

**HENIPAVIRUS
STANDARD OPERATING PROCEDURES:
1. OVERVIEW OF ETIOLOGY AND ECOLOGY**

FAD PReP

**Foreign Animal Disease
Preparedness & Response Plan**



**United States
Department of
Agriculture**

United States Department of Agriculture • Animal and Plant Health Inspection Service • Veterinary Services

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The Foreign Animal Disease Preparedness and Response Plan (FAD PreP) Standard Operating Procedures (SOPs) provide operational guidance for responding to an animal health emergency in the United States.

These draft SOPs are under ongoing review. This document was last updated in **November 2013**. Please send questions or comments to:

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Nipah Virus

Etiology & Ecology Quick Summary

Disease

Nipah virus encephalitis; porcine respiratory and encephalitis syndrome (PRES); porcine respiratory and neurologic syndrome, barking pig syndrome, Hendra-like virus

Mortality & Morbidity

High morbidity, low mortality in pigs except in piglets; morbidity and mortality in humans variable, but mortality in humans may range from 40%–75%.

Susceptible Species

Primarily swine; humans. Infections also reported in dogs, cats, goats, horses, and sheep.

Zoonotic Potential?

High.

Reservoir

Fruit bats (of the genus *Pteropus*).

Transmission

Direct contact with infective materials of fruit bats, contaminated feed, fruit, or water, materials from other infected animals. Virus present in urine, saliva, respiratory secretions, feces, and placental fluids.

Persistence in the Environment

Moderately stable in the environment (tolerates heat up to 60°C, pH 4.0–10.0). Susceptible to most soaps and disinfectants.

Animal Products and By-Products

Can survive in urine and contaminated fruit juice for days.

Hendra Virus

Etiology & Ecology Quick Summary

Disease

Hendra; equine morbillivirus pneumonia; acute equine respiratory syndrome.

Mortality & Morbidity

Low morbidity, high mortality in horses and humans.

Susceptible Species

Horses and humans. Cats and guinea pigs have been infected experimentally.

Zoonotic Potential?

High.

Reservoir

Fruit bats (of the genus *Pteropus*).

Transmission

Direct contact with infective materials of fruitbats, contaminated feed, fruit, or water, materials from other infected animals. Virus present in urine, saliva, respiratory secretions, feces, and placental fluids.

Persistence in the Environment

Moderately stable in the environment (tolerates heat up to 60°C, pH 4.0–10.0); susceptible to most soaps and disinfectants.

Animal Products and By-Products

Can survive in urine and contaminated fruit juice for days.

1.1 Introduction

Nipah and Hendra are both emerging diseases, having been first described in the 1990's. Nipah virus (NiV) and Hendra (HeV) virus are in the same family (Paramyxoviridae) and genus (Henipavirus), and the clinical course of each disease is similar. Both viruses are zoonotic. Domestic swine are the primary animal species affected by NiV, while horses are the primary animal species affected by HeV.

NiV encephalitis was first identified as causing acute fever and respiratory symptoms in pigs and encephalitis in humans in 1998–1999 epidemics in the Malaysian Peninsula. HeV, presenting as an acute respiratory syndrome, was first recognized in Australia in 1994. Neither NiV nor HeV has ever been reported in the United States. For both henipaviruses, flying foxes/fruit bats (in the genus *Pteropus*) appear to be the primary reservoir host of the virus. Secretions from infected fruit bats appear to be highly infective.

The morbidity and mortality rates of henipaviruses have varied over the course of various outbreaks. NiV is highly contagious and morbidity in swine is frequently high, and can be as high as 100 percent depending on density of the affected population and age of the animal. Mortality is higher in piglets (40 percent) than in young swine or older animals (<5 percent). The case fatality rate for humans is estimated between 40 percent and 75 percent. For HeV, morbidity in horses is relatively high, though the infection in horses does not appear to be highly contagious.^{1,2} The case fatality rate is high in both humans and horses, though an estimate of the mortality rate is hard to provide given the relatively few outbreaks that have occurred.³

1.1.1 Goals

As a preparedness goal, the Animal and Plant Health Inspection Service (APHIS) will provide etiology and ecology summaries for Nipah and Hendra, and update these summaries at regular intervals.

As a response goal, the Unified Command and stakeholders will have a common set of etiology and ecology definitions and descriptions, to ensure proper understanding of henipaviruses when establishing or revising goals, objectives, strategies, and procedures.

1.1.2 Further Information

This document is intended to be an overview, focusing on NiV and HeV in domestic animal species. Additional resources on NiV and HeV, as well as the articles referenced in this SOP, are listed in [Attachment 1.A](#). Foreign Animal Disease Preparedness and Response Plan (FAD PRoP) documents are available on the APHIS public website (http://www.aphis.usda.gov/animal_health/emergency_management) or on the APHIS Intranet (<http://inside.aphis.usda.gov/vs/em/fadprep.shtml>) for APHIS employees. Case definitions and

¹ Field H, Young P, Yob, JM, Mills J, Hall L, Mackenzie J. 2001. "The natural history of Nipah and Hendra viruses." *Microbes and Infection*. 307-314.

² Eaton BT, Broder CC, Middleton D, Wang LF. 2006. "Hendra and Nipah viruses: different and dangerous." *Nature Rev Microbio*. 4, 23-35.

³ New South Wales Government. 2011. "Hendra Virus: National guidelines for public health units." Available from <http://www.health.nsw.gov.au/factsheets/guideline/hendra.html> (accessed January 2012).

laboratory criteria are also available, from the APHIS Centers for Epidemiology and Animal Health.

1.2 Purpose

This document provides responders and stakeholders with a common understanding of the disease agent.

1.3 Etiology

1.3.1 Name

Nipah virus encephalitis is also known as Porcine Respiratory and Encephalitis Syndrome (PRES), Porcine Respiratory and Neurologic Syndrome, Barking Pig Syndrome, and Hendra-like virus. The name is derived from the village in Malaysia, Sungai Nipah, where pig farmers first become sick with the virus.

Hendra takes its name from a suburb of Brisbane, Australia where the first occurrence of an acute, highly fatal pneumonia in horses and humans during 1994-95 took place. HeV is otherwise known as Equine Morbillivirus Pneumonia or Acute Equine Respiratory Syndrome.

1.3.2 Virus Characteristics

According to the International Committee on Taxonomy of Viruses⁴, both NiV and HeV are categorized as follows:

- Family: Paramyxoviridae
 - Subfamily: Paramyxovirinae
 - Genera: Henipavirus
- Genome characteristics: (-) ssRNA.

An additional novel Henipavirus was characterized in bats in pteropid bats in 2012, Cedar Virus (CedPV). To-date, there is not evidence to suggest that CedPV causes clinical disease in domestic animals.⁵

1.3.3 Morphology

Both Nipah and Hendra are enveloped viruses that have non-segmented genomes composed of single-stranded ribonucleic acid (RNA) which codes for six structural proteins: nucleocapsid, phosphoprotein, matrix protein, fusion protein, glycoprotein or attachment protein, and large protein or RNA polymerase.

NiV and HeV are closely related, and the antibodies from these viruses will cross-react.⁶

⁴ International Committee on Taxonomy of Viruses. Available at: <http://ictvonline.org/> Accessed January 2012.

⁵ Marsh GA, de Jong C, Barr JA, Tachedjian M, et al. 2012. "Cedar virus: a novel Henipavirus isolated from Australian bats." *PLoS Pathog* 8(8).

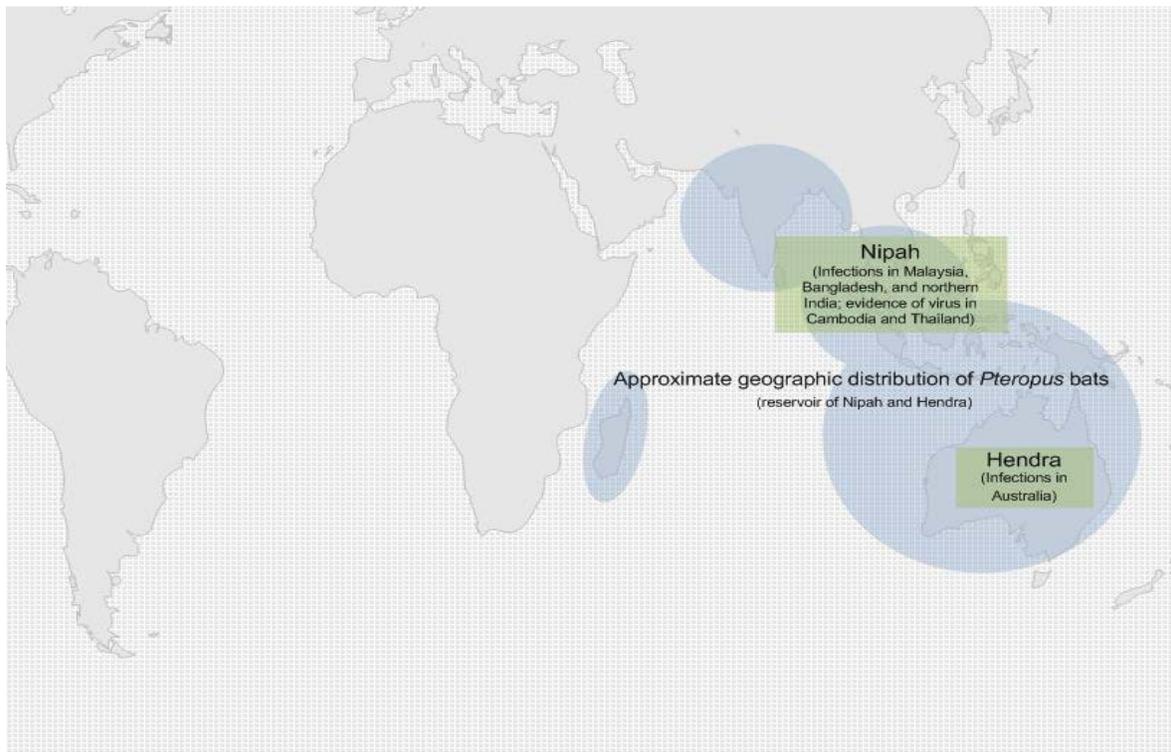
⁶ Wang L, Harcourt BH, Yu M, Tamin A, Rota PA, et al. 2001. "Molecular biology of Hendra and Nipah viruses." *Microbes and Infection* 3, 279-287.

Antibodies to CedPV will also cross-react with NiV and HeV.⁷

1.4 Ecology

1.4.1 General Overview

Nipah and Hendra are both emerging, highly pathogenic zoonotic viral diseases which have only been described since 1994. HeV has caused multiple outbreaks of mild to fatal pulmonary disease and encephalitis among horses and humans in Brisbane, Queensland and New South Wales, Australia including cases in horses in 2011, 2012, and 2013. NiV has caused similar syndromes in domestic swine and humans since 2001 in Malaysia, Singapore, Bangladesh, and India, including cases in humans in 2011, 2012, and 2013 in Bangladesh.



1.4.2 Susceptible Species

1.4.2.1 Nipah

Swine are the most susceptible domestic species and act as amplifying hosts of the virus. Humans can be infected with direct contact through infected swine, as well as thru direct or indirect contact with infected bats. Human-to-human transmission was observed in the Bangladesh outbreak. Dogs, cats, horses, and goats can also be affected by NiV.

⁷ Marsh GA, de Jong C, Barr JA, Tachedjian M, et al. 2012. "Cedar virus: a novel Henipavirus isolated from Australian bats." *PLoS Pathog* 8(8).

1.4.2.2 Hendra

HeV has been reported only in horses and humans, though antibodies have been detected in dogs. Cats have been experimentally infected, but natural infection with HeV has not been detected. Human-to-human transmission has not been observed in past outbreaks; humans have been infected with HeV by direct exposure with sick and necropsied horses.

1.4.3 Reservoir and Carriers

The only natural reservoir of Nipah and Hendra viruses is fruit bats (flying foxes) of the genus *Pteropus*. The geographic distribution of these animals is limited to the western Indian Ocean and Southeast Asia, including parts of Pakistan and India, as well as the southwest Pacific Islands and Australia. They have been reported to be somewhat nomadic and to travel long distances (up to 600 km) over both land and water. During the 1998–1999 Nipah outbreak in Malaysia the prevalence of virus antigen or antibody isolated from bats ranged from 7-58 percent. A serological survey following the outbreaks of Hendra in Australia found a crude seroprevalence of 47 percent in flying foxes.^{8, 9, 10}

1.4.4 Introduction and Transmission of Henipaviruses

Henipaviruses are primarily introduced through direct contact with infected animals and contaminated environment, fomites, feed/fruit, or water. Among bats, transmission is horizontal rather than vertical. Although the routes of transmission from bats to horses or pigs is uncertain, the viruses have been isolated from urine, saliva, fetal or uterine tissues, blood, feces, and other secretions from asymptotically infected bats. It has been hypothesized that as a result of clearing and deforestation and the subsequent reduction of their habitat, bats have come closer in proximity to horses, pigs, and other peridomestic species, including rats, dogs, and chickens, which may facilitate the spread from bats to domestic livestock.

Hendra virus may spread between horses within an enclosed environment (such as a stable) via inhalation, ingestion, or environmental contamination, but contact with aerosols such as infective saliva, respiratory secretions, or tissues from an ill or dead horse in a pasture situation is not considered an efficient means of transmission. Subsequent zoonotic transmission to humans from infective bodily fluids or aerosols has occurred due to close contact with infected horses or during necropsies. Human-to-human spread has not been observed.

Nipah is transmitted efficiently among pigs, as they are an amplifying host, by direct contact or via fomites contaminated with respiratory secretions, saliva, and possibly urine.

In the first outbreak of Nipah among humans in Malaysia and Singapore, zoonotic transmission via contact with urine, feces, and respiratory secretions of pigs were identified as possible routes of infection.¹¹ In later outbreaks in Bangladesh, virus spread from bats to humans was implicated via drinking contaminated raw date palm sap or direct contact with bats,⁸ and

⁸ Field H, Young P, et al. 2001 "The natural history of Hendra and Nipah viruses." *Microbes and Infection*, 3:307-314.

⁹ Luby SP, Gurley ES, Hossain MJ. 2009. "Transmission of human infection with Nipah Virus." *Clinical Infectious Disease*, 49(11):1743-1748.

¹⁰ Yob JM, Field H, et. al. 2001. "Nipah virus infection in bats (order Chiroptera) in peninsular Malaysia. *Emerging Infectious Diseases*, 7(3):439-441.

¹¹ Chew MHL, Arguin PM, et. al. 2000. "Risk factors for Nipah virus infection among Abattoir workers in Singapore." *Journal of Infectious Diseases*, 181:1760-1763.

subsequent person-to-person transmission was observed to occur via direct contact.^{12, 13}

1.4.5 Incubation Period

The incubation period for both Nipah and Hendra is different among infected humans and animals. In animals, the incubation period is 7–14 days for Nipah and 5–16 days for Hendra. Among humans, the incubation periods are 4–20 days and 5–12 days, for Nipah and Hendra, respectively.

1.4.6 Morbidity and Mortality

Hendra is very minimally contagious, but highly fatal in both horses and humans. Apart from outbreaks featuring clusters of cases, the incidence of illness has been very low. Mortality is much higher, with up to 75 percent of infected horses having died.¹⁴

Unlike Hendra, the morbidity and mortality of Nipah is variable depending on the age of the populations affected. Young piglets experience high morbidity and mortality (up to 40 percent), although illness in sows may have contributed to fatalities. In pigs older than 4 weeks, morbidity may reach 100 percent, but mortality is usually low (1–5 percent).

1.4.6.1 In Humans

Since the first described outbreak in 1994 there have been seven confirmed Hendra infections in humans with four deaths, making the case fatality rate over 50 percent. All cases have been epidemiologically linked to infections in horses; humans are dead-end hosts as there is no evidence of human-to-human transmission.¹⁵

Nipah virus infections in humans have a highly variable case fatality rate of approximately 40 – 75 percent, sometimes becoming significantly higher. Of those who survive infection about 20 percent have permanent neurological problems, such as persistent convulsions or changes in personality. Relapse or delayed onset of disease is also a possibility.¹⁶

Because of the mortality and long-term health consequences in people, Hendra and Nipah have become a great concern for both animal and human health. There are no medical countermeasures or vaccines currently available, however research is ongoing. Because NiV and HeV are so closely related it is likely that a cross-reactive vaccine that protects against both viruses is possible.^{17, 18}

¹² Gurley ES, Montgomery JM, et. al. 2007. "Person-to-Person transmission of Nipah virus in a Bangladeshi community." *Emerging Infectious Diseases*, 13(7):1031-1037. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2878219/>. Accessed January 2012.

¹³ Hsu VP, Hossain MJ, et. al. 2004. "Nipah virus encephalitis reemergence, Bangladesh." *Emerging Infectious Diseases*, 10(12):2082-2087.

¹⁴ New South Wales Government. 2011. "Hendra Virus: National guidelines for public health units." Available at: <http://www.health.nsw.gov.au/factsheets/guideline/hendra.html>. Accessed January 2012.

¹⁵ Paterson BJ, MacKenzie JS, Durrheim DN, Smith D. 2011. "A review of the epidemiology and surveillance of viral zoonotic encephalitis and the impact on human health in Australia." *New South Wales Public Health Bulletin*. 22(6):99-104.

¹⁶ World Health Organization. 2011. "Weekly Epidemiological Record." 41:451-455. Available at <http://www.who.int/wer/2011/wer8641.pdf> (Accessed January 2012).

¹⁷ Pallister J, Middleton D, Wang LF, Klein R, et al. 2011. "A recombinant Hendra virus G glycoprotein-based subunit vaccine protects ferrets from lethal Hendra virus challenge." *Vaccine*. 29(34):5623-5630.

¹⁸ McEachern JA et al. 2008. "A recombinant subunit vaccine formulation protects against lethal Nipah virus challenge in cats." *Vaccine*. 26(31): 3842-3852.

1.4.6.2 Clinical Signs

Horses and humans are the only species demonstrated to contract natural infection of Hendra. Cases in horses begin as mild to severe influenza-like illness, with fever, depression, and respiratory symptoms. Neurologic signs may present early in the disease and acute death from pulmonary edema occurs in 1–3 days after disease onset.

Humans with Hendra infections experience a similar course of fever, respiratory distress, and meningoencephalitis that may relapse into fatal neurologic disease. Experimentally infected cats also demonstrate this progression of fever, respiratory distress, and encephalitis, often fatal within 24 hours.¹⁹

Natural infection with Nipah has been observed in pigs, humans, dogs, and cats. Clinical presentation varies by the age of the population affected. In pigs 1–6 months of age, fever and respiratory signs mainly occur with some neurologic deficits. In older animals, fever and marked central nervous system signs with occasional respiratory involvement is observed. Although rare, fulminant death may also occur in this group.

Among dogs signs of clinical infection that have been reported include distemper-like syndrome, characterized by fever, depression, respiratory, and oculonasal signs. Among cats acute respiratory fevers has been observed.

The signs of human infections of Nipah can range from mild or subclinical influenza-like signs to more acute encephalitic symptoms, with 50 percent developing loss of consciousness and brainstem dysfunction, and relapses may occur as long as 4 years post-recovery. Rare cases show respiratory difficulty, and the most severe infections cause septicemia, gastrointestinal bleeding, and renal impairment, in some cases leading to death.

1.4.7 Vaccines for Animals

Currently, there are not medical countermeasures or vaccines available for domestic animals for either Nipah or Hendra. However, there are several clinical trials ongoing, and experiments have preliminarily demonstrated in the laboratory that ferrets and monkeys were be protected by novel vaccines.^{20, 21, 22}

1.5 Environmental Persistence of Hendra/Nipah

The survival characteristics of henipaviruses in the environment are not well known. However, the OIE cites features of other Paramyxoviridae viruses and expects that Nipah and Hendra would share similar characteristics.

¹⁹ Barclay AJ and Paton DJ. 2000. "A Review of Hendra disease." *The Veterinary Journal*, 160:169-176.

²⁰ Pallister JA, Klein R, Arkinstall R, Haining J et al. 2013. "Vaccination of ferrets with a recombinant G glycoprotein subunit vaccine provides protection against Nipah virus disease for over 12 months." *Virology*.10: 237.

²¹ Pallister J, Middleton D, Wang LF, Klein R et al. 2011. "A recombinant Hendra virus G glycoprotein-based subunit vaccine protects ferrets from lethal Hendra virus challenge." *Vaccine*. 29(34):5623-5630.

²² Bossart KN, Rockx B, Feldmann F, Brining D, et al. 2012. "A Hendra Virus G Glycoprotein Subunit Vaccine Protects African Green Monkeys from Nipah Virus Challenge." *Sci Trans Med*, 4(146), 146ra107.

Table 1-1. Resistance of Henipaviruses to Physical and Chemical Action²³

Action	Resistance
Temperature	Other animal <i>Paramyxoviruses</i> are inactivated by 60°C/60 minutes.
pH	Stable between pH 4.0 and 10.0.
Chemicals/Disinfectants	<i>Paramyxoviruses</i> are susceptible to common soaps and disinfectants; lipid solvents (alcohol and ether) and sodium hypochlorite solutions were used effectively in outbreaks for cleaning and disinfection.
Survival	Survives for long periods in favorable conditions; survives for days in fruit bat urine and contaminated fruit juice.

Source: OIE Technical Disease Card for Nipah, 2009.

1.6 Risk of Introduction to the United States

The risk for introduction of Hendra and Nipah into the United States appears to be fairly low. This is due to the fact that the fruit bats that are known to be the natural reservoir of both viruses, genus *Pteropus*, are only found in the Indian and western Pacific Ocean regions, and they have never been reported in North or South America, Europe, Africa, or mainland Asia.²⁴ Further, infections with these viruses have never been reported outside of India and the island nations mentioned above (sections 1.1 and 1.4.1). Specific analyses and risk assessments are needed to better estimate the likelihood of introduction into the United States, with consideration of the movements of domestic livestock and wildlife, human transport, and import and export data.

²³ World Organization for Animal health (OIE). 2009. Nipah. *OIE Technical Disease Card*. <http://www.oie.int>.

²⁴ Field H, Young P, et. al. 2001. "The natural history of Hendra and Nipah viruses." *Microbes and Infection*, 3:307-314.

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Pallister J, Middleton D, Wang LF, Klein R, et al. 2011. "A recombinant Hendra virus G glycoprotein-based subunit vaccine protects ferrets from lethal Hendra virus challenge." *Vaccine*. 29(34):5623–5630.

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Attachment 1.B Abbreviations

APHIS	Animal and Plant Health Inspection Service
CedPV	Cedar Valley Virus
FAD PReP	Foreign Animal Disease Preparedness and Response Plan
HeV	Hendra
NiV	Nipah
OIE	World Organization for Animal Health
PRES	Porcine Respiratory and Encephalitis Syndrome
RNA	Ribonucleic acid
USDA	United States Department of Agriculture