



**GLANDERS  
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

SEPTEMBER 2016

File name:	Glanders_FAD_PReP_E&E_Sept2016	
Lead section:	Preparedness and Incident Coordination	Version number: Draft 1.0
Effective date:	September 2016	Review date: September 2018

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 **September 2016**. Please send questions or comments to:

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# Contents

1.1	Background and Introduction.....	1-2
	1.1.1 Further Information.....	1-2
	1.1.2 Goals .....	1-3
1.2	Purpose.....	1-3
1.3	Etiology.....	1-3
	1.3.1 Name .....	1-3
	1.3.2 Bacterial Characteristics.....	1-3
	1.3.3 Morphology .....	1-4
1.4	Ecology .....	1-4
	1.4.1 Susceptible Species.....	1-4
	1.4.2 Transmission.....	1-4
	1.4.3 Morbidity and Mortality.....	1-5
	1.4.4 Clinical Signs.....	1-5
	1.4.5 Differential Diagnosis .....	1-7
1.5	Environmental Persistence of Glanders.....	1-7
1.6	Public Health Significance.....	1-7
	Attachment 1.A References and Resources.....	1-9
	Attachment 1.B Acronyms .....	1-11

## Tables

Table 1–1.	Clinical Signs and Their Frequencies among Glandered Equines (n=86) .....	1-5
Table 1–2.	Resistance of Glanders to Physical and Chemical Action .....	1-7

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## **Glanders**

### **Etiology and Ecology Quick Summary**

#### **Disease**

Glanders is an infectious disease primarily of equines and is also known as farcy. It is a zoonotic disease and has been used as a biological weapon. Glanders was eradicated from the United States in the 1940's.

#### **Mortality and Morbidity**

Presumed high—difficult to determine since animals are euthanized to prevent disease spread.

#### **Clinical Species**

Signs consistent with respiratory infections and skin lesions in animals.

#### **Susceptible Species**

Primarily horses, mules, donkeys, and other animals, including humans.

#### **Causative Agent**

The bacteria *Burkholderia mallei*.

#### **Zoonotic Potential**

Yes, humans are susceptible to this disease, however naturally occurring human cases are rare. Glanders has been used as a biological weapon.

#### **Transmission**

Direct contact with infected animals or via fomites or ingestion.

#### **Persistence in the Environment**

*B. mallei* can survive up to 2 weeks in the environment, on average, depending on environmental conditions. However, the bacteria can possibly survive over 6 weeks to months in certain conditions.

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## 1.1 Background and Introduction

Glanders is one of the oldest recorded diseases in history—described by Aristotle in the 3rd century. It is caused by the bacteria, *Burkholderia mallei*, primarily infecting equids; however, it is zoonotic though naturally occurring cases are rare. The disease is characterized by the combination of cutaneous lesions with nasal and pulmonary signs that can be fatal to both humans and animals.

Glanders is considered a biological warfare weapon, category B Select Agent,<sup>1</sup> and has been used as a biological weapon in the past. It was used in both world wars by infecting horses and subsequently soldiers. Most recently, the Soviet Army was accused of using *B. mallei* in the Afghan War.<sup>2,3</sup>

Glanders was evident during the American Civil War in epidemic proportions due to the sheer number and close proximity of horses which enabled disease spread.<sup>4</sup> Glanders was later eradicated in the United States during the 1940s. Since then, there has only been one human case, which occurred in 2000 when a researcher was infected while working with the bacteria at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID).<sup>5</sup> The disease remains endemic in Africa, Asia, the Middle East, Central America, and South America.

Although it has been eradicated from the United States, glanders poses a threat to U.S. equines. The United States has the largest equine population worldwide and is one of the leading exporters of horses. In addition, competition horses frequently travel internationally, including to endemic regions. If glanders was reintroduced into the United States it may not have the potential impact on production agriculture as other foreign animal diseases, but still poses great risks to the equine industry and humans due to the disease's zoonotic nature and biowarfare potential.

### 1.1.1 Further Information

This document is intended to be an overview of glanders. Resources as well as the references in this standard operating procedure (SOP) are listed in [Attachment A](#). The occurrence of glanders infection and laboratory criteria are defined in the World Organization for Animal Health (OIE)

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<sup>1</sup> Category B are those agents that are moderately easy to disseminate, result in lower morbidity and mortality rates than category A, and require specific enhancements for diagnostic capacity and enhanced disease surveillance. Retrieved from National Institute of Allergy and Infectious Diseases <https://www.niaid.nih.gov/topics/biodefenserelated/biodefense/pages/cata.aspx>.

<sup>2</sup> Khan, I., et al. (2013). Glanders in animals: a review on epidemiology, clinical presentation, diagnosis and countermeasures. *Transboundary and Emerging Diseases*, 60(3), 204–221. <http://onlinelibrary.wiley.com/doi/10.1111/j.1865-1682.2012.01342.x/abstract>.

<sup>3</sup> Gilad, J., et al. (2007). *Burkholderia mallei* and *Burkholderia pseudomallei* as bioterrorism agents: national aspects of emergency preparedness. *Israeli Medical Association Journal*, 9(7), 499–503. Retrieved from <http://www.ima.org.il/FilesUpload/IMAJ/0/46/23087.pdf>.

<sup>4</sup> Wagg, D.M. & DeShazer, D. (2005). Glanders, new insights into an old disease. In *Biological Weapons Defense: Infectious Disease and Counterbioterrorism* (Chapter 10). Retrieved from <https://books.google.com/books?isbn=1592597645>.

<sup>5</sup> The Centers for Disease Control (CDC). (2000, May). Laboratory-acquired human glanders—Maryland, May 2000. *Morbidity and Mortality Weekly Report (MMWR)*, 49(24), 532–535. Retrieved from <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm4924a3.htm>.

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*Terrestrial Animal Health Code* (2016)<sup>6</sup> and *Terrestrial Animal Health Manual* (2015),<sup>7</sup> respectively. Other Foreign Animal Disease Preparedness and Response Plan (FAD PRoP) documents are available on the Animal and Plant Health Inspection Service (APHIS) public website, <http://www.aphis.usda.gov/fadprep>.

### 1.1.2 Goals

As a preparedness goal, APHIS will provide etiology and ecology summaries for glanders 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 glanders when establishing or revising goals, objectives, strategies, and procedures.

## 1.2 Purpose

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

## 1.3 Etiology

### 1.3.1 Name

Glanders is caused by infection from the bacterium *Burkholderia mallei*. Previously known as *Pseudomonas mallei*, *B. mallei* was named by Aristotle after the Latin word *malleus* meaning malignant disease. It is important to distinguish this organism from *Burkholderia pseudomallei* which causes melioidosis, as this is closely related but completely distinct bacterium—with many phenotypic and genetic differences.<sup>8</sup>

### 1.3.2 Bacterial Characteristics

*B. mallei* has the following taxonomy:

- Order: Burkholderiales
- Family: *Burkholderiaceae*
- Genus: *Burkholderia*
- Species: *B. mallei*.

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<sup>6</sup> World Organization for Animal Health (OIE). (2016). Chapter 12.10. Glanders. *Terrestrial Animal Health Code*. Retrieved from [http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre\\_glanders.htm](http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_glanders.htm).

<sup>7</sup> OIE. (2015). Chapter 2.5.11. Glanders. *Terrestrial Animal Health Manual*. Retrieved from [http://www.oie.int/fileadmin/Home/eng/Health\\_standards/tahm/2.05.11\\_GLANDERS.pdf](http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.05.11_GLANDERS.pdf).

<sup>8</sup> Galyov, E.E., Brett, P.J., and DeShazer, D. (2010). Molecular insights into *Burkholderia pseudomallei* and *Burkholderia mallei* pathogenesis. *Annual Review of Microbiology*, 64, 495–517. doi: 10.1146/annurev.micro.112408.134030.

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### 1.3.3 Morphology

*B. mallei* is a gram-negative rod, non-motile, non-encapsulated, and non-spore-forming intracellular zoonotic pathogen. It is 1–5 microns long and 0.3–1 microns wide.

## 1.4 Ecology

### 1.4.1 Susceptible Species

The primary hosts for *B. mallei* are horses, mules and donkeys (solipeds). Other susceptible species include members of the feline family, from domesticated cats to lions. Post mortem cases have been reported in dogs, bears, wolves, jackals, and hyenas after consuming glanderous meat. Camels, sheep, and goats can also be infected.<sup>9,10</sup> Experimental infections have occurred in most other domesticated mammals including guinea pigs, hamsters, and rodents; but pigs, cattle, and birds are resistant.<sup>11</sup>

### 1.4.2 Transmission

Glanders can be spread through direct or indirect contact primarily with horses, donkeys, or mules presenting either the acute or chronic form. The most common route of bacteria transference occurs through the ingestion of contaminated food or water containing respiratory secretions. Carnivores are most often infected when contaminated meat is consumed. The bacteria can spread through skin abrasions, mucous membranes, inhalation of aerosols, or contact with fomites such as horse harnesses or grooming tools. Animals can secrete the organism in feces, urine, saliva, and tears—horses shed *B. mallei* sporadically or continually. Animal density, proximity, and high-stress environments can intensify disease spread.<sup>12,13,14,15</sup>

#### 1.4.2.1 Incubation Period

The incubation period ranges from a few days to 6 weeks; however, feline species may have an extended incubation time. The OIE recognizes the incubation period for glanders as 6 months.<sup>16</sup>

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<sup>9</sup> The Center for Food Security and Public Health (CFSPH), Iowa State University. (2015, February). Glanders. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/glanders.pdf>.

<sup>10</sup> Verma, A.K., et al. (2014). Glanders-A re-emerging zoonotic disease: a review. *Journal of Biological Sciences*, 14(1). 38–51. doi: 10.3923/jbs.2014.38.51.

<sup>11</sup> CFSPH. (2015). Glanders. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/glanders.pdf>.

<sup>12</sup> OIE, (2013). Glanders. *Technical Disease Card*. Retrieved from [http://www.oie.int/fileadmin/Home/eng/Animal\\_Health\\_in\\_the\\_World/docs/pdf/Disease\\_cards/GLANDERS.pdf](http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/GLANDERS.pdf).

<sup>13</sup> Timoney, J.F. (2013). Overview of glanders (Farcy). *Merck Veterinary Manual*. Retrieved from [http://www.merckvetmanual.com/mvm/generalized\\_conditions/glanders/overview\\_of\\_glanders.html](http://www.merckvetmanual.com/mvm/generalized_conditions/glanders/overview_of_glanders.html).

<sup>14</sup> CFSPH. (2015). Glanders. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/glanders.pdf>.

<sup>15</sup> Verma, A.K., et al. (2014). Glanders-a re-emerging zoonotic disease: a review. *Journal of Biological Sciences*, 14(1). 38–51. doi: 10.3923/jbs.2014.38.51.

<sup>16</sup> OIE. (2016). Chapter 12.10. Glanders. *Terrestrial Animal Health Code*. Retrieved from [http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre\\_glanders.htm](http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_glanders.htm)

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### 1.4.3 Morbidity and Mortality

Exact morbidity and mortality data is difficult to determine since infected animals are euthanized to prevent disease spread, although it is suspected to be high. The acute form causes death within a few days to 1–4 weeks in animals. In humans, there is a 95 percent case fatality rate.<sup>17</sup>

### 1.4.4 Clinical Signs

Glanders is categorized into three forms of disease that can present independently or most often in combination: nasal, pulmonary, and cutaneous. It can manifest as either acute, typically seen in donkeys and mules, or chronic, most associated with horses. Some animals can become latently infected.

Table 1–1 depicts results from a study assessing the clinical signs of 86 horses presented to the Veterinary Medical Teaching Hospital, University of Agriculture, Faisalabad (Pakistan). This table was chosen based on the limited publicly available research from an animal health standpoint to provide a representation of associated clinical signs.

**Table 1-1. Clinical Signs and Their Frequencies among Glandered Equines (n=86)<sup>a18</sup>**

Clinical Signs	Frequency (before malleinization <sup>a</sup> )	Percent (before malleinization <sup>a</sup> )
Fever	56/86	65.1
Inappetence	84/86	97.6
Debility	71/86	82.5
Quick loss of stamina (when exercised)	77/86	89.5
Cough	61/86	70.9
Dyspnea	78/86	90.7
Abnormal respiratory sounds	59/86	68.6
Nasal discharge	71/86	82.5
Nasal septum ulcers	77/86	89.5
Cutaneous ulcers	69/86	80.2
Enlargement of submaxillary lymph nodes	86/86	96.5
Odema of hind legs	39/86	45.3
Orchitis	31/96	44.92

<sup>a</sup> The Mallein test is delayed hypersensitivity testing that can result in fever, swelling, or efflux of pus from the eye in positive animals.

Note: This table has been summarized for the purposes of this document.

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<sup>17</sup> CFSPH. (2015). Glanders. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/glanders.pdf>.

<sup>18</sup> Khan, I., et al. (2013). Glanders in animals: a review on epidemiology, clinical presentation, diagnosis and countermeasures. *Transboundary and Emerging Diseases*, 60(3), 204–221. <http://onlinelibrary.wiley.com/doi/10.1111/j.1865-1682.2012.01342.x/abstract>.

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#### 1.4.4.1 Nasal Form

The nasal form occurs acutely with the following clinical signs:

- High fever and loss of appetite
- Labored breathing with coughing
- Sticky yellowish-green nasal discharge
- Ocular discharge
- Ulcers and nodules in the nasal passage
- Scabbed ulcers in star shape.

#### 1.4.4.2 Pulmonary Form

The pulmonary form is the most common and takes longer to develop than the nasal form; however, this form is still acute in nature, alike the nasal form. The following are clinical signs most often seen with this form:

- Dry coughing
- Labored breathing
- Nodules and/or abscesses in the lungs
- Pneumonia may be present
- Infection into the upper respiratory tract.

#### 1.4.4.3 Cutaneous Form

The cutaneous form is a chronic process—unlike the other two forms—that results in prolonged infection beginning with mild to unseen signs leading to a debilitating state. The following signs predominately occur:

- Episodes of exacerbation
- Cough
- Fever
- Skin nodules that rupture and ulcerate
- Nodule discharge
- Slow nodule healing
- Lymph node enlargement
- Joint swelling.

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### 1.4.5 Differential Diagnosis

Glanders presents clinically similar to the following conditions:<sup>19</sup>

- Strangles (*Streptococcus equi*)
- Ulcerative lymphangitis (*Corynebacterium pseudotuberculosis*)
- Botryomycosis
- Sporotrichosis (*Sporotrix schenckii*)
- Pseudotuberculosis (*Yersinia pseudotuberculosis*)
- Epizootic lymphangitis (*Histoplasma farciminosum*)
- Horsepox
- Tuberculosis (*Mycobacterium tuberculosis*)
- Trauma and allergy.

## 1.5 Environmental Persistence of Glanders

Table 1-2. Resistance of Glanders to Physical and Chemical Action<sup>20</sup>

Action	Resistance
Temperature	Destroyed through heating to 55°C (131°F) for 10 minutes, or with ultraviolet irradiation.
Chemicals/Disinfectants	Susceptible to many common disinfectants such as iodine, mercuric chloride in alcohol, potassium permanganate, benzalkonium chloride (1/2000), sodium hypochlorite (500 parts per million available chlorine), 70 percent ethanol, 2 percent glutaraldehyde; less susceptible to phenolic disinfectants.
Survival	Sensitive to sunlight with inactivation in 24 hours of direct exposure and heat as above; possible survival for over 6 weeks to various months in contaminated areas; can remain viable in tap water for at least 1 month; agent is susceptible to desiccation as humid/wet conditions favor survival. Polysaccharide capsule of bacterium is considered an important virulence factor and enhances survival.

## 1.6 Public Health Significance

Glanders is a disease with public health significance. It is zoonotic and certain characteristics make it well suited for use as a biological weapon (appropriate notifications—at local, State, and Federal levels—must occur if glanders is suspected or confirmed in any species):

- As a zoonotic agent, it can be highly infectious in the aerosolized form, such as within a laboratory environment. Direct transmission from horses to humans is rare, however, and

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<sup>19</sup> OIE. (2013). Glanders. *Technical Disease Card*. Retrieved from [http://www.oie.int/fileadmin/Home/eng/Animal\\_Health\\_in\\_the\\_World/docs/pdf/Disease\\_cards/GLANDERS.pdf](http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/GLANDERS.pdf).

<sup>20</sup> OIE. (2013). Glanders. *Technical Disease Card*. Retrieved from [http://www.oie.int/fileadmin/Home/eng/Animal\\_Health\\_in\\_the\\_World/docs/pdf/Disease\\_cards/GLANDERS.pdf](http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/GLANDERS.pdf).

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in such cases human symptoms may be mild or absent.<sup>21</sup> This is likely due to a high infectious dose of agent or bacteria being necessary for human infection.<sup>22</sup>

- Still, glanders is an occupational hazard for those working in direct contact with equids (i.e., veterinarians, animal caretakers, mounted workers, researchers, etc.), as most reported naturally occurring cases in the past were from close and frequent contact with either live equids or tissues.<sup>23,24</sup>
- Infection in humans may be systemic with a case fatality rate over 50 percent with traditional antibiotic treatment.<sup>25</sup>
  - Little is known about antibiotic susceptibility of *B. mallei* since glanders mostly disappeared before the development and wide use of antibiotics.
  - A recent antimicrobial study indicates that *B. mallei* is highly resistant to common antibiotics that are categorized into classes such as  $\beta$ -lactum antibiotics, aminoglycosides, and macrolides.<sup>26</sup>
- There is currently no glanders vaccine for either animals or humans.

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<sup>21</sup> CFSPH. (2015). Glanders. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/glanders.pdf>.

<sup>22</sup> Van Zandt, K.E., Greer, M.T., and Gelhaus, H.C. (2013). Glanders: an overview of infection in humans. *Orphanet Journal of Rare Diseases*, 8, 131. doi: 10.1186/1750-1172-8-131.

<sup>23</sup> CFSPH. (2015). Glanders. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/glanders.pdf>.

<sup>24</sup> Gilad, J., et al. (2007). *Burkholderia mallei* and *Burkholderia pseudomallei* as bioterrorism agents: national aspects of emergency preparedness. *Israeli Medical Association Journal*, 9(7), 499–503. Retrieved from <http://www.ima.org.il/FilesUpload/IMAJ/0/46/23087.pdf>.

<sup>25</sup> CDC. (2012, January). Information for health care workers. *Glanders*. Retrieved from <http://www.cdc.gov/glanders/health-care-workers.html>.

<sup>26</sup> Thibault, F. M., Hernandez, E., Vidal, D. R., Girardet, M., & Cavallo, J. D. (2004). Antibiotic susceptibility of 65 isolates of *Burkholderia pseudomallei* and *Burkholderia mallei* to 35 antimicrobial agents. *Journal of Antimicrobial Chemotherapy*, 54(6), 1134–1138. doi: 10.1093/jac/dkh471.

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## Attachment 1.A References and Resources

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## Attachment 1.B Acronyms

APHIS	Animal and Plant Health Inspection Service
CDC	Centers for Disease Control
CFSPH	Center for Food Security and Public Health
FAD PReP	Foreign Animal Disease Preparedness and Response Plan
MMWR	Morbidity and Mortality Weekly Report
NIAID	National Institute of Allergy and Infectious Diseases
NIH	National Institutes of Health
OIE	World Organization for Animal Health
SOP	standard operating procedure
USAMRIID	United States Army Medical Research Institute of Infectious Diseases
USDA	United States Department of Agriculture