

Report on the Potential Exposure to Ebola Virus

Centers for Disease Control and Prevention

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Executive Summary

This report describes an incident involving the potential exposure of a laboratory technician at the Centers for Disease Control and Prevention (CDC) to live (non-inactivated) Ebola virus. The incident occurred on December 22, 2014, on CDC's Roybal Campus in Atlanta during procedures for a study being conducted as part of the public health response to the ongoing West Africa Ebola outbreak. The potential exposure of the laboratory technician resulted from the inadvertent transfer of potentially live Ebola virus from one of CDC's high containment biosafety level 4 (BSL-4) laboratories to a lower biosafety level 2 (BSL-2) laboratory, where the laboratory technician processed the material. The laboratory technician completed 21 days of monitoring and reported no illness. Subsequent studies conducted at CDC have determined that the mistakenly transferred samples likely did not contain live virus, and posed no safety risk to CDC staff or the broader community.

Description of the incident

The incident involved staff from CDC's Viral Special Pathogens Branch (VSPB), which conducts public health research on highly pathogenic viruses and has played a central role in the Agency's response to the current Ebola outbreak. Staff involved in the incident were conducting an animal-model study to gain information to help determine if the current strain of Ebola virus was more virulent compared to other outbreak strains and if oral fluid swabs could be used in disease diagnosis efforts. The study involved taking two oral swabs daily from each of the study animals and then placing the swabs in two sets of tubes—one designated for live-virus studies and the other for studies with inactivated material. The tubes were distinguishable only by colored caps and pre-printed labels. The incident occurred when the tubes designated for live-virus studies were mistakenly prepared for transfer out of the BSL-4 laboratory and then subsequently taken to the BSL-2 laboratory for additional studies. On December 23, CDC laboratory scientists involved in the study discovered the problem, took immediate steps to minimize the possible risk to workers in the BSL-2 laboratory, and promptly reported the incident to their leadership, with standard notifications made for select agent or toxin exposures. Leadership of the CDC BSL-4 laboratory where this incident occurred immediately suspended transfers out of the laboratory until a full review of the incident is completed and appropriate improvements are implemented. In addition to the internal investigation of the incident described in this report, per standard protocol, CDC's Division of Select Agent and Toxins and the Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture has conducted an investigation.

Internal investigation

An internal investigation was conducted by a team of CDC laboratory scientists from other parts of the Agency, who interviewed persons directly involved with the incident as well as others who had specific knowledge of the incident and related activities. The overriding causes of this incident were related to inadequate safeguards, including lack of a written study plan that had been approved by a supervisor and a workflow that was not designed to sufficiently minimize the possibility that human error could result in exposure. Other underlying factors included lack of a centralized point of contact in VSPB for laboratory safety and select-agent compliance; lack of project oversight and continuity in day-to-day leadership; and the lack of full implementation of recent laboratory safety enhancement requirements, which may have had the potential to reduce the likelihood of this incident.

Recommendations

This report describes specific actions underway at CDC to improve laboratory safety, recommended actions for VSBP to address factors that may have caused or contributed to the incident, and actions to address issues identified from this incident that may have implications for all CDC BSL-3 and BSL-4 laboratories. Examples include ensuring full understanding and implementation of actions recommended as part of CDC's ongoing laboratory safety improvement efforts, such as proper completion of a required form for materials taken out of CDC's high containment laboratories to lower biosafety level laboratories and appropriate secondary verification measures for critical safety control points. New remediation actions specific for the VSPB laboratory include the designation of a senior scientist to ensure select-agent compliance. Broader recommendations for CDC's BSL-3 and BSL-4 laboratories include the establishment of a peer review system of written research plans to help optimize workflows and minimize safety errors; the use of multiple, visual safeguards (e.g., coloring for liquids, distinctive size and shape for specimen handling and storage containers); and steps to improve safety for laboratory staff working outside of normal work hours.

Laboratory safety at CDC

Ongoing efforts to ensure that appropriate lab safety procedures are followed and that continuous improvements occur are essential for safeguarding CDC staff and the broader community. Although this incident clearly highlights the importance of ongoing efforts to identify and address potential gaps in laboratory safety at CDC, progress has been made over the past several months. Actions include creation of a new position of CDC Associate Director for Laboratory Science and Safety; review and approval of all inactivation methods for highly pathogenic organisms; an inventory of all stored biologic materials; and broader engagement of CDC laboratory staff and stakeholders to better inform laboratory safety recommendations. As part of these efforts, CDC has formed an external laboratory safety working group, under the Advisory Committee to the Director, composed of experts in biosafety and related areas, as well as an internal Laboratory Safety Improvement Workgroup (LSIW), which has worked closely with CDC laboratory scientists and leadership to identify and implement new safety procedures. Moving forward, CDC will continue to work to identify and implement systems and procedures that can further improve the Agency's laboratory operations and reduce safety risks, including those that may result from human error.

Background

On December 22, 2014, material from an Ebola virus experiment that could have contained live Ebola virus was inadvertently transported from one of the Centers for Disease Control and Prevention's (CDC) high containment biosafety level 4 (BSL-4) laboratories to a lower biosafety level laboratory (biosafety level 2 [BSL-2]). Both laboratories were part of the same CDC organizational branch and were select-agent approved. Although appropriate inactivation procedures were conducted, samples that had been prepared for viral culture studies and that were to be maintained in the BSL-4 laboratory were mistakenly thought to be the inactivated material, placed in a sealed transfer container, then moved out of the BSL-4 laboratory to the BSL-2 laboratory for additional studies. One laboratory technician worked with the material in the BSL-2 laboratory and had the potential to be exposed to live virus (the technician did not become ill, and subsequent studies have determined that the samples likely did not contain live virus). On December 23, CDC laboratory scientists involved in the study discovered the problem and promptly reported it to their leadership, with standard notifications made for select agent or toxin exposures. The CDC BSL-4 laboratory where this incident occurred immediately suspended transfers out of the laboratory until a full review of the incident is completed and appropriate improvements are implemented. This report reviews the circumstances related to this event, outlines how the event happened, and provides recommendations for preventing similar incidents in the future.

Ebola viruses

Ebola virus disease (Ebola), previously known as Ebola hemorrhagic fever, is a rare and frequently fatal disease caused by infection with one of the Ebola virus species. Ebola viruses can cause disease in humans and nonhuman primates (monkeys, gorillas, and chimpanzees). Ebola viruses are found in several African countries. Ebola was first discovered in 1976 near the Ebola River in what is now the Democratic Republic of the Congo; outbreaks have since appeared sporadically in Africa. In 2014, the largest outbreak of Ebola on record began in West Africa, resulting in an unprecedented public health crisis in the region and potentially throughout the world.

Laboratories involved in the incident

The incident involved staff from CDC's Viral Special Pathogens Branch (VSPB), which conducts public health research on highly pathogenic viruses, many of which cause hemorrhagic manifestations in humans. Examples include Ebola virus, Marburg virus, Lassa fever virus, Rift Valley fever virus, Crimean-Congo hemorrhagic fever virus, and other arenavirus and hantavirus species. Because of the severity of illness they cause and lack of effective treatment, almost all of these viruses are classified as BSL-4 pathogens and as such must be handled in special facilities designed to contain them safely. VSPB operates one of the world's few BSL-4 laboratories. Among its responsibilities, VSPB provides technical and research support and diagnostic materials to many international laboratories and collaborators. VSPB staff members are trained to respond to global disease outbreaks and provide assistance for disease detection and control measures. The Branch also is responsible for developing, evaluating, and improving methods for treatment, prevention, and laboratory diagnosis of hazardous disease agents. VSPB has approximately 50 staff members organized into seven teams. VSPB is located in CDC's Division of High-Consequence Pathogens and Pathology (DHCPP), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID).

The incident occurred during a study being conducted as part of the public health response to the ongoing West Africa Ebola outbreak. The study team included five staff members: two veterinary scientists (Scientists 1 and 2), and three laboratory technicians (Laboratory Technicians 1, 2, and 3). The incident directly involved Laboratory Technician 1, Laboratory Technician 2, and Scientist 2. However, only Laboratory Technician 2 worked with the material outside of the BSL-4 laboratory. Laboratory Technician 1 was a veterinary technician, and Laboratory Technician 2 was trained in molecular virology. Laboratory Technician 3, also a veterinary technician, had been previously assisting Laboratory Technician 1. Scientist 1 (the research group lead) and Laboratory Technician 3 were on leave the day of the incident.

Methods Used in Reviewing this Incident

In conducting an internal review of the incident, a team of CDC laboratory scientists from other parts of the Agency interviewed the persons directly involved with the incident as well as others who had specific knowledge of the incident and related activities. Each person was interviewed individually; interviews included a standard set of questions, as well as specific questions based on the individual's role and responsibilities. Relevant standard operating procedures, protocols, and training records were also reviewed.

Description of the Event

Appendix A provides a timeline of major events.

Study Design

The study, involving animal models, was designed to determine if the current strain of Ebola virus was more virulent compared to previous prototype strains (1976 Mayinga strain and the guinea pig-adapted virus variant) and to evaluate whether oral fluid swabs could be used to confirm disease diagnosis and determine infectiousness. These data would help guide and inform response activities in Ebola-affected areas, which has been a critical need in the ongoing Ebola outbreak, and build a collection of postmortem specimens for pilot testing rapid diagnostic tests on oral fluids prior to their use in humans in West Africa. Collectively, this information could be used to further understand and develop more informed guidelines for appropriate timing of Ebola virus diagnostics in the field and to provide data to supplement analyses of data generated from human patient materials collected during CDC's Ebola surveillance activities in West Africa.

CDC's Institutional Animal Care and Use Committee (IACUC) had approved the protocol for the animal work that was done. In addition, CDC's Laboratory Safety Improvement Workgroup (LSIW) had reviewed and approved the protocol for the inactivation procedures used in the study (consistent with recently implemented requirements), and the laboratory staff performing the study followed this protocol (including completion of checklist and supervisory notification of start and end of inactivation) on the day of the incident. However, although the study researchers had discussed and rehearsed the steps involved in the study, there was no detailed, written study plan covering all aspects of the study.

Two swabs were collected from each animal daily for 15 days. The two swabs were placed in separate vials, each containing different solutions: one vial contained lysis buffer for virus inactivation and subsequent nucleic acid testing, and the second vial contained virus transport media (VTM) for subsequent virus isolation attempts. Although both were clear, uncolored solutions and were in the same type of tube (2.0 ml Sarstedt™ tubes), the tubes for VTM had a preprinted “Virus Transport Media” label and a blue cap, compared to unlabeled, noncolored-capped tubes, for the lysis-buffer. For the study, both the VTM and the lysis-buffer tubes were hand-labeled with sequential numbers, corresponding to each animal number tested. All sample preparation work was performed in the VSPB BSL-4 select agent-registered laboratory; the nucleic acid testing was done in a VSPB select agent-registered BSL-2 laboratory after inactivation of the virus was complete.

How the incident occurred

The incident occurred on Monday, December 22, 2014 (14 days after the beginning of the study). On that day, Laboratory Technician 1 prepared two sets of tubes in the BSL-4 laboratory as described above and placed them into a tube rack for sample collection from each experimental animal. After weighing, each animal was briefly swabbed in the oral cavity with two long, polyester-tipped swabs (a noninvasive and nondistressful procedure) taking approximately 10 seconds per animal. On previous days, this procedure had been typically done by Laboratory Technician 1 and Laboratory Technician 3 together, but on this day was completed by Laboratory Technician 1 only. The research group lead (Scientist 1), along with the rest of the study team, had determined previously that one experienced animal technician could safely complete this task.

During sample collection, one swab was placed into each of the separate tubes (containing lysis buffer or VTM). The VTM tubes were to remain in the BSL-4 laboratory for later virus isolation attempts. By study design, one swab per animal was to be placed directly into a VTM tube and then the swab handle snapped off. After swabs were taken, the VTM tubes were to be resealed with their original blue-colored caps and placed in the -80°C freezer in the BSL-4 laboratory.

Unlike the VTM tubes, the lysis-buffer-containing tubes were hand-labeled with the animal number only (no pre-printed label or colored cap), since these tubes were just a temporary container used prior to the same-day transfer of the liquid from them into a 96-well deep block. The swab handles for the lysis-buffer tube specimens were not snapped off so that the swabs could be removed from lysis buffer and discarded by the laboratory technician responsible for the transfer of lysis buffer samples to the BSL-2 laboratory.

After sample collection was complete, normal procedure for this experiment was for the laboratory technician who took the swabs from the animals to leave the rack with the lysis-buffer tubes containing the long-handle swabs in the BSL-4 animal room biosafety cabinet (BSC) for later transfer to a 96-well block by a second laboratory technician. To prevent any possibility of non-inactivated particles being present on the lysis-buffer tubes, the transfer of the tube contents to the block was performed in the BSC of the BSL-4 animal room. The lysis buffer used (MagMax®, guanidinium chaotrope) requires a 10-minute inactivation time, which was generously exceeded due to the practical nature of the collection step from each animal and the time required to organize the tubes and then to physically transfer their contents to the 96-well block.

On the day of the incident, Laboratory Technician 1 snapped the handles off of the swabs in the lysis-buffer tubes instead of those in the VTM tubes, and stored them in the -80°C freezer in the

BSL-4 laboratory. Consequently, the VTM tubes, with intact swabs, were left in the BSC in the BSL-4 animal room for subsequent processing by Laboratory Technician 2. When processing the mistakenly placed VTM tubes from the BSC, Laboratory Technician 2 did not notice the “Viral Transport Media” label present on all of the specimen tubes. Also, since the long swabs were left in the tubes, the colored caps were not present for Laboratory Technician 2 to see, and visually the tubes looked identical to the lysis-buffer tubes, except for the label. Laboratory Technician 2 removed and discarded the swabs, transferred the specimens from the VTM tubes to a 96-well plastic block, heat-sealed the block with foil, placed the sealed block into the BSL-4 disinfectant dunk tank (which ensures no virus is present on the outside of the block), and contacted Scientist 2 to retrieve the specimen block from the outer corridor side of the dunk tank. In retrieving the 96-well block in the outer corridor, Scientist 2 visually inspected it for sample volume and adequate sealing; however, since the fluid colors of the lysis buffer and VTM were the same, there was no indication that the liquid in the block came from the VTM tubes. The block with the VTM material was then placed in a secondary container and taken from the BSL-4 outer corridor to the BSL-2 laboratory.

Laboratory Technician 2 left the BSL-4 laboratory (through standard, decontamination exiting procedures) and went to the BSL-2 laboratory and processed the specimens following approved protocols for nucleic acid assay. Because of the mix-up in the sample tubes, Laboratory Technician 2 could have been exposed to Ebola virus while transferring the specimens into the laboratory equipment that was used to process the specimens for the assay. However, subsequent studies have determined that the samples likely did not contain live virus at this stage, and Laboratory Technician 2 did not become ill.

On December 23, 2014, Scientist 2 entered the BSL-4 laboratory and noticed that the previous day’s specimens in the freezer did not have VTM labels, suggesting the wrong samples may have been transferred out of the BSL-4 laboratory the previous day. Scientist 2 immediately notified Scientist 1 and Laboratory Technician 1, and then immediately called the BSL-2 laboratory and asked all personnel to leave the laboratory until the potential inappropriate transfer had been confirmed or refuted. Scientist 1 and Laboratory Technician 3 visually confirmed the sample mix-up by examining the BSL-4 waste area and finding the VTM-labeled tubes. This indicated that the contents of the VTM tubes rather than the contents of the lysis-buffer tubes had been taken to the BSL-2 laboratory for nucleic acid testing on December 22.

The VSPB Branch and Division leadership immediately notified the CDC’s Responsible Official for select agent or toxin exposure and the Director of CDC’s Environment, Safety, and Health Compliance Office (ESHCO), following standard protocol. CDC leadership was notified and informed officials at the Department of Health and Human Services (HHS).

Findings

VSPB Results from Ebola Virus Isolation Studies: As part of the post-incident assessment, swab samples that had been collected the work days before and after the incident (December 19 and 23, respectively) were studied to evaluate if detectable live virus could have been present in the samples removed from the BSL-4 laboratory on December 22 (samples from the day of the incident had been destroyed during the nucleic acid assay process). VSPB reported no detectable Ebola virus present from swabs collected

on both December 19 and December 23, suggesting that there was likely no live virus in the samples that were mistakenly taken out of the BSL-4 laboratory on December 22.

Causes of the Laboratory Incident

The overriding causes of this relate to inadequate safeguards:

1. Lack of a written study plan that had been approved by a supervisor

Although there was an IACUC-approved protocol for animal handling and sampling and an LSIW-approved protocol for the study's inactivation procedures (consistent with requirements), there was not a written, approved study plan that outlined each of the steps that were to be followed in the experiment. Approval of overall study plans is not currently required.

2. A study plan workflow that was not designed to sufficiently minimize the possibility that human error could result in exposure

The study included placing identical oral swab samples from guinea pigs into two different sets of tubes, one for inactivation with nucleic acid extraction and one for virus isolation. The tubes were identical in brand and size, except for a blue cap and preprinted label on the tubes for virus isolation. Because the caps had been removed so the swabs could be collected and placed into the tubes, the tube caps did not provide the visual cue that was intended to distinguish between the two types of tubes. The collection of specimens and the extraction procedure were done by two different individuals, which also could have contributed to the error.

The two laboratory technicians and the laboratory scientist directly involved in the incident are experienced researchers, each with 5-10 years of experience working in BSL-4 laboratories, and had conducted these procedures uneventfully for the prior 2 weeks. Their inattentiveness regarding the differences in the tubes being used for inactivation and for virus growth media indicated an incomplete understanding of the workflow process as well as inadequacies in the workflow process itself, both of which could have contributed to the mix up of the sample tubes.

Other underlying factors that contributed to these direct causes include the following:

1. Lack of centralized point of contact for both laboratory safety and select agent compliance

VSPB does not have a designated individual responsible for monitoring laboratory safety and regulatory compliance. VSPB is part of a high containment laboratory (HCL) suite of BSL-4 laboratories that includes other CDC organizational groups. Other user groups in the HCL suite have dedicated safety and compliance points of contact that are knowledgeable of regulations, protocols, and procedures, and have accountability to ensure safety is prioritized and adherence to select agent requirements is followed.

2. Lack of project oversight and day-to-day leadership continuity

While an established HCL manager provides oversight for all groups in the HCL suite (e.g., oversight of physical facility issues, ensuring new users have appropriate training), VSPB does not have a full-time laboratory manager, and principal investigators are expected to provide oversight and management for their own studies. In addition, for the last 6 months, the Branch Chief has been deployed for the Ebola response and there have been several staff rotations to fill this critical role.

3. Lack of full implementation of recent laboratory safety enhancement requirements

In the last several months, CDC has implemented a number of safety enhancements. One of these includes the requirement that a Material Transfer Certificate (MTC) be completed for transfer of any material from high containment laboratories to lower biosafety level laboratories, including internal transfers. These certificates must describe all inactivation methods used and be signed by involved parties. This new procedure had not been fully implemented by the VSPB laboratories, and was not done for the transfer of specimens out of the VSPB BSL-4 laboratory to the VSPB BSL-2 laboratory on December 22.

An additional recently implemented laboratory safety improvement measure has been the requirement for secondary verification of critical safety control points, such as those involving inactivation of infectious agents. To fully meet these requirements, VSPB was taking steps to install a camera system to allow for additional verification that procedures were performed following protocol.

Full implementation of these two requirements may have had the potential to reduce the likelihood of this incident. VSPB is working to implement these two recommendations prior to resuming full BSL-4 operations. The camera systems are currently being installed in the BSL-4 laboratory, and the laboratory has received clear instructions on the intended use of the MTC.

Recommendations

In addition to recommendations for VSPB relating to this specific event, the incident has also highlighted issues that have implications for other CDC high containment laboratories. These actions are now being addressed as part of CDC's overarching laboratory science and safety improvement efforts, which began after earlier laboratory errors were identified (<http://www.cdc.gov/about/lab-safety/index.html>), and have resulted in the implementation of new safety enhancement actions. The recommendations are outlined across three categories:

I. Continued implementation of ongoing CDC laboratory safety improvement efforts

1. Leadership should ensure full understanding and implementation of previously recommended laboratory safety improvement actions, including the following:
 - The completion of an MTC for transfer of any material from high containment laboratories to lower biosafety level laboratories. MTCs must describe all inactivation methods used and be signed by involved parties. In situations where a hand off of materials between laboratory staff must be made, the MTC should ensure that the transfer is made in person and that both the originator and the recipient of the materials understand exactly what material is being exchanged and how it has been processed. Acknowledgment by both parties of the nature of the materials being handed off creates an additional checkpoint where errors might be recognized and corrected. Reduction in the number of steps and handoffs is well known in the medical field as a measure to prevent error.
 - Appropriate secondary verification of critical safety control points, including additional installation of camera systems for review and verification of critical steps in a protocol.

II. Additional safety enhancements recommended specifically for VSPB

2. Enlist a team to evaluate preparations that have been performed by the laboratory technicians involved in this incident to confirm that similar errors related to processing the wrong tubes for nucleic acids did not occur.
3. Identify a designated, senior scientist who understands the scientific basis for the procedures used in both the diagnostic and research activities of the Branch, maintains select agent compliance, ensures appropriate competency-based training, and serves as a resource for scientists if they have safety or security questions. This person should enter the laboratory on a routine basis (preferably daily) to provide consistent oversight. Having a designated, experienced laboratory safety point of contact will be increasingly critical as laboratories adopt new diagnostic and analytic technologies that may necessitate changes in safety measures.
4. Ensure mission-critical work is not affected when key leaders are deployed or on detail to support other public health priorities. To the extent possible, a consistent leader should be available to provide day-to-day oversight and prioritization of activities, enabling laboratory scientists to minimize lower priority work. Leadership should determine which, if any, activities (including both programmatic and research) can be eliminated or suspended without significant impact. And, for the remainder of the current Ebola response, VSPB should identify a single point of contact (with designated backup) to serve as Acting Branch Chief to provide consistent, on-site leadership.

III. Additional safety enhancements recommended for CDC high containment (BSL-3 and BSL-4) laboratories

5. Work with CDC scientists from high containment laboratories to establish a peer-review system of written research plans to foster critical thinking on how to optimize workflows and minimize error.
6. Enhance standard operating procedures for materials intended for inactivation and removal from laboratories:
 - Ensure that all materials are in standard, appropriately labeled tubes.
 - Ensure the use of multiple, redundant visual safeguards (e.g., coloring for liquids, distinctive size and shape specimen handling and storage containers) so that laboratory staff can more easily determine that the correct material is being taken out of a high containment laboratory.
 - Unless exceptions are reviewed and cleared by a supervisor, establish a requirement that inactivation procedures for a single protocol be performed or, at a minimum, checked by a single, highly trained individual within that team who understands the scientific reasons for each step of the procedure. This “from beginning to end” concept of processing high-risk pathogens intended for transfer from high containment laboratories to lower biosafety level laboratories would help ensure a greater sense of the personal responsibility required for these processes, given the commensurate risks of managing these pathogens unsafely.

- When possible and not detrimental for the end use of the materials, samples coming out of the BSL-4 laboratory should undergo gamma irradiation sufficient to inactivate any virus present. Materials not irradiated should require extra attention to verification of the inactivation procedures employed.
7. Because of the unique circumstances of BSL-4 work, further enhance safety for individuals working in the BSL-4 laboratory outside of normal work hours:
- Establish an on-call system to ensure after-hours availability of a BSL-4 supervisor or designee. These individuals should be experienced laboratory scientists who have access to the facility, are familiar with the process to enter and exit the laboratory, are authorized to enter the laboratory, and are capable of responding if health or technical issues arise.
 - Develop a standard operating procedure that
 - requires laboratory staff entering the BSL-4 laboratory after hours and on weekends to inform the on-call individual of their plans, and
 - contains steps to ensure that laboratory staff have exited safely.
8. When possible, scientists should not work in the BSL-4 laboratory unaccompanied.

Conclusions

Ongoing efforts to ensure that appropriate lab safety procedures are followed and that continuous improvements occur are essential for safeguarding CDC staff and the broader community. While the incident described in this report highlights the need for continued improvements in laboratory safety practices across the Agency, progress has been made in this area over the past several months. In addition to the recently implemented laboratory safety measures described earlier in this report, the LSIW has also worked with CDC laboratory scientists and leadership to identify other areas for improvements, including expansion of biosafety training and improvements in research standards and protocols. The Agency has also undertaken an inventory of all stored biologic materials, and engaged CDC laboratory staff and stakeholders to better inform recommendations for improving laboratory safety. As part of these efforts, CDC formed an external Laboratory Safety Workgroup of the Advisory Committee to the Director, comprising experts in biosafety and related areas, and has established a new position of Associate Director for Laboratory Science and Safety.

After the recommendations outlined in this report have been implemented, CDC will convene an external review of safety and security procedures, processes, policies, and organizational effectiveness of VSPB. The review will be conducted by an independent, non-conflicted external group in order to facilitate transparency and objectivity in their findings. The group will include members of the external Laboratory Safety Workgroup as well as other scientists with extensive experience working in BSL-4 laboratory settings and with technical expertise in biosafety, biosecurity, records management, informatics, and regulatory affairs. Consistent with standard procedures, APHIS has also conducted an investigation of this incident, and any additional recommendations from this review will also be implemented by CDC.

The new position of Associate Director for Laboratory Science and Safety will report to the CDC Director and have responsibility to provide Agency-wide leadership and accountability for laboratory science, safety, and quality. The position announcement was posted on USAJobs (<https://www.usajobs.gov/>); the position has closed, and recruitment is underway. Moving forward, this individual will engage leadership from high containment laboratories both within and outside of CDC to gather lessons learned and establish practices and standardization across CDC that can directly and effectively enhance laboratory safety.

CDC is committed to ongoing efforts to identify and implement systems and procedures that can further improve the Agency's laboratory operations and eliminate as much risk as possible.

Appendix A. Timeline of Major Events

December 19 (Friday)

- Viral Special Pathogens (VSPB) staff member prepares 500 µl-aliquot of MagMax® lysis buffer into clean, 2.0 ml microtubes (Sarstedt™) in VSPB's BSL-4 laboratory for use in an animal-model study undertaken as part of the ongoing Ebola outbreak response. Aliquots of 500 µL of virus transport media (VTM) had been previously obtained from CDC's Core Facility, pre-prepared into clean 2.0 ml microtubes (Sarstedt™). Although both solutions were in 2.0 ml Sarstedt™ microtubes, VTM tubes have a pre-printed "Virus Transport Media" label and a blue cap to prevent confusion.
- Aliquots were stored in refrigeration in the BSL-4 laboratory over the weekend

December 22 (Monday)

- Following study protocol and using the above-described microtubes, a veterinary technician (Laboratory Technician 1) took 2 oral swabs from each animal and placed individual swabs into separate tubes containing lysis buffer (for inactivation) or VTM (for future virus isolation studies)
- In error, Laboratory Technician 1 left the VTM tubes instead of the lysis-buffer tubes in the BSL-4 biosafety cabinet (BSC). The lysis-buffer tubes were placed in the BSL-4 freezer.
- Following safety protocols approved for removal of RNA specimens from the BSL-4 laboratories and assuming the VTM tubes were the lysis-buffer tubes, a second laboratory technician (Laboratory Technician 2) transferred the liquid from the VTM tubes into a 96-well block, foil sealed the block, and placed the sealed block into the disinfectant dunk tank
- Following normal protocol, a study team member (Scientist 2) transported the specimen block in a secondary container from the VSPB BSL-4 laboratory to a VSPB BSL-2 laboratory, where it was stored sealed in the laboratory's refrigerator
- Laboratory Technician 2 left the BSL-4 laboratory, went to the BSL-2 laboratory, and processed the specimens following approved protocols for nucleic acid assay, which included decontamination of equipment and work areas with bleach solution between steps and after completion.

December 23 (Tuesday)

- Scientist 2 noticed that the frozen tubes remaining in the BSL-4 were the lysis tubes and not the VTM tubes, and notified the research group lead (Scientist 1). Visualization by study team members of the empty VTM tubes in the BSL-4 waste confirmed the mistake.
- Upon verification, all areas of the VSPB BSL-2 laboratory where the sample processing occurred were surface decontaminated and all waste autoclaved.
- Personnel who were present in the VSPB BSL-2 laboratory at any point between time of processing and decontamination were identified. Laboratory Technician 2 was determined to have some risk of potential exposure and began a 21-day monitoring period, per current guidance.
- Following standard notification protocol, VSPB Branch and Division leadership notified CDC's Responsible Official (RO) of a potential select agent or toxin exposure, as well as the Director of the CDC Environment, Safety, and Health Compliance Office (ESHCO) and CDC leadership
- CDC leadership notified HHS of incident
- Summary of incident forwarded to CDC Division of Select Agent and Toxin (DSAT), as an initial select agent notification

December 24 (Wednesday)

- USDA's Animal and Plant Health Inspection Services (APHIS) officially notified of the incident
- Notification of the incident sent to CDC employees
- CDC notification of news media

December 27 (Saturday)

- APHIS/CDC Form 3 Report submitted by CDC RO
- DSAT acknowledges receipt of APHIS/CDC Form 3 Report

December 29 (Monday)

- Initial internal review meeting held

December 30 (Tuesday)

- Additional decontamination of affected areas complete.
- Personnel interviews began as part of the CDC internal review.

January 5 (Monday)

- Personnel interviews completed.

January 6 (Tuesday)

- APHIS/DSAT visits CDC to conduct an inspection in response to the laboratory incident.

January 9 (Thursday)

- APHIS/DSAT inspection completed.

January 10 (Saturday)

- ESCHO report with recommendations regarding re-entry of personnel into the affected BSL-2 laboratory is completed and shared with senior leadership.

January 12 (Monday)

- 21-day monitoring period completed. No symptoms or illness reported.

Appendix B. Definitions and Terms

Animal and Plant Health Inspection Services (APHIS) – A multi-function agency within the United States Department of Agriculture (USDA) responsible for protecting and promoting U.S. agricultural health, regulating genetically engineered organisms, administering the Animal Welfare Act, and carrying out wildlife damage management activities. The Agricultural Select Agent Service (AgSAS) is part of this agency.

Biosafety cabinet (BSC) (also called biological safety cabinet) – The primary means of containment used for working safely with infectious microorganisms that are designed to provide personnel, environmental, and product protection.

Biosafety Level (BSL) – The risk criteria used to define the four ascending levels of containment, referred to as biosafety levels 1 through 4 based on infectivity, severity of disease, transmissibility, and the nature of the work conducted.

Decontamination – The treatment of environmental surfaces (e.g., laboratory areas) to render any infectious materials sterile and nonpathogenic.

High Containment Laboratory (HCL) – Any biosafety level 4 (BSL-4) or biosafety level 3 (BSL-3) laboratory.

Inactivation – The process of treating an infectious agent to render it noninfectious and nonpathogenic.

Institutional Animal Care and Use Committee (IACUC) – an oversight body mandated by the Animal Welfare Act to review all research studies involving animals at CDC to ensure compliance with animal welfare standards.

Laboratory Safety Improvement Workgroup (LSIW) – A group established by the CDC Director to accelerate improvements in CDC laboratory safety and monitor incident recommendations.

Personal Protective Equipment (PPE) – Equipment that is worn to minimize exposure to workplace injuries or illnesses.

Responsible Official (RO) – The individual designated by an entity with the authority to ensure compliance with the Select Agent Regulations at the entity.