

Hantavirus Guidelines (BRM033)

Table of Contents

<i>Research with Hantavirus (Orthohantavirus)</i>	1
<i>Scope</i>	1
Agent	1
Incidence	2
Species	2
Occupational infections	2
Sequelae	2
Laboratory Hazards and Communicability	2
Susceptibility to Disinfectants	3
<i>GUIDELINES</i>	3
<i>Biosafety Levels</i>	3
<i>Response to Potential Employee Exposures</i>	4

Research with Hantavirus (Orthohantavirus)

The University of Pittsburgh has developed guidelines to establish a system of education and safeguards to ensure compliance with the NIH Guidelines for Research Involving Recombinant and Synthetic Nucleic Acid Molecules (NIH Guidelines), and other applicable biosafety guidelines and best practices for all personnel working with wildtype and recombinant strains of Hantavirus.

The NIH Guidelines define specific work practices and administrative controls for work with recombinant forms of certain Risk Group 3 viruses, including recombinant strains of Hantavirus. These Biorisk Management Guidelines apply to work involving wild-type or recombinant Hantavirus strains.

Scope

Agent – Hantavirus spp. are enveloped negative-sense RNA viruses belonging to the family *Hantaviridae* within the order *Bunyavirales*. Hantaviruses are spherical enveloped particles 90-100 nm in diameter. Hantaviruses are globally distributed, zoonotic viruses, and the geographic ranges of each strain of virus are dependent on

its associated host species. The host range of Hantaviruses includes rodents, shrews, moles, bats, reptiles, and fish. Only a limited number of Hantaviruses have been identified as causing human disease. Hantaviruses are divided into two broad categories, Old World and New World viruses.

Incidence – The World Health Organization estimates between 10,00 to 100,000 cases per year worldwide.

Hantaviruses found in North, Central, and South America are linked with causing Hantavirus cardiopulmonary syndrome (HCPS) in humans.

- United States: 890 cases of Hantavirus were reported between 1993 -2023, with the majority of cases found in the southwest United States.
- Americas: South American countries (Argentina, Brazil, and Chile) have an estimated 100 cases per year.

Hantaviruses found in Europe and Asia are known to cause hemorrhagic fever with renal syndrome (HFRS)

The case fatality rate of HFRS ranges from less than 1% to 15%, while for HPS it is 30–60% .

Species: Rodents, deer mice, shrews, moles, bats, reptiles and fish. Potential hazard when performing field studies with wild rodents. Transmission to other species of animals, including pigs, rabbits, deer, and cattle, has been observed with specific strains of Hantavirus.

Occupational infections – Documented laboratory-acquired infections have occurred in individuals working with Hantaviruses. Extreme caution must be used when performing procedures that may create aerosols. Two recent researcher infections with Hantavirus Pulmonary Syndrome (HPS) cases (1 fatal), associated with trapping of rodents in field studies.

Sequelae- In humans, symptoms can begin between 1 and 8 weeks after exposure, depending on the strain of Hantavirus, and typically include fever, headache, muscle aches, and gastrointestinal symptoms including abdominal pain, nausea, or vomiting.

Laboratory Hazards and Communicability –

Use of Hantavirus is restricted to Biosafety Level 3 facilities at the University of Pittsburgh. Hantaviruses that cause illness in humans are primarily transmitted by rodents. In rodents, hantaviruses usually cause an asymptomatic, persistent infection. Virus can spread through contact with aerosols, droplets from infected laboratory materials, infected animals' feces, urine, saliva, and blood, and tissue. Hantavirus can survive at room temperature for up to 10 days, and 18 days at 4 C.

Laboratory transmission of hantaviruses to humans via the aerosol route is well documented. Other laboratory routes of transmission include ingestion, contact with infectious materials through mucous membranes or broken skin, and animal bites.

Human-to-human transmission of the Andes virus has been reported through close contact with infected individuals.

Susceptibility to Disinfectants – Susceptible to 1% sodium hypochlorite, 2% glutaraldehyde, and EPA-registered disinfectants appropriate for Hantavirus. Sensitive to heat.

GUIDELINES

All Principal Investigators (PIs) using wild-type or recombinant Hantavirus strains must be registered with the Institutional Biosafety Committee (IBC; recombinant) and the Division of Biorisk Management (wild-type). PIs may register by completing a protocol application in the MyIBC system (myibc.pitt.edu).

Biosafety Levels

Biosafety Level 3, with enhanced work practices, administrative controls, containment equipment, and facilities, is required for all *in vitro* activities involving the use or manipulation of wild-type or recombinant Hantavirus strains.

Potentially infected animal materials, including tissue samples, should be handled in BSL-2 facilities in accordance with BSL-3 practices (currently defined as BSL-2+ at the University of Pittsburgh).

BSL-2 practices with BSL-3 practices (BSL-2+), containment equipment, and facilities are required for handling of clinical samples from persons potentially infected with Hantavirus.

Biosafety Cabinets and other physical containment devices should be used whenever work with Hantavirus is performed, especially when performing aerosol-generating procedures.

All live animal work with Hantavirus must be performed in a BSL-4 facility, and may not be performed at the University of Pittsburgh.

In vitro work practices and administrative controls shall include: Change of gloves and sleeve covers (at a minimum) after full decontamination of the work area, after work with Hantavirus. Separate reagents to be used solely for Hantavirus work.

A protocol-specific Biosafety Level 3 Manual is required for all research with wild-type or recombinant strains of Hantavirus, and must be approved by Biorisk Management and the University Biohazards Committee prior to initiating research. Laboratories shall be inspected by Biorisk Management at least annually to verify appropriate Biosafety Level 3 containment, including facility enhancements, enhanced work practices, and restricted access.

Occupational Health Requirements

All personnel entering any BSL-3/ABSL-3 facility at the University of Pittsburgh where Hantavirus is in use must be enrolled in the University's Respiratory Protection Program and must wear a Powered Air-Purifying Respirator (PAPR).

All personnel entering BSL-3/ABSL-3 facilities must have undergone a BSL-3 Worker Health Screening through Employee Health Services within the previous 12 months.

Response to Potential Employee Exposures

In the event of potential exposure to wild-type or recombinant Hantavirus strains, personnel shall follow the post-exposure response procedures outlined in this document and the PI's incident response plan and/or biosafety manual.

Risk assessment regarding the potential for exposure to result in infection will be performed collectively by the Employee Health Services Medical Director, PI, and Biorisk Management.

If work is planned with strains of Hantavirus that are known, or determined by risk assessment to be likely, to spread via person-to-person transmission (e.g., Andes virus), a research-informed consent SOP must be developed in collaboration with Employee Health Services and Biorisk Management as part of the PI's incident response plan and/or biosafety manual. In the event of a known exposure that poses a high risk of infection during research with a person-to-person transmissible strain, appropriate post-exposure response procedures will be determined through a risk assessment conducted jointly by the Employee Health Services Medical Director, PI, Biorisk Management, and applicable public health and/or subject-matter experts.

Any incident that may pose an exposure risk should be reported immediately to Employee Health Services, Biorisk Management, and the employee's supervisor. Personnel should report to the MyHealth@Work clinic or the Presbyterian Emergency Room as appropriate for exposure evaluation and post-exposure follow-up. Additional information is found in the University's BSL-3 Exposure Memo available to all personnel working in BSL-3/ABSL-3 facilities in exposure response kits and electronic form in shared document systems.

If personnel who have had a potential exposure begin to develop signs and/or symptoms of Hantavirus infection, depending on the strain of Hantavirus involved in the exposure (1 and 8 weeks after exposure, depending on the strain of Hantavirus, and typically include fever, headache, muscle aches, and gastrointestinal symptoms including abdominal pain, nausea or vomiting) they shall immediately inform Employee Health Services.

It shall be the responsibility of the Principal Investigator and/or individuals responsible for control of access to a facility where wild-type or recombinant strains of Hantavirus are used to assure that individuals handling Hantavirus or Hantavirus-exposed materials are:

- Enrolled in the occupational health requirements of this Guideline
- Listed on any relevant IBC and/or IACUC protocol,
- Approved for access to BSL-3 laboratories at the University of Pittsburgh,

CDC guidelines at <https://www.cdc.gov/hantavirus/index.html>