

Expanded Access Investigational New Drug (IND) Protocol: Booster
Dose Immunization with Ervebo[®] (Ebola Zaire Vaccine, Live) for
Domestic Pre-exposure Prophylaxis (PrEP) Vaccination of Adults (≥ 18
years of age) at Potential Occupational Risk for Exposure to *Zaire*
ebolavirus

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ABBREVIATIONS/DEFINITIONS

ACIP	Advisory Committee on Immunization Practices
AE	Adverse event
BSL-4	Biosafety level 4
CDC	Centers for Disease Control and Prevention
ELISA	Enzyme-linked immunosorbent assay
EU/mL	Endotoxin units per milliliter
EVD	Ebola virus disease
FDA	Food and Drug Administration
HCP	Healthcare Personnel
HIV	Human Immunodeficiency Virus
IgG	Immunoglobulin G
IM	Intramuscular
IND	Investigational New Drug
IP-10	γ -inducible protein 10
IRB	Institutional Review Board
NHPs	Nonhuman primates
PCR	Polymerase chain reaction
PFU	Plaque-forming units
PrEP	Pre-exposure prophylaxis
PREVAIL	Partnership for Research on Ebola Virus in Liberia study
rVSV	Recombinant vesicular stomatitis virus
rVSV Δ G-ZEBOV-GP	Recombinant vesicular stomatitis virus with envelope glycoprotein replaced by <i>Zaire ebolavirus</i> (Kikwit 1995 strain) glycoprotein (V920)
SAE	Serious adverse event
SDV	Single-dose vial
SNS	Strategic National Stockpile
STRIVE	Sierra Leone Trial to Introduce a Vaccine against Ebola
VAERS	Vaccine Adverse Event Reporting System

1 INTRODUCTION and BACKGROUND

Ebola virus is a zoonotic pathogen that causes severe hemorrhagic fever in humans known as Ebola virus disease (EVD). The virus is transmitted through contact with body fluids from infected patients. There are four species of Ebola virus that have been known to cause disease in humans. Of these, species *Zaire ebolavirus* is the most lethal with case fatality rates of 70-90% if left untreated.

Importation of EVD to the U.S. from an epidemic region through an infected traveler or healthcare worker is a recognized risk with potential for secondary transmission. There were 11 people treated for EVD in the U.S. during the 2014–2016 Ebola outbreak in West Africa. Of the 11 domestically-treated EVD patients that resulted in 2 deaths, two were imported cases of EVD, seven were persons with EVD symptoms transported from West Africa to U.S. hospitals, and two were domestic healthcare workers who cared for the first travel-associated EVD case diagnosed in the U.S. The patient died but both healthcare workers recovered.¹

The 2014–2016 Ebola outbreak in West Africa and the 2018 Ebola outbreak in the Democratic Republic of the Congo (DRC) heighten the importance of pre-event preparedness and response, including vaccine availability and access, to protect high-risk groups who may have potential occupational exposure to Ebola virus (e.g., laboratorians, healthcare workers, emergency responders) for pre-exposure prophylaxis (PrEP) against *Zaire ebolavirus*. Ervebo® (Ebola Zaire Vaccine, Live also known as V920, rVSVΔG-ZEBOV-GP or rVSV-ZEBOV) was approved by the U.S. Food and Drug Administration (FDA) on December 19, 2019 for the prevention of disease caused by *Zaire ebolavirus* in individuals 18 years of age and older as a single dose administration. Since the FDA-approved dosing of Ervebo is a single dose administration only, a booster dose is considered an unapproved use. Therefore, the Centers for Disease Control and Prevention (CDC) is sponsoring this expanded access Investigational New Drug (IND) program to allow booster dose administration for domestic PrEP use in adults (≥ 18 years of age) with potential risk of occupational exposure to *Zaire ebolavirus*. Ervebo is not planned for commercial marketing, but is maintained in the Strategic National Stockpile (SNS) with vaccine access within the United States facilitated by the U.S. government.

Ervebo is manufactured by Merck Sharp & Dohme Corp., NJ, USA. The vaccine is a replication-competent, live, attenuated recombinant vesicular stomatitis virus (rVSV) vaccine with the gene for the *Zaire ebolavirus* Kikwit strain glycoprotein (ZEBOV-GP) replacing the gene for the native VSV glycoprotein.² The FDA's approval of the vaccine was based on the data from 12 clinical trials in which a total of 15,399 adults received a dose of $\geq 2 \times 10^7$ (plaque-forming units) pfu. Clinical efficacy of the vaccine was supported by an open-label, randomized cluster (ring) vaccination study during the 2014-2016 outbreak in Guinea (Ebola Ça Suffit trial), in which 3,537 contacts and contacts of contacts of individuals with laboratory-confirmed EVD received either immediate or delayed (21 days or later) vaccination. Clinical immunogenicity was assessed in three studies conducted in Liberia, Sierra Leone, United States (U.S.), Canada, and Spain.

In well-controlled clinical trials in adults, Ervebo was demonstrated to be a safe and effective vaccine for preventing EVD infection. The vaccine has been shown to elicit rapid immune response in 14 days after a single dose. Seroconversion in adults peaked between 28 and 35 days for most clinical trial subjects.³ However, Ervebo does not provide cross protection against other species of *Ebolavirus* or *Marburgvirus*. Since the evaluation of clinical efficacy and immunogenicity has not been done in the same study, it is not possible to define a correlate of protection at the individual level. The duration of protection conferred by Ervebo is unknown, and effectiveness of the vaccine when administered concurrently with antiviral medication, immune globulin, and/or blood or plasma transfusion is also unknown.

Preliminary data from vaccine response during the 2018 outbreak in DRC confirm efficacy of Ervebo against disease.⁴ Vaccine efficacy evaluation and safety monitoring during the vaccine response in DRC

will provide additional data as they become available. See **Section 8, Efficacy and Safety Information of Ervebo for EVD** for a summary of efficacy and safety information from clinical studies and clinical experiences of the vaccine during the West Africa Ebola outbreak.

On February 26, 2020, the [Advisory Committee on Immunization Practices \(ACIP\)](#) recommended PrEP vaccination with Ervebo for adults ≥ 18 years of age in the U.S. population who are at potential occupational risk of exposure to Ebola virus (species *Zaire ebolavirus*) because they are responding or may respond to an outbreak of EVD; laboratorians or other staff working at biosafety-level 4 facilities in the U.S.; or healthcare personnel working at federally-designated Ebola Treatment Centers in the U.S.⁵

2 EXPANDED ACCESS IND PROGRAM DESCRIPTION

Ervebo is approved by FDA for prevention of EVD in people 18 years of age and older as a single dose only. Therefore, initial doses of Ervebo will proceed under its FDA-approved indication. However, the duration of protection conferred by Ervebo is unknown. Given booster dose vaccination is not covered under Ervebo's FDA-approved indication, CDC is sponsoring this expanded access IND protocol to provide an appropriate regulatory mechanism to allow for booster dose administration of Ervebo.

There is need for PrEP vaccination of individuals with occupational risk of Ebola virus exposure, especially for those deploying to areas with Ebola outbreaks. Ervebo is not commercially marketed in the United States and access to vaccine maintained in SNS is through licensed healthcare provider request to CDC. Ervebo available under this IND program is for domestic use in the United States, its territories and U.S. embassy or military installations outside of the U.S., in individuals who have been previously vaccinated and are at potential occupational risk for exposure to *Zaire ebolavirus* and meet eligibility criteria, including individuals in occupational risk groups described in the February 26th, 2020 ACIP recommendations.

The procedures set forth in this expanded access IND program are to help ensure that CDC, the sponsor of the IND, and the healthcare providers, their institutions/sites, and affiliated personnel involved in the request receipt, handling, administration, and disposal of Ervebo are informed of and abide by the FDA regulations regarding IND and human subjects protections requirements (21 CFR Parts 312, 50, and 56). CDC will provide Ervebo upon receipt of request of a booster dose(s) by licensed healthcare providers from institutions/sites with identified individuals who meet the eligibility criteria under this IND protocol (see **Section 2.1, Inclusion Criteria/Eligibility**). Under this expanded access IND program, the requesting healthcare providers will serve as site investigators to assume the oversight responsibility, including any delegated activities, regarding vaccine receipt, handling and use at their institutions/sites, and monitoring and reporting of serious adverse events (SAEs) resulting from Ervebo administration. See **Section 5, Procedures**, and **Section 7, Program Responsibilities**, for further details.

2.1 Inclusion Criteria/Eligibility

In order to be eligible to receive a booster dose with Ervebo under this expanded access IND program, individuals must be adults (≥ 18 years of age) in the U.S. population who have previously received Ervebo and/or any other Ebola vaccine in the past (e.g., ≥ 6 months since prior vaccination). Eligible individuals include those at potential high risk of occupational exposure to Ebola virus (species *Zaire ebolavirus*) such as those who:

- Are responding or may respond to an outbreak of Ebola virus disease (e.g., persons who would be expected to provide care for Ebola patients or be deployed to an outbreak area)
or
- Work as laboratorians or other staff at biosafety-level 4 (BSL-4) facilities in the U.S. Personnel working at non-BSL-4 facilities in the Laboratory Response Network may be eligible to receive Ervebo depending on specific circumstances of public health needs and the Ebola preparedness and/or response activities at such facilities.

or

- Work as healthcare personnel (HCP)** at federally-designated Ebola Treatment Centers in the U.S. HCP working at state-designated Ebola healthcare facilities or other facilities may be eligible to receive Ervebo depending on specific circumstances of public health needs and the Ebola preparedness and/or response activities at such facilities.

**Healthcare personnel refers to all paid and unpaid persons serving in healthcare settings who have the potential for direct or indirect exposure to Ebola patients or infectious materials, including body substances (e.g., blood, tissue, and specific body fluids); contaminated medical supplies, devices, and equipment; contaminated environmental surfaces; or contaminated air. These healthcare personnel include, but are not limited to, emergency medical service personnel, nurses, nursing assistants, physicians, physician assistants, technicians, clinical laboratory personnel, autopsy personnel, therapists, phlebotomists, pharmacists, students and trainees, contractual staff not employed by the healthcare facility, and persons not directly involved in patient care, but who could be exposed to infectious agents that can be transmitted in the healthcare setting (e.g., clerical, dietary, environmental services, laundry, security, engineering and facilities management, administrative, billing, and volunteer personnel). Adapted from <https://www.cdc.gov/infectioncontrol/guidelines/healthcare-personnel/index.html>

Final eligibility decisions of booster doses, including dose interval (e.g., ≥ 6 months after initial vaccination), will be assessed on an individual case-by-case basis depending on clinical judgement of the risks and benefits and circumstances warranting booster dose administration (e.g., outbreak response, suspected waning immunity, vaccination strategy, and/or projected duration of elevated risk).

Please see the **Occupational Risk/Vaccine Eligibility Assessment Form** (Appendix A1) to help identify vaccine candidates and complete the **Ervebo Request and Use Agreement Form**, and **Form FDA 1572** (Appendix A2) to submit the vaccine request to CDC.

2.2 Exclusion Criteria

Ervebo should not be given to individuals with any of the following:

- Known severe allergy, such as anaphylaxis, to Ervebo or any component of the vaccine, including rice protein
- Clinical evidence (e.g., oral temperature $>38^{\circ}\text{C}$ [100.4°F], systemic symptoms) of a systemic infection or other acute intercurrent illness at the scheduled time of vaccination[†]
- Presence of any clinically significant medical condition, past medical history, pre-existing illness (e.g., acute malignancy, history of Guillain-Barré syndrome, history of neurologic disorder that may increase risk, active autoimmune disorder or immunosuppression) that in the opinion of the healthcare provider (i.e., site investigator) may place the individual at an unreasonably increased risk by getting the vaccine
- Unwilling to complete the informed consent process and sign the consent form

[†]Vaccination may be rescheduled at a later date if the conditions resulting in ineligibility are no longer present.

While pregnancy and lactation are not absolute exclusion criteria for receiving Ervebo, live, attenuated vaccines are generally contraindicated during pregnancy. Women of reproductive age should be counseled on the potential fetal risk(s) of vaccination, and determination of whether to receive Ervebo should be made on an individual basis, in consultation with a healthcare provider, based on the risk/benefit of vaccination against the risk of exposure to Ebola virus.

Laboratory and healthcare workers at risk for occupational exposure to *Zaire ebolavirus* receiving Ervebo must continue to adhere to recommended biosafety guidelines and infection prevention and control procedures. Individuals responding to an EVD outbreak must wear recommended personal protective equipment and follow proper procedures to prevent infection upon direct contact or contact with body fluids from a suspected or confirmed Ebola patient even if they received Ervebo.

3 PRECAUTIONS/SPECIAL POPULATIONS/ADVERSE EVENTS

3.1 Precautions

- Among the 15,399 adult subjects vaccinated with Ervebo during the clinical development of the vaccine, there were two reports of serious vaccine-related pyrexia and two reports of non-fatal anaphylaxis. Following vaccination with Ervebo, monitor the vaccinated individuals for signs and symptoms of hypersensitivity reactions. Appropriate medical treatment and supervision must be available in case of an anaphylactic event following the vaccine administration. Each vaccinated individual should be observed for a minimum of 30 minutes post-vaccination.
- Vaccination with Ervebo may not protect all individuals. Vaccinated individuals should continue to adhere to recommended infection control practices to prevent *Zaire ebolavirus* infection and transmission.
- The safety and effectiveness of Ervebo have not been assessed in immunocompromised individuals. The effectiveness of Ervebo in immunocompromised individuals may be diminished. To date, a small number of HIV-positive adult subjects have been vaccinated with Ervebo in the Partnership for Research on Ebola Virus in Liberia (PREVAIL) first study (PREVAIL I) that evaluated two Ebola vaccines.⁶ Additional studies are ongoing to evaluate the use of Ervebo in HIV-positive subjects without severe immune compromise. The risk of vaccination with Ervebo, a live virus vaccine, in immunocompromised individuals should be weighed against the risk of disease due to *Zaire ebolavirus*.
- Because Ervebo is produced with rice derived recombinant human serum albumin, precaution should be taken with individuals allergic to rice. Individuals with a history of severe allergic reaction (e.g., anaphylaxis) to rice protein should not receive Ervebo.
- Vaccine virus RNA has been detected by reverse-transcription polymerase chain reaction in urine (up to 7 days post-vaccination), blood and saliva (up to 14 days post-vaccination), and fluid from skin vesicles (up to 20 days post-vaccination) of vaccinated adults.^{3,7-10} Transmission of vaccine virus through close personal contact is a theoretical possibility. Healthcare providers administering vaccine should exercise appropriate infection control practices. Vaccine recipients should avoid:
 - sharing needles, razors, toothbrushes, eating utensils, drinking from the same cup, and open-mouth kissing for 2 weeks after vaccination; if oral sores develop after receiving vaccine, avoid these activities until the sores heal.
 - close contact and association with high-risk individuals (e.g., immunocompromised individuals, pregnant or breastfeeding women, infants (< 1 year of age)) for up to 6 weeks following vaccination.
 - exposure of livestock to blood and bodily fluids for up to 6 weeks following vaccination.

Additional post-vaccination instructions for vaccinated individuals are detailed in **Appendix B1, Informed Consent Form**.

3.2 Considerations for Special Populations

Pregnancy

There are no adequate well-controlled studies of Ervebo in pregnant women, and human data available from clinical trials with Ervebo are insufficient to establish the presence or absence of vaccine-associated risk during pregnancy. In the randomized, unblinded Phase 2/3 Sierra Leone Trial to Introduce a Vaccine against Ebola (STRIVE) study that evaluated Ervebo, there were 84 pregnant women; 31 and 18 pregnant women in the immediate and deferred crossover vaccination arms, respectively, became pregnant within 60 days after vaccination, and 35 in the unvaccinated group became pregnant within 60 days of enrollment. Of the pregnant women with known outcomes, no statistical difference in pregnancy loss, defined as spontaneous abortion and still birth, was observed between pregnant women in the immediate vaccination (14/31; 45%) and unvaccinated (11/33; 33%) arms. No external congenital anomalies were

detected among 44 live-born infants examined (born to 28 vaccinated and 16 unvaccinated pregnant women).¹²

The World Health Organization recommends the use of Ervebo in pregnant and breastfeeding women during an active *Zaire ebolavirus* outbreak in affected areas, in the context of rigorous research or in accordance with a compassionate use protocol.¹³ Vaccination for pregnant women should consider the risk of exposure to *Zaire ebolavirus* against potential vaccine-related risk during pregnancy based on individual informed decisions.

Lactation

Human data are not available to assess the impact of Ervebo on milk production, its presence in breast milk, or its effects on the breastfed child. The development and health benefits of breastfeeding should be considered along with the mother's clinical need for Ervebo and any potential adverse effects on the breastfed child from Ervebo or from the underlying maternal condition. For preventative vaccines, the underlying condition is susceptibility to disease prevented by the vaccine.

Older Adults

A total of 542 subjects ≥ 65 years of age received Ervebo during clinical development of the vaccine. Although this was inadequate to determine whether the immune response in older adults (≥ 65 years) is different from younger participants, the FDA-approval of Ervebo for prevention of disease caused by *Zaire ebolavirus* in adults (≥ 18 years) is inclusive of older adults without an upper age limit.

3.3 Possible Adverse Events with Ervebo

The most commonly reported injection-site adverse events among the adult subjects vaccinated with Ervebo during clinical development were injection-site pain (70%), swelling (17%), and redness (12%). The most commonly reported systemic adverse events following vaccination with Ervebo were headache (37%), feverishness (34%), muscle pain (33%), fatigue (19%), joint pain (18%), nausea (8%), arthritis (5%), rash (4%) and abnormal sweating (3%). A limited number of adult subjects received a second dose 28 days after initial dose; reactogenicity at the injection site and systemic reactogenicity were less severe after the second dose than after the first dose. The potential for previously not known, rare, serious events following vaccination may be possible. Monitor individuals for signs and symptoms of reactions following vaccination. Appropriate medical treatment and supervision must be available in case of an anaphylactic event.

4 PRODUCT DESCRIPTION

Ervebo is a live, attenuated recombinant Vesicular Stomatitis Virus (rVSV) with a deletion of the VSV envelope glycoprotein that is substituted with the *Zaire ebolavirus* (Kikwit 1995 strain) surface glycoprotein. The vaccine virus is grown in serum-free Vero cell cultures, harvested from the cell culture medium, and purified to produce bulk drug substance before being aseptically added to a drug product stabilizer solution. The filled final vaccine is supplied as single-dose vials containing a 1-mL dose and stored frozen at -80°C to -60°C (-112°F to -76°F) for long-term storage.

Each 1 mL dose contains a minimum of 72 million plaque forming units (7.2×10^7 pfu) of vaccine virus in a stabilizer solution containing 10 mM Tromethamine (Tris) and 2.5 mg/mL rice-derived recombinant human serum albumin. Each 1 mL dose may contain residual amounts of host cell DNA (≤ 10 ng) and benzonase (≤ 15 ng). The vaccine may contain trace amounts of rice protein. The product contains no preservatives. The vaccine vial stopper is not made with natural rubber latex.

Frozen vaccine will be shipped from the SNS to the participating sites at $\leq -60^{\circ}\text{C}$ on dry ice in an insulated shipping container containing a temperature monitoring device. The preference is to maintain Ervebo frozen at -80°C to -60°C until use to the extent possible. The vaccine should be thawed completely at

room temperature since it is sensitive to slow thawing at refrigerated temperature. Once thawed, vaccine can be stored refrigerated at 2°C to 8°C (35.6°F to 46.4°F) for a total time of **no more than 14 days** or at room temperature (up to 25°C; 77°F) for a total time of **no more than 4 hours**.

5 PROCEDURES

Ervebo will be provided upon CDC's receipt and review of request from licensed healthcare providers for individuals who have previously received Ervebo and/or any other Ebola vaccine (e.g., ≥ 6 months since prior vaccination) and with occupational risk of exposure to *Zaire ebolavirus*. After verifying requests, CDC will coordinate shipment of frozen vaccine(s) to participating sites directly from the SNS. Also see **Section 7, Program Responsibilities**, for related information.

5.1 Vaccine Request and Release Decision

- Before requesting Ervebo, identify individuals with occupational risk for *Zaire ebolavirus* using the **Occupational Risk/Vaccine Eligibility Assessment Form** (Appendix A1).
 - This form is provided for site use to aid in determining individuals for whom vaccination is appropriate. The vaccine eligibility under the IND is for the 3 occupational risk groups as indicated under Section 2.1 (EVD responders, BSL-4 workers, and Healthcare personnel).
- Complete and submit the **Ervebo Request and Use Agreement Form**, and **Form FDA 1572** (Appendix A2) with curriculum vitae (CV) to CDC by fax (404-471-2526) or a scanned copy via email (spathvax@cdc.gov).
 - By submitting the completed and signed forms in Appendix A2, the licensed healthcare providers at participating sites acknowledge that they understand and agree to assume oversight responsibility, including any delegated activities, regarding vaccine receipt, storage, handling, use and disposal under the CDC-sponsored IND program at their institutions/sites, including ensuring informed consent, monitoring and reporting of SAEs resulting from Ervebo administration, in accordance with this expanded access IND protocol and applicable FDA IND regulations.
- Upon receipt, CDC will review, verify and/or discuss the information with the requesting institution/site as needed to make a release decision, and initiate vaccine shipment, accordingly, which will be coordinated by SNS.
- CDC will not approve vaccine if upon review, eligibility criteria per the protocol are not met, or if there is incomplete information, any known or cited violation with FDA regulations, and/or any reason for which the requesting institution/site will not be able to comply with the requirements of the IND protocol.

5.2 Shipment of Vaccine

CDC will notify the requesting healthcare provider or designee once the vaccine release decision has been made.

- Ervebo will be shipped by SNS to the address indicated in the **Ervebo Request and Use Agreement Form**, and **Form FDA 1572** (Appendix A2). Shipment information with estimated delivery date will be provided once arranged.
- The vaccine is maintained at -80°C to -60°C (-112°F to -76°F) for long-term storage. The vaccine will be shipped to requesting sites frozen at ≤-60°C (≤-76°F). A temperature monitoring device will be included in each vaccine shipment. See **Table 1** and **Section 5.3, Vaccine Receipt and Handling at Participating Sites**, for further information on storage conditions and durations.

5.3 Vaccine Receipt and Handling at Participating Sites

- Upon receipt of vaccine shipment, delivered by SNS frozen (≤-60°C (≤-76°F)), at the participating site, slowly open the insulated shipping container packed with dry ice and point the lid away from the body and others in the area.

- Remove the primary shipping box containing the vaccine vials from the outer, insulated shipping container and place immediately into a -80°C to -60°C (-112°F to -76°F) freezer, if available at the participating site. Preference is to maintain vaccine vials at -80°C to -60°C (-112°F to -76°F) until use to the extent feasible.
 - If -80°C to -60°C (-112°F to -76°F) freezer capacity is not available, then thaw vials completely at room temperature until no visible ice is present (approximately 10 to 15 minutes). Thaw vaccine vials **at room temperature only** as vaccine is sensitive to slow thawing at refrigerated temperature. Once fully thawed, store immediately at 2°C to 8°C (35.6°F to 46.4°F) and use within the use-by-period indicated in Table 1 below.

Table 1: Use-by-Period Once Thawed²

Storage Temperature	Maximum Storage Duration
2°C to 8°C (35.6°F to 46.4°F)	14 days
9°C to 25°C (48°F to 77°F)	4 hours

- Transfer time from dry ice of the shipper to the -80°C to -60°C (-112°F to -76°F) freezer at the participating site, if available, or thawing at room temperature followed by refrigeration, if no freezer at the participating site, should be kept to a minimum.
- Protect vaccine from light. Do **NOT** re-freeze.
- After appropriately storing the vaccine into the freezer or refrigerator, locate the temperature monitoring device included in the shipment. Plug it into the USB port of a laptop or desktop computer immediately to stop the temperature recordings. The screen on the device may be blank as it warms up while plugged into the USB port. Do not wait to thaw the temperature monitoring device prior to plugging into a USB port as this can lead to potential inaccurate temperature recordings.
 - If a temperature excursion is indicated on the device, notify the CDC. CDC, in coordination with SNS, will provide clarification on if the vaccine can still be used or if it is unacceptable for administration and the appropriate next steps to take (e.g. discard on site).
- Similarly, notify CDC if a temperature excursion occurs at any time during vaccine storage at the participating site for determination on product impact and usability of the vaccine.

5.4 Vaccination and Post-vaccination Procedures at Participating Sites

- Ervebo administration at the participating sites will proceed with a designated licensed healthcare provider serving as a site investigator. Consultation with CDC Ebola subject matter experts is available as needed (e.g., eligibility criteria, expected adverse events, clinical consideration for a booster dose).
- Inform vaccinated individuals that if they choose to be vaccinated, then they will receive a brief voluntary electronic Post-Vaccination Adverse Events Survey from CDC via email or text on or around days 7, 14, 21, and 28 after vaccination to monitor for specific adverse events. Show an example paper copy of **the CDC Post-Vaccination Adverse Events Survey** (Appendix B2) to eligible individuals with the informed consent form (ICF).
- For each eligible participant, conduct informed consent process (see **Appendix B1, Informed Consent Form**) and obtain a signed ICF prior to administering the vaccine. Provide a copy of the signed ICF to participants.
- On the day of vaccination, use the **Vaccination Record Form** (Appendix C) to assess and document vaccine eligibility, administration, and any or no occurrence of SAEs during the minimum 30-minute observation period following vaccination.
- The completed Vaccine Record Form for each vaccinated individual must be returned to CDC no later than 3 calendar days of vaccination. If any SAEs are observed, report to CDC

- by returning the completed VRF **as soon as possible** and **no later than 3 calendar days (72 hours)** of SAE occurrence. Any subsequent AEs/SAEs experienced by the vaccinated individuals that the site investigator becomes aware of should be reported to VAERS.
- Remind vaccinated individuals of post-vaccination care and precautionary measures as outlined under the “**What you need to know AFTER you get the Ebola vaccine**” in the ICF (e.g., covering vaccination site, avoiding sharing razors, toothbrushes, eating utensils for 2 weeks after vaccine, avoid pregnancy for 8 weeks after vaccination by use of effective barrier prophylaxis and/or birth control, etc.).
 - Within 14 calendar days of completing vaccination (i.e., having used received vaccines) or final vaccine disposition, complete the **Vaccine Product Accountability and Disposal Record Form** (Appendix D) and return to CDC by fax (404-471-2526) or a scanned copy via email (spathvax@cdc.gov). Failure to comply may result in further action and denial of future vaccine requests.

When the booster dose usage of Ervebo under the CDC-sponsored IND is determined no longer necessary (e.g., discontinuation of CDC-sponsored IND program), the participating sites will be notified with instructions to either discard or return the unused vaccines. Disposal and/or return must be appropriately documented in the **Vaccine Product Accountability and Disposal Record Form** (Appendix D).

6 DOSAGE AND ADMINISTRATION

Practice aseptic technique and standard precautions when preparing and administering the vaccine intramuscularly (IM).

6.1 Preparation, Dosage and Administration

Supplies required:

- Ervebo (supplied as 1-mL single dose vial containing $\geq 7.2 \times 10^7$ pfu)
- Sterile syringe (e.g., 3-mL syringe)
- Sterile needle for IM administration (e.g., 22-25 gauge, 1- to 1.5-inch length needle)

If frozen, thaw the vaccine vial completely **at room temperature** until no visible ice is present (approximately 10 to 15 minutes). Do not thaw the vial in a refrigerator as the vaccine is sensitive to slow thawing. Gently invert the vial several times. The vaccine is a colorless to slightly brownish-yellow liquid with no particulates visible. Do not use if particulate matter or discoloration exist. Use the vaccine immediately after thawing. If not used immediately, the vaccine may be stored for up to 14 days at 2°C to 8°C (35.6°F to 46.4°F) or for up to 4 hours at room temperature (up to 25°C; 77°F) protected from light.

Do NOT re-freeze.

Using aseptic technique, withdraw a 1 mL dose using a sterile syringe with a sterile injection needle and administer the vaccine by IM injection in the deltoid area of the non-dominant arm at a 90° angle into the muscle tissue using a needle long enough to ensure IM deposition of the vaccine.

- Do not inject the vaccine intravascularly.
- No data are available for administration via the subcutaneous or intradermal routes.

After administration of the vaccine, the used vial and syringe should be disposed of as biohazardous waste in accordance with the participating sites' policy, as applicable. Used vials and syringes can be disposed of in normal biohazard containers, as the product does not contain Ebola virus.

7 PROGRAM RESPONSIBILITIES

CDC Principal Investigator

The CDC Principal Investigator is located at the CDC and has the oversight responsibility of this expanded access IND protocol to allow booster dose vaccination for adults (≥ 18 years) with potential high risk of occupational exposure to EVD and who have previously received Ervebo and/or any other Ebola vaccine. The Principal Investigator will monitor the appropriate use of Ervebo, including review of vaccination requests, evaluation of eligibility requirements and reported SAEs, and provide consultation to requesting healthcare providers (i.e., site investigators) as needed.

Licensed Healthcare Providers (Site Investigators)

By requesting and obtaining Ervebo under the CDC-sponsored IND 16337, the requesting licensed healthcare providers serve as site investigators for use of Ervebo at their sites under this expanded access IND program and are responsible for ensuring appropriate handling, procedures and use of Ervebo at their institutions/sites in accordance with this IND protocol, and FDA IND regulations. By completing and signing the required **Ervebo Request and Use Agreement Form**, and **Form FDA 1572** (Appendix A2), the site investigator acknowledges and agrees to the responsibilities and also affirms the following to the best of their knowledge:

- The participating site has not been:
 - i. Debarred under the provisions of the Generic Drug Enforcement Act of 1992, 21 U.S.C. § 335a(a) and (b); or
 - ii. Suspended by the Office for Human Research Protections as a clinical research site under 45 C.F.R. Part 46, and
- No persons performing activities in connection with the IND program has been disqualified as a clinical investigator under 21 C.F.R. Part 312.70 and/or convicted of a felony under federal law for conduct:
 - i. Relating to the development or approval, including, but not limited to, the process for development or approval, of any drug, product, medical device, New Drug Application, Pre-Market Application, 510(k) or IND or similar application; or
 - ii. Otherwise relating to the regulation of any drug product or medical device under the Food Drug & Cosmetic Act.

7.1 Required Data Collection Forms, Monitoring and Safety Reporting

All required forms under this IND protocol must be completed and maintained at the institutions/participating sites and made available upon request by CDC or FDA. As mentioned in **Section 5, Procedures**, the following forms are provided for use, completion and/or return to CDC as specified below:

Appendix A1: Occupational Risk/Vaccine Eligibility Assessment Form - Optional.

For internal use by the vaccine-requesting institutions/participating sites to help identify individuals eligible for vaccine per occupational exposure risk assessment.

Appendix A2: Ervebo Request and Use Agreement Form, and Form FDA 1572 - Required.

Used to request vaccine. Must include the names of vaccine eligible individuals with their occupational risk categories. Submit the completed forms to CDC by email (spathvax@cdc.gov) or fax (404-471-2526).

Appendix B1: Informed Consent Form (ICF) – Required and must be obtained prior to vaccination.

Provide participants a copy of their signed ICF. Retain the original, signed ICFs at the participating sites.

Appendix B2: Example Copy of the CDC Post-Vaccination Adverse Events Survey – Required.

Inform the eligible individuals that they will receive a brief electronic survey from CDC via email or text on or around days 7, 14, 21, and 28 after vaccination to monitor for specific adverse events. The survey is expected to take less than 5 minutes to complete and will ask questions specific to the occurrence and severity of 5 specific adverse events (muscle pain, joint pain, joint swelling, skin lesions and/or oral lesions). Show an example paper copy of the survey to eligible individuals with the ICF.

Appendix C: Vaccination Record Form (VRF) – Required.

Complete and return a VRF for each vaccinated individual to CDC no later than 3 calendar days of vaccination by email (spathvax@cdc.gov) or fax (404-471-2526). Retain copies at the participating sites. **All observed SAEs during the 30-minute post-vaccination period must be recorded on the VRF and reported to CDC as soon as possible and no later than 3 calendar days (72 hours)** of SAE occurrence, irrespective of whether the healthcare provider/site investigator considers the event to be vaccine-related or not. Any subsequent AEs/SAEs experienced by the vaccine recipients that the site investigator becomes aware of should be reported to VAERS (<https://vaers.hhs.gov/>).

Appendix D: Vaccine Product Accountability and Disposal Record Form – Required.

Complete and return to CDC within **14 calendar days** of completing vaccination (i.e., having used received vaccines) or final vaccine disposition by email (spathvax@cdc.gov) or fax (404-471-2526). Failure to comply may result in further action and denial of future vaccine requests.

7.1.1 Definitions of AEs and SAEs per 21 CFR 312.32

An **Adverse Event** (AE) is any untoward medical occurrence associated with the use of Ervebo in humans, whether or not considered related to Ervebo. It can be any unfavorable and unintended sign (e.g., an abnormal laboratory finding), symptom, or disease temporally associated with the use of Ervebo, without any judgment about causality.

A **Suspected Adverse Reaction** is any AE for which there is a reasonable possibility that Ervebo caused the AE. It is a subset of all AEs for which there is a reasonable possibility that Ervebo caused the event. “Reasonable possibility” means there is evidence to suggest a causal relationship between Ervebo and the AE. “Suspected adverse reaction” implies a lesser degree of certainty about causality than “adverse reaction.”

An **Adverse Reaction** is any AE caused by Ervebo. Adverse reactions are a subset of all suspected adverse reactions for which there is a reason to conclude that Ervebo caused the event (i.e., in greater degree of certainty than “suspected” adverse reaction).

Unexpected: An AE is considered “unexpected” if it is not listed in this protocol or Package Insert, or is not listed at the specificity or severity observed.

Serious Adverse Event (SAE) or Serious Adverse Reaction (SAR): An AE or suspected adverse reaction is considered “serious” if, in the view of either the treating physician or CDC, it results in any of the following outcomes:

- death
- a life-threatening AE
- inpatient hospitalization or prolongation of existing hospitalization
- a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions
- a congenital anomaly/birth defect

Serious and Unexpected Suspected Adverse Reaction (SUSAR): A suspected adverse reaction that is both unexpected (not consistent with the observed or expected risk information applicable to Ervebo) and also meets the definition of “serious” described above.

NOTE: Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the patient and may require medical or surgical intervention to prevent one of the outcomes previously listed.

Life-Threatening: An AE or suspected adverse reaction is considered “life-threatening” if, in the view of either the treating physician or CDC, its occurrence places the patient at immediate risk of death. It does not include an AE or suspected adverse reaction that, had it occurred in a more severe form, might have caused a death.

Healthcare providers (i.e., site investigators) must report SAEs **as soon as possible** and no later than 72 hours of observed occurrence or his or her awareness, irrespective of whether the healthcare provider considers the event to be vaccine-related or not. CDC will review all SAEs received and report serious, unexpected suspected adverse reactions to FDA within 15 calendar days of initial receipt or after determining that the information qualifies for reporting under 21 CFR 312.32(c)(1). CDC will report all serious and unexpected suspected adverse reactions and incidents to CDC IRB according to CDC IRB’s policy and procedures.

7.2 Regulatory and Administrative Requirements

CDC, the sponsor of the IND, and all licensed healthcare providers (serving as site investigators) who request and receive Ervebo under this IND protocol will abide by the Code of Federal Regulations (in particular, 21 CFR Parts 50, 56, and 312) and FDA good clinical practice guidelines. The IND protocol is subject to FDA’s review and authorization as well as review and approval by an Institutional Review Board (IRB). CDC IRB will serve as central IRB for approval and continuing review of this IND protocol, which is determined non-research (i.e., does not constitute human subjects per 45 CFR 46.102(l)). Therefore, participating sites may use CDC IRB’s approval of this protocol that meets the FDA’s requirements regarding IRB review per 21 CFR Parts 50 and 56.

Any change or modification to this expanded access IND program that affects the purpose, procedures, or significant data or administrative aspects will require a formal amendment to the protocol. Such protocol amendments will be approved by the CDC IRB and submitted to FDA prior to implementation.

Information about specific site investigators (i.e., names, CVs, or Form FDA 1572) and/or participating sites may be shared with FDA, and local public health jurisdictions, and the vaccine manufacturer. Any information pertaining to site investigators and/or participating sites that are provided to the vaccine manufacturer is limited to use in the manufacturer’s discussions with health authorities concerning this CDC-sponsored IND program.

7.3 Confidentiality

Although the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule generally prohibits the use or disclosure of private health information without the written authorization of the participant, there are several exceptions to this requirement, including an exception for public health. Representatives from CDC, FDA, and the vaccine manufacturer may review medical and program records related to the Ervebo use as a part of their responsibility to protect persons in this expanded access IND program. No personal data will be used in any external communication or publication.

All proprietary and confidential information provided under and/or in association with this expanded access IND protocol for Ervebo should only be used for the stated purpose and scope of the IND protocol in accordance with the applicable IND regulatory requirements. This protocol and its contents should not be further distributed or disclosed for any other purpose without prior authorization from the CDC. All proprietary and confidential information provided under and/or in association with the CDC-sponsored IND program to the participating sites and site investigators must be regarded and kept as confidential information.

7.4 Financial Remuneration and Insurance

CDC is providing Ervebo under this expanded access IND program at no cost. Participating sites that request, receive, handle, and administer the vaccines under the IND will be responsible for any cost or resources associated with vaccine administration. Should a participant be injured as a direct result of receiving Ervebo, he/she should be treated as indicated clinically and may be entitled to medical care for that injury. However, CDC does not set aside funds to pay for this kind of medical care. The participant or participant's insurer, Medicare, or Medicaid will have to pay for any care that is needed. The participant should understand that signing the consent does not constitute a waiver or release of legal rights. This is addressed in the Informed Consent.

8 EFFICACY and SAFETY INFORMATION of ERVEBO for EVD

The summary of Ervebo efficacy and safety information can be found in the Ervebo package insert.

8.1 Immunogenicity and Efficacy of PrEP

Since the evaluation of clinical efficacy and immunogenicity has not been done in the same study, immune correlates for protection against *Zaire ebolavirus* infection are unknown. One study revealed strong and early innate immune activation following vaccination with Ervebo. A subset of early innate markers, encompassing interferon γ -inducible protein 10 (IP-10) and subsets of monocytes, dendritic cells, and NK cells as well as an early gene signature linked to the IP-10 pathway, were identified as innate immune signatures, that correlated with the GP-specific antibody response on day 28 and beyond.¹⁴

In the PREVAIL I study, there was a considerable increase in antibody titers 1-month post-vaccination (GMT EU/ml [95% CI] of 1000 [910–1099] rVSVΔG-ZEBOV-GP vs. 75 [69–80] placebo) with the antibody response rate of 83.7% in the Ervebo vaccinated group (vs. 2.8% placebo). At 12 months, the titer levels remained elevated but declined (818 [752–889] vs. 90 [83–96] placebo) with antibody response rate of 79.5% in the Ervebo vaccinated group (vs. 6.8% in placebo).⁶ In unpublished data of extended follow-up of the original PREVAIL I cohort, antibody titer levels decreased to 496 (442–557) and 65.1% sero-positive by three years. Additionally, antibody titer results in West African adults receiving single vs. boosted (day 56) Ervebo vaccination demonstrated short lived 4-month increase in serologic responses which return to same level of the single dose thereafter.

Another study found that at 365 days after vaccination, 77/77 (100%) study participants who received at least 1×10^7 pfu of Ervebo vaccine and returned for follow-up were seropositive (≥ 58.84 EU/mL) for ZEBOV-GP-specific IgG antibodies. At 730 days, 45/45 (100%) participants who received at least 1×10^7 pfu of Ervebo vaccine and returned for follow-up were seropositive for ZEBOV-GP-specific IgG antibodies.¹⁵ However, the contribution of these long-term persistent ZEBOV-GP-specific IgG antibodies to the protection against disease caused by *Zaire ebolavirus* in humans is unclear.

The duration of protection following a single dose of Ervebo is unknown. In unpublished animal studies, 2/6 nonhuman primates (NHPs) vaccinated with 3×10^6 pfu and challenged with 1000 pfu of *Zaire ebolavirus* (Kikwit 7U) 3 months later survived; 3/7 NHPs vaccinated with either 3×10^6 or 3×10^4 pfu and challenged with 1000 pfu of *Zaire ebolavirus* 1 year later survived. At one-year post vaccination, there was no clear association between survival and pre-challenge antibody response as measured by ELISA or

pseudovirion neutralization assay. It is unclear to what extent a similar waning of immune protection over time may be expected in humans receiving Ervebo. A follow-up study is in progress to assess durability of protection in NHPs vaccinated with one or two doses (60 days apart) of the full human vaccine dose ($>7.2 \times 10^7$ pfu) that were challenged with 1000 pfu of *Zaire ebolavirus* four months after the last vaccine dose. Survival was 100% in the single-dose vaccine group, 88% in the two-dose vaccine group, and 0% in the saline control group. Histological and immunological sample testing results are pending.¹¹

Among the 673 EVD patients enrolled in the PALM trial, Ervebo vaccination status was available via self-report for 620 patients. Of these, 60 patients with EVD reported receiving the vaccine ≥ 10 days before their admission to an Ebola Treatment Center.¹⁶ Preliminary, unpublished data from an ongoing CDC study examining long-term immune responses found that antibodies against glycoproteins of both Ebola virus strains Mayinga 1976 and DRC2018 were detected in 44/45 (97.8%) samples collected 8–31 months after vaccination (median: 16 months). The majority of the samples tested negative for the presence of neutralizing antibodies using live virus focus-reduction neutralization assay.

Until additional data on the duration of protection following the initial vaccination becomes available, booster dosing should be considered on a case-by-case basis in individuals that were previously vaccinated ≥ 6 months and are at potential occupational risk for exposure to Ebola virus.

8.2 Safety

The clinical development program for Ervebo included 12 clinical studies conducted in North America, Europe, and Africa, in which a total of 15,399 adult subjects received a dose of Ervebo; 1,712 in double-blind, placebo-controlled trials and 13,687 in open label trials.

A report of four Phase 1, multi-center clinical trials of the Ervebo vaccine in 158 healthy adults in Africa and Europe reported mild to moderate early-onset reactogenicity including fever in 30% of vaccinees and vaccine viremia in 95% of vaccinees. Arthritis affecting one to four joints was reported in 22% of vaccinees at a study site in Geneva with onset approximately 7-14 days after vaccination. Pain lasted a median of 8 days and virus was identified in the synovial fluid aspirate and in skin vesicles of two other vaccinees. At six months, 10 of 11 participants with arthritis were symptom-free. Three vaccinees with arthritis also developed a mild maculopapular rash with rare vesicles on fingers and toes. Analysis of one papule identified the Ervebo vaccine strain by reverse transcriptase polymerase chain reaction (PCR).⁷ Other phase 1 and 2 studies (total number vaccinated = 601) have also described similar vaccine reactogenicity, although rates of arthritis were lower in other studies.^{8,17,18} Available clinical data suggest that a second dose of Ervebo may have an acceptable safety profile. A Phase 1 dose-escalation study included administration of two doses on Day 0 and 28 at three dosage levels (3×10^6 pfu, 2×10^7 pfu, and 1×10^8 pfu). Reactogenicity at the injection site and systemic reactogenicity were less severe after the second dose than after the first dose.¹⁹

Although earlier analyses had revealed no association between the presence of arthritis and vaccine dose, age, sex, earlier arthralgia, or peak viremia, a more recent post-hoc multivariate analysis of risk factors for arthritis in Ervebo dose-tolerability studies was undertaken by Merck and evaluated the following factors: treatment dose, body mass index, age (18 to 45 years vs. 46 to 65 years), sex, medical history of arthritis (composite term), and race. The analysis identified an association with female sex and a past or current medical history of arthritis as two potential risk factors for the development of arthritis post-vaccination.²⁰

A Phase 2/3 randomized, non-blinded trial with phased introduction of Ervebo vaccination in Sierra Leone (STRIVE) administered one IM dose of 2×10^7 pfu of vaccine to healthcare and frontline response workers in 5 districts. Vaccine recipients were randomized to immediate or deferred vaccination and followed for 6 months post-vaccination. In total, 7,998 enrollees were vaccinated. No vaccine-related serious adverse events were reported. A vaccine safety substudy was conducted amongst 205 vaccinated

participants. In this substudy population, vaccine reactogenicity was assessed, with the most commonly reported symptoms including pain at injection site (81%), headache (71%), subjective fever (50.7%), fatigue (50.7%), joint pain (31.7%), muscle pain (28.8%), and objective fever (20.5%). Skin vesicles were reported in seven (3.4%) vaccinees. The vaccine was generally well-tolerated, with most symptoms being mild to moderate in severity and resolving within 5 days.²¹ Among 84 women inadvertently vaccinated in early pregnancy or that became pregnant \leq 60 days after vaccination or enrollment, 45% (14/31) of women in the immediate vaccination group reported pregnancy loss, compared with 33% (11/33) of unvaccinated women with contemporaneous pregnancies (RR 1.35, 95% CI 0.73-2.52).¹² No congenital anomalies were detected among 44 live-born infants examined.

The Phase 2/3 randomized, double-blind, placebo-controlled PREVAIL I trial in Liberia enrolled 1,500 adult volunteers with 500 participants randomized to each of three arms: ChAd3-EBO-Z, Ervebo, or placebo. As incidence of Ebola virus disease in Liberia declined, the study protocol was amended to focus on safety and longer-term 5-year immunogenicity. During the 12-month study period, 47 SAEs were reported in the Ervebo group compared to 59 in the placebo group ($p=0.68$); the majority of SAEs were attributable to malaria. Participants reported primarily grade 1 symptoms, with few grade 2 symptoms. The most commonly reported targeted symptoms in the Ervebo group were headache (31.9%), feverishness (30.5%), muscle pain (26.9%), and fatigue (15.4%). A two-week post-vaccination assessment for arthritis did not reveal a significant difference between the three groups.⁶

A Phase 3 ring vaccination trial of Ervebo in Guinea administered one IM dose of 2×10^7 pfu of vaccine to 5,837 non-pregnant individuals $>$ 6 years of age. Among all vaccinees ($n=5837$), the most frequently experienced solicited adverse events within 14 days of vaccination were: headache (33.3%), fatigue (25.4%), muscle pain (18.1%) arthralgia (17.9%), and myalgia (16.8%). Severity of these adverse events was also assessed. Among all vaccinees who experienced headache, 91% reported the headache as mild, 8.7% as moderate, and 0.4% as severe. Among all vaccinees who experienced fatigue within 14 days of vaccination, 84.3% reported the fatigue as mild, 14.2% as moderate, and 1.5% as severe. Amongst all vaccinees who experienced muscle pain within 14 days of vaccination, 83.3% reported muscle pain as mild, 15.7% as moderate, and 1% as severe. Amongst all vaccinees who experienced arthralgia within 14 days of vaccination, 89.1% reported the arthralgia as mild, 10.1% as moderate, and 0.7% as severe. Mean duration of arthralgia in adults was 2 days (interquartile range (IQR) 2-4). In addition, two serious vaccine-related adverse events were reported; one febrile reaction and one anaphylactic reaction, both of which resolved without sequelae.²²

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APPENDIX A1: Occupational Risk/Vaccine Eligibility Assessment Form

Instructions:

- Use this form to help identify individuals at high potential occupational risk of exposure to Ebola virus (species *Zaire ebolavirus*).
- This form is for internal use by each vaccine requesting site and does NOT need to be returned to CDC.

Appendix A1: Occupational Risk/Vaccine Eligibility Assessment Form

Instructions: This form is provided to help each participating site identify individuals at high potential occupational risk for exposure to Ebola virus (species *Zaire ebolavirus*) for whom Ervebo may be appropriate. This form is for internal use by each participating site at its discretion and does NOT need to be returned to CDC. To request Ervebo, each participating site must complete and submit the **Ervebo Request and Use Agreement Form**, and **Form FDA 1572** (required for booster dose use under CDC-sponsored IND) to CDC. All vaccine candidates identified using this form must be listed under Section 3 of the **Ervebo Request and Use Agreement Form**.

Vaccine may be requested for pre-exposure vaccination of adults 18 years of age or older in the U.S. population who are at potential occupational risk of exposure to Ebola virus (species *Zaire ebolavirus*) such as those in the following groups:

- Responders to an Ebola virus (species *Zaire ebolavirus*) outbreak.
- Laboratorians and support staff working at biosafety level 4 (BSL-4) facilities (Table 1) with replication-competent Ebola virus (species *Zaire ebolavirus*) or with specimens suspected to contain replication-competent Ebola virus (species *Zaire ebolavirus*). Personnel working at non-BSL-4 facilities in the Laboratory Response Network may be eligible to receive Ervebo depending on specific circumstances of public health needs and the Ebola preparedness and/or response activities at such facilities.
- Healthcare personnel (HCP)* at federally-designated Ebola Treatment Centers (Table 2) involved in the care and transport of patients infected or suspected to be infected with Ebola virus (species *Zaire ebolavirus*). HCP working at state-designated Ebola healthcare facilities or other facilities may be eligible to receive Ervebo depending on specific circumstances of public health needs and the Ebola preparedness and/or response activities at such facilities.

*Healthcare personnel refers to all paid and unpaid persons serving in healthcare settings who have the potential for direct or indirect exposure to Ebola patients or infectious materials, including body substances (e.g., blood, tissue, and specific body fluids); contaminated medical supplies, devices, and equipment; contaminated environmental surfaces; or contaminated air. These healthcare personnel include, but are not limited to, emergency medical service personnel, nurses, nursing assistants, physicians, physician assistants, technicians, clinical laboratory personnel, autopsy personnel, therapists, phlebotomists, pharmacists, students and trainees, contractual staff not employed by the healthcare facility, and persons not directly involved in patient care, but who could be exposed to infectious agents that can be transmitted in the healthcare setting (e.g., clerical, dietary, environmental services, laundry, security, engineering and facilities management, administrative, billing, and volunteer personnel). Adapted from <https://www.cdc.gov/infectioncontrol/guidelines/healthcare-personnel/index.html>

Table 1: Biosafety-level 4 Facilities in the United States

- | | |
|---|---|
| <ul style="list-style-type: none">• CDC, GA• Galveston National Laboratory, TX• Georgia State University, GA• Shope Laboratory, TX• National Emerging Infectious Disease Laboratories, MA | <ul style="list-style-type: none">• Texas Biomedical Research Institute, TX• Integrated Research Facility/NIH, MD• USAMRIID, MD• Rocky Mountain Laboratories, MT• National Biodefense Analysis and Countermeasures Center, MD |
|---|---|

Table 2: Federally-designated Ebola Treatment Centers

- | | |
|---|---|
| <ul style="list-style-type: none">• Emory University, GA• Nebraska Medical Center, NE• NYC Health + Hospitals/Bellevue, NY• Denver Health Medical Center, CO• Johns Hopkins Hospital, MD• Providence Sacred Heart Medical Center and Children's Hospital, WA | <ul style="list-style-type: none">• Cedars-Sinai Medical Center, CA• University of Minnesota Medical Center, MN• University of Texas Medical Branch at Galveston, TX• National Institutes of Health, MD• Massachusetts General Hospital, MA |
|---|---|

Note to Sites: Use the assessment form on the next page to identify each vaccine candidate. This form is for internal use by the sites that will be requesting Ervebo.

Section 1: Vaccine Candidate Information

Name of the individual being assessed:

Section 2: Occupational Risk Groups and Activities

To be eligible for pre-exposure vaccination with Ervebo, the individual must be an adult (≥ 18 years) at potential high risk of occupational exposure to Ebola virus (species *Zaire ebolavirus*). Listed below are types of activities that would be associated with high potential for occupational risk exposure but may not be exhaustive. Check ALL the boxes that apply to the individual being assessed for vaccine eligibility. Given the definition of Healthcare personnel above, including at eligible state-designated Ebola healthcare facilities or other facilities, if none of the listed activities below apply to the individual being assessed yet vaccination still needs consideration, please call Viral Special Pathogens Branch (470-312-0094) to discuss further.

1. Responders to an Ebola virus (species *Zaire ebolavirus*) outbreak

	Persons who provide care for patients infected, or suspected to be infected, with Ebola virus (species <i>Zaire ebolavirus</i>); or persons who would be expected to provide care for patients if an outbreak were to occur.
	Persons who transport patients infected, or suspected to be infected, with Ebola virus (species <i>Zaire ebolavirus</i>) to include intra/inter-facility transport; or persons who would be expected to transport patients if an outbreak were to occur.
	Persons who collect or process specimens suspected to contain replication-competent Ebola virus (species <i>Zaire ebolavirus</i>); or persons who would be expected to collect or process specimens if an outbreak were to occur.
	Persons who provide direct, hands-on support (including custodial support) to the containment equipment or facilities in the spaces associated with the care of persons infected with Ebola virus (species <i>Zaire ebolavirus</i>), to include patient care areas and diagnostic laboratories; or persons who would be expected to provide such support if an outbreak were to occur.
	Persons who enter room(s) or associated spaces when samples suspected to contain replication-competent Ebola virus (species <i>Zaire ebolavirus</i>) are being manipulated; or persons who would be expected to enter room(s) or associated spaces if an outbreak were to occur.
	Persons who live and/or work in areas of active Ebola virus (species <i>Zaire ebolavirus</i>) transmission.

2. Laboratorians and support staff working at biosafety level 4 (BSL-4) facilities or eligible non-BLS-4 facilities in the Laboratory Response Network with replication-competent Ebola virus (species *Zaire ebolavirus*) or with specimens suspected to contain replication-competent Ebola virus (species *Zaire ebolavirus*)

	Persons who work with replication-competent Ebola virus (species <i>Zaire ebolavirus</i>).
	Persons who collect specimens suspected to contain replication-competent Ebola virus (species <i>Zaire ebolavirus</i>).
	Persons who enter laboratory rooms housing animals infected with Ebola virus (species <i>Zaire ebolavirus</i>) or who touch contaminated animal bedding or cages.
	Persons who provide direct, hands-on support (including custodial support) to the containment equipment and/or enter the room(s) or interstitial spaces associated with room(s) where replication-competent Ebola virus (species <i>Zaire ebolavirus</i>) is being manipulated.

3. Healthcare personnel at federally-designated Ebola Treatment Centers or eligible state-designated Ebola healthcare facilities or other facilities involved in the care and transport of patients infected or suspected to be infected with Ebola virus (species *Zaire ebolavirus*)

	Persons who provide care for patients infected, or suspected to be infected, with Ebola virus (species <i>Zaire ebolavirus</i>).
	Persons who transport patients or specimens infected, or suspected to be infected, with Ebola virus (species <i>Zaire ebolavirus</i>).
	Persons who collect or process specimens that contain, or are suspected to contain, replication-competent Ebola virus (species <i>Zaire ebolavirus</i>).
	Persons who provide direct, hands-on support (including custodial support) to the containment equipment or facilities in the spaces associated with the care of patients infected, or suspected to be infected, with Ebola virus (species <i>Zaire ebolavirus</i>), including patient care areas and diagnostic laboratories.
	Persons who may enter the patient care areas or associated spaces during an emergency or other incident where normal operational controls are not present.
	Persons who may enter the laboratory areas or associated spaces where replication-competent Ebola virus (species <i>Zaire ebolavirus</i>) specimens are being manipulated during an emergency or other incident where normal operational controls are not present.

If the vaccine candidate is 18 years of age or older and has one or more of the above eligibility criteria, please continue to Section 3: Exclusion Criteria for Vaccination. If the vaccine candidate does not fit any of the eligibility criteria, please continue to Section 4: Final Eligibility Determination and mark the candidate as 'not eligible'.

Section 3: Exclusion Criteria for Vaccination

Refer to IND protocol, section 2.2, or the package insert for vaccine exclusion criteria and contraindications. Does this vaccine candidate have any of the exclusion criteria or contraindications outlined in the IND protocol or package insert?

- No exclusion criteria are met. Individual is eligible for vaccination with Ervebo.
- One or more exclusion criteria apply to this vaccine candidate. Individual MAY NOT receive Ervebo.

Section 4: Final Eligibility Determination

Based on the vaccine candidate's age, Ebola vaccination history, occupational risk, and assessment of vaccine exclusion criteria, this vaccine candidate is:

- eligible
- not eligible

to receive the Ebola vaccination.

Name and/or signature of the site official determining eligibility for Ervebo vaccination

Date

If the vaccine candidate is eligible and would like to receive a dose of Ervebo, be sure to include the candidate's name in Section 3 of the **Ervebo Request and Use Agreement Form**.

APPENDIX A2: Ervebo Request and Use Agreement Form, and Form FDA 1572

Instructions:

In order to receive Ervebo under this CDC-sponsored expanded access IND program:

- Complete the Ervebo Request and Use Agreement Form.
- The licensed healthcare provider serving as a site investigator with oversight responsibility of vaccine receipt, handling, use, and disposition at the institution/organization/site must complete Form FDA 1572 (Statement of Investigator).
- Please submit the completed forms along with the Curriculum Vitae and healthcare provider license of the site investigator to CDC by fax (404-471-2526) or a scanned copy via email (spathvax@cdc.gov).

Appendix A2: Ervebo Request and Use Agreement Form, and Form FDA 1572

Instructions: Ervebo is FDA-approved for the prevention of disease caused by *Zaire ebolavirus* in individuals 18 years of age and older and is made available through the Centers for Disease Control and Prevention (CDC) for pre-exposure vaccination of civilian adults (≥ 18 years) in the U.S. with potential occupational risk such as those included in the recommendations by [the Advisory Committee on Immunization Practices \(ACIP\)](#). Booster dose administration of Ervebo is considered an unapproved use by the Food and Drug Administration (FDA), therefore the CDC is sponsoring an expanded access IND protocol to provide an appropriate regulatory mechanism to allow for booster dose administration of Ervebo.

To request Ervebo for eligible-individuals, complete and return this Ervebo Request form to CDC by email (spathvax@cdc.gov) or fax (404-471-2526).

Individuals who fall into one of the 3 occupational categories below are eligible to receive Ebola vaccine:

- 1. Ebola virus disease (EVD) responders:** Individuals responding to an outbreak due to Ebola virus (species *Zaire ebolavirus*).
- 2. Biosafety level 4 (BSL-4) workers:** Laboratorians and support staff working at BSL-4 facilities with replication-competent Ebola virus (species *Zaire ebolavirus*) or with specimens suspected to contain replication-competent Ebola virus (species *Zaire ebolavirus*). Personnel working at non-BSL-4 facilities in the Laboratory Response Network may be eligible to receive Ervebo depending on specific circumstances of public health needs and the Ebola preparedness and/or response activities at such facilities.
- 3. Healthcare personnel (HCP)*:** HCP at federally-designated Ebola Treatment Centers involved in the care and transport of patients infected or suspected to be infected with Ebola virus (species *Zaire ebolavirus*). HCP working at state-designated Ebola healthcare facilities or other facilities may be eligible to receive Ervebo depending on specific circumstances of public health needs and the Ebola preparedness and/or response activities at such facilities.

*Healthcare personnel refers to all paid and unpaid persons serving in healthcare settings who have the potential for direct or indirect exposure to Ebola patients or infectious materials, including body substances (e.g., blood, tissue, and specific body fluids); contaminated medical supplies, devices, and equipment; contaminated environmental surfaces; or contaminated air. These healthcare personnel include, but are not limited to, emergency medical service personnel, nurses, nursing assistants, physicians, physician assistants, technicians, clinical laboratory personnel, autopsy personnel, therapists, phlebotomists, pharmacists, students and trainees, contractual staff not employed by the healthcare facility, and persons not directly involved in patient care, but who could be exposed to infectious agents that can be transmitted in the healthcare setting (e.g., clerical, dietary, environmental services, laundry, security, engineering and facilities management, administrative, billing, and volunteer personnel). Adapted from <https://www.cdc.gov/infectioncontrol/guidelines/healthcare-personnel/index.html>

Please refer to the **Occupational Risk/Vaccine Eligibility Assessment Form** to help identify individuals with occupational exposure risk for *Zaire ebolavirus* at your institution/organization. Vaccine-eligible individuals for whom the vaccine supply is being requested must be entered in Section 3 of this form.

If Ervebo use is under the CDC-sponsored expanded access IND protocol for booster dose administration, the **licensed healthcare provider** serving as the site investigator for a participating site is responsible for the oversight and management of the vaccine receipt, storage, handling, use and disposal at the receiving site (i.e., participating site); ensuring informed consent, monitoring and reporting of serious adverse events (SAEs) in accordance with the IND Protocol and applicable Food and Drug Administration (FDA) IND regulations, including good clinical practice; and protecting the welfare and safety of participants. The licensed healthcare provider serving as the site investigator must complete this form and agree to all requirements outlined in **Section 4**. The licensed healthcare provider must also include a signed Form FDA 1572 (Statement of Investigator), his/her current CV, and current healthcare provider license when submitting the Ebola Vaccine Request and Use Agreement form to CDC. Once reviewed and approved by CDC for vaccine release, the participating site will not require a resubmission of Form FDA 1572 for the same licensed healthcare provider/site investigator for subsequent request for additional Ebola vaccine supplies.

Section 1: Vaccine Requesting Institution Details

Name of the institution/organization/site		Date of Request
Street	Building	Suite
City	State	Zip Code
Does the institution have freezer capacity to store the vaccine frozen at $\leq -60^{\circ}\text{C}$ ($\leq -76^{\circ}\text{F}$)? <input type="checkbox"/> Yes <input type="checkbox"/> No		
If no, is there capacity to store the vaccine refrigerated at 2°C to 8°C (35.6°F to 46.4°F)? <input type="checkbox"/> Yes <input type="checkbox"/> No		

Section 2: Vaccine Requesting Personnel Details**Licensed healthcare provider (i.e., site investigator)**

Name (First, middle, last name)	Title	Health provider category	<input type="checkbox"/> M.D.	<input type="checkbox"/> D.O.
			<input type="checkbox"/> P.A.	<input type="checkbox"/> N.P.
			<input type="checkbox"/> Other: _____	
	Current license #			
Email	Phone	Fax		

Alternate point of contact (e.g., delegated personnel under the site investigator)

Name (First, middle, last name)	Title	Health provider category	<input type="checkbox"/> M.D.	<input type="checkbox"/> D.O.
			<input type="checkbox"/> P.A.	<input type="checkbox"/> N.P.
			<input type="checkbox"/> Other: _____	
	Current license #			
Email	Phone	Fax		

Section 3: Identified Individuals Eligible to Receive a Dose of Ervebo

Eligible Individual		Occupational Risk Category			Description of Occupational Risk		Ebola Vaccine History	
Name (Last, First, MI)	Age	EVD responder	BSL-4 worker	Healthcare personnel	Position	Duties	Has the individual previously received Ebola vaccination?	If yes, name of vaccine and date(s) of previous dose(s)
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	
		<input type="radio"/>	<input type="radio"/>	<input type="radio"/>			<input type="checkbox"/> Yes <input type="checkbox"/> No	

Attach additional pages if necessary

Section 4: Vaccine Use Agreement

Licensed healthcare provider/Site Investigator: I have read and understood the conditions outlined in this agreement and understand that I must abide by them to receive and use Ervebo. I agree to the following:

1. As the licensed healthcare provider/site investigator, I am responsible for the oversight and management of Ervebo receipt, storage, handling, use, and disposal at my site for the purposes of administering Ervebo to eligible individuals at risk of occupational exposure. If Ervebo use is under the CDC-sponsored expanded access IND protocol for booster dose administration, I will submit a completed Form FDA 1572 with my CV to CDC with this Ebola Vaccine Request and Use Agreement form.
2. Ervebo is provided as a public health service. Ervebo provided by CDC will only be used for vaccination of individuals who are at potential occupational risk of exposure to Ebola virus (species *Zaire ebolavirus*) and under no circumstances will the vaccine be used for any other purposes (e.g., human or non-human research, treatment of any clinical condition).
3. If Ervebo use is under the CDC-sponsored expanded access IND protocol for booster dose administration, then qualified and trained personnel under my direction and supervision, who are involved in the procedures and activities of the IND protocol, will adhere to the requirements of applicable U.S., state and local laws, regulations and guidelines.
4. The vaccine will be administered only by me and/or qualified and trained personnel under my direction and supervision. All vaccinations will be documented in the Vaccination Record Form and returned to CDC no later than 3 calendar days of vaccination.
5. I will ensure that I and all qualified, trained personnel under my direction and supervision involved in Ervebo vaccination activities at my site will report, as soon as possible and no later than 72 hours of occurrence, any serious adverse events (SAEs) experienced by vaccinees during the 30-minute observation period following vaccination to CDC by completing the Vaccination Record Form. Any subsequent adverse events (AEs) or SAEs experienced by vaccinees will be reported utilizing the Vaccine Adverse Events Reporting System (VAERS).
6. I assume the oversight responsibility, including delegated responsibility, for monitoring vaccinated individuals, recording and ensuring the integrity of reported data, and for protecting the welfare and safety of vaccinated individuals.
7. I will retain full control of Ervebo received at my site, and further agree not to transfer the vaccine to any other party. Upon completion of all vaccinations, I or the delegated personnel under my direction and supervision will return or destroy any remaining supplies of vaccine and document the return or destruction by completing the Vaccine Product Accountability and Disposal Record Form within 14 calendar days of completion of vaccination or final vaccine disposition. Failure to comply may result in further action and denial of future vaccine requests.
8. By administering Ebola vaccine to eligible individuals, I agree not to claim, infer, or imply United States Governmental endorsement of the institution, institution's activities, or personnel activities or any resulting commercial product(s). Unless prohibited by law from doing so, I agree to hold the United States Government harmless and to indemnify the United States Government for all liabilities, demands, damages, expenses, and losses arising out of use of Ebola vaccine.
9. I understand that any false or misleading statements made, presented or submitted to the U.S. Government, including any relevant omissions, under this agreement are subject to all applicable civil and criminal statutes including Federal statutes 31 USC § §3801-3812 (civil liability) and 18 USC §1001 (criminal liability including fine(s) and/or imprisonment).
10. By signing below, I warrant that all of the statements and representations in this agreement are true and accurate.

Name (Print)	Title	Signature	Date

Return the completed and signed form to CDC by email (spathvax@cdc.gov) or by fax (404-471-2526)

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

STATEMENT OF INVESTIGATOR
(TITLE 21, CODE OF FEDERAL REGULATIONS (CFR) PART 312)
(See instructions on reverse side.)

Form Approved: OMB No. 0910-0014
Expiration Date: March 31, 2022
See OMB Statement on Reverse.

NOTE: No investigator may participate in an investigation until he/she provides the sponsor with a completed, signed Statement of Investigator, Form FDA 1572 (21 CFR 312.53(c)).

1. NAME AND ADDRESS OF INVESTIGATOR

Name of Clinical Investigator

Address 1

Address 2

City

State/Province/Region

Country

ZIP or Postal Code

2. EDUCATION, TRAINING, AND EXPERIENCE THAT QUALIFY THE INVESTIGATOR AS AN EXPERT IN THE CLINICAL INVESTIGATION OF THE DRUG FOR THE USE UNDER INVESTIGATION. ONE OF THE FOLLOWING IS PROVIDED (Select **one** of the following.)

Curriculum Vitae

Other Statement of Qualifications

3. NAME AND ADDRESS OF ANY MEDICAL SCHOOL, HOSPITAL, OR OTHER RESEARCH FACILITY WHERE THE CLINICAL INVESTIGATION(S) WILL BE CONDUCTED

CONTINUATION PAGE
for Item 3

Name of Medical School, Hospital, or Other Research Facility

Address 1

Address 2

City

State/Province/Region

Country

ZIP or Postal Code

4. NAME AND ADDRESS OF ANY CLINICAL LABORATORY FACILITIES TO BE USED IN THE STUDY

CONTINUATION PAGE
for Item 4

Name of Clinical Laboratory Facility

Address 1

Address 2

City

State/Province/Region

Country

ZIP or Postal Code

5. NAME AND ADDRESS OF THE INSTITUTIONAL REVIEW BOARD (IRB) THAT IS RESPONSIBLE FOR REVIEW AND APPROVAL OF THE STUDY(IES)

CONTINUATION PAGE
for Item 5

Name of IRB

Centers for Disease Control and Prevention Human Research Protection Office

Address 1

1600 Clifton Rd, MS D-73

Address 2

City

Atlanta

State/Province/Region

GA

Country

United States

ZIP or Postal Code

30329

6. NAMES OF SUBINVESTIGATORS (If not applicable, enter "None")

7. NAME AND CODE NUMBER, IF ANY, OF THE PROTOCOL(S) IN THE IND FOR THE STUDY(IES) TO BE CONDUCTED BY THE INVESTIGATOR

IND #16337/CDC IRB # 7298: Expanded Access Investigational New Drug (IND) Protocol: Booster Dose Immunization with Ervebo® (Ebola Zaire Vaccine, Live) for Domestic Pre-exposure Prophylaxis (PrEP) Vaccination of Adults (≥ 18 years of age) at Potential Occupational Risk for Exposure to Zaire ebolavirus

8. PROVIDE THE FOLLOWING CLINICAL PROTOCOL INFORMATION. (Select **one** of the following.)

- For Phase 1 investigations, a general outline of the planned investigation including the estimated duration of the study and the maximum number of subjects that will be involved.
- For Phase 2 or 3 investigations, an outline of the study protocol including an approximation of the number of subjects to be treated with the drug and the number to be employed as controls, if any; the clinical uses to be investigated; characteristics of subjects by age, sex, and condition; the kind of clinical observations and laboratory tests to be conducted; the estimated duration of the study; and copies or a description of case report forms to be used.

9. COMMITMENTS

I agree to conduct the study(ies) in accordance with the relevant, current protocol(s) and will only make changes in a protocol after notifying the sponsor, except when necessary to protect the safety, rights, or welfare of subjects.

I agree to personally conduct or supervise the described investigation(s).

I agree to inform any patients, or any persons used as controls, that the drugs are being used for investigational purposes and I will ensure that the requirements relating to obtaining informed consent in 21 CFR Part 50 and institutional review board (IRB) review and approval in 21 CFR Part 56 are met.

I agree to report to the sponsor adverse experiences that occur in the course of the investigation(s) in accordance with 21 CFR 312.64. I have read and understand the information in the investigator's brochure, including the potential risks and side effects of the drug.

I agree to ensure that all associates, colleagues, and employees assisting in the conduct of the study(ies) are informed about their obligations in meeting the above commitments.

I agree to maintain adequate and accurate records in accordance with 21 CFR 312.62 and to make those records available for inspection in accordance with 21 CFR 312.68.

I will ensure that an IRB that complies with the requirements of 21 CFR Part 56 will be responsible for the initial and continuing review and approval of the clinical investigation. I also agree to promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to human subjects or others. Additionally, I will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human subjects.

I agree to comply with all other requirements regarding the obligations of clinical investigators and all other pertinent requirements in 21 CFR Part 312.

**INSTRUCTIONS FOR COMPLETING FORM FDA 1572
STATEMENT OF INVESTIGATOR**

1. Complete all sections. Provide a separate page if additional space is needed.
2. Provide curriculum vitae or other statement of qualifications as described in Section 2.
3. Provide protocol outline as described in Section 8.
4. Sign and date below.
5. FORWARD THE COMPLETED FORM AND OTHER DOCUMENTS BEING PROVIDED TO THE SPONSOR. The sponsor will incorporate this information along with other technical data into an Investigational New Drug Application (IND). INVESTIGATORS SHOULD NOT SEND THIS FORM DIRECTLY TO THE FOOD AND DRUG ADMINISTRATION.

10. DATE (mm/dd/yyyy)

11. SIGNATURE OF INVESTIGATOR

Sign

(WARNING: A willfully false statement is a criminal offense. U.S.C. Title 18, Sec. 1001.)

The information below applies only to requirements of the Paperwork Reduction Act of 1995.

The burden time for this collection of information is estimated to average 100 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden to the address to the right:

Department of Health and Human Services
Food and Drug Administration
Office of Operations
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

**DO NOT SEND YOUR COMPLETED FORM
TO THIS PRA STAFF EMAIL ADDRESS.**

APPENDIX B1: Informed Consent Form

Instructions:

- Prior to booster dose vaccination with Ervebo, Informed Consent must be obtained.
- Conduct informed consent process to help the individual eligible for booster dose vaccination with Ervebo to make an informed, voluntary decision on whether to get vaccinated based on information regarding risks and benefits of the vaccine and the purpose of the IND program, with opportunity to ask questions.
 - Print two copies of the signed ICF
 - Retain the original, signed ICF as part of the program records at the medical facility administering the vaccine
 - Provide one copy of the signed ICF to the individual to keep
 - Show the individual an example paper copy of **the CDC Post-Vaccination Adverse Events Survey** (Appendix B2)

Booster Dose of Ebola Vaccine for Pre-exposure Prophylaxis of Ebola Virus Disease

Please read this consent form carefully and ask any questions that you may have. If you choose to get a booster dose of the Ebola vaccine, then you will be asked to sign this consent form. You will receive a copy of the consent form to keep.

What is Ebola virus disease?

Ebola virus disease (EVD) is a rare disease caused by Ebola virus. It is severe and can cause death. Symptoms usually start 2 to 21 days after a person has contact with the virus. In most cases, symptoms start around days 8 to 10. First, a person may develop “dry” symptoms. These include fever, aches and pains, and fatigue. They may have “wet” symptoms (such as diarrhea and vomiting) as they get sicker. The most common Ebola symptoms are:

- Fever
- Aches and pains, such as severe headache, muscle and joint pain, and stomach pain
- Weakness and fatigue
- Diarrhea, vomiting, and stomach pain
- Unexplained bleeding or bruising

Other symptoms may include red eyes, skin rash, and hiccups.

The Ebola virus spreads between people. People can only spread the virus to other people after they develop Ebola symptoms. The virus spreads through direct contact (such as through broken skin or mucous membranes in the eyes, nose, or mouth) with:

- the blood or body fluids of someone who is sick with or died from EVD. Body fluids can include urine, spit, sweat, feces, breast milk, or semen.
- objects (clothes, bedding, needles, or medical equipment) that has body fluids from a person who is sick with or has died from EVD on it.

Staff who work in labs and handle or have contact with patient samples or infectious materials containing the Ebola virus may also be at risk for EVD.

What is Ervebo?

Ervebo is a vaccine that can help protect you from getting EVD if you come in contact with the Ebola virus. Ervebo helps the body’s natural defense (immune) system fight off the Ebola virus. The vaccine contains a weakened part of the Ebola virus that will not make you sick with Ebola.

The vaccine only protects against EVD due to *Zaire ebolavirus*. Ervebo was shown to be safe and protective against *Zaire ebolavirus* during previous outbreaks. These include the largest Ebola outbreak in West Africa in 2014-16 and the one in 2018 in the Democratic Republic of Congo.

Ervebo was approved by the U.S. Food and Drug Administration (FDA) in December 2019 to prevent disease caused by *Zaire ebolavirus* in adults 18 years of age and older as a single dose. The vaccine might not protect everyone who gets it. This vaccine does not treat or cure people who are sick with EVD.

What is the purpose of this program?

Ervebo is approved by the FDA as a single dose administration. A booster dose is considered investigational since it is not part of the FDA-approved indication for Ervebo. We do not know how long the vaccine protects you from EVD. So the Centers for Disease Control and Prevention (CDC) is providing this vaccine as a booster dose if your prior Ebola vaccination was 6 months ago or longer and

your work activities place you at risk of exposure to Ebola. A booster dose is based on an individual assessment of your need for another dose of the vaccine.

A booster dose of the vaccine is offered under CDC's Investigational New Drug (IND) program to adults (≥ 18 years of age) that have been previously vaccinated and are at potential risk of Ebola due to their jobs. This includes those who:

- Are responding or may respond to an outbreak of EVD such as people who care or may need to care for Ebola patients or could deploy to an Ebola outbreak
or
- Work at a biosafety-level 4 lab or another eligible lab in the Laboratory Response Network in the U.S.
or
- Work as healthcare staff at a federally-designated Ebola Treatment Center or eligible state-designated healthcare facility or other facility in the U.S.

The booster dose use of Ervebo is based on an individual case-by-case assessment and has been reviewed and allowed by FDA and CDC's Institutional Review Board (IRB).

You can choose whether to receive a booster dose of Ervebo under this program. You may drop out at any time without penalty.

Who should NOT receive Ervebo?

The following people should not receive Ervebo:

- People who have an allergy, including anaphylaxis, to the vaccine or any component of the vaccine, including rice protein.
- People who are moderately or severely ill (such as those with an oral temperature $>38^{\circ}\text{C}$ (100.4°F)). However, these people can get the vaccine once they have recovered.
- People with a serious medical condition. These can include cancer, Guillain-Barré syndrome, history of brain disorder, active autoimmune disorder or weakened immune system. These conditions may place the person at an unreasonably increased risk by getting this vaccine.

Who should get more advice before getting Ervebo?

Tell the healthcare provider giving you the shot if you:

- have ever had a bad reaction to an Ebola vaccine or any other vaccine.
- are pregnant or planning to become pregnant.
 - Ervebo has not been studied in pregnant women. There are not enough data to know if there is a risk. It is also not known whether Ervebo is passed into breast milk. If you are pregnant, talk to your doctor about the risks of you getting ill with EVD and the potential benefits of the vaccine.
- have a weakened immune system or take medicines or treatments that might weaken your immune system.
- have close contact with anyone who has a weakened immune system.

What happens if you choose to receive a booster dose of Ervebo?

If you choose to get this vaccine, you will get one shot of Ervebo into the muscle of your upper arm. You will need to stay at the clinic for 30 minutes afterward. This will allow staff to monitor you for fainting or a serious allergic reaction. CDC will email or text you a brief survey on or around days 7, 14, 21, and 28 after receiving the vaccine. The survey will ask if any of five side effects occurred. If so, it will ask how severe they were. The survey should take about 5 minutes. An example of the survey will be shown to you before you sign this consent form. Responding to the survey is voluntary. However, we would appreciate it and it will help us monitor and assess side effects from this vaccine. CDC may potentially

contact you in the future about your interest in taking part in any future studies of individuals who have been vaccinated with Ervebo (for example, to understand long-term immune responses after vaccination). Your decision to get vaccinated under this IND program does not require participation in future studies.

What are the benefits of Ervebo?

The vaccine may help protect you from getting EVD, but we do not know for sure. If the vaccine protects you against EVD, we do not know how long this protection might last. Because there is limited information on how long protection might last, you are being offered a booster dose because your previous Ebola vaccination was 6 months ago or longer.

What are the risks/side effects of Ervebo?

Side effects of Ervebo include:

- Pain, swelling, or redness at the injection site
- Excessive sweating
- Joint pain
- Fever
- Nausea
- Joint swelling
- Headache
- Feeling tired
- Skin rash or blisters
- Chills
- Muscle aches
- Mouth cuts or sores

The number of white blood cells someone has can decrease after vaccination. But this does not mean you are ill. They will go back to normal on their own.

Most side effects go away within a few days. Joint pain and swelling may last for weeks to years in some people. These symptoms may come back after going away.

Ervebo is made from a virus called vesicular stomatitis virus (VSV) that does not normally cause serious health problems in adults. Natural infection with VSV can cause mouth sores.

Fainting does not occur often. When it does, it is usually within the first 15 minutes after getting a vaccine. There may be other side effects from the vaccine that we do not know about yet.

The safety of booster vaccination is not established but an early phase 1 study involving two doses 28 days apart showed the local and systemic reactions were less severe after the second dose compared to the first dose.

Serious side effects:

Some people have had serious allergic reactions to Ervebo. Tell your healthcare provider promptly about any unusual or severe symptoms you have after getting this vaccine. See a doctor right away if you have signs of an allergic reaction, which may include:

- wheezing or difficulty breathing
- swelling of the face, lips, tongue, or other parts of the body
- all-over itching, redness, or itchy bumps on the skin
- a weak and rapid pulse
- nausea, vomiting or diarrhea
- dizziness or fainting

You will be observed for 30 minutes after receiving the vaccine for any immediate allergic reactions and will receive treatment for any reactions.

What should you do if you have side effects?

- If you have a severe allergic reaction, call 9-1-1, or go to the nearest hospital.
- Tell a healthcare provider right away that you just received Ervebo.

- Report any vaccine side effects that you have to the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or <http://www.vaers.hhs.gov> and choose “Ebola Zaire (Ervebo)” under the “Vaccine (type and brand)” category.
- If you have muscle or joint pain, joint swelling, or skin or mouth sores, notify CDC on the surveys you will receive on days 7, 14, 21, and 28 after vaccination.

Are there other options besides Ervebo?

There are no other vaccines FDA-approved to prevent EVD at this time. Whether you’ve received the vaccine or not, use of recommended personal protection and infection control practices must also be followed for best prevention of Ebola virus infection and transmission of vaccine virus.

There are currently two FDA-approved treatments for EVD, but they are for treatment of patients who become sick from *Zaire ebolavirus*.

What you need to know AFTER you get the Ervebo?

- Ervebo may not protect everyone who gets it. You should still protect yourself from Ebola virus. Reduce contact with those who have EVD. Wear appropriate personal protective equipment (such as masks, gloves, etc.) when exposed to Ebola patients or infectious materials.
- Cover your shot site with a bandage (such as an adhesive bandage or gauze and tape) that provides a physical barrier to protect against direct contact.
- If you develop a rash with blisters after receiving the vaccine, cover the blisters until they heal. The bandage may be removed when you can’t see any fluid leaking.
- If you develop mouth sores after getting the vaccine, tell your healthcare provider.
- It has not been seen so far, but there is a possible risk that you could pass vaccine virus (not Ebola virus) to other people or animals. This is because the vaccine virus’s genetic material (RNA) can stay in the body. The RNA has been found in urine for up to 7 days. It has been found in blood and saliva for up to 14 days after vaccination. Whether you may be infectious after vaccination and for how long are not known. To reduce possible risk to others, you should **avoid**:
 - sharing needles, razors, toothbrushes, eating utensils, drinking from the same cup, and open-mouth kissing for 2 weeks after vaccination. If you get mouth sores after getting the vaccine, avoid these activities until the sores heal.
 - close contact with people who have a condition that weakens the immune system or who take medicines that weaken the immune system.
 - close contact with pregnant or breastfeeding women, and infants (< 1 year of age) for up to 6 weeks after vaccination.
 - donating blood for at least 6 weeks after vaccination.
 - doing anything that may expose livestock to your blood and bodily fluids for up to 6 weeks following vaccination.
- Pregnancy should be avoided for 8 weeks following vaccination. Women of child-bearing potential should use an effective contraceptive method.
- Regardless of childbearing status or sexual orientation, use effective barrier protection, such as latex condoms, during any sexual interaction for 8 weeks after vaccination.
- If you are a healthcare worker caring for patients, adhere to recommended infection control standards.
- The vaccine may cause you to have a positive test for Ebola, even if you don’t have the disease. Tell your healthcare provider that you received the vaccine.

What are the costs?

Ervebo is provided at no cost. Choosing to get the vaccine should not affect any health insurance that you have. This includes private insurance, Medicare, or Medicaid you use for routine medical costs not related to this program.

What about your privacy?

We will keep all facts about you private to the extent allowed by law. People who work for CDC, FDA, U.S. Department of Health and Human Services, local/state health departments, and the vaccine manufacturer may look at your medical records. This may include your name and personal information. This is to monitor the proper and safe use of Ervebo. If this information is shared with anyone else, your name and personal information will not be used or listed. This includes reports or articles in scientific journals. However, CDC can give your name to public health or medical people who, for example, need to monitor the safety of Ervebo. Also, CDC may potentially reach out to you using the contact information you provided under this IND program about your interest in taking part in any future studies of individuals who have been vaccinated with Ebola vaccine (for example, to understand long-term immune responses after vaccination).

What if you are harmed or have problems or questions?

If you are harmed by being in this program, you will be treated. You (or your insurer, Medicare, or Medicaid) will have to pay for your care. If you feel you were harmed by your participation, please contact Dr. Mary Choi at 404-639-1155. If you have questions about the vaccine or the program, please call the CDC Viral Special Pathogens Branch (470-312-0094) to discuss your questions with an Ebola subject matter expert.

If you sign this consent form and agree to receive the Ebola vaccine, you are not giving up any rights. If you have questions about your rights in this program, please contact CDC’s Human Research Protection Office at 800-584-8814. Please leave a message that includes your name, and telephone number, and refer to CDC IRB protocol #7298. Someone will return your call as soon as possible.

Documentation of Informed Consent: I have read this form, or it has been read to me. I have had a chance to ask questions and they were answered. I agree to get the Ebola vaccine as a booster dose. I have been given this consent form. I have been told that I will not lose any legal rights by being in this program.

<hr/>		
Name of Individual (Printed)	Date of Birth of Individual (mm/dd/yy)	
<hr/>		
Signature of Individual	Date/Time	
<hr/>		
Printed Name of Person Conducting Consent Interview	Signature of Person Conducting Consent Interview	Date

Translator Documentation (if applicable)
Translator to document if informed consent process was given in another language other than English.

<hr/>	
Name of Translator	Language
<hr/>	
Signature of Translator	Date

APPENDIX B2: Example Copy of the CDC Post-Vaccination Adverse Events Survey

Instructions:

- Inform vaccinees to expect the CDC post-vaccination adverse events survey via email or text on or around days 7, 14, 21 and 28 after vaccination. Show this example paper copy of the survey and encourage their participation in responding to the surveys.
- Inform vaccinated individuals that their responses to the Post-Vaccination Adverse Events Survey from CDC will be submitted to the Vaccine Adverse Event Reporting System (VAERS) and they will likely receive follow-up questions from VAERS in the future.

Appendix B2: Example Copy of the CDC Post-Vaccination Adverse Events Survey

You're receiving this brief survey from the Centers for Disease Control and Prevention (CDC) regarding the dose of Ebola vaccine you received. At the time of vaccination, you were informed that CDC will be sending you a survey by email or text on or around days 7, 14, 21 and 28 after vaccination (a total of 4 times) to ask questions on 5 specific adverse events (side effects). The survey is expected to take less than 5 minutes. Your response to the survey is much appreciated and will greatly help monitor specific side effects regarding this vaccine. Please note that your responses to the survey that indicate adverse events will be added to the Vaccine Adverse Event Reporting System (VAERS). You may be contacted by the CDC VAERS team with follow-up questions.

1. Was this your first time receiving the Ervebo Ebola vaccine or was this a booster dose?
 First vaccine Booster dose
2. If booster dose, what was the name of the vaccine and date you received your first dose?
 Name of vaccine: _____ Date received: _____ (mm/dd/yyyy)
3. In the past 7 days, have you experienced any of the following adverse events?

Adverse Events	If yes, when did it start?	If yes, has it resolved?
<p>a. Muscle pain <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><i>If yes, how would you describe the muscle pain?</i></p> <input type="checkbox"/> Mild <input type="checkbox"/> Moderate, some interference with daily activity <input type="checkbox"/> Severe, prevents daily activity <input type="checkbox"/> Requires medical attention/intervention	<p style="text-align: center;">____/____/____ MM/DD/YYYY</p> <input type="checkbox"/> Date unknown	<p style="text-align: center;"><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><i>If yes, when did it resolve?</i></p> <p style="text-align: center;">____/____/____ MM/DD/YYYY</p> <input type="checkbox"/> Date unknown
<p>b. Joint pain <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><i>If yes, which joints are affected?</i></p> <p>_____</p> <p><i>If yes, how would you describe the joint pain?</i></p> <input type="checkbox"/> Mild <input type="checkbox"/> Moderate, some interference with daily activity <input type="checkbox"/> Severe, prevents daily activity <input type="checkbox"/> Requires medical attention/intervention	<p style="text-align: center;">____/____/____ MM/DD/YYYY</p> <input type="checkbox"/> Date unknown	<p style="text-align: center;"><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><i>If yes, when did it resolve?</i></p> <p style="text-align: center;">____/____/____ MM/DD/YYYY</p> <input type="checkbox"/> Date unknown
<p>c. Joint swelling <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><i>If yes, which joints are affected?</i></p> <p>_____</p>	<p style="text-align: center;">____/____/____ MM/DD/YYYY</p> <input type="checkbox"/> Date unknown	<p style="text-align: center;"><input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><i>If yes, when did it resolve?</i></p> <p style="text-align: center;">____/____/____ MM/DD/YYYY</p> <input type="checkbox"/> Date unknown
<p>d. Skin lesion (rash, pustule, vesicle) <input type="checkbox"/> Yes <input type="checkbox"/> No</p>	<p style="text-align: center;">____/____/____ MM/DD/YYYY</p>	<p style="text-align: center;"><input type="checkbox"/> Yes <input type="checkbox"/> No</p>

If yes, where is the skin lesion? <hr/>	<input type="checkbox"/> Date unknown	<input type="checkbox"/> Yes <input type="checkbox"/> No If yes, when did it resolve? ____/____/____ <input type="checkbox"/> Date unknown MM/DD/YYYY
e. Oral lesion (blister, sore, vesicle) <input type="checkbox"/> Yes <input type="checkbox"/> No	If yes, when did it start? ____/____/____ MM/DD/YYYY <input type="checkbox"/> Date unknown	If yes, has it resolved? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, when did it resolve? ____/____/____ <input type="checkbox"/> Date unknown MM/DD/YYYY
f. Any other adverse events? If yes, describe.	If yes, when did it start? ____/____/____ MM/DD/YYYY <input type="checkbox"/> Date unknown	If yes, has it resolved? <input type="checkbox"/> Yes <input type="checkbox"/> No If yes, when did it resolve? ____/____/____ <input type="checkbox"/> Date unknown MM/DD/YYYY
4. Have you missed work because of any of the adverse event(s) you experienced in the past 7 days? <input type="checkbox"/> Yes <input type="checkbox"/> No a. If yes, how many days of work did you miss? _____		
5. Have you seen a healthcare provider for any of the adverse event(s) you experienced within the past 7 days? <input type="checkbox"/> Yes <input type="checkbox"/> No a. If yes, did you have any diagnostic testing performed? <input type="checkbox"/> Yes <input type="checkbox"/> No i. If yes, what diagnostic testing did you have? _____ b. If yes, did you receive a diagnosis? <input type="checkbox"/> Yes <input type="checkbox"/> No i. If yes, please list the diagnosis(es) _____		
<p><i>This is the end of the survey. Thank you for your participation! If any adverse events occur after completing all of the surveys (a total of 4 times), please report them to the VAERS at 1-800-822-7967 or http://www.vaers.hhs.gov. If you experience adverse events that you're concerned about or have questions on, consult a healthcare provider and inform them that you recently received the Ebola vaccine.</i></p>		

APPENDIX C: Vaccination Record Form

Instructions:

- Complete and return the Vaccine Record Form for each participant to CDC no later than 3 calendar days of vaccination via email (spathvax@cdc.gov) or fax (404-471-2526).
- If any serious adverse events (SAE) occur during the 30-minute post-vaccination observational period, report to CDC **as soon as possible** and no later than **3 calendar days (72 hours)** of the SAE occurrence by returning the completed Vaccine Record Form that documents the SAEs via email (spathvax@cdc.gov) or fax (404-471-2526).
- Maintain the Vaccine Record Form for each vaccinated individual.

Appendix C: Vaccination Record Form: Complete and return to CDC no later than 3 calendar days of vaccination for each vaccine recipient

DEMOGRAPHIC INFORMATION				
Name (Last, First, Middle)		Sex <input type="checkbox"/> Male <input type="checkbox"/> Female <input type="checkbox"/> Other		DOB (MM/DD/YYYY)
Age (Years)				
Residence City: State:		Contact Information Phone: Email:		Occupational Risk Category <input type="checkbox"/> EVD Responder <input type="checkbox"/> BSL-4 Worker <input type="checkbox"/> Healthcare Personnel
BASELINE INFORMATION: <i>Healthcare provider, please interview the individual and record responses prior to vaccination with Ervebo.</i>				
1. Has the individual previously received an Ebola vaccination? <input type="checkbox"/> Yes <input type="checkbox"/> No If Yes, date(s) of prior vaccination: _____ Name or manufacturer of the prior Ebola vaccine: _____				
2. Does the individual have a known severe allergy, such as anaphylaxis, to Ervebo or any component of the vaccine, including rice protein? (if yes, then do not administer Ervebo)				<input type="checkbox"/> Yes <input type="checkbox"/> No
3. Is the individual moderately or severely ill (e.g., has an oral temperature >38°C (100.4°F) or systemic symptoms)?				<input type="checkbox"/> Yes <input type="checkbox"/> No
4. Does the individual have a clinically significant medical condition, past medical history, pre-existing illness (e.g., acute malignancy, history of Guillain-Barré syndrome, history of neurologic disorder that may increase risk, active autoimmune disorder or immunosuppression) that in the clinical opinion of the healthcare provider may place the individual at an unreasonably increased risk by getting the vaccine?				<input type="checkbox"/> Yes <input type="checkbox"/> No
5. Has the individual ever had Ebola virus disease?				<input type="checkbox"/> Yes <input type="checkbox"/> No
6. Has the individual ever had a bad reaction (e.g., allergic reactions) to any vaccine?				<input type="checkbox"/> Yes <input type="checkbox"/> No
7. Is the individual a female of child-bearing age or currently pregnant?				<input type="checkbox"/> Yes <input type="checkbox"/> No <input type="checkbox"/> NA
If answered "no" to all Questions 2-7, then skip questions A & B below, and proceed to Question 8. If answered "yes" to any of the Questions 2-7, and the clinical opinion of the healthcare provider is to avoid vaccination or reschedule to a later date if the condition(s) affecting vaccine eligibility is no longer present, document accordingly here: _____				
For precautionary conditions, advise/remind the individual of the information in the Ervebo Patient Information sheet and/or Informed Consent Form regarding risks/side effects of Ervebo, what conditions individuals have that they should tell their healthcare provider about before getting Ervebo, and what to do if there are side effects				
A. Was the individual advised of the potential risks/side effects of Ervebo?				<input type="checkbox"/> Yes <input type="checkbox"/> No
B. Did the individual want to proceed with Ervebo?				<input type="checkbox"/> Yes <input type="checkbox"/> No
8. For a booster dose, has the individual signed the informed consent form? <i>If no, then do not proceed with vaccination</i>				<input type="checkbox"/> Yes <input type="checkbox"/> No
9. Has the individual been informed about and provided with a copy of the post-vaccination survey from CDC?				<input type="checkbox"/> Yes <input type="checkbox"/> No
ERVEBO ADMINISTRATION: <i>Please enter date(s) in MM/DD/YYYY format and time in HH:MM military time format (e.g., 16:30)</i>				
Date/Time of thawed vaccine vial:		OR Vaccine expiration date:		
Date/Time of vaccine administration:		Vaccine lot #:		
Dose administered: <input type="checkbox"/> 1 mL	Route of administration: <input type="checkbox"/> IM		Site of injection (Arm): <input type="checkbox"/> L <input type="checkbox"/> R	
Healthcare provider administering vaccine:		Individual completing this form (if different):		
OBSERVATION AFTER VACCINATION: <i>Please keep the individual in the observation area for a minimum of 30 minutes after vaccination.</i>				
Did any serious adverse event (SAE) <input type="checkbox"/> Yes <input type="checkbox"/> No <i>If yes, complete table below and report to CDC as soon as possible; NLT 72 hours.</i>				
Type of SAE	Description	Duration of	Treatment/Management	Outcome
1. Difficulty breathing <input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Recovered without sequelae <input type="checkbox"/> Recovered with sequelae Describe:
2. Swelling of lips/tongue or face <input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Recovered without sequelae <input type="checkbox"/> Recovered with sequelae Describe:
3. Severe rash <input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Recovered without sequelae <input type="checkbox"/> Recovered with sequelae Describe:
4. Other serious adverse event <input type="checkbox"/> Yes <input type="checkbox"/> No				<input type="checkbox"/> Recovered without sequelae <input type="checkbox"/> Recovered with sequelae Describe:
Return completed form to CDC by email (spathvax@cdc.gov) or by fax (404-471-2526) no later than 3 calendar days of vaccination.				

APPENDIX D: Vaccine Product Accountability and Disposal Record Form

Instructions: This form serves to document product accountability and disposition of Ervebo received under the CDC-sponsored IND 16337.

- Please complete and return the Vaccine Product Accountability and Disposal Record Form within 14 calendar days of vaccination completion or final vaccine disposition to CDC by fax (404-471-2526) or a scanned copy via email (spathvax@cdc.gov).
- Retain a copy for your record in accordance with 21 Code of Federal Regulations 312.57 regarding investigational products (e.g., until 2 years after receipt of Ervebo shipment and administration under the IND).

Appendix D: Vaccine Product Accountability and Disposal Record Form

Instructions: Complete and return this form to CDC within 14 calendar days of completion of vaccination or final vaccine disposition. Failure to comply may result in further action and denial of future vaccine requests.

Ebola Vaccine Receipt: Please complete the fields below for the vials received at your site

Participating Site Name/Address		Name/Title of the receiving person
Date received	Total number of vials received	Lot numbers (no. of vials per lot, if more than one lot received in the shipment)

Storage:

Were Ebola vaccines received frozen at -80°C to -60°C (-112°F to -76°F) without any temperature excursion? Yes No
 If no, did the temperature excursion result in unacceptability of vaccine for use? Yes No
 Were Ebola vaccines maintained frozen at -80°C to -60°C (-112°F to -76°F) until use? Yes No
 Were Ebola vaccines stored refrigerated at 2°C to 8°C (35.6°F to 46.4°F) at any time? Yes No
 If yes, were they used (or discarded if not used) within 14 days of thawing? Yes No NA
 Were temperature excursions experienced at any time during the vaccine storage at your facility/site? Yes No

If yes, describe:

Outcome of any impact to vaccine vials:

Accountability: Please complete the fields below to document the use and disposition of vaccine at your facility/site

Vaccine Recipient Name (Last, First, MI)	Sex	Age	Vaccination Date	EVD Responder	BSL-4 Worker	Healthcare Personnel	Vaccination in Series		
							Initial*	Booster*	Date(s) of vaccination
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	
				<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	

*Initial doses are under FDA-approved use and booster doses are under CDC sponsored IND

[Link to additional line to enter vaccine usage/vaccinee information fields if needed]	No. Vials Used	No. Vials Unused
No. Vials Destroyed or Returned	Date Destroyed or Returned	Method of Destruction
Name/Title of Individual completing this form (<i>print</i>)	(signature)	Date

Return the completed and signed form to CDC by email (spathvax@cdc.gov) or by fax (404-471-2526)
 Retain a copy for your record until 2 years after receipt of Ervebo shipment and use under the IND.