VII. ELEMENTS OF THE RISK ASSESSMENT SCENARIOS

Overview

The purpose of evaluating the risk scenarios described in this section was to determine the impacts of the four exotic diseases being studied (Ebola HF, Brazilian HF- caused by Sabia virus, Rift Valley Fever, and Monkeypox) on three distinctly different communities resulting from accidental release through fictitious events. The Boston-BUMC, MA, Tyngsborough, MA, and Peterborough, NH communities represent urban, suburban, and rural placement of the NEIDL, respectively. (See Section VI)

The risk assessment scenarios described in this section have been designed to cause infection in the index patient 100% of the time. This ***is a gross overstatement of the risk.*** In reality transmission rates of diseases are rarely, if ever, 100% in a given population due to modifiers of susceptibility that differ among individuals and populations (e.g., health, nutritional, and immune status; genetic susceptibility; pregnancy; drugs such as chemotherapeutic agents or steroids) and exposure cannot be directly equated to disease development 100% of the time. Through interactions with the hypothetically infected individual in the home, at work or during other social situations, the exotic diseases of interest were introduced into each simulated community. The probability for the index (i.e., first) case in each scenario is set at 1.0 (100%) to ensure that there is a chance for further dissemination of disease into the simulated communities. If an initial infection was not established, there would be no risk to the community and there would be no impacts to compare. This extreme and unrealistic approach to modeling disease transmission was necessary because the exotic agents that so concern the community and that are reported upon in the lay press (e.g., Ebola) are indeed infectious; they are not, however, highly communicable or highly contagious.

Fictitious scenarios were developed to address concerns expressed by citizens in Boston. (See Section II and below). The scenarios were purposely contrived to accomplish disease introduction into each simulated community. Wherever possible, information used in the development of the scenarios was based on scientific, public health and epidemiologic literature but in every case the assumptions and inputs used for simulations vastly overstated any actual risk. Probabilities were assigned to events that, in fact, have not occurred in nature or been reported in the scientific literature (e.g., Sabia transmission through close contact; sexual transmission of Ebola virus; transmission of monkeypox from a human to a hamster, etc.) to ensure transmission of simulated disease into the three communities. Scenarios were designed to “force” or ensure the occurrence of an infection beyond the laboratory and the index case so that a hypothetical, simulated threat to the three communities could be compared to determine if one community would be impacted more than the other two.

It is important to note that no public health interventions were included in the simulations; for example the use of insect repellents, immunizations, “sharp safe” or needleless medical devices, condoms and so on. In using this extreme and unrealistic modeling approach, the risks of infection by Ebola virus, Sabia virus, Rift Valley Fever

virus, and monkeypox and the associated simulated outcomes (morbidity and mortality) of the computational modeling are greatly overstated. This highly contrived approach, however, was necessary to acquire data sufficient to cause impacts that could then be compared in the three communities to answer the following questions:

1) Does location of the NEIDL in an urban, suburban, or rural setting represented by Boston-BUMC, Tyngsborough and Peterborough, respectively, affect the incidence of disease or transmission of disease as a result of the introduction of an infectious agent through each scenario?
2) Does the population of the community in which the NEIDL will be sited affect the incidence of disease or transmission of disease as a result of the introduction of the infectious agent through each scenario?
3) Are Environmental Justice communities, if present, subjected to disproportionate health impacts as a result of siting the NEIDL near these communities in the unlikely event that an infectious agent was released?

As was discussed earlier in Section II, the NIH believed it was critically important that concerned citizens have input into development of the model and specifically development of the release scenarios studied through simulation modeling. To that end, the NIH conducted a series of three public meetings to openly discuss the types of infectious disease agents to be studied and the scenarios through which potential releases could occur. Additionally, an e-mail address and telephone number were established through which citizens could provide comments and suggestions. Through these outreach activities, citizens made it known that they wanted to see the following situations that, in their opinions, could be associated with high containment laboratories or agents included in the risk assessments.

- A transportation accident with subsequent release of an infectious agent
- A release of a vector-borne disease
- A release of an infected arthropod
- A laboratory incident concerning mislabeling of a specimen or stock culture
- A release of a recombinant organism (**Please Note:** NIH recognizes that rDNA use requiring containment defined as "BL4" by the NIH Guidelines for Research Involving Recombinant DNA Molecules shall not be permitted in the City of Boston. This scenario was added in response to a written comment received from the community)
- A laboratory incident involving Ebola virus
- A laboratory incident involving a poxvirus
- An incident involving a school or school-aged children
- An incident requiring transport of an infected patient

Furthermore, one commenter wrote, “If public safety is the focus of this new risk assessment, then the assessment cannot be limited to one possible scenario, since there are many scenarios that could result in public danger. Also, true-life complexity cannot

be left out of the model for the sake of making the problem tractable. This risk assessment must capture the real world complications in order to have any value in protecting public safety". To that end, the NIH used both the A-BEST and MLAB-ST modeling approaches (see Section VI) to model the requested "true-life complexities" and "real world complications" through the scenarios described herein.

EBOLA VIRUS SCENARIO

Rationale Used for Development of the Ebola Virus Scenario

Outside of two extremely rare laboratory-acquired infections in England and Russia (Emonds 1977, ITAR-TASS News Agency 2004, Akinfeeva 2005), Ebola virus infection of humans has been limited to the African continent. Most of the events contributing to the spread of Ebola Hemorrhagic Fever (EHF) in African villages and towns do not occur in the United States including ritual cleansing of a body before burial, handling and/or consuming "bush meat"; re-use of needles and syringes; and the use of non-barrier nursing techniques. Activities involving exposure to infective blood or other body fluids should be considered high risk. Studies following household contacts of EHF convalescents have been done. While virus or viral RNA has been found in seminal fluid in patients recovering from Ebola infection (Emond 1977, Rodriguez 1999), there is no direct evidence of sexual transmission of Ebola virus (Rowe, et al., 1999; Rodriguez, et al., 1999). These studies also showed that the risk of transmission of EHF to household contacts from convalescent patients is exceedingly low.

Bearing in mind the cultural differences and the availability and practice of healthcare in developing African nations, potential routes of transmission of Ebola virus infection can be identified and adapted to hypothetical situations in developed nations such as the United States. A-BEST modeling and simulation techniques can be used to explore the consequences of exposure to an Ebola-infected individual in urban, suburban and rural environments such as Boston-BUMC, Tyngsborough and Peterborough, respectively. The results of casual societal interactions with an Ebola-infected individual, which is not known to be risk for infection, can be also be explored through A-BEST simulation.

After review of the scientific literature and discussions with recognized Ebola virus scientific experts, the potential for infection from four types of societal contacts with an index case were studied through A-BEST simulation modeling techniques:

- Casual contacts - person to person societal interactions outside the household
- Household contacts - close interactions between family or household members
- Intimate contacts - interactions involving the exchange of one or more body fluids
- Healthcare contacts – contacts occurring during the provision of healthcare

Using A-Best modeling techniques, in conjunction with the fictitious scenario described below, potential disease transmission was studied including 1) casual contacts such as

interactions with others in a shop, school or on public transportation; 2) household contacts such as daily interactions within a family; 3) intimate contacts such as sexual intercourse or other exchanges of body fluids; and 4) healthcare worker contacts such as performing injections, blood draws, respiratory therapy treatments, invasive procedures or other activities that place the worker in close proximity to blood and other body fluids.

The Ebola Virus Scenario

A 37-year-old, male scientist working with Ebola virus in the maximum containment laboratory setting sustains a percutaneous (through broken skin) exposure to the virus but does not recognize the exposure and thus does not report it. He has a 36-year-old wife, who is also a scientist, and a six-year-old daughter and four-year-old son with whom he lives. On day 7 post-exposure, he begins to feel "unwell" and displays symptoms including fever, chills and general malaise (tiredness) which progressed to vomiting and diarrhea similar to those symptoms seen in his children who are suffering from a common childhood viral illness.

On day 9 post-exposure, his wife takes him to a local emergency room where he is placed in a routine non-isolation bed for four hours. Upon completion of a history and physical, he is moved to an "isolation room" and started on intravenous (IV) fluids. An infectious diseases (ID) specialist is called to provide a consult. (In Tyngsborough and Peterborough, an ID specialist is not immediately available.) After transfer to the isolation room a healthcare worker (HCW) sustains a needlestick injury exposing her to the patient's blood. This exposure was reported per hospital protocols and the HCW was placed on a "fever watch" in her home.

The index (first) patient is transferred and admitted to a large tertiary care hospital and is isolated in a manner exceeding CDC Interim HFV Guidelines (CDC 2005). The index patient survives and is discharged on day 35 post onset of symptoms. In accordance with CDC recommendations, the patient is counseled to refrain from intimate relations for 90 days to be "on the safe side". The discharge summary and written patient instructions for self-care and follow-up by the ID specialist are provided to the patient upon release from the hospital. These instructions included a written reminder to refrain from intimate relations for 90 days.

On day 62 post onset of symptoms, the convalescing (recovering) man visits a woman in nearby Town B with whom he has had prior contact in the years preceding his illness. He and the woman share intimate relations. Twenty-one days later the woman begins to run a very low-grade fever, but in the intervening time has intimate relations with three other men resulting in the exchange of multiple body fluids. The next day the woman begins to feel unwell and on day 4 of her symptoms she is admitted to the local emergency department (ED). At the ED she is prescribed fluids, antipyretics (fever reducing medications) and bed rest, and is sent home with a tentative diagnosis of a viral infection that is "going around". She becomes gravely ill and is readmitted to the local hospital and subsequently transferred to BU Medical Center by helicopter following a diagnosis of tentative viral hemorrhagic fever (VHF). She is diagnosed with Ebola Hemorrhagic

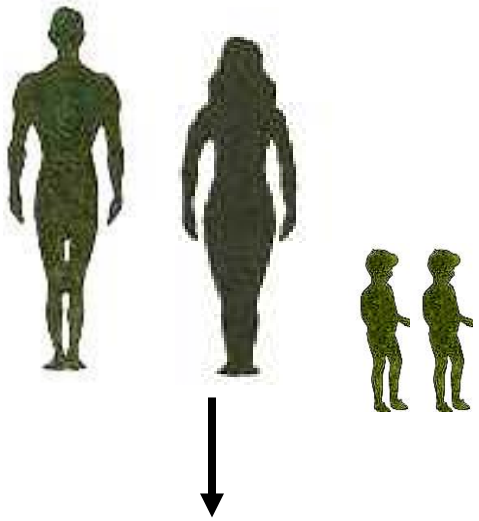
Fever at BU Medical Center. The woman was deceased by day 23 after onset of her symptoms. Her contacts were identified for the prior 30 days.

The hypothetical events described in this scenario were simulated using A-BEST modeling for each of the three communities of Boston-BUMC, Tyngsborough and Peterborough. A simplified diagram of this scenario can be in found in Figure VII-1.

Note: *The events described in the above scenario are highly contrived and are based on exaggerated assumptions. Specifically, the scientist 1) did not recognize a break in the double glove containment barrier that protected him from percutaneous exposure to Ebola virus; 2) did not notice the break in the integrity of the outer glove during the routine decontamination protocol following completion of work in the BSL-4 laboratory; and 3) did not notice the loss of pressure in his suit the next time he inspected it prior to wear. Furthermore, a secondary case was arbitrarily established through sexual contact and was not a result of actual transmission dynamics The potential exposure and the required mitigation measures should an exposure occur are subjects of exhaustive and repeated training prior to and during work requiring BSL-4 containment. Laboratory workers who conduct research on organisms requiring BSL-4 containment must report all fevers and other symptoms to the institutional Environmental Health and Safety Office and an appropriate, identified medical authority. The institutional Responsible Official and CDC Select Agent Program must also be notified in the event of a possible exposure to a select agent. Exposed workers are considered to be potentially infected with the agent(s) they are working with until this is proven not to be the case. In this instance, the scientist would have been placed on a "fever watch" and isolated for the duration of the 21-day incubation period. If any symptom occurred that may have resulted from an Ebola infection he would have been admitted immediately to the hospital under isolation procedures in a manner meeting or exceeding CDC Interim HFV Guidelines (CDC 2005). Under these conditions, the secondary exposure to the health care worker who was inadvertently exposed to EHF by a needle stick would likely not have occurred. Finally, there is no direct evidence in the medical literature to support the contention that EHF can be transmitted through sexual contact. Therefore the infection of the woman in the neighboring town, described in the above scenario, is highly contrived solely in an attempt to ensure spread of disease into the simulated community for the purpose of computational modeling.*

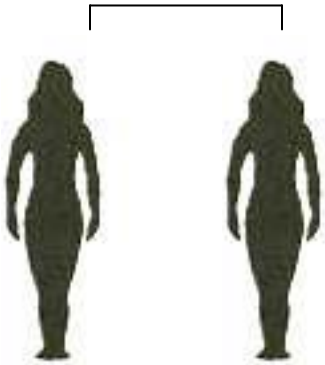
Ebola virus Scenario Diagram

1. Male sustains unrecognized percutaneous exposure to Ebola virus resulting in undiagnosed illness as small children in household are suffering a viral illness causing fevers, diarrhea and vomiting; he requires hospitalization for unknown illness



2. HCW sustains needlestick with hollow bore needle

3. During convalescence, man visits woman in neighboring Town B with whom he has intimate contact



4. Woman in Town B becomes infected and is beginning to run a slight fever during which time she has intimate contacts with three men. In one instance there is exchange of multiple body fluids

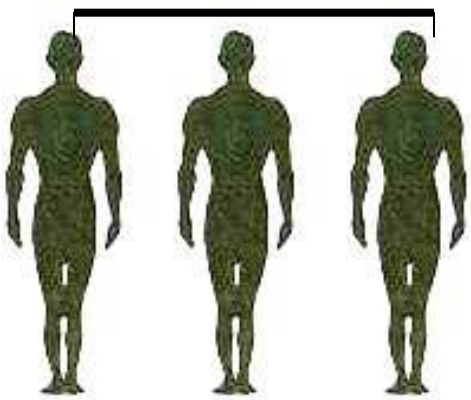


Figure VII-1. Flowchart depicting contacts of index Ebola-infected man. See the rationale for development of the Ebola virus scenario. See the Ebola scenario and Note above for detailed information regarding the potential exposures depicted in this diagram.

RECOMBINANT MONKEYPOX SCENARIO

Rationale Used for Development of the Recombinant Monkeypox Scenario

Most individuals under the age of 16 in the United States have no immunity to smallpox or the other non-smallpox orthopoxviruses such as monkeypox. Since the global eradication of smallpox was certified by the World Health Assembly (WHA) in 1980 (APHA 2004), civilians have not been immunized against smallpox and the World Health Organization (WHO) recommends against cross-immunization for monkeypox using the smallpox vaccine (APHA 2004). Monkeypox has occurred sporadically in African rainforest countries since 1970 as smallpox disappeared. The disease affects all age groups though historically children under the age of 16 make up the greatest proportion of cases. Among unvaccinated children, the case fatality rate ranges from 1% to 14% (APHA 2004). Infection in humans may be acquired through physical contact or respiratory droplets and the nasopharyngeal, oropharyngeal, or cutaneous routes. The route of transmission in animals is less clear. The virus might be transmitted to animals through the nasopharynx or oropharynx route, through skin abrasions, or through the ingestion of infected animal tissue. (Jezek and Fenner 1988) Epidemiological data suggests a secondary attack rate of about 8% (Hutin 2000). In Africa, extended transmission has occurred in a hospital setting. Prolonged outbreaks in humans are generally attributed to lack of vaccination and an enzootic (continued low-level presence of disease in an animal host) situation. In 2003, an outbreak of the disease occurred in six midwestern and Central States of the US (IL, IN, KS, MO, OH and WI). This outbreak was subsequently traced to pet prairie dogs that were infected by exotic rodents imported from Africa (MMWR 2003). Direct contact with infected animals poses a considerable risk as demonstrated by this recent outbreak. Of the 71 human monkeypox cases, 18 (i.e., 25%) were in veterinarians or veterinary staff who had contact with pet prairie dogs infected with the virus (MMWR 2003). There is no direct evidence of transfer of monkeypox from man to animals but the potential must be considered. The CDC warns animal handlers who may have been exposed to monkeypox virus to avoid contact with small ‘pocket pets’ such as hamsters and gerbils (CDC 2003). Further, veterinarians or other personnel “who are diagnosed with monkeypox should not examine animals during their illness because they may pose a risk of disease transmission to animals and should isolate themselves at home to minimize contact with other persons and animals” (CDC 2003).

Based on the aforementioned evidence in the scientific, epidemiologic and public health literature, it was determined that the potential for spread of monkeypox in a simulated community could most appropriately be studied through the use of A-BEST simulation modeling techniques and three types of societal contacts:

- Casual contacts - person to person societal interactions outside the household
- Household contacts - close interactions between family or household members
- Healthcare contacts – contacts occurring during the provision of healthcare

Using A-Best modeling techniques, in conjunction with the fictitious scenario described below, potential disease transmission was studied including 1) casual contacts such as interactions with others in a shop, school or on public transportation; 2) household contacts such as daily interactions within a family; 3) intimate contacts such as sexual intercourse or other exchanges of body fluids; and 4) healthcare worker contacts such as performing injections, blood draws, respiratory therapy treatments, invasive procedures or other activities that place the worker in close proximity to blood and other body fluids.

Recombinant Monkeypox Scenario

A 46-year-old male virologist lives in a household with his wife, six-year-old daughter and a family pet hamster. The virologist is performing pathogenesis studies involving aerosolization of recombinant monkeypox virus carrying a green fluorescent protein (gfp) marker gene in a nonhuman primate (NHP) model. He was vaccinated against smallpox when he was 10 years old prior to "living abroad" with his family. He currently experiences periodic episodes of allergic eczema and was not revaccinated prior to beginning work with monkeypox.

During the necropsy (autopsy) of a NHP infected with the recombinant monkeypox, the virologist sustains an unrecognized percutaneous exposure due to a breach in the integrity of his glove. Fourteen days after this exposure he has mild flu-like symptoms (low-grade fever, body aches and sore throat) that resolve within 48 hours at which time he does some yard work. Three days after onset of his symptoms, he notices a raised nonpruritic (non-itching) vesicle on the palm of his right hand and two days later a similar vesicle appears on the back of his neck. He does not seek medical attention as he determines he "just got into something" in the yard. Together, the man and his daughter have a daily routine of handling and caring for the family's pet hamster each evening and continue to do so after the vesicles appear on his hand.

The mother and daughter take the hamster to visit the daughter's first grade class as an activity during the class study of mammals. The visit lasts two hours and 26 children, including the daughter, handle or are in close proximity to the hamster. The mother returns home with pet hamster and notices the animal is lethargic and upon closer inspection it seems to be 'gagging' or coughing periodically and has some discharge from an eye. The mother believes the hamster is suffering the ill effects of being handled too much or too roughly during the classroom visit. The hamster's symptoms worsen and it dies five days later.

Fourteen days after the school visit, the mother begins to have symptoms involving what appears to be a skin infection. Her primary care doctor refers the mother to a dermatologist who diagnosed a staphylococcal (bacterial) skin infection and treated her accordingly with an antibiotic. That evening the daughter is running a fever and has skin eruptions so the father takes her to the Emergency Department (ED) where she is diagnosed with a streptococcal (bacterial) infection. She is treated with an antibiotic and an antipyretic (fever reducing medication) and released. The daughter's condition worsens and the father becomes suspicious because differing diagnoses have been

provided for the mother and daughter. He returns to ED with his daughter at which time the ED physician obtains the father's employment history and an infectious diseases (ID) consult is requested. (In Tyngsborough and Peterborough no ID consultation is immediately available). The daughter's condition continues to worsen and she is placed in intensive care for stabilization and subsequent transport to a tertiary care hospital. As her condition continues to deteriorate, severe neurological disease develops and she requires mechanical ventilation to assist her breathing. The daughter is transferred to BUMC Intensive Care Unit and placed in contact and airborne isolation.

The hypothetical events described in this scenario were simulated using A-BEST modeling for each of the three communities of Boston-BUMC, Tyngsborough and Peterborough. A simplified diagram of this scenario can be in found in Figure VII-2.

Note: *The events described in the above scenario are highly contrived and are based on the exaggerated assumptions that 1) the virologist was not appropriately immunized with the smallpox vaccine; 2) he would continue to work with the monkeypox virus even during an outbreak of his allergic eczema; 3) he did not notice the penetration of his glove and the subsequent monkey blood underneath the glove; and 4)he did not use adequate double gloving techniques to protect himself during work with monkeypox infective tissues and body fluids. Further, there is no direct evidence that monkeypox is transmitted from man to animals (in this case, the hamster). The potential for such exposure and required mitigation measures should such an exposure occur is the subject of exhaustive and repeated training prior to and during work involving exotic agents. This would have included guidance to avoid contact with small 'pocket pets' such as hamsters and gerbils. (CDC 2003) Laboratory workers who conduct research with exotic agents must report all fevers and other relevant symptoms to the institutional Responsible Official (42 CFR Part 73), the Environmental Health and Safety Office and an appropriate, identified medical authority. Previously established response and treatment protocols would have been followed. The CDC Select Agent Program must also be notified in the event of a possible exposure to monkeypox (42 CFR Part 73). Workers with a known exposure are considered to be potentially infected with the agent(s) they are working with until proven not to be the case. In this instance, the virologist would have been placed on a "fever watch" for the duration of the 21 day incubation period. If any symptom occurred that may have resulted from a monkeypox infection, he would have been treated in accordance with CDC recommendations "Updated Interim Guidance for Use of Smallpox Vaccine, Cidofovir and Vaccinia Immunoglobulin (VIG) for Prevention and Treatment in the Setting of an Outbreak of Monkeypox Infections" (2003). Finally, evidence suggests that diminishing numbers of cases of monkeypox in successive generations are likely and eventual cessation of transmission is probable (Jezek 1987). Under these conditions, the secondary exposure to the hamster and subsequent exposures of the mother, daughter and other children would not have occurred.*

The infection of the scientist, described in the above scenario, is highly contrived solely in an attempt to ensure spread of disease into the simulated community for computational modeling. Results of that modeling will far overstate the actual risk.

Recombinant Monkeypox Scenario

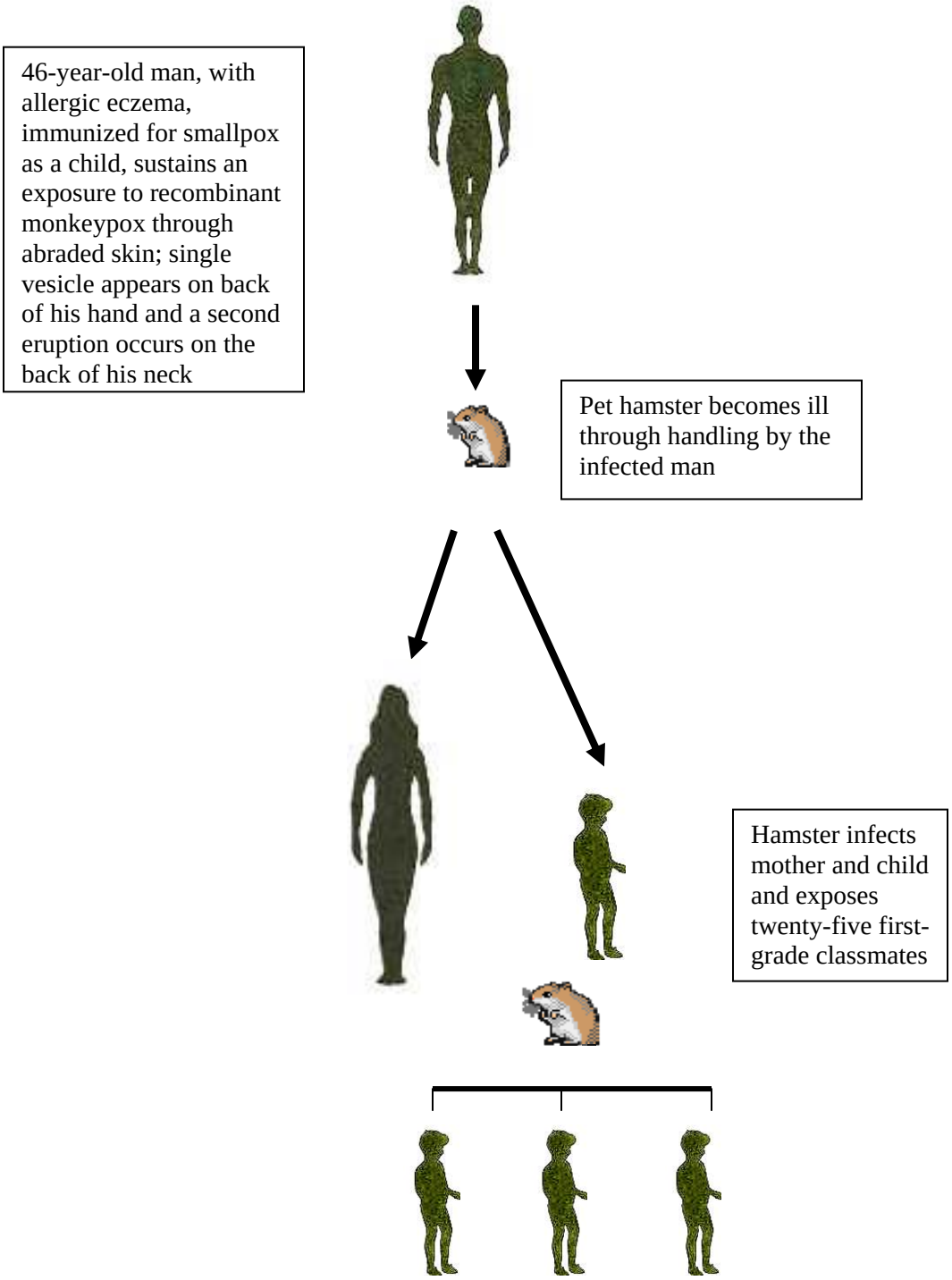


Figure VII-2. Flowchart depicting contacts of recombinant monkeypox infected man. See the rationale for development of the monkeypox virus scenario. See the monkeypox scenario and Note above for detailed information regarding the potential exposures depicted in this diagram.

SABIA VIRUS SCENARIO

Rationale Used for Development of the Sabia Virus Scenario

Three cases of Brazilian hemorrhagic fever (BrHF) caused by Sabia virus (SABV) have been reported since it was first detected in 1990. The index case was a 25-year old woman in Sabia, Brazil (PAHO 2003). Her infection was naturally acquired, but the other two cases that followed were laboratory-acquired. The second case was a laboratory technician who was working to identify the infectious agent isolated from the first case (Coimbra et. al. 1994). A third case occurred in 1994 in a virologist at Yale University who was working to characterize the newly discovered virus (MMWR 1994). While BrHF was lethal in the first patient, the other two cases recovered (Coimbra et.al., 1994, CDC/MMWR 1994). Given the small number of cases, it is difficult to determine definitely the possible mode(s) of transmission. Natural infections with other arenaviruses tend to occur through exposure to dried excreta (often urine) from infected rodents. These exposures occur through inhalation (contaminated dust or bedding), ingestion (contaminated food or water) or though direct contact with broken or abraded skin or mucosal membranes (Borio et al 2002). Natural infection by SABV is thought to occur in a similar manner. Inhalation of virus-laden particles has been responsible for transmission of other hemorrhagic fevers and this is the most likely route of exposure for the two laboratory-acquired Sabia virus infections (MMWR 1994, Peters 2002). Also, while not known to be true in BrHF, person-to-person transmission of other viral hemorrhagic fever viruses is known to have occurred through direct contact with secretions (Borio et.al. 2002). Some arenaviruses, such as Lassa and Machupo viruses, have been associated with secondary person-to-person and nosocomial (health-care setting) transmission. Airborne transmission has also been reported in connection with certain arenaviruses (CDC-Arenavirus Fact Sheet). Person-to-person transmission of arenaviruses may occur during the acute febrile phase when the virus is present in the throat and is easily aerosolized (USA-CHPPM accessed March 2007, Peters 2002). This method of transmission must be taken into consideration when choosing methods for prevention and containment of BrHF.

Based on the aforementioned evidence in the scientific, epidemiologic and public health literature, it was determined that the potential for spread of Sabia virus in a simulated community could most appropriately be studied through using A-BEST simulation modeling techniques of three types of societal contacts and one laboratory exposure through inhalation of infectious aerosols:

- Casual contacts - person to person societal interactions outside the household
- Household contacts - close interactions between family or household members
- Healthcare contacts – contacts occurring during the provision of healthcare

Using A-BEST modeling techniques, in conjunction with the hypothetical scenario described below, potential disease transmission was studied including 1) casual contacts such as those in schools, on mass transit, or places of worship during the acute febrile phase of illness; 2) household contacts such as inter-familial interactions, close contacts

between a mother and a child or through contaminated household articles; and 3) healthcare worker contacts such as exposure to respiratory and pharyngeal secretions, blood and body fluids, contaminated bedding and other linens.

Sabia Virus Scenario

A male virologist-physician removes what he believes to be a BSL-2 arenavirus (Tacaribe) from the laboratory freezer on a Monday morning and expands the virus in a cell culture system. On Thursday, high speed centrifugation of cell culture fluids in the laboratory results in some spillage through a crack in the seal of a centrifuge bottle. Two other workers are present in the lab but are remote from the centrifuge. The virologist notifies his co-workers of the spill and he cleans it up. Co-worker 1 chooses to leave the lab and go on a coffee break while Co-worker 2 remains at the bench remote from the centrifuge during clean up. The spill is not considered significant by any worker and is not reported.

Co-worker 1 is a single mother with three small children under the age of five. Co-worker 2 is married and lives with her husband and a teen-aged son.

Friday afternoon virologist travels to/remains in Boston for the weekend and visits with friends in their home. While returning home on Sunday night he begins to feel unwell (7 days post exposure). He treats himself with ibuprofen for two days as symptoms worsen. He seeks treatment from his primary care physician because he fears he may be having a relapse of an untreated malarial infection. The primary physician orders thick blood smears for malaria but they are negative. Further review of work history reveals that the virologist has worked with a variety of arenaviruses including Sabia (but only in a BSL-4 laboratory so this is not the agent of highest suspicion). He is hospitalized and given supportive therapy while patient specimens are subjected to a variety of testing to identify the virus. After specimens are collected, patient is begun on ribivirin antiviral therapy (day 13 post exposure).

Fourteen days after the spill incident, Co-worker 1 feels unwell experiencing fever, malaise (tiredness), etc. but attributes it to becoming ill with the “cold” all three of her young children have and that is passing through their daycare center. She does not seek healthcare and because she was at home with a sick child she does not hear about the virologist’s hospitalization. In addition, 14 days post exposure, Co-worker 2 begins to feel unwell and reports her illness to her lab chief who directs her to the ED for evaluation of possible arenavirus infection.

The hypothetical events described in this scenario were simulated using A-BEST modeling for each of the three communities of Boston-BUMC, Tyngsborough and Peterborough. A simplified diagram of this scenario can be in found in Figure VII-3.

Note: *The events described in the above scenario are highly contrived and are based on the exaggerated assumptions that 1) the male virologist could have mistakenly handled*

an arenavirus requiring BSL-4 containment (Sabia virus) in a BSL-2 laboratory; 2) the virologist did not inspect the centrifuge bottle prior to use and failed to use a containment rotor in the centrifuge or open it only within a biological safety cabinet; 3) inappropriate spill clean-up procedures were employed and that none of the workers thought the potential exposure was significant; 4) no one reported the spill or potential exposures; 5) a select agent was mislabeled and unaccounted for; 6) close contact can result in person-to-person disease transmission; 7) the lab chief would not notify Co-worker 1 of the virologist's arenavirus infection and subsequent hospitalization; and 8) appropriate barrier nursing techniques would not be used and may result in hospital-acquired or work-related infections in healthcare staff. The potential for exposure and required mitigation measures are the subjects of exhaustive and repeated training prior to and during work involving agents requiring BSL-4 containment. Laboratory workers who conduct research on exotic organisms such as arenaviruses must report fevers and other symptoms to the institutional Environmental Health and Safety Office and an appropriate, identified medical authority. The CDC Select Agent Program must also be notified in the event of a possible exposure to or infection from a select agent as does the institutional Responsible Official. Exposed workers are considered to be potentially infected with the agent(s) they work with until proven not to be the case. In this instance, all three workers would have been place on a "fever watch" for the duration of the 5 to 16 day incubation period. If any symptom occurred that may have resulted from a Sabia infection the workers would have been admitted immediately to the hospital under isolation procedures in a manner meeting or exceeding CDC Interim HFV Guidelines (CDC 2005). Institution of these measures in the above scenario would have dramatically reduced the potential for an occupationally-acquired infection in a healthcare worker. Under these conditions, the secondary exposure to a health care worker who may have been inadvertently exposed to BrHF through a needle stick, or respiratory or oropharyngeal secretions would likely not have occurred. The viruses cannot be spread through casual contact (including skin-to-skin contact without exchange of body fluids).

With regard to the failure to properly identify and control a Sabia virus sample, the impact of release of a highly dangerous biological agent or toxin – whether intentional or accidental – can be significant. Thus, tight controls over such agents and toxins are paramount to prevent use as a weapon or inadvertent release. Consequently, the United States strictly regulates possession, use, and transfer of certain biological agents and toxins (select agents) that have the potential to pose a severe threat to public health and safety. (42 CFR Part 73) The Agricultural Bioterrorism Protection Act of 2002 authorized the strict regulation of select agents and toxins that have the potential to pose a severe threat to animal and plant health, or to animal and plant products. (7 CFR Part 331, 9 CFR Part 121) Failure to maintain appropriate control over a select agent is also against the law and a person violating the possession restrictions on select biological agents and toxins may be subjected to criminal prosecution (18 U.S.C. § 175b). A case in point; in late 2003, the United States prosecuted a medical researcher in Texas for inappropriately handling and transferring a select agent. A jury convicted the researcher of, among other charges, shipping select agent samples without the proper permit and mislabeling the mailing package. A federal court sentenced the researcher to two years

imprisonment. The probability of mislabeling a sample or losing select agent inventory, in the current climate, is extremely remote.

The infections of the laboratory workers, described in the above scenario, are highly contrived solely in an attempt to ensure spread of disease into the simulated community for the purpose of computational modeling. Results of that modeling will far overstate the actual risks.

Sabia virus Scenario

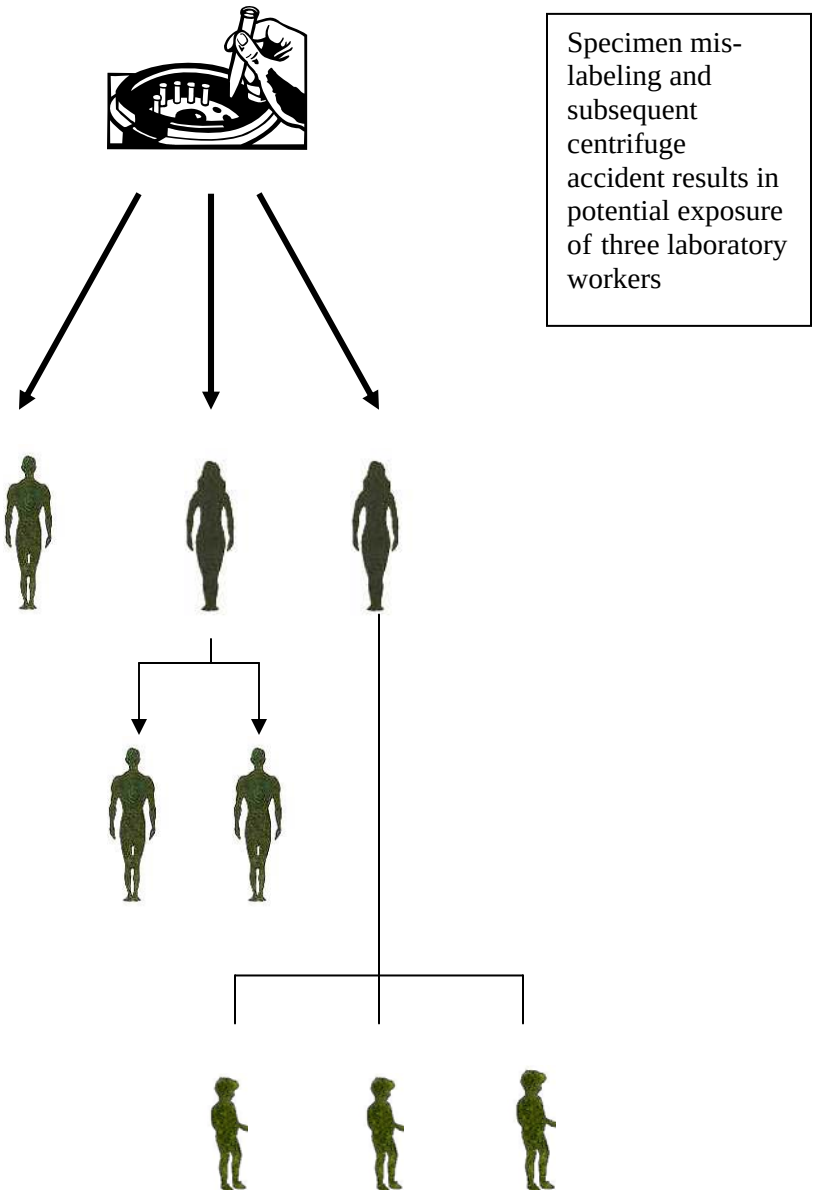


Figure VII-3. Flowchart depicts three laboratory exposures to a mislabeled arenavirus culture as a result of a centrifuge accident. See the rationale for development of the Sabia virus scenario. See the Sabia scenario and Note above for detailed information regarding the potential exposures depicted in this diagram.

RIFT VALLEY FEVER TRANSPORTATION ACCIDENT SCENARIO

Rationale Used for Development of the Rift Valley Fever Virus Scenario

Rift Valley Fever is primarily a veterinary public health problem on the African continent that provokes abortion among pregnant ungulates (animals having hooves) and often fatal in young animals (Shimshony et al. 1983). Humans are also highly susceptible to infection. Humans can get RVF as a result of bites from mosquitoes and possibly other bloodsucking insects that serve as vectors; RVF is not transmitted from person-to-person. However, protective measures should be taken to prevent infection by aerosols produced during the handling of infected fetuses and tissues of livestock and in laboratory procedures. Veterinarians and livestock industry personnel are at risk. Exposure can result from the slaughtering or handling of infected animals or by touching contaminated meat during the preparation of food. In endemic areas, an animal vaccination program is critical in preventing the disease but it is not used in the US because RVF does not exist on the North American continent.

Susceptible hosts in which viral amplification can occur are present in the United States (cattle and other livestock). Mosquitoes (arthropods) transmit RVF and an aggressive human- and animal-biting species of mosquitoes capable of transmitting RVF in laboratory studies (Gargan 1988) is present in both Massachusetts and New Hampshire. Unlike some other VHFs, RVF has the ability to be spread beyond the initial introduction point by mosquito vectors present in the United States (Peters 2005, Gargan, et al., 1988). It is unknown whether this can occur via interhuman transmission mediated by arthropods or if viremic domestic animals are required (Peters 2005). Virus titers in infected humans are high enough to infect mosquitoes (Meegan, et al., 1979; Gargan et al.1988) so there is a theoretical possibility that after biting infected humans, those mosquitoes can, in turn, transmit virus to other vertebrate hosts or introduce virus into new areas. (Hoogstraal et al.1979, Mebus 1998, Gerdis 2004). It is unknown whether this can occur via interhuman transmission mediated by arthropods or if viremic domestic animals are required (Peters 2005).

Infection has resulted from contact with laboratory specimens and laboratory-generated aerosols containing the virus. Laboratory-acquired infections of RVF through inhalation of infective aerosols have been recorded (Sabin and Blumberg 1947, Harding and Byer 2006) and there have been 103 laboratory-acquired RVF infections, resulting in four deaths, published in the scientific literature (Paragas and Endy 2006). An inactivated vaccine for humans, not available commercially, has been used under an investigational new drug (IND) application, in the U.S. to protect laboratory workers from RVF.

Based on the aforementioned evidence in the scientific, epidemiologic and public health literature, it was determined that the potential for spread of RVF virus in a simulated community could most appropriately be studied through the use of A-BEST simulation modeling techniques and two types of societal contacts, animal or veterinary work-related activities and HCW contacts. Mosquito transmission of disease must also be considered.

- Occupational contact- handling or having other contact with animal tissues or body fluids
- Household contacts- close interactions between family or household members
- Contact with Mosquitoes
- Healthcare worker contacts

Using A-Best modeling techniques, in conjunction with the fictitious scenario described below, potential disease transmission was studied including 1) household contacts such as inter-familial interactions between a mother and a child or through contaminated household articles; 2) healthcare worker contacts with bloodborne exposure to infective blood and body fluids such as needle sticks or splashes of body fluids to mucous membranes; 3) occupational exposure of veterinarians, abattoir workers, farmers or butchers; and 4) mosquito-borne disease both interhuman disease mediated by the mosquito and mosquito-borne disease facilitated through amplification hosts. MLAB-ST modeling was also applied to this scenario.

Rift Valley Fever Transportation Accident Scenario

A lab chief who is studying the pathogenesis of the Rift Valley Fever virus causing the current epidemic in east Africa asks a postdoctoral fellow to package a vial of virus for transportation to a colleague's lab across the country. In doing so, the "post-doc" places a small amount of dry ice in the infectious agent shipping container and seals the container preparing it for courier pick up. The courier places the package in the back of a step van and proceeds to drive down the street (Albany Street, Tyng Road, or Camp Sargent Road) toward a main road when he hits a "pot hole". The jarring of the package causes the over-pressurized shipping container to explode frightening the driver who crashes the step van into a utility pole along the side of the road. RVF virus is released into the interior of the van. Local emergency responders handle the incident; the driver, while shaken up and has a mild concussion, is not otherwise injured.

Within the next week the driver begins to run a fever and feels very tired and stays home from work early in his illness. Hoping to feel better the driver takes a walk around his wooded backyard in the evening while waiting for his wife to come home from work. While in the backyard, he sustains a mosquito bite on the neck before returning inside.

The hypothetical events described in this scenario were simulated using A-BEST modeling for each of the three communities of Boston-BUMC, Tyngsborough and Peterborough. A simplified diagram of this scenario can be in found in Figure VII-4. A-BEST Modeling begins when the infected mosquito population reaches 10,000 infected mosquitoes per acre of suitable water habitat, flooded land or still water in each community. MLAB-ST modeling begins when the mosquito bites the infected van driver.

Note: *The events described in the above scenario are highly contrived and are based on the exaggerated assumptions that: 1) The postdoctoral fellow would ignore the clear*

warning on the infectious disease shipping container stating "Do Not Place Dry Ice in Shipper"; 2) that the Lab Chief would allow an inexperienced scientist to pack a select agent; 3) the infected courier would be bitten by a North American mosquito capable of vectoring RVF during the stage of his illness when viral titer in his blood would be high enough to infect the mosquito; 4) amplification hosts would be present in the communities for which the simulation was conducted;5) the mosquito would live long enough to take a blood meal and infect a cow or sheep; and 6) amplification would result in 10,000 infected mosquitoes per acre of appropriate water habitat (for A-BEST modeling and simulation). The MLAB-ST was used to simulate disease transmission beginning from one infected mosquito.

The potential for such exposure and required mitigation measures should such an exposure occur is the subject of exhaustive and repeated training prior to and during work involving exotic agents and especially select agents. All potential exposures such as that experienced by the courier must be reported to the Environmental Health and Safety Office and appropriate, identified medical authority. The CDC Select Agent Program must also be notified in the event of a possible exposure to or infection from a select agent as must the institutional Responsible Official. Exposed workers are considered to be potentially infected with the agent(s) they are working with until this proven not to be the case. In this instance, the courier would have been place on a "fever watch" for the duration of the 2-6 day incubation period. If any symptom occurred that may have resulted from a RVF infection the courier would have been admitted immediately to the hospital under isolation procedures in a manner meeting or exceeding CDC Interim HFV Guidelines (CDC 2005). Institution of these measures in the above scenario would have dramatically reduced the potential for an occupationally-acquired infection in a healthcare worker. Lack of an amplification host in any of the communities simulated would have reduced the probability of establishing RVF in the environment to levels so low as to be undetectable. The postdoctoral fellow would have been required to attend certified shipper's training prior to packaging infectious agents for transport, as well as registered and approved by the CDC and USDA Select Agent Programs prior to having access to as select agent such as RVF. Furthermore, if workers are unvaccinated RVF is worked with in BSL-4 facilities.

The infection of the courier, described in the above scenario, is highly contrived solely in an attempt to ensure spread of disease into the simulated community for the purpose of computational modeling. Results of that modeling will far overstate the actual risks.

Rift Valley Fever Transportation Accident Scenario

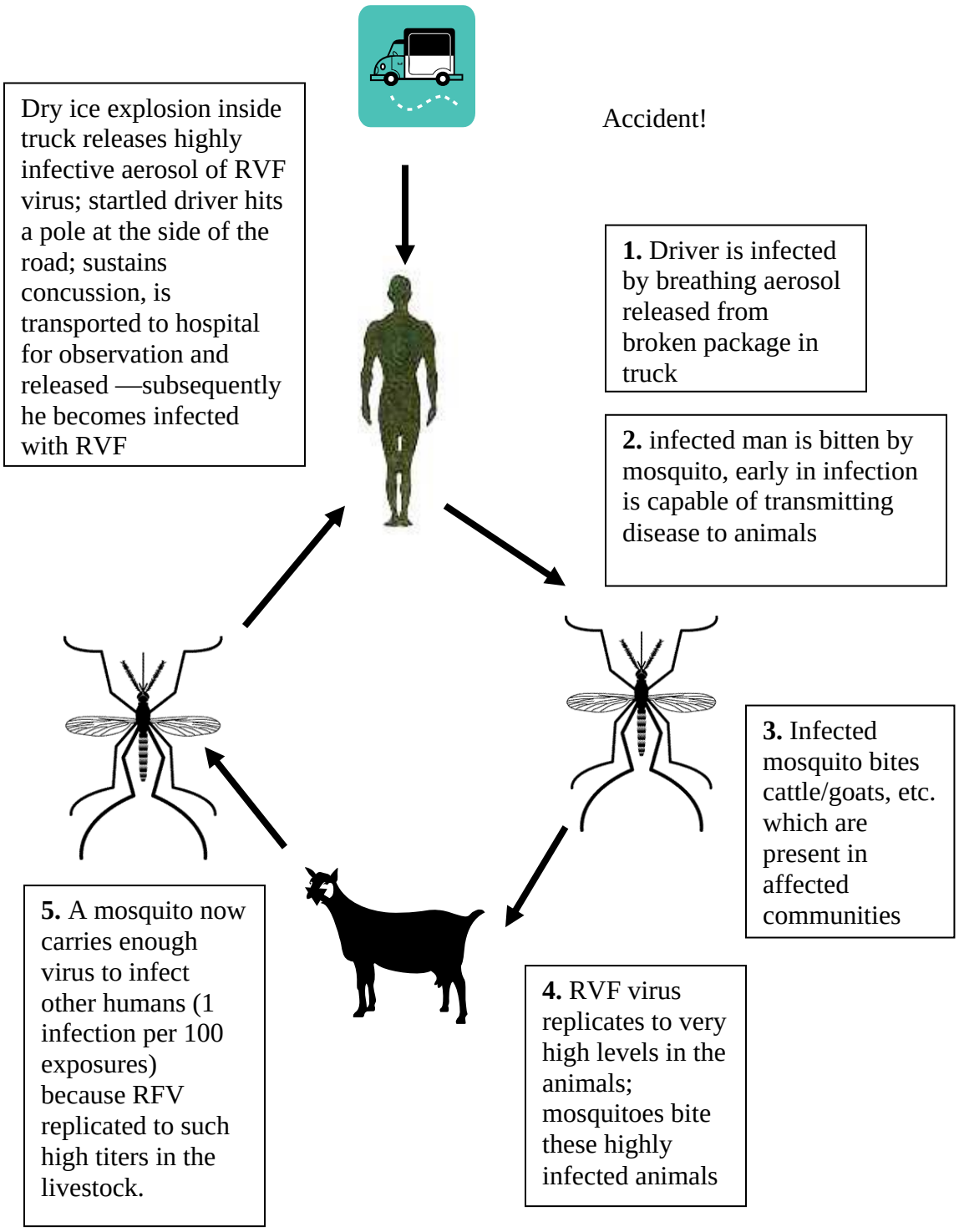


Figure VII-4. Flowchart of Rift Valley Fever introduction into the community. See the rationale for development of the Sabia virus scenario. See the RVF scenario and Note above for detailed information regarding the potential exposures depicted in this diagram.