military Aviation - Small Aircraft	1.22E-05
Total of Non-airport Operations Aircraft Crash Frequency		1.7E-04
Total Aircraft Crash Frequency		**3.5E-04**

Accident Sequence

The accident is defined as the NBAF experiencing a significant impact from an aircraft crash with the subsequent release of biological material from the facility. The aircraft crash event has substantial energy to affect a relatively small area (relative to the seismic event above) of the facility structure and systems or components inside. There is, however, only small amounts of direct energy to provide a mechanism for transport of pathogens outside of the facility. For the purposes of this analysis, the aircraft is assumed to crash into the facility with the greatest amount of viral pathogens present. Because of this assumption, the total amount of infectious agents released into the environment is considered to be large.

In this accident scenario, the operability of the protective systems available to mitigate or prevent a release is dependent on the design and construction of the facility. For this accident scenario, the base case is the conceptual design provided in the feasibility study. For the unmitigated case, the structure and safety systems are assumed to fail catastrophically from the impact of the aircraft.

Preventive Features (preventing the release, not the accident)

- Robust storage containers (BSCs, containers, cabinets, etc.) resistant to mechanical insults

Mitigative Features

- Facility structure
- Ventilation and confinement systems
- Working inventory is minimized

An accident leading to the release of biological material is considered to occur if all the events in the prescribed sequence are compromised or fail. Should any one event succeed, the accident is prevented or mitigated. The following sections describe the qualitative failure frequency.

Aircraft Crash Into the NBAF Occurs – Because the initiating event is a natural phenomena event, the occurrence frequency is based on the likelihood values presented above.

Facility Structure Resists Mechanical Insult – Given the current design specification for the NBAF, the likelihood that the structure would resist the event is low. An aircraft crash would likely involve an airplane with an engine (propellar) shaft that could be on the order of 500 lb traveling at a speed greater than 90 knots (103 mph) and would penetrate the building along with large cracks and significant spalling and likely loss of safety systems inside the facility.

Active Ventilation Operates – Because the ventilation is segmented, the loss of this safety system would likely be limited to the area where the aircraft crashed. It is also possible that there would be a loss of power to the fans along with a subsequent loss of the differential pressure across the confinement barriers.

Passive Confinement System Intact and Functional – The confinement system consists of the intake and exhaust HEPA filters and plenums, the duct work from the plenums to the structure, and the NBAF structural shell (including doors). The confinement system and ventilation is essential in preventing a release from the NBAF, thereby maintaining the confinement boundary. Under the stresses imposed from the postulated accident there, it is likely that only the duct work in the immediate area would be affected. The remainder of the passive ventilation system could survive and provide some residual protection.

Accident Sequence Results – Evaluation of the range of accident sequences that can result from the failure or success of each event shows that the most likely accident sequence for a release of pathogens from an aircraft crash event ranges on the low side of no release to complete penetration of the facility and the loss of associated safety systems leading to a large release of pathogens.

Source Term Analysis

The possibility exists that an aircraft crash event could occur resulting in the release of pathogen from the facility.

MAR – The MAR is the same for this scenario and is assumed to be a significant number of viable pathogens on the order of 3×10^{12} that could be available for release. (Considers single laboratory area with maximum volumes of viable pathogens. The single maximum volume considered is the 30-L cGMP.)

The source of pathogen would include the cGMP facility considered for operation in the NBAF that is capable of processing tens of liters of pathogen-rich solution. In addition, NBAF also houses the inventory of infected animals as discussed in previous accident scenarios.

DR – The DR is the fraction of material affected during the accident. All of the MAR in the facility is affected by the natural phenomena event, so the DR is set equal to 1.0.

ARF – The ARF for this event is considered to be essentially the same as a spill. While an aircraft crash has much greater energy than a 3-m drop, the energy is dissipated by the structure and the subsequent impact to the BSCs or storage areas is considered to be similar to the spill event evaluated previously.

Therefore, the ARF for this accident is 1×10^{-4} and the RF is 1.0 for both the unmitigated and mitigated accident cases

LPF – For the unmitigated analysis in which the aerosolized material escapes the NBAF without being filtered or otherwise mitigated by the building confinement system, the LPF is set to 1.0. For the mitigated analysis, the LPF is also set to unity based on the current conceptual design specifications for the area affected by the aircraft.

The parameters of the source term formula are summarized in Table E.4.3.1-5. The unmitigated consequence calculation shows the need for improved safety controls over what was identified in the Feasibility Study. The mitigated LPF calculation includes the NBAF confinement system as a credited safety control. This includes the NBAF structure, intake and exhaust HEPA filters, and duct work between the plenums and the structure.

Table E.4.3.1-5 — Aircraft Crash Source Term Calculation Parameters

Scenario	Source	MAR	DR	ARF	RF	LPF
Unmitigated Aircraft Crash	Solutions of biological materials	3×10^{12}	1	1×10^{-4}	1	1
Mitigated – Aircraft Crash	Solutions of biological materials	3×10^{8}	1	1	1	1×10^{-5} based on upgrade of facility structure to resist insult

Unmitigated Source Term

Therefore, the unmitigated respirable source terms from these accidents are:

$$Q = 3\times10^{12} \text{ viable pathogens}\times1\times1\times10^{-4}\times1 = 3\times10^{12} \text{ virions}$$

It is clear that this level of release from the NBAF would cause considerable environmental damage.

Mitigated Source Term

The facility structure and safety systems may not be adequate to prevent or mitigate the release from the postulated accident. Design of the facility to resist mechanical insults could reduce the release to much less than the MID of 10 virions.

Consequence Analysis

Unmitigated Off-Site Consequences – The dose to a receptor outside of the NBAF (animal or human) is represented by the exposure due to inhalation pathway. Once the pathogens are in the environment, however, all pathways are available for transmission. The exposure time is considered to be approximately 1 hour (3,600 seconds) for situations where there is a release of biological materials to the environment, and the typical breathing rate for humans is taken to be 3×10^{-4} m^3/s (the breathing rate for pigs or cows is significantly different, where cows breathing rate is approximately 6 m^3/hour or 1.6×10^{-3} m^3/s and a pig would be approximately the same as a human).

$$\text{Exposure} = Q \times BR \times \chi/Q \times ET$$

Where:

Q = source term calculated from the five-factor formula (mitigated or unmitigated) [virions]
BR = breathing rate [m^3/s]
χ/Q = the 95th percentile normalized distribution of pathogen in the air at the receptor location [s/m^3]

The calculated χ/Q is site specific and varies with distance from the facility. Because the unmitigated release is large, there is a greater chance for significant downwind transport of the pathogens in a concentration that would result in an exposure. The highest χ/Q value for any site at a distance of 50 m (approximate NBAF fence line) is 1.61×10^{-1} s/m^3 and is approximately 3×10^{-5} s/m^3 at a distance of 10 km. Using these values to determine exposure results in a total inhalation of approximately 2×10^{15} virions/m^3 at 50 m and 3×10^{11} virions/m^3 at 10 km for the seismic event. The high-wind event will result in 1×10^{4} more virions. At these exposure levels there is significant potential for widespread infection in the environment.

Mitigated Off-Site Consequences – Under these proposed conditions, there is no mitigated consequence estimates.

Comparison to MID of 10 Virions – The unmitigated and mitigated consequence or dose to the receptor was conservatively based on a loss of function of the current design of the facility structure and the confinement and containment systems. This mitigated accident is not able to mitigate or prevent the release and exposure of pathogen to the environment.

Table E.4.3.1-6 — Summary of Safety Barriers and Procedural Controls

Control	Description
Safety Barriers	The NBAF confinement system, including the NBAF structure, intake and exhaust HEPA filters, and duct work between the plenums and the structure, provides a barrier against pathogen release to the environment. Additional safety barriers to provide redundant containment in the event of a large release accident to include BSC, MAR containers, and compartmentalization philosophies.
Procedural Controls	Conduct of engineering and operations consider maintenance, contamination control, PPE use, training, specialized operational procedures, etc. Operational MAR limit (Use of small quantities of pathogen in all operations).

E.4.4 Site-Specific Analyses

This section provides the summary of consequences from operations, accidents, and intentional acts for each of the proposed sites. Site-specific consequences are based on the estimates of pathogens released from the bounding accidents and the estimation of exposure previously. The exposure to pathogens is based on the results of the transport of viral pathogens as aerosols after release as calculated using the Gaussian Plume model. Tables E.4.4-1 and E.4.4-2 present summary results for several downwind distances of the normalized air and ground concentrations. These results are multiplied by the estimated quantity of pathogens released in a specific accident to arrive at the estimated concentrations for each accident and site.

For each site, the normalized time-integrated air and ground concentrations are presented for both near- and far-field perspectives. The near-field presentation focuses on distances up to 1 km from the release. The results of the Gaussian Plume model for the 95% estimates of the air concentrations, for ground-level releases, tend to be greatest at distances close to the point of release. In addition, the ground deposition typically is greatest close to the release point. Focusing in on distances less than 1 km from the release provides an opportunity to discern subtle differences in the air and ground concentrations. For small accidents (and mitigated large accidents), the majority of pathogens that would be released will be within this area. The initial response to an accident will also focus on the magnitude of the problem close to the source. The far-field perspective is provided for distances out to 10 km to illustrate the potential downwind transport of pathogens in the unmitigated accidents.

The consideration of the use of flat terrain, no building wake, the same boundary layer height, a ground-level release, and a single year of site-specific meteorological data for each of the sites resulted in the Kansas, Mississippi, Texas, and New York sites having the same 95% χ/Q values up to 10 km distances from the release. These results illustrate that there is little differentiation between any of the sites based purely on the meteorology. Site-specific consequences, however, consider the exposed populations of humans, animals, and the environment.

Table E.4.4-1 — Unmitigated Site-Specific χ/Q Normalized Air Concentration Estimates s/m^3

Radial Distance from Release Point Meters	GA	NC	KS	MS	TX	NY
χ/Q Normalized Air Concentration (s/m^3)						
50	9.34×10^{-2}	8.11×10^{-2}	1.61×10^{-1}	1.61×10^{-1}	1.61×10^{-1}	1.61×10^{-1}
200	9.00×10^{-3}	7.80×10^{-3}	1.57×10^{-2}	1.57×10^{-2}	1.57×10^{-2}	1.57×10^{-2}
600	1.66×10^{-3}	1.44×10^{-3}	2.91×10^{-3}	2.91×10^{-3}	2.91×10^{-3}	2.91×10^{-3}
1,000	7.69×10^{-4}	6.66×10^{-4}	1.35×10^{-3}	1.35×10^{-3}	1.35×10^{-3}	1.35×10^{-3}
6,000	1.43×10^{-5}	1.46×10^{-5}	2.54×10^{-5}	9.08×10^{-5}	4.02×10^{-5}	9.08×10^{-5}
10,000	7.56×10^{-6}	5.44×10^{-6}	1.18×10^{-5}	1.55×10^{-5}	1.36×10^{-5}	3.01×10^{-5}

Table E.4.4-2 — Unmitigated Site-Specific Normalized Ground Concentration Estimates 1/m^2

Radial Distance from Release Point Meters	GA	NC	KS	MS	TX	NY
Normalized Ground Concentration (1/m^2)						
50	1.54×10^{-4}	9.97×10^{-5}	1.59×10^{-4}	2.12×10^{-4}	1.64×10^{-4}	2.38×10^{-4}
200	2.76×10^{-5}	1.73×10^{-5}	1.92×10^{-5}	3.03×10^{-5}	1.98×10^{-5}	3.19×10^{-5}
600	5.95×10^{-6}	4.49×10^{-6}	3.16×10^{-6}	6.08×10^{-6}	3.86×10^{-6}	6.95×10^{-6}
1,000	2.73×10^{-6}	2.33×10^{-6}	1.93×10^{-6}	2.89×10^{-6}	2.05×10^{-6}	3.00×10^{-6}
6,000	1.29×10^{-8}	1.30×10^{-8}	1.66×10^{-8}	2.73×10^{-8}	2.27×10^{-8}	3.14×10^{-8}
10,000	5.92×10^{-9}	5.73×10^{-9}	8.22×10^{-9}	1.16×10^{-8}	1.01×10^{-8}	1.91×10^{-8}

The resultant ground concentrations differ between each of the sites due to the different rainfall estimates, which influence the wet deposition rates.

For each of the accidents considered in this analysis, specific concentration terms were developed based on site-specific meteorological data obtained from the nearest measurement location. From these data, normalized concentration terms for the air and ground deposition were determined on a site-specific basis. Tables E.4.4-3 and E.4.4-4 present the air and ground concentrations for each site for the spill accident to illustrate the potential for infections to result downwind of the NBAF. Since Nipah and RVF are not considered to be any more infectious than FMD, the minimum infectious dose of 10 virions also serves as a reasonably conservative estimate of the infectious dose for these viruses.

For a specific example, since the breathing rate for a cow is estimated to be on the order of 1.6×10^{-3} m^3/s and using the calculated air concentration for the Kansas site at a distance of 50 m for the spill event of 1.6×10^{5} virions-s/m^3, then the total exposure to the cow via inhalation is on the order of 2.6×10^{2} (260) virions (50 m is the minimum calculated distance for the Gaussian Plume model). This exposure is approximately 25 times greater than the minimum infectious dose and therefore would represent a relatively high likelihood for the cow to acquire the disease via the inhalation of the virions in the air.

(*Note: the air concentration of 1.6×10^{5} virions is the product of the χ/Q value from Table E.4.4-1 for the Kansas site at 50 m (1.6×10^{-1} s/m^3) and the source term for the spill accident 1×10^{6} virions released.*)

For calculation of the ground concentration and a resultant exposure, the results are not independent in time, as were the χ/Q values. Therefore, in order to assess the potential risk to cattle grazing on grass where viral pathogens have been deposited, an estimate of the total time that the receptor is exposed is necessary. As a an example, if one were to assume that a cow eats nearly 100 lb of feed per day (8 lb/hour, assuming that cows eat 12 hours out of 24) and that the yield for typical pasture grass on the order of approximately 3.5 lb/m^2, then a cow would need to cover nearly 30 m^2/day at a average rate of 2.5 m^2/hour to meet the food intake of a 100 lb.

Consider the unmitigated ground concentration for the Kansas site at a distance of 1 km for the seismic event (source term of 1×10^{11} virions) is 1.9×10^{5} virions/m^2, the exposure to a cow for a single day would be on the order of 5.7×10^{6} virions or 5.7×10^{5} (570,000) times greater than the infectious dose. It is unlikely that a release of this magnitude would go unnoticed or without intervening emergency response. Assuming that the grazing time is limited to a single hour—the reasonable time period before emergency plans could be implemented—the unmitigated exposure would not be reduced significantly.

(*Note: the ground concentration of 1.9×10^{5} virions is the product of the normalized ground concentration value from Table E.4.4-2 for the Kansas site at 1 km (1.9×10^{-6} $1/m^2$) and the source term for the spill accident 1×10^{11} virions released*.)

Site-specific consequences were developed using the source terms provided from the accident analysis. The site-specific consequences are presented for both unmitigated, without the benefit of safety controls, and mitigated, taking credit for the safety controls that reduce quantity of pathogens released in an accident, consequences.

The determination of the consequences for all of the accidents is based on the specific hazards posed by FMDV, RVFV, and Nipah virus. FMDV has a known infectious dose and are highly infectious and are transmitted mainly by aerosols and simple contact with fomites (contaminated materials, inanimate objects, clothing, veterinary equipment, vehicles, foodstuffs, manure, soil, and vegetation). Viruses are excreted from and present in blood and body fluids, including respired air, saliva, vesicular fluids, and tissues of the vesicles, which are a hallmark of the infection; semen; vaginal fluids; urine; feces; meats; and milk. Infected animals can excrete high concentrations of virus in respired air, secretions, and fluids. For example, cattle may excrete up to 1.26×10^{5} or 126,000 virions respired in a 24-hour period. Therefore, there are nearly 1×10^{4} infectious doses of the FMDV respired from a single bovine animal per hour. Swine (pigs) have been measured at rates up to 3.9×10^{8} virions/24 hours in expired air. Doses as low as 10 to 20 virions could infect a sheep and a steer, respectively (J. H. Sorensen: An integrated model to predict the atmospheric spread of foot-and-mouth disease virus. *Epidemiol Infect* 124:577-590, 2000). The minimum dose of natural aerosol to infect a pig has not been determined, but some observations suggest that it is probably much higher than that for other species (A. Donaldson: Airborne spread of foot-and-mouth disease. *Microbiology Today* 26:118-119, 1999). The Canadian Food Inspection Agency presents in the Pathogen Safety Data Sheet for Foot and Mouth Disease that as few as 10 infectious particles can produce disease. The minimum infectious dose for Nipah virus and RVFV are not readily known and are, for the purposes of evaluating hazards and accidents, conservatively assumed to be the same as that for FMD (10 infectious particles or virions) (CFIA 2005a; CFIA 2005b; CFIA 2005c; Goh 2000; NEEG 2007).

Furthermore, based on mission objectives and regulatory requirements, an individual package containing biological materials may contain approximately 100 mL. Typical concentrations of viral pathogens are estimated based on a specific volume of culture medium. Culture media is used to grow and maintain cells at an appropriate temperature and gas mixture (typically, 37°C, 5% CO_2) in a cell incubator. Culture conditions vary widely for each cell type, and variation of conditions for a particular cell type can result in different phenotypes being expressed. Aside from temperature and gas mixture, the most commonly varied factor in culture systems is the growth medium. Recipes for growth media can vary in pH, glucose concentration, growth factors, and the presence of other nutrient components. The growth factors used to supplement media are often derived from animal blood, such as calf serum. Nearly all of the culture media are essentially in the form of liquids or gels.

For the purposes of the hazard and accident analysis, the concentration in a milliliter (1/1,000 of a liter or a cubic-centimeter) is taken to be approximately 1×10^{8} viable virions. Therefore, there could be a total inventory of approximately 1×10^{11} viable virions/L of media. The biological materials consist of various forms but are considered to aerosolize upon impact. Using these concentrations of virions in typical media and the numbers of virions respired from a typical infected cow, estimates for the site-specific consequences from the MAR for each accident were developed.

Table E.4.4-3 — Unmitigated Site-Specific Air Concentration Estimates From a Spill Release of Aerosol Pathogen (Source Term = 1×10^{6}; MAR = 1×10^{10} virions * ARF = 1×10^{-4})

Radial Distance from Release Point Meters	GA	NC	KS	MS	TX	NY
Air Concentration (virions-s/m^3)						
50	9.3×10^{4}	8.1×10^{4}	1.6×10^{5}	1.6×10^{5}	1.6×10^{5}	1.6×10^{5}
200	9.0×10^{3}	7.8×10^{3}	1.6×10^{4}	1.6×10^{4}	1.6×10^{4}	1.6×10^{4}
600	1.7×10^{3}	1.4×10^{3}	2.9×10^{3}	2.9×10^{3}	2.9×10^{3}	2.9×10^{3}
1,000	7.7×10^{2}	6.7×10^{2}	1.4×10^{3}	1.4×10^{3}	1.4×10^{3}	1.4×10^{3}
6,000	1.4×10^{1}	1.5×10^{1}	2.5×10^{1}	9.1×10^{1}	9.1×10^{1}	9.1×10^{1}
10,000	7.6	5.4	1.2×10^{1}	1.6×10^{1}	1.6×10^{1}	3.0×10^{1}

Table E.4.4-4 — Unmitigated Site-Specific Ground Concentration Estimates From a Spill of Aerosol Pathogen (Source Term = 1×10^{6}; MAR = 1×10^{10} * virions ARF = 1x 10^{-4})

Radial Distance from Release Point Meters	GA	NC	KS	MS	TX	NY
Ground Concentration (virions/m^2)						
50	1.5×10^{2}	1.0×10^{2}	1.6×10^{2}	2.1×10^{2}	1.6×10^{2}	2.4×10^{2}
200	2.8×10^{1}	1.7×10^{1}	1.9×10^{1}	3.0×10^{1}	2.0×10^{1}	3.2×10^{1}
600	6.0	4.5	3.2	6.0	3.9	7.0
1,000	2.7	2.3	1.9	2.9	2.0	3.0
6,000	1.3×10^{-2}	1.3×10^{-2}	1.7×10^{-2}	2.7×10^{-2}	2.3×10^{-2}	3.1×10^{-2}
10,000	5.9×10^{-3}	5.7×10^{-3}	8.2×10^{-3}	1.2×10^{-2}	1.0×10^{-2}	1.9×10^{-2}

Table E.4.4-5 — Accident Risk Rank Summary

Accident	Accident Case	Risk Rank	Frequency Category	Severity Category
Operational Accident 1	Unmitigated	1	II	A/B
	Mitigated	4	IV	D/C
Operational Accident 2	Unmitigated	1	I	B
	Mitigated	4	III	E
Operational Accident 3	Unmitigated	1	II	A
	Mitigated	3	III	E
Operational Accident 4	Unmitigated	1	II	A
	Mitigated	3	III	D
Operational Accident 5	Unmitigated	2	III	A/A
	Mitigated	4	IV	D/C
Operational Accident 6	Unmitigated	2	III	A/A
	Mitigated	4	IV	D/D
NPH	Unmitigated	2	IV	A/A
	Mitigated	4	V	E/D
Aircraft	Unmitigated	2	IV	A/A
	Mitigated	4	V	E/D

The unmitigated accident risk ranking resulted in a risk rank of either 1 or 2. These rankings were the result of operational accident frequencies between 1×10^{-2} and 1×10^{0} (NPH and aircraft crash accident frequencies were lower because of the likelihood of the initiating events was much smaller). Likewise, the consequences for the unmitigated operational, NPH, and external accidents were all "A" to the public and "A" or "B" to the worker, indicating high potential for large quantities of virions to be released.

The mitigated accident risks were significantly reduced (often by more than one category for both frequency and consequence) by taking factoring in improvements in safety barriers and controls. Two of the mitigated accidents (loss of an infected animal and release of contaminated wastes) had risk ranks of 3, indicating the need for considering additional controls. This risk rank was assigned because the mitigated accident frequency only dropped by one bin from a FC II to FC III after factoring in the controls. Overall, however, the risk reduction in the mitigated accidents illustrates the effectiveness of the safety controls.

These risk ranks, however, do not provide information that can be used to discriminate between the proposed NBAF sites to assess the site-specific impacts from a postulated release of FMDV, RVFV, or Nipah virus. To evaluate the site-specific risks, a coupling of the risk ranks for the accidents, which are generic in that all of the release scenarios could occur at any of the proposed NBAF sites, with the site-specific characteristics is necessary.

Since risk is the product of the likelihood and consequence of an accident and the accident frequency is a characteristic of the NBAF structure and operations, then the frequency of the accidents can be assumed to be constant across the proposed sites. In other words, moving from one site to another does not change the accident frequency; therefore, only the change in consequences is needed to assign a site-specific risk.

Therefore, based on the unmitigated air and ground concentrations possible from a release of viral pathogens as a result of the postulated accidents, a coupled site-specific risk ranking was developed to compare released inventories to potential infections downwind from the NBAF (Asante-Duah 2002; Greenberg 1991; Cohrssen 1989). The data presented in the table are based on the 10 virion minimum infectious dose for each of the three pathogens. While other livestock would have a different MID for each of the viruses, the bounding scenario is to consider all of the livestock to be at the same level of susceptibility.

The risk ranking, based on the change in site-specific consequences, ranges from a minimum of "none" to a maximum of "high" based on the MID. A review of the site-specific unmitigated air and ground concentrations shows that a minimum of 1×10^4 (10,000) virions is necessary to be released before there is a credible possibility for multiple infections downwind of the release. For example, a potential infection is expected to result from a release such that the exposure (inhalation, contact, or ingestion) of at least 10 virions. Taking the air concentration at 50 m of 1.6×10^{-1} for the Mississippi site, the product of the source term, a cow's breathing rate, and the air concentration (1.6×10^{-1} * 1.6×10^{-3} * 1×10^4) yields nearly 3 virions, which is less than one-third of the MID of 10 virions indicating that no infection would likely result. The risks presented in the accident analysis section were based on qualitative estimates of exposure based on the magnitude of the unmitigated and mitigated source terms. This phase of the risk ranking takes the site independent consequences calculated in the accident analysis and incorporates the site-specific aspects for population, wildlife, agriculture, and other environmental factors for the purpose of differentiating one proposed site from another.

Table E.4.4-6 — Site-Specific Risk Ranking Based on Potential Infections

Site-Specific Risk Category	Label	Description	Viable Pathogens Released
I	High	Likelihood of receptor infection approaches certainty (dose is greater than 10 times the infectious dose)	$VP > 1\times10^6$
II	Moderate	Likelihood of receptor infection increases with concentration (dose is equal to or greater than the infectious dose)	$1\times10^4 < VP \leq 1\times10^6$
III	None or Low	Likelihood of receptor infection approaches zero (dose is less than MID)	$VP \leq 1\times10^4$

The interpretation of the site-specific risk ranks includes the unmitigated and mitigated site-independent accident frequencies. Because these frequencies do not change from one site to another, they are not repeated in the following site-specific discussions.

In each of the site-specific cases, the effective mitigation of risk is dependent on the incorporation of robust safety controls into the design, construction, and operation of the NBAF. The need for robust safety controls is emphasized in federal regulations and executive orders to ensure that operation of the facility does not result in adverse consequences to the workers, public, or environment. To meet this objective, it is essential that the identified safety controls, including both the primary and secondary barriers, are able to meet their

intended safety function during normal and credible abnormal conditions. Because of the nature of the pathogens anticipated in the operation of the NBAF, there is a need for the increased assurance on the performance of safety equipment. This specifically means safety controls need to ensure that viral pathogens are contained during all operations, external mishaps, and after credible natural phenomena events.

The evaluation of site-specific consequences illustrates that with the exception of Plum Island, each of the proposed sites resides in an area where the wildlife, vegetation, agriculture, and human populations provide ample opportunity for each of the viruses (FMDV, RVFV, and Nipah virus) to become established and spread rapidly once released from the NBAF. For this reason, the focus of the hazards, accident, and risk analysis was on the containment of the viruses within the NBAF and the importance of both the engineered and administrative controls to prevent or mitigate accidents.

Site-specific consequences for the proposed NBAF sites were depicted in terms of the postulated accidents. Each of the accidents has the potential to release pathogens to the environment. The site-specific analysis considered differences in topography, weather, and agricultural uses near each site.

To assess the site-specific consequences from the postulated bounding accidents, it was necessary to evaluate the results of the transport modeling and the development of specific air and ground concentrations of viral pathogens estimated to have been released in each accident. Resultant air and ground concentrations for each unmitigated accident at specific radial distances. The combination of these concentration tables and the figures representing the near- and far-field results provide the basis for evaluating the impacts to the population and environment after a hypothetical release at the proposed NBAF sites.

The normalized air concentrations (for Flora, MS, as an example) site range from 1.6×10^{-2} at distances of 200 m to 1.4×10^{-3} at a distance of 1,000 m (1 km) from a release. The ground concentrations for these same radial distances range from a high of 3×10^{-5} to a low of 2.9×10^{-6}. Taking into consideration the source terms for each of the specific accidents, the normalized air and ground concentration values represent the potential for significant concentrations in the air and on the ground for the larger accidents such as over-pressure, seismic, and fire events. This effect is similar at all of the six proposed NBAF sites.

Individual Site Characteristics

As with the previous discussion, the majority of the NBAF would be within the 200-m radial distance. Significant releases of pathogens from the NBAF as a result of accidents could be expected to occur only from the higher containment areas. The site boundary would be located at approximately 250 m from the center of the NBAF. For the purposes of the analysis, it is assumed that distances past 200 m essentially represents an off-site release.

For each site, the area outside of the 4-km distance from the site was evaluated to determine if the environment would hinder or enhance the spread and growth of the three pathogens in the event of a release. Consideration of vegetation (e.g., wooded forestland, grasses, crops, etc.) and the presence of streams or rivers and wetlands were factored into the evaluation of the environmental characteristics for each site.

The agriculture of the area, out to significant distances (>10 km) was also considered. The presence of grazing livestock and the crops to support them is critical to understanding the potential infections that could result in the event of a release of FMDV, RVFV, and Nipah virus. The site-specific evaluations factored in the details of terrestrial wildlife in the vicinity of the proposed NBAF sites. Attention to the numerous species of mammals, birds, reptiles, and insects (mosquitoes and ticks) that inhabit the area around the proposed sites was also evaluated. Various species of mammals, including white tail deer, wild boar, elk, and others, are critical in determining whether there are viable hosts for the pathogens that were considered in the risk assessment. The wildlife and livestock in the vicinity of the site are prime candidates for acquiring or transmitting the FMDV and RVFV and to some extent the Nipah virus in pigs. While the FMDV, RVFV, and

Nipah virus each have different characteristics related to transmission and viability, however, the unmitigated concentrations near the proposed NBAF sites are potentially significant. The location of the proposed NBAF sites provides a significant opportunity for the spread of viruses via vectors and infected wildlife. In addition, the atmospheric modeling indicates that downwind transport is a credible scenario given a sufficiently large release of pathogens.

For all of the proposed sites, except Plum Island, NY, there was a potential for viral pathogens to be transported significant distances by the wind. The results of the modeling indicate that this transport pathway is not limited, as was the case for Plum Island. It is considered likely that deer, wild boar, and other wildlife or livestock could act to spread disease over long distances. In addition, common vectors such, as mosquitoes, can be transported long distances.

The counties surrounding each of the proposed NBAF sites contain significant numbers of livestock potentially exposed to any off-site release. Data related to the distribution of livestock in the vicinity of the NBAF was obtained from a DHS tasking response dated August 6, 2007. The specific task was to collect information about livestock in the areas of the proposed NBAF sites to support the determination as to whether accidental laboratory releases at these locations could have the potential to affect nearby livestock (DHS 2007). The normalized downwind air and ground concentrations up to distances of 10 km from the proposed NBAF sites was found to be susceptible to the spread and growth of disease.

Site-Specific Consequences for FMDV

FMDV spreads quickly through herds and flocks of susceptible animals. With an incubation period of as little as 12 hours, the disease can spread quite rapidly. Cattle are often considered to act as indicators because of the low infectious dose, sheep act as maintenance hosts, and swine act as amplifiers of FMDV. The livestock and wildlife (deer and boar) in the vicinity of the proposed sites provides ample opportunity for FMDV to establish in the environment upon a release. FMDV can persist in the human upper respiratory tract for up to 48 hours, making humans potential vectors if they are exposed. In addition, the ability for FMDV to be spread by fomites and with the large human population in the area, the ability for FMD to spread over large areas also exists. The consequences of a large release of FMD virions would be as severe as that of RVFV or Nipah virus in this area.

Site-Specific Consequences for RVFV

RVFV is an acute mosquito-borne (vector-based disease) viral disease affecting mainly ruminants (e.g., cattle, sheep, deer) and humans. In animals, RVF causes abortions and high mortality in young. In humans, RVF causes severe influenza-like syndrome. The area around each of the proposed sites would provide an environment for the RVFV to be easily transmitted once released. The inhalation pathway to humans and wind-borne dispersal of infected vectors can transmit RVFV, and infected livestock and people movement are a means of spreading RVF. Mosquitoes are a reservoir for RVFV, and the virus can remain dormant in the eggs of the mosquito in dry soil of grassland depressions. With adequate rainfall, the infected mosquitoes develop and infect ruminants. The virus can be spread by many mosquito species. The consequences of a large release of RVF virions would be as severe as that of FMDV or Nipah virus in this area.

Site-Specific Consequences for Nipah Virus

In pigs, the Nipah virus appears to cause a high rate of febrile illness but a low rate of sickness and death, yet it can appear as sudden death syndrome in mature swine. In humans, Nipah virus is characterized by severe febrile encephalitis, fever, headache, dizziness, and vomiting with a high mortality rate. The host range of Nipah virus is in pigs, cats, dogs, and possible in horses and goats. Because Nipah virus is transmitted by direct contact and exchange of bodily fluids, mechanical transmission, and aerosol transmission, there is

substantial opportunity for the Nipah virus to spread rapidly in the area. The consequences of a large release of Nipah virions would be as severe as that of RVFV or FMD in this area.

The final risk rank for the mitigated accident scenarios for the proposed NBAF sites is 3 (none) for all accidents except over-pressure and fire, which are designated as risk rank 2 (moderate) for distances close to the release. Because of the potential for easy spread of the FMDV, RVFV, and Nipah virus via infected livestock, wildlife, and vectors, the overall risk for the five mainland sites is designated as risk rank 2 (moderate). The Plum Island site is assigned a site-specific risk rank of 3 due to the reduction in the likelihood of spreading disease off of the island.

E.5 SUMMARY

The hazards evaluations, accident analyses, and the assessment of risks for the NBAF was predicated on the basis that the three representative pathogens (FMDV, RVFV, and Nipah virus) present the opportunity for serious hazards and potential adverse consequences if not handled appropriately. The NBAF is a high-risk, high-hazard facility that can be designed, constructed, and operated safely using existing methods, techniques, and safety systems. The design and construction precedents exist; the operating philosophy exists; operating protocols exist—in short, the technology exists. The risk will never be zero, but it can be made to be acceptably low.

This risk assessment addresses issues and incorporates the appropriate analysis, presented to NIH by the National Research Council's Committee on Technical Input on the NIH's Draft Supplemental Risk Assessment and Site Suitability Analysis (DSRASSA) associated with the siting and operation of the National Emerging Infectious Diseases Laboratory (NEIDL) at Boston University. As such, this risk assessment provides a defensible foundation for understanding the hazards, potential consequences, requisite safety controls, and the risks posed by the operation of the NBAF. This risk assessment of the NBAF provides the requisite information with sufficient basis and at the appropriate level for the decisions that formed the motivation for the study.

With the exception of the proposed Plum Island NBAF site location in NY, the other site alternatives are in population areas (high densities of people and animals) and the surrounding ecosystems that provide favorable environments to support pathogen spread and growth in the event of a release. The analysis provides consistent, credible, and bounding risk information to support the specified decisions.

The hazards associated with operating the proposed NBAF were compiled using methodology described in the American Institute of Chemical Engineers' *Guidelines for Hazard Evaluation Procedures* (CCPS-1). A full list of the hazards, their estimated unmitigated (no protective controls applied) and mitigated (protective controls applied) frequencies and consequences, existing controls, and recommended additional controls were presented. From this list of hazards, six operational accidents were analyzed in detail, as well as one natural phenomena accident and one external man-made event. These accidents are:

- Spill/Uncontrolled Release of Pathogens
- LAI
- Loss of Infected Animal/Insect
- Release of Contaminated Wastes
- Large Room or Facility Fire
- Over-Pressure Event from a Deflagration
- Seismic Event
- Aircraft Crash into the Facility

The potential risks associated with intentional acts were also evaluated based on the separate Threat Risk Assessment. These accidents were chosen to represent reasonable upper-bound consequences to the workers and the public from potential NBAF operations. Consequences for each of the six prospective sites were calculated considering site-specific meteorological data for airborne releases, as well as topography and population estimates of animals and humans in the surrounding areas. Overall unmitigated and mitigated risk ranks were estimated based on the unmitigated and mitigated probabilities and consequences of each accident for each site. The risk was ranked from 1 (high risk = high probility and high consequence) to 4 (low probability and low consequences).

Summary of Site-Specific Risk Ranks

Site		Site-Specific Risk Rank[a]	Site-Independent Accident Risk Range[b]	Accident Frequency Range[c]	Accident Severity Range[d]
Plum Island	Unmitigated		1–2	I–II	A/A – A/B
	Mitigated	III–Low	3–4	III–IV	D/C – E/D
Mississippi	Unmitigated		1–2	I–II	A/A – A/B
	Mitigated	II–Moderate	3–4	III–IV	D/C – E/D
Kansas	Unmitigated		1–2	I–II	A/A – A/B
	Mitigated	II–Moderate	3–4	III–IV	D/C – E/D
Texas	Unmitigated		1–2	I–II	A/A – A/B
	Mitigated	II–Moderate	3–4	III–IV	D/C – E/D
North Carolina	Unmitigated		1–2	I–II	A/A – A/B
	Mitigated	II–Moderate	3–4	III–IV	D/C – E/D
Georgia	Unmitigated		1–2	I–II	A/A – A/B
	Mitigated	II–Moderate	3–4	III–IV	D/C – E/D

[a]The primary differentiator among sites is the ability for FMDV, RVFV, and Nipah virus to become established and spread considering the hosts, vectors, and vehicles.
[b]Site-independent accident frequencies do not vary across sites.
[c]NPH and aircraft crash accidents have unmitigated frequency IV and mitigated frequency V.
[d]Accident severity categories were assigned based on NBAF operations and structure not on location.

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NATIONAL BIO AND AGRO-DEFENSE FACILITY

Science and Technology Directorate/Office of National Laboratories

NATIONAL BIO AND AGRO DEFENSE FACILITY DEIS

APPENDIX F

NEPA DISCLOSURE STATEMENT

U.S. DEPARTMENT OF HOMELAND SECURITY

NEPA DISCLOSURE STATEMENT FOR PREPARATION OF THE *NATIONAL BIO AND AGRO-DEFENSE FACILITY ENVIRONMENTAL IMPACT STATEMENT*

CEQ Regulations at 40 CFR 1506.5(c) require contractors who will prepare an EIS to execute a disclosure specifying that they have no financial or other interest in the outcome of the project. The term "financial interest or other interest in the outcome of the project" for purposes of this disclosure is defined in the March 23, 1981 guidance "Forty Most Asked Questions Concerning CEQ's National Environmental Policy Act Regulations," 46 FR 8026-18038 at Question 17a and b.

"Financial or other interest in the outcome of the project" includes "any financial benefit such as a promise of future construction or design work in the project, as well as indirect benefits the contractor is aware of (e.g., if the project would aid proposals sponsored by the firm's other clients)." 46 FR 18026-18038 at 18031.

In accordance with these requirements, the offeror and any proposed subcontractors hereby certify as follows: (check either (a) or (b) to assure consideration of your proposal).

(a) __X__ Offeror and any proposed subcontractor have no financial or other interest in the outcome of the project.

(b) _____ Offeror and any proposed subcontractor have the following financial or other interest in the outcome of the project and hereby agree to divest themselves of such interest prior to award of this contract.

Financial or Other Interests

1.

2.

3.

Certified by

Signature

Lee Swain, Vice President

Printed Name and Title

Dial Cordy and Associates Inc..

Company

February 26, 2008

Date

NEPA DISCLOSURE STATEMENT FOR PREPARATION OF THE *NATIONAL BIO AND AGRO-DEFENSE FACILITY ENVIRONMENTAL IMPACT STATEMENT*

CEQ Regulations at 40 CFR 1506.5(c) require contractors who will prepare an EIS to execute a disclosure specifying that they have no financial or other interest in the outcome of the project. The term "financial interest or other interest in the outcome of the project" for purposes of this disclosure is defined in the March 23, 1981 guidance "Forty Most Asked Questions Concerning CEQ's National Environmental Policy Act Regulations," 46 FR 8026-18038 at Question 17a and b.

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(a) __X__ Offeror and any proposed subcontractor have no financial or other interest in the outcome of the project.

(b) _____ Offeror and any proposed subcontractor have the following financial or other interest in the outcome of the project and hereby agree to divest themselves of such interest prior to award of this contract.

Financial or Other Interests

1.

2.

3.

Certified by

Signature

Mark Smith, Vice President

Printed Name and Title

Tetra Tech, Inc.

Company

February 24, 2008

Date