EBOLA VIRUS

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PATHOGEN SAFETY DATA SHEET - INFECTIOUS SUBSTANCES

SECTION *I* - INFECTIOUS AGENT

NAME: *Ebola virus*

SYNONYM OR CROSS REFERENCE: African haemorrhagic fever, Ebola haemorrhagic fever (EHF, Ebola HF), filovirus, EBO virus (EBOV), *Zaire ebolavirus* (ZEBOV), *Sudan ebolavirus* (SEBOV), Ivory Coast ebolavirus (ICEBOV), Ebola-Reston (REBOV), Bundibugyo ebolavirus (BEBOV), and Ebola virus disease [1, 2].

CHARACTERISTICS: Ebola was discovered in 1976 and is a member of the Filoviridae family (previously part of Rhabdoviridae family, which were later given a family of their own based on their genetic structure). It is an elongated filamentous molecule, which can vary between 800 - 1000 nm in length, and can reach up to14000 nm long (due to concatamerization) with a uniform diameter of 80 nm [2-5]. It contains a helical nucleocapsid, (with a central axis) 20 - 30 nm in diameter, and is enveloped by a helical capsid, 40 - 50 nm in diameter, with 5 nm cross-striations [2-6]. The pleomorphic viral fragment may occupy several distinct shapes (e.g., in the shape of a "6", a "U", or a circle), and are contained within a lipid membrane [2, 3]. Each virion contains one molecule of single-stranded, non-segmented, negative-sense viral genomic RNA [3, 7].

Five Ebola subtypes have been identified: *Zaire ebolavirus* (ZEBOV), which was first identified in 1976 and is the most virulent; *Sudan ebolavirus*, (SEBOV; *Ivory Coast ebolavirus* (ICEBOV); Ebola-Reston (REBOV), and Bundibugyo ebolavirus (BEBOV) [1, 3, 8, 9]. Reston was isolated from cynomolgus monkeys from the Philippines in 1989 and is less pathogenic in non-human primates. It was thought to be the only subtype that does not cause infection in humans until 2009, when it was strongly speculated to have been transferred from pigs to humans. Bundibugyo was discovered in 2008, and has been found to be most closely related to the ICEBOV strain [9].

SECTION *II* - HAZARD IDENTIFICATION

PATHOGENICITY/TOXICITY: The Ebola virions enter the host cells through endocytosis and replication occurs in the cytoplasm. Upon infection, the virus targets the host blood coagulative and immune defence system and leads to severe immunosuppression [6, 10]. Early signs of infection are non-specific and flu-like, and may include sudden onset of fever, asthenia, diarrhea, headache, myalgia, arthralgia, vomiting, and abdominal pains [11]. Less common early symptoms such as conjunctival injection, sore throat, rashes, and bleeding may also appear. Shock, cerebral oedema, coagulation disorders, and secondary bacterial infection may co-occur with onset of infection [4]. Haemorrhaging symptoms begin 4 - 5 days after onset, which includes hemorrhagic conjunctivitis, pharyngitis, bleeding gums, oral/lip ulceration, hematemesis, melena, hematuria, epistaxis, and vaginal bleeding [12]. Hepatocellular damage, marrow depression (such as thrombocytopenia and leucopenia), serum transaminase elevation, and proteinuria may also occur. Persons that are terminally ill typically present with obtundation, anuria, shock, tachypnea, normothermia, arthralgia, and ocular diseases [13]. Haemorrhagic diathesis is often accompanied by hepatic damage and renal failure, central nervous system involvement, and terminal shock with multi-organ failure [1, 2]. Contact with the virus may also result in symptoms such as severe acute viral illness, malaise, and maculopapular rash. Pregnant women will usually abort their foetuses and experience copious bleeding [2]. Fatality rates range between 50 - 100%, with most dying of dehydration caused by gastric problems [14]. Subtype Ebola-Reston manifests lower levels of pathogenicity in non-human primates and has not been recorded to be infectious in humans; however, sub-clinical symptoms were observed in some people with suspected contact after

they developed antibodies against the virus [8].

Pathogenicity between different subtypes of Ebola does not differ greatly in that they have all been associated with hemorrhagic fever outbreaks in humans and non-human primates. The Ebola-Zaire and Sudan strains are especially known for their virulence with 53 - 90% fatality rate. Less virulent strains include the Côte d'Ivoire ebolavirus and the Reston strain, and the latter has only been observed to cause sub-clinical infections to humans, with transmission from pigs [9]. The major difference between the strains lies in the genome, which can vary by 30 - 40% from each other. This difference might be the cause of the varying ecologic niches of each strain and their evolutionary history. The newly discovered Bundibugyo strain, which caused a single outbreak in Uganda, has a genome with 30% variance from the other strains. It is most closely related to the Côte d'Ivoire ebolavirus strain; however, it has been found to be more virulent as 37 fatal infections were recorded.

EPIDEMIOLOGY: Occurs mainly in areas surrounding rain forests in central Africa [6] with the exception of Reston which occurs in the Phillipines [9]. No predispositions to infection have been identified among infected victims; however, the 20 - 30-year-old age group seems to be particularly susceptible.

Outbreaks:

Democratic Republic of the Congo (formerly Zaire): The first outbreak was recorded in 1976 with 318 cases (88% fatality); in 1995 with 315 cases (81% fatality); in 2001 with 59 cases (75% fatality); in 2003 as two separate outbreaks with 143 cases (90% fatality) and 35 cases (83% fatality), respectively; and recently in 2007 with reports of 372 cases involving 166 deaths [1, 2, 15, 16].

Sudan: The first outbreak was recorded in 1976 with 284 cases (53% fatality); and a second was recorded in 1979 with 34 cases (65% fatality) [1, 2, 15].

Gabon: The first outbreaks were recorded in 1994 with 52 cases (60% fatality); in 1996 as two separate outbreaks with 37 cases (57% fatality) and 60 cases (74% fatality), respectively; and in 2001-2 with 65 cases (82% fatality) [1, 2, 15].

Côte-d'Ivoire: Single non-fatal case of a scientist infected during a necropsy of an infected chimpanzee in the Tai Forest [17].

Uganda: Outbreaks were recorded in 2000 with 425 cases (53% fatality); and recently in 2007 with reports of 93 cases involving 22 deaths [2, 15, 18].

Philippine: In 2009, local authorities and international agencies confirmed for the first time that the Ebola Reston virus was strongly likely to have been transmitted from pigs to humans, when it was discovered that 5 out of 77 people who had come in contact with the pigs had developed antibodies to the EBOV virus, no other clinical signs were observed [19].

United States: An outbreak of REBOV in monkeys in 1989 in a shipment of animals from the Philippines, and a second outbreak occurred in 1996 in Texas among animals from the same Phillipine supplier [20].

Western Uganda: The outbreak in 2007 in the townships of Bundibugyo and Kikyo in the Bundibugyo district marked the discovery of the fifth strain of the virus, the Bundibugyo ebolavirus [9]. The outbreak lasted for 2 months, with 149 suspected cases and 37 deaths.

HOST RANGE: Humans, various monkey species, chimpanzees, gorillas, baboons, and duikers [1-3, 15, 16, 18, 21-23]. The Ebola virus genome was recently discovered in two species of rodents and one species of shrew living in forest border areas, raising the possibility that these animals may be intermediary hosts [24]. Other studies of the virus have been done using guinea pig models [25]. A survey of small vertebrates captured during the 2001 and 2003 outbreaks in Gabon found evidence of asymptomatic infection in three species of fruit bat (*Hypsignathus monstrosus*, *Epomops franqueti*, and *Myonycteris torquata*) [26].

INFECTIOUS DOSE: 1 - 10 aerosolized organisms are sufficient to cause infection in humans [21].

MODE OF TRANSMISSION: In an outbreak, it is hypothesized that the first patient becomes infected as a result of contact with an infected animal [15]. Person-to-person transmission occurs via close personal contact with an infected individual or their body fluids during the late stages of infection or after death [1, 2, 15, 27]. Nosocomial infections can occur through contact with infected body fluids due to the reuse of unsterilized syringes, needles, or other medical equipment contaminated with these fluids [1, 2]. Humans may be infected by handling sick or dead non-human primates and are also at risk when handling the bodies of deceased humans in preparation for funerals, suggesting possible transmission through aerosol droplets [2, 6, 28]. In the laboratory, infection through small-particle aerosols has been

demonstrated in primates, and airborne spread among humans is strongly suspected, although it has not yet been conclusively demonstrated [1, 6, 13]. The importance of this route of transmission is not clear. Poor hygienic conditions can aid the spread of the virus [6].

INCUBATION PERIOD: Two to 21 days, more often 4 - 9 days [1, 13, 14].

COMMUNICABILITY: Communicable as long as blood, secretions, organs, or semen contain the virus. Ebola virus has been isolated from semen 61 days after the onset of illness, and transmission through semen has occurred 7 weeks after clinical recovery [1, 2].

SECTION *III* - DISSEMINATION

RESERVOIR: The natural reservoir of Ebola is unknown [1, 2]. Antibodies to the virus have been found in the serum of domestic guinea pigs, with no relation to human transmission [29]. The virus can be replicated in some bat species native to the area where the virus is found, thus certain bat species may prove to be the natural hosts [26].

ZOONOSIS: Probably transmitted from animals (non-human primates and/or bats) [2, 15, 26].

VECTORS: Unknown.

SECTION *IV* - STABILITY AND VIABILITY

DRUG SUSCEPTIBILITY: Unknown. S-adenosylhomocysteine hydrolase inhibitors have been found to have complete mortality protection in mice infected with a lethal dose of Ebola virus [30].

DRUG RESISTANCE: There are no known antiviral treatments available for human infections.

SUSCEPTIBILITY TO DISINFECTANTS: Ebola virus is susceptible to sodium hypochlorite, lipid solvents, phenolic disinfectants, peracetic acid, methyl alcohol, ether, sodium deoxycholate, 2% glutaraldehyde, 0.25% Triton X-100, β-propiolactone, 3% acetic acid (pH 2.5), formaldehyde and paraformaldehyde, and detergents such as SDS [20, 21, 31-34].

PHYSICAL INACTIVATION: Ebola are moderately thermolabile and can be inactivated by heating for 30 minutes to 60 minutes at 60ºC, boiling for 5 minutes, gamma irradiation (1.2 $x10^6$ rads to 1.27 $x10^6$ rads), and/or UV radiation [3, 6, 20, 32, 33].

SURVIVAL OUTSIDE HOST: The virus can survive in liquid or dried material for a number of days [23]. Infectivity is found to be stable at room temperature or at 4°C for several days, and indefinitely stable at -70°C [6, 20]. Infectivity can be preserved by lyophilisation.

SECTION *V* - FIRST AID / MEDICAL

SURVEILLANCE: Monitor anyone suffering from an acute febrile illness that has recently travelled to rural sub-Saharan Africa, especially if haemorrhagic manifestations occur [3]. Diagnosis can be quickly done in an appropriately equipped laboratory using a multitude of approaches including ELISA based techniques to detect anti-Ebola antibodies or viral antigens [12], RT-PCR to detect viral RNA, immunoelectron microscopy to detect Ebola virus particles in tissues and cells, and indirect immunofluorescence to detect antiviral antibodies [1, 2, 12, 21]. It is useful to note that the Marburg virus is morphologically indistinguishable from the Ebola virus, and laboratory surveillance of Ebola is extremely hazardous and should be performed in a Containment Level 4 facility [1, 2, 12, 35].

Note: All diagnostic methods are not necessarily available in all countries.

FIRST AID/TREATMENT: There is no effective antiviral treatment [23, 26]. Instead, treatment is supportive, and is directed at maintaining renal function and electrolyte balance and combating haemorrhage and shock [15]. Transfusion of convalescent serum may be beneficial [3]. Post-exposure treatment with a nematode-derived anticoagulation protein and a recombinant vesicular stomatitis virus vaccine expressing the Zaire Ebola virus glycoprotein have been shown to have 33% and 50% efficacy, respectively, in humans [4]. Recent studies have shown that small interfering RNAs (siRNAs) can be potentially effective in silencing Zaire Ebola virus RNA polymerase L, and treatments in rhesus macaque monkeys have resulted in 100% efficacy when administered everyday for 6 days; however, delivery of the nucleic acid still remains an obstacle.

IMMUNIZATION: None [23].

PROPHYLAXIS: None. Management of the Ebola virus is solely based on isolation and barrier-nursing with symptomatic and supportive treatments [4].

SECTION *VI* - LABORATORY HAZARDS

LABORATORY-ACQUIRED INFECTIONS: One reported near-fatal case following a minute finger prick in an English laboratory (1976) [36]. A Swiss zoologist contracted Ebola virus after performing an autopsy on a chimpanzee in 1994 [2, 37]. An incident in Germany in 2009 when a laboratory scientist pricked herself with a needle that had just been used to infect a mouse with Ebola, however infection has not be confirmed. Additional incidents were recorded in the US in 2004, and a fatal case in Russia in 2004 [4].

SOURCES/SPECIMENS: Blood, serum, urine, respiratory and throat secretions, semen, and organs or their homogenates from human or animal hosts [1, 2, 35]. Human or animal hosts, including non-human primates, may represent a further source of infection [35].

PRIMARY HAZARDS: Accidental parenteral inoculation, respiratory exposure to infectious aerosols and droplets, and/or direct contact with broken skin or mucous membranes [35].

SPECIAL HAZARDS: Work with, or exposure to, infected non-human primates, rodents, or their carcasses represents a risk of human infection [35].

SECTION *VII* - EXPOSURE CONTROLS / PERSONAL PROTECTION

RISK GROUP CLASSIFICATION: Risk Group 4 [38].

CONTAINMENT REQUIREMENTS: Containment Level 4 facilities, equipment, and operational practices for work involving infectious or potentially infectious materials, animals, and cultures.

PROTECTIVE CLOTHING: Personnel entering the laboratory must remove street clothing, including undergarments, and jewellery, and change into dedicated laboratory clothing and shoes, or don full coverage protective clothing (i.e., completely covering all street clothing). Additional protection may be worn over laboratory clothing when infectious materials are directly handled, such as solid-front gowns with tight fitting wrists, gloves, and respiratory protection. Eye protection must be used where there is a known or potential risk of exposure to splashes [39].

OTHER PRECAUTIONS: All activities with infectious material should be conducted in a biological safety cabinet (BSC) in combination with a positive pressure suit, or within a class III BSC line. Centrifugation of infected materials must be carried out in closed containers placed in sealed safety cups, or in rotors that are unloaded in a biological safety cabinet. The integrity of positive pressure suits must be routinely checked for leaks. The use of needles, syringes, and other sharp objects should be strictly limited. Open wounds, cuts, scratches, and grazes should be covered with waterproof dressings. Additional precautions should be considered with work involving animal activities [39].

SECTION *VIII* - HANDLING AND STORAGE

SPILLS: Allow aerosols to settle and, wearing protective clothing, gently cover spill with paper towels and apply suitable disinfectant, starting at the perimeter and working towards the centre. Allow sufficient contact time before clean up [39].

DISPOSAL: Decontaminate all materials for disposal from the containment laboratory by steam sterilisation, chemical disinfection, incineration or by gaseous methods. Contaminated materials include both liquid and solid wastes [39].

STORAGE: In sealed, leak-proof containers that are appropriately labelled and locked in a Containment Level 4 laboratory [39].

SECTION *IX* - REGULATORY AND OTHER INFORMATION

REGULATORY INFORMATION: The import, transport, and use of pathogens in Canada is regulated under many regulatory bodies, including the Public Health Agency of Canada, Health Canada, Canadian Food Inspection Agency, Environment Canada, and Transport Canada. Users are responsible for ensuring they are compliant with all relevant acts, regulations, guidelines, and standards.

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