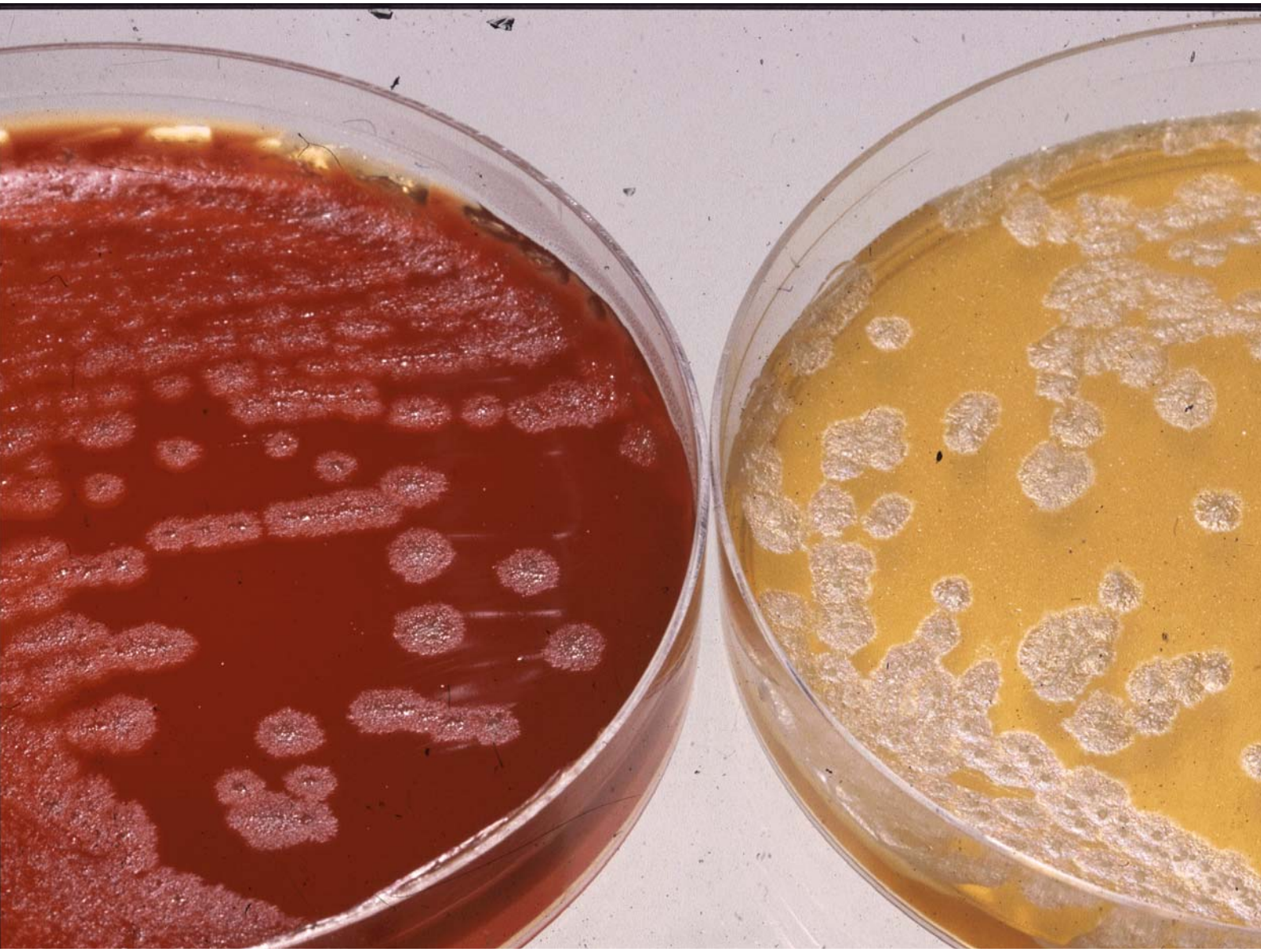

Bioterrorism

A review of Potential Bioterrorism Agents

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AUSTRIAN
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INTRODUCTION

Bioterrorism is defined by the unlawful, intentional or threatened use of microorganisms or of toxins derived from living organisms to cause death or diseases in humans, animals or plants and to generate fear in the population.
The use of biological agents is so attractive to the terrorist because of the ease of acquisition, of the ease and economy of production also because of low visibility, and the ease and stealth of delivery. Throughout the world, countries have set up new administrative and operational structures and adapted their preparedness and response plans in order to deal with the new threat. On the wider international level, global health security measures to strengthen the public health response to the threat of international biological, chemical and radio-nuclear terrorism have been initiated. Governments and international entities with responsibilities related to maintenance of peace, security, safety and health protection have made it a priority to review their political, economic, diplomatic, military and legal capacity to face up to such attacks and have embarked on major efforts to increase their preparedness.

Web pages of the following academic infectious disease institutions, infectious disease control societies, civilian and military intelligence experts, and law enforcement officials were consulted with respect to potential biological weapons threats.

- WHO
- CDC
- HPA, Health Protection Agency
- NATO
- Federation of American Scientists
- United Nations Office on Drugs and Crime
- APIC, Association for Professionals in Infection Control and Epidemiology
- Weapons of Mass Destruction Commission (WMDC)
- U.S. Army Medical Research (USAMRIID)
- United States Department of Agriculture (USDA), Animal and Plant Health Inspection Service (APHIS)
- National selected agency registry (NSAR), Department of Health and Human Services (HHS)
- Washington state university WSU
- Monterey Institute of International Studies
- Center for Infectious Disease Research and Preparedness (CIDRAP)
- ECDC
- EU Health Security Plan
- EMEA, The European Agency for the Evaluation of Medicinal Products
- RKI
- Deutsches BUNDESVERWALTUNGSAMT, Zentralstelle für Zivilschutz
- Bundesamt für Bevölkerungsschutz und Katastrophenhilfe
- Bulletin zur schweizer Sicherheitspolitik
- Österreichisches Bundesheer

Document	SOURCE
Specific Bioterrorism Agents A–Z List of Agents	2007 CDC http://www.bt.cdc.gov/bioterrorism/
Biosecurity and Biodefence Resource	Federation of American scientists (FAS) http://www.fas.org/biosecurity/resource/agents.htm
Biologische Gefahren I Handbuch zum Bevölkerungsschutz Biologische Gefahren II Entscheidungshilfen zu medizinisch angemessenen Vorgehensweisen in einer B-Gefahrenlage	2007 Bundesamt für Bevölkerungsschutz und Katastrophenhilfe RKI, Bonn http://www.bbk.bund.de/cln_027/DE/00__Home/homepage__node.html__nnn=true
Kehren die Seuchen zurück? (Neue) Gefahren durch biologische Kampfstoffe	2002 Deutsches BUNDESVERWALTUNGSAMT Zentralstelle für Zivilschutz Akademie für Krisenmanagement, Notfallplanung und Zivilschutz; Schriftenreihe: Wissenschafts-Forum Band 3 http://www.bbk.bund.de/cln_027/nn_398732/SharedDocs/Publikationen/Wissenschaftsforum/Band-3__Seuche-II,templateId=raw,property=publicationFile.pdf/Band-3_Seuche-II.pdf
HHS AND USDA SELECT AGENTS AND TOXINS	2006 The Departments of Agriculture (USDA) and Health and Human Services (HHS); http://www.cdc.gov/od/sap/docs/salist.pdf
Risiko und Verwundbarkeitsanalyse Bioterrorismus	2005 Bulletin zur schweizer Sicherheitspolitik Michael Guery http://cms.isn.ch/public/docs/doc_10755_259_de.pdf
EU list of high threat pathogens	2005 Technical guidance on generic preparedness planning – interim document – April 2005 EU Health Security Programme http://ec.europa.eu/health/ph_threats/Bioterrorisme/keydo_bio_01_en.pdf
Bioterrorism and Threat Assessment no22	2005 Weapons of Mass Destruction Commission (WMDC)

	GARY A. ACKERMAN AND KEVIN S. MORAN http://www.wmdcommission.org/files/No22.pdf
WHO - Public health response to biological and chemical weapons – WHO guidance	2004 WHO guidance http://www.who.int/csr/delibepidemics/biochemguide/en/index.html
USAMRIID's MEDICAL MANAGEMENT OF BIOLOGICAL CASUALTIES HANDBOOK	2004 Fifth Edition August 2004 Lead Editors CAPT Robert G. Darling, MC, USN, Lt Col Jon B. Woods, MC, USAF http://www.usamriid.army.mil/searchresults.cfm?sSearch=bioterrorism
Mikrobiologie - eine militärische und militärmedizinische Herausforderung	2004 Bundesminister für Landesverteidigung Tom Pustelnik http://www.bmlv.gv.at/pdf_pool/publikationen/09_vu3_04_mbh.pdf
CFR-Listed Agent and Toxin Summaries SANDIA REPORT	2003 Compiled and Edited by Natalie Barnett Prepared by Sandia National Laboratories Albuquerque, New Mexico 87185 and Livermore, California 94550 Sandia is a multiprogram laboratory operated by Sandia Corporation, a Lockheed Martin Company, for the United States Department of Energy's National Nuclear Security Administration under Contract DE-AC04-94AL85000. http://www.terrorisminfo.mipt.org/pdf/Biosecurity-Reference-CFR-Listed-Agent-Toxin-Summaries.pdf
BIOLOGICAL WARFARE AND ITS CUTANEOUS MANIFESTATIONS	Thomas W. McGovern, MD, MAJ, MC George W. Christopher, LTC, USAF, MC The Internet Dermatology Society, Inc. All rights reserved. 1995-2001 http://telemedicine.org/biowar/biologic.htm
Biological weapons: what's what?	UNODC - UNITED NATIONS Office on drugs and crime http://www.un.org/issues/docs/d-disarm.html
Bacteria of potential health concern	2003 N.F. Lightfoot World Health Organization (WHO). Heterotrophic Plate Counts and Drinking-water Safety. Edited by J. Bartram J. Cotruvo, M. Exner, C. Fricker, A.

	Glasmacher. Published by IWA Publishing, London, UK. ISBN: 1 84339 025 6. http://www.who.int/water_sanitation_health/dwq/HPC5.pdf
EMEA/CPMP Guidance document on use of medicinal products for treatment and prophylaxis of biological agents that might be used as weapons of bioterrorism	2002 The European Agency for the Evaluation of Medicinal Products, London, 25 July 2002, CPMP/4048/01 http://www.emea.europa.eu/htms/human/bioterror/bioterror.htm http://www.emea.europa.eu/pdfs/human/bioterror/404801.pdf
WORKING PAPER Bioterrorism and Biocrimes The Illicit Use of Biological Agents Since 1900	2001 W. Seth Carus August 1998; February 2001 Revision Center for Counter proliferation Research National Defense University Washington, D.C. http://www.fas.org/irp/threat/cbw/carus.pdf
MICROBIOLOGY 101 INTERNET TEXT	2000 Washington state university WSU CHAPTER XV, ADDENDUM: BIOLOGICAL WEAPONS; MALIGNANT BIOLOGY http://www.slic2.wsu.edu:82/hurlbert/micro101/pages/101biologicalweapons.html
Bioterrorism Agents	APIC, Association for Professionals in Infection Control and Epidemiology http://www.apic.org/Content/NavigationMenu/PracticeGuidance/Topics/Bioterrorism/Bioterrorism_Agents.htm
Biologische Sicherheit	Robert Koch Institut http://www.rki.de/nn_196322/DE/Content/Infekt/Biosicherheit/biosicherheit__node.html?__nnn=true
Biokampfstoffe und Terrorismus	Österreichisches Bundesheer Wolfgang Schallenberger http://www.bmlv.gv.at/pdf_pool/publikationen/09_ztt_07_scha.pdf
BIO Terry®	http://www.bioterry.com/
SELECT AGENTS AND TOXINS POSSESSED, USED, OR TRANSFERRED BY ENTITY	GUIDANCE DOCUMENT FOR APPLICATION FOR REGISTRATION FOR POSSESSION, USE, AND TRANSFER OF SELECT AGENTS AND TOXINS (APHIS/CDC FORM 1) NSAR – National selected agency registry HHS (Department of Health and Human Services) USDA (United States Department of Agriculture

	SECTION 3 http://www.selectagents.gov/resources/APHIS-CDC%20Form%201Pt1.pdf http://www.selectagents.gov/index.html
BWC draft Protocol	2001 Ad Hoc Group of the States Parties to the Convention on the Prohibition, Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on their Destruction, document BWC/AD HOC GROUP/56-2, at pp 465-466, which is in Annex A of the Chairman's Composite Text for the BWC Protocol
Biological and Chemical Terrorism: Strategic Plan for Preparedness and Response. Recommendations of the CDC Strategic Planning Workgroup	2000 Centers for Disease Control and Prevention. Morbidity and Mortality, Weekly Report, 2000; 49 (No.RR-4):1–14.
Bioterrorism Readiness Plan: A Template for Healthcare Facilities	1999 APIC Bioterrorism Task Force Judith F. English, Mae Y. Cundiff, John D. Malone, Jeanne A. Pfeiffer CDC Hospital Infections Program Bioterrorism Working Group, Michael Bell, Lynn Steele, J. Michael Miller, 4/13/99 http://www.cdc.gov/ncidod/dhqp/pdf/bt/13apr99APIC-CDCBioterrorism.PDF
Potential Biological Weapons Threats	1999 CDC Mark G. Kortepeter and Gerald W. Parker Emerging Infectious Disease Special Issue; Vol. 5, No. 4, July-August 1999 Potential Biological Weapons Threats U.S. Army Medical Research Institute of Infectious Diseases, Fort Detrick, Maryland, USA http://www.cdc.gov/ncidod/EID/vol5no4/kortepeter.htm http://www.bt.cdc.gov/bioterrorism/
The Threat of Deliberate Disease in the 21st Century	1998 Graham S. Pearson Department of Peace Studies, University of Bradford, UK; This article is reproduced by kind permission of the Henry L. Stimson Center. It first appeared in the Henry L. Stimson Centre Report No. 24, Biological Weapons Proliferation: Reasons for Concern, Courses of Action' January 1998) http://www.brad.ac.uk/acad/sbtwc/other/disease.htm

Potential Biological Agents Operational Data Charts	1996 NATO HANDBOOK ON MEDICAL ASPECTS OF NBC DEFENSIVE OPERATIONS PART II - BIOLOGICAL, ANNEX C POTENTIAL BIOLOGICAL AGENTS OPERATIONAL DATA CHARTS http://www.fas.org/nuke/guide/usa/doctrine/dod/fm8-9/2appc.htm#tabc_iip2
BWC, CBM-F	1992 UN Office of Disarmament Affairs, compilation of declarations of information by BWC States Parties in accordance with the extended confidence-building measures agreed at the Third Review Conference, DDA/4-92/ BW3 plus Add.1, Add.2 and Add.3, data from Section 2, *Past offensive biological R&D programmes*, of Form F as filed by Canada, France, Russian Federation, UK, and USA in 1992
Australia Group document AG/Dec92/BW/Chair/30 dated June 1992	1992 Australia Group
Health aspects of chemical and biological weapons	1970 WHO, Report of a WHO group of consultants, Geneva
Chemical and bacteriological (biological) weapons and the effects of their possible use	1969 United Nations, Report of the Secretary-General, New York

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Selection of potential agents for reviewing

More than 180 pathogens have been reported to be potential agents for bioterrorism. In order to create a list of agents that would be feasible to the scope of effective review, it was necessary to narrow down the number of agents significantly. The logic behind implementing such a reduction is supported by the World Health Organization's stated approach in their 2004 Second Edition of "Public Health Response to Biological and Chemical Weapons": *"A central consideration in such preparedness planning is that it is neither possible nor necessary to prepare specifically for attack by all possible biological and chemical agents. If a country is seeking to increase its preparedness to counter the effects of biological and chemical attacks, the targeting of its preparation and training on a limited but well chosen group of agents will provide the necessary capability to deal with a far wider range of possibilities. Knowledge of the general properties of this representative group of agents will enable certain measures to be taken against virtually any other agent. In addition to being impractical from a preparedness perspective, long and exhaustive lists of agents also give a misleading impression of the extent of possible threats."*[1]

The preliminary reduction of the number of agents was carried out based upon the findings of how frequently the agents were considered as potential bioterrorism agents by the competent bodies. Around 55 agents were selected which are mentioned between 4 and 28 times by the competent bodies as possible bioterrorist threats (table 1, 2, 3).

These agents were subsequently chosen for reviewing the literature for their potential as a bioterrorist threat.

Selected potential bioterrorism agents

Table 1. Agents – Bacteria considered as potential agents of bioterrorism by the competent bodies.

	Agent	WHO 2004	USAMRIID	SANDIA REPORT	Center for Counter proliferation Research	NATO Handbook	The Internet Dermatology Society	UN office drugs of crime	FAS	Department of Peace Studies, University of Bradford, UK	EU list of high threat pathogens	Deutsches Bundesverwaltungsamt	WHO (N.F. Lightfoot)	EMEA	WSU	CDC a-z	RKI	Zur schweizer Sicherheitspolitik Bulletin	APIC	Österreichisches Bundesheer (W. S)	BMLV (Tom Pustelnik)	bio terry®	HHS, USDA LISTS	Eurosurveillance - BICHAT LL	UN 1969	WHO 1970	BWC CMB 1992	Australia group 1992	Nato 1996	BWC/AD HOC 2001
1	Bacillus anthracis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
2	Yersinia pestis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
3	Brucella suis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
4	Francisella tularensis	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
5	Brucella abortus	X		X		X	X	X	X		X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
6	Coxiella burnetti	X	X	X	X	X	X	X	X	X	X		X	X	X	X	X				X	X	X		X	X	X	X	X	X
7	Brucella melitensis	X				X	X	X	X		X	X	X	X	X	X	X	X		X	X	X	X	X	X	X	X	X	X	X
8	Burkholderia pseudmallei	X		X		X	X		X		X	X	X	X	X	X				X	X		X	X	X	X	X	X	X	X
9	Ricettsia prowatcekii	X	X	X	X	X		X			X		X	X	X	X							X		X	X	X	X	X	X
10	Salmonella typhi	X	X		X	X	X	X			X			X	X	X	X	X								X	X		X	X	
11	Vibrio cholerae	X	X		X	X	X	X	X		X			X	X	X					X					X	X		X	X	
12	Burkholderia mallei	X		X							X	X	X	X	X	X					X		X	X	X	X	X	X		X
13	Rickettsia rickettsii	X		X		X		X			X		X		X								X		X	X		X	X	X
14	Shigella species	X	X		X			X			X			X	X	X									X				X	
15	Chlamydia psittaci	X				X		X			X			X	X	X									X				X	

16	Orienta Tsutsugamushi	X				X		X			X																		X	X
17	Salmonella Typhimurium		X		X									X		X	X	X												
18	EHEC O157							X			X			X	X	X														
19	Salmonella paratyphi				X						X					X		X												

Table 2. Agents – Fungi and Viruses considered as potential agents of bioterrorism by the competent bodies.

	Agent	WHO 2004	USAMRIID	SANDIA REPORT	Center for Counter proliferation Research	NATO Handbook	The Internet Dermatology Society	UN office drugs of crime	FAS	Department of Peace Studies, University of Bradford, UK	EU list of high threat pathogens	Deutsches Bundesverwaltungsamt	WHO (N.F. Lightfoot)	EMEA	WSU	CDC a-z	RKI	Zur Schweizer Sicherheitspolitik Bulletin	APIC	Österreichisches Bundesheer (W. S)	BMLV (Tom Pustelnik)	bio terry®	HHS, USDA LISTS	Eurosurveillance - BICHAT LL	UN 1969	WHO 1970	BWC CMB 1992	Australia group 1992	Nato 1996	BWC/AD HOC 2001
20	Coccidioides immitis	X		X				X			X												X		X	X		X	X	X
21	Monkeypox virus	X		X				X			X				X								X		X	X		X	X	X
22	Variola vera	X	X	X	X	X	X	X	X		X	X	X	X	X	X		X	X	X	X	X	X		X	X		X	X	X
23	Chikungunya-Virus	X				X		X			X				X										X	X		X	X	
	Haemorrhagic fever virus (HFV)		X		X							X		X		X	X	X				X								
24	Yellow fever virus	X	X		X	X		X			X			X	X	X		X							X	X		X	X	X
25	Ebola-Virus	X	X	X	X		X	X	X		X			X	X	X		X					X					X	X	X
26	Rift Valley fever virus	X		X		X	X	X	X		X				X								X	X		X		X	X	X
27	Lassa fever virus	X		X		X	X	X			X				X	X		X					X					X	X	X
28	Crimean-Congo haemorrhagic fever virus	X		X		X	X	X	X		X				X								X			X		X	X	X
29	Hantaan virus	X				X	X	X			X			X	X	X										X		X	X	
30	Dengue virus	X				X	X	X							X			X						X	X	X		X	X	
31	Machupo virus	X					X	X			X				X	X							X	X				X	X	
32	Marburg-Virus			X			X	X			X			X	X	X		X					X							
33	Junin virus	X					X	X			X				X	X							X	X				X	X	
34	Omsk haemorrhagic fever virus	X				X		X			X				X														X	

35	Kyasanur Forest virus						X	X			X				X								X							
	Encephalitis Virus (EV)		X		X							X		X		X														
36	Venezuelan equine EV	X		X		X	X	X	X	X	X			X	X	X							X	X	X	X		X	X	X
37	Eastern equine EV	X		X		X		X			X			X	X	X					X		X	X	X	X		X	X	X
38	Western Equines EV	X				X		X			X			X	X	X								X		X		X		X
39	Tick-borne EV	X						X															X	X	X	X		X	X	X
40	Japanese EV	X						X			X				X									X		X		X		
41	Nipah Virus			X							X			X		X							X							
42	Murray Valley-EV							X			X				X									X						
43	Lymphocytic choriomeningitis virus							X			X				X									X						
44	Powassan Virus							X			X				X									X						
45	Rocio Virus							X			X				X									X						
46	Louping ill Virus							X			X				X									X						
47	Hendra-Virus			X							X												X	X						

Table 3. Agents – Toxines considered as potential agents of bioterrorism by the competent bodies.

	Agent	WHO 2004	USAMRIID	SANDIA REPORT	Center for Counter proliferation Research	NATO Handbook	The Internet Dermatology Society	UN office drugs of crime	FAS	Department of Peace Studies, University of Bradford, UK	EU list of high threat pathogens	Deutsches Bundesverwaltungsamt	WHO (N.F. lightfoot)	EMEA	WSU	CDC a-z	RKI	Zur schweizer Sicherheitspolitik Bulletin	APIC	Österreichisches Bundesheer (W. S)	BMLV (Tom Pustelnik)	bio terry®	HHS, USDA LISTS	Eurosurveillance – BICHAT LL	UN 1969	WHO 1970	BWC CMB 1992	Australia group 1992	Nato 1996	BWC/AD HOC 2001
48	Clostridium botulinum toxin		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X	X							
49	Ricin		X	X	X	X	X	X	X	X	X	X		X	X	X	X			X	X	X	X							
50	Staph. Enterotoxin B		X	X	X	X	X	X	X	X		X	X	X		X				X	X	X	X							
51	Saxitoxin			X		X		X	X	X	X	X			X							X		X						
52	T2 mycotoxin			X		X		X	X						X					X	X	X	X							
53	C. perfringens epsilon					X		X	X					X	X	X								X						
54	Shigatoxin			X				X							X									X						
55	Abrin			X				X							X									X						

Additionally listed by WHO 2004

Bartonella quintana	X													X														X		
O´nyong-nyong V	X																									X				
Toxoplasma gondii	X																						X							

Description of the selected potentially bioterroristic agents

The selected agents were described by their clinical manifestation(s) and by epidemiological measures.
The epidemiological measures used were as follows:

Table 4. Epidemiological Measures and Definitions

Reservoir	An ecological niche where a pathogen lives and multiplies.
Incubation Period	Period starting from the moment a person is infected until he/she develops symptoms of disease.
Environmental Stability	Tenacity; description of an organism' ability to live and/or multiply outside of a host. E.g. viability in the presence of dryness, lack of nutrients, light, heat, oxygen.
Infectious Dose	Number of bacteria or viruses required to cause an infection.
Transmission Chain	The directional chain of pathogen transmission between environmental, animal and human hosts— e.g. animal-human (zoo-anthroponotic), animal-animal (enzootic), vector-human.
Transmission Route	Classified into two categories: Direct - Direct and essentially immediate transfer of infectious agents to a receptive portal of entry through which human or animal infection may take place. Indirect - The transmission of an agent carried from a reservoir to a susceptible host by animate (vector) or inanimate (vehicle) intermediaries.
Transmission Mode	Descriptive categorizations of transmission routes: Direct: Physical contact - including effective contact that is skin to skin, skin to mucosa (including sexual contact), mucosa to mucosa, or skin and/or mucosa to microbe-containing secretions or body fluids (e.g. infected saliva or blood) Droplet spread - effective contact between the mucosal membranes of the conjunctiva, nose or mouth and the spray of relatively large, short-ranged, pathogen-carrying droplets produced by sneezing, coughing or talking Faecal-oral inoculation - self inoculation through the accidental ingestion of the contaminated faeces of an infected animal reservoir Indirect: Vehicle transmission - effective contact (whether it be through ingestion, inhalation, etc.) with contaminated food, water, air (aerosols), soil, plants, or human-made environments, surfaces or fomites

	Vector transmission - infection via pathogen-carrying arthropods (effective bites, contact with secretions).
Transmission Risk	The proportion of people who become ill out of all the susceptible persons exposed. This value will likely vary depending on the specific transmission mode being investigated.
Effective Contact Rate	(denoted β): The measure of effective contacts per unit time. This can be expressed as the total contact rate (the total number of contacts, effective or not, per unit time, denoted γ), multiplied by the risk of infection, given contact between an infectious and a susceptible individual. This risk is called the transmission risk and is denoted *p*. Thus: formula: $\beta = \gamma \times p$.
Reproduction Number	The basic reproduction number (R0) is the number of secondary cases which one case would produce in a completely susceptible population. It depends on the duration of the infectious period, the probability of infecting a susceptible individual during one contact, and the number of new susceptible individuals contacted per unit of time.
Attack Rate	The proportion of those exposed to an infectious agent who become ill.
Infectious Period	The length of time during which a person can transmit a disease.
Lethality	A measure of the proportion of deaths out of all cases of the disease (given as a ratio or %)
Chemoprophylaxis	Antimicrobial treatments given pre or post-exposure.
Vaccine (pre and/or post exposure)	A drug intended to induce active artificial immunity against a pathogen by causing the body to produce antibodies and/or specialized lymphocytes which will prevent disease in the cased of later exposure. Vaccines are described as means of "immuno-prophylaxis".
Vaccine Production/ Availability status	Where and by what companies vaccines are being produced and relevant information about distribution for the means of prophylaxis in the case of an outbreak.
Immunity	Status associated with the presence of specific antibodies and/or cells having a specific combative action on the microorganism concerned with a particular infectious disease or on its toxin. "Cellular immunity" refers to T-lymphocyte sensitization to particular agents. "Humoral immunity" refers to B-lymphocyte response.

Not for all agents every epidemiological measure was available or relevant.

CDC assessed the bioterroristic threat associated with selected agents based on the following 4 criteria –
1) public health impact based on illness and death;
2) delivery potential to large populations based on stability of the agent, ability to mass produce and distribute a virulent agent, and potential for person-to-person transmission of the agent;
3) public perception as related to public fear and potential civil disruption; and
4) special public health preparedness needs based on stockpile requirements, enhanced surveillance, or diagnostic needs) and on weighting.

Subsequently the agents were placed in one of three priority categories for initial public health preparedness efforts: A, B or C.

CDC – Definition of the three priority categories

Agents in Category A have the greatest potential for adverse public health impact with mass casualties, and most require broad-based public health preparedness efforts (e.g., improved surveillance and laboratory diagnosis and stockpiling of specific medications). Category A agents also have a moderate to high potential for large-scale dissemination or a heightened general public awareness that could cause mass public fear and civil disruption.

Most Category B agents also have some potential for large-scale dissemination with resultant illness, but generally cause less illness and death and therefore would be expected to have lower medical and public health impact. These agents also have lower general public awareness than Category A agents and require fewer special public health preparedness efforts. Agents in this category require some improvement in public health and medical awareness, surveillance, or laboratory diagnostic capabilities, but presented limited additional requirements for stockpiled therapeutics beyond those identified for Category A agents. Biological agents that have undergone some development for widespread dissemination but do not otherwise meet the criteria for Category A, as well as several biological agents of concern for food and water safety, are included in this category.

Biological agents that are currently not believed to present a high bioterrorism risk to public health but which could emerge as future threats were placed in Category C.

These agents will be addressed non-specifically through overall bioterrorism preparedness efforts to improve the detection of unexplained illnesses and ongoing public health infrastructure development for detecting and addressing emerging infectious diseases.
Category A agents are being given the highest priority for preparedness. For Category B, public health preparedness efforts will focus on identified deficiencies, such as improving awareness and enhancing surveillance or laboratory diagnostic capabilities. Category C agents will be further assessed for their potential to threaten large populations as additional information becomes available on the epidemiology and pathogenicity of these agents.

The **EU Health Security Programme** elaborated an agreed updateable list of biological and chemical agents that are susceptible to be used in attacks or threats of attack, together with their characteristics and associated symptoms and diseases and indications that permit their timely detection and identification/diagnosis with agreed levels of certainty.
The agents were placed in one of two priority categories:
Agents with VERY HIGH threat (I) and Agents with HIGH threat (II).

CDC – Priority Categories – Agents / Diseases

Priority Category A - Diseases/Agents

The U.S. public health system and primary healthcare providers must be prepared to address various biological agents, including pathogens that are rarely seen in the United States. High-priority agents include organisms that pose a risk to national security because they

- can be easily disseminated or transmitted from person to person
- result in high mortality rates and have the potential for major public health impact
- might cause public panic and social disruption and
- require special action for public health preparedness

Agents/Diseases

Bacillus anthracis | Anthrax

Clostridium botulinum toxin / Botulism

Yersinia pestis | Plague

Variola major / Smallpox

Francisella tularensis | Tularemia

Filoviruses (e.g. Ebola, Marburg), Arenaviruses (e.g., Lassa, Machupo / Viral

hemorrhagic fevers

Priority Category B - Diseases/Agents

Second highest priority agents include those that

- are moderately easy to disseminate
- result in moderate morbidity rates and low mortality rates and
- require specific enhancements of CDC's diagnostic capacity and enhanced disease surveillance

Agents/Diseases

Brucella species / Brucellosis

Epsilon toxin of *Clostridium perfringens*

Salmonella species, *Escherichia coli* O157:H7, *Shigella*, e.g. */* Food safety threats

Burkholderia mallei / Glanders

Burkholderia pseudomallei / Melioidosis

Chlamydia psittaci / Psittacosis

Coxiella burnetii / Q fever

Ricin toxin from *Ricinus communis* (castor beans)

Staphylococcal enterotoxin B

Rickettsia prowazekii / Typhus fever

Alphaviruses (e.g. Venezuelan equine encephalitis, Eastern equine encephalitis, Western equine encephalitis) / Viral encephalitis

V*ibrio cholerae*, *Cryptosporidium parvum,* e.g. / Water safety threats

Priority Category Category C - Diseases/Agents

Third highest priority agents include emerging pathogens that could be engineered for mass dissemination in the future because of

- availability
- ease of production and dissemination and
- potential for high morbidity and mortality rates and major health impact

Emerging infectious diseases such as Nipahvirus and Hantavirus.

EU Health Security Programme

The establishment of a list of agents was foreseen in the plan for the EU Health Security Programme: "Elaboration of an agreed updateable list of biological and chemical agents that are susceptible to be used in attacks or threats of attack, together with their characteristics and associated symptoms and diseases and indications that permit their timely detection and identification/diagnosis with agreed levels of certainty".

Similar lists have been developed elsewhere with a more or less defined goal of identifying the most dangerous agents for which certain activities, like export control, need to be implemented. Other lists aim for the most dangerous pathogens if used against humans or the agents that have most potential to be developed into a bio-weapon. In order to do this a number of variables have obviously been examined and this has been described more or less openly. There is medical literature, when it comes to the CDC list but less obvious for other lists. These lists were obtained from analysing the vulnerability along many variables.

List of diseases	**Agents with VERY HIGH threat**
Anthrax	*Bacillus anthracis*
Botulism	Clostridium botulinum toxin
Glanders	*Burkholderia mallei*
Haemorrhagic fever	Congo-Crimean haemorrhagic fever virus
	Ebola virus
	Guanarito
	Junin virus
	Lassa fever virus
	Machupo virus
	Marburg virus
	Omsk Haemorrhagic Fever Virus
	Sabia
Plague	*Yersinia pestis*
Smallpox	Variola major
Toxic syndromes	Ricin
	Tetrodotoxin
	Viscum album lectin 1 (Viscumin
Tularemia	*Francisella tularensis*

List of diseases	Agents with HIGH threat
Brucellosis	*Brucella abortus*
	Brucella melitensis
	Brucella spp
	Brucella suis
Cholera	*Vibrio cholerae*
Coccidoidomycosis	*Coccidioides immitis*
Diphtheria	*Corynebacterium diphtheriae*
Dysentery	*Shigella dysenteriae*
Fever	*Chikungunya virus*
Hantavirus pulmonary syndrome	Hantaan virus
Heamorrhagic fever	Nipah virus
	Rift Valley fever virus
Histoplasmosis	*Histoplasma capsulatum*
HUS	*E. coli 0157:H7*
Influenza	Influenza virus (new strain)
Legionellosis	*Legionella pneumophila*
Melioidosis	*Burkholderia pseudomallei*
Monkey pox fever	Monkey pox
Neurological syndrome	Palytoxin
Paratyphoid fever	*Salmonella paratyphi*
Psittacosis	*Chlamydia psittaci*
Q fever	*Coxiella burnetii*
Rocky mountain spotted fever	*Rickettsia rickettsii*
Scrub typhus	*Orienta tsutsugamushi*
Toxic syndrome	Conotoxin
	Microcystin (Cyanginosin)
	Saxitoxin
Tuberculosis	*Mycobacterium tuberculosis*
Typhoid fever	*Salmonella typhi*
Typhus fever(Epidemic louseborne typhus)	*Rickettsia prowazekii*
Viral encephalitis	*Eastern equine encephalitis virus*
	Getah Virus
	Hendra (formely: Equine Morbilli Virus)
	Herpesvirus simiae (B virus)
	Japanese encephalitis virus
	Kyasanur Forest Virus
	La Crosse
	Louping III Virus
	Lymphocytic choriomeningitis virus
	Murray Valley Encephalitis Virus
	Powassan Virus
	Rocio Virus
	St. Louis Encephalitis Virus
	Tick-borne encephalitis virus
	Toscana
	Venezuelan equine encephalitis virus
	West Nile
Yellow fever	Yellow fever virus

Priority Categorisation of the bioterroristic threat of selected agents by CDC (A, B, C) and the EU Health Security Programme (I, II)

Agents	Clinical manifestation	CDC A,B,C	EU HSP[1] I, II
Bacillus anthracis	Inhalational anthrax	A	I
Yersinia pestis	Plague	A	I
Brucella suis, mellitnesis, abortus	Brucellosis	B	II
Francisella tularensis	Tularemia	A	I
Variola Virus	Variola major/smallpox	A	I
Coxiella burnetti	Q-fever	B	II
Burkholderia pseudomallei	Mellloidose	B	II
Botulinum toxin	Botulismus	A	I
Rickettsia prowazekii	Typhus Fieber	B	II
Venezuelan equine encephalitis virus	Virale encephalitis	B	II
Ricin	Toxic syndrom	B	I
Staphylococcal enterotoxin B	Toxic syndrom	B	Not given
Salmonella typhi	Typhoid fever	B	II
Vibrio cholerae	Gastroenteritis	B	II
Ebola-virus	Heamorrhagic fever	A	I
Ost-Equines encephalitis virus	Virale encephalitis	B	II
Burkholderia mallei	Glanders	B	I
Rift valley fever virus	Heamorrhagic fever	Not given	II
Yellow fever virus	Heamorrhagic fever	C	II
Rickettsia rickettsii	Rocky mountain spotted fever	Not given	II
Lassa-fever virus	Heamorrhagic fever	A	I
Congo-Crimean- heamorrhagic fever virus	Heamorrhagic fever	A	I
Hantaan virus	HPS (HFRS)	C	II
Monkey pox virus	Monkey pox fever	C	II
West-Equines encephalitis virus	Virale encephalitis	B	II
Coccidioides immitis	Coccidoidomycosis	Not given	II
Shigella species	Gastroenteritis	B	II
Bolivianisches HFV(Machupo Virus)	Heamorrhagic fever	A	I
Tickborne encephalitis virus	Virale encephalitis	C	II
Marburg virus	Heamorrhagic fever	A	I
Argentinisches HFV(JuninVirus)	Heamorrhagic fever	A	I
Chikungunya virus	Fever	Not given	II
Chlamydia psittaci	Psittacosis	B	II
Japanische encephalitis virus	Virale encephalitis	C	II
Orienta tsutsugamushi	Scrub typhus	Not given	II
Salmonella Typhimurium	Gastroenteritis	B	Not given
Omsk heamorrhagic fever virus	Heamorrhagic fever	A	I
Kyasanur Forest virus	Virale encephalitis	Not given	II
EHEC O157	HUS	B	II
Nipah Virus	Heamorrhagic fever	C	II
Salmonella paratyphi	Parathyphoid fever	B	II
Murray Valley encephalitis virus	Virale encephalitis	Not given	II
LCMV	Virale encephalitis	Not given	II
Powassan virus	Virale encephalitis	Not given	II
Rocio virus	Virale encephalitis	Not given	II
Louping Ill virus	Virale encephalitis	Not given	II
Hendra virus	Virale encephalitis	Not given	II
West Nile virus	Virale encephalitis	C	II

[1] EU HSP: EU Health Security Program

Description of the selected biological agents[2] by clinical and epidemiological characteristics

Agents
Bacillus anthracis
Yersinia pestis
Brucella suis, mellitensis, abortus
Francisella tularensis
Variola Virus
Coxiella burnetti
Burkholderia pseudomallei
Botulinum toxin
Rickettsia prowazekii
Venezuelan equine encephalitis virus
Ricin
Staphylococcal enterotoxin B
Salmonella typhi
Vibrio cholerae
Ebola-virus
Ost-Equines encephalitis virus
Burkholderia mallei
Rift valley fever virus
Yellow fever virus
Rickettsia rickettsii
Lassa virus
Congo-Crimean- heamorrhagic fever virus
Hantaan virus
Monkey pox virus
West-Equines encephalitis virus
Coccidioides immitis
Shigella species
Bolivianisches HFV(Machupo Virus)
Tickborne encephalitis virus
Marburg virus
Argentinisches HFV(JuninVirus)
Chikungunya virus
Chlamydia psittaci
Japanische encephalitis virus
Orienta tsutsugamushi
Salmonella Typhimurium
Omsk heamorrhagic fever virus
Kyasanur Forest virus
EHEC O157
Nipah Virus
Salmonella paratyphi
Murray Valley encephalitis virus
LCMV
Powassan virus
Rocio virus
Louping Ill virus
Hendra virus
West Nile virus

[2] agents in blue: description for these agents currently available in this document

1 Biological agent	Bacillus anthracis
Microbiology	Spore-forming bacterium
Forms of Disease	Inhalational form Cutaneous form Gastrointestinal form
Relevant disease manifestation	Inhalational form
Reservoir	Animals - mostly herbivores, both livestock and wildlife; spores are usually shed in terminal haemorrhages or through blood at or near the time of death.[2]
Incubation Period	Inhalational form: 1- 6 days[3]; periods up to 60 days are possible[4] Cutaneous form: generally 1-7 days Gastrointestinal form: generally 1-7 days
Environmental Stability	Spores, which, rather than the bacilli themselves, are generally responsible for transmission of the disease. They have no detectable metabolism and can survive in relatively adverse environments for long periods of time. They are resistant to drying, heat, ultra-violet light, gamma irradiation and many disinfectants. Spores may persist in certain types of soil, animal products (e.g. meat, eggs, ect.), or in appropriate industrial settings (e.g. processing plants for animal products such as hides, wool, and certain textiles) for years to decades.[5] The pathogen itself is not thought to proliferate significantly outside of the body and is rarely active in the actual transmission process (except possibly in the case of fly bites in which the pathogen can occur in its vegetative form). Vitality: 30-40 years
Infectious Dose	Inhalational form: estimated to be 8.000-10.000 spores[6]. This number can be significantly less depending on the susceptibility of the exposed person (e.g. elderly, immunocompromised, etc.) or on whether the spores have been intentionally modified somehow. Certain estimates have postulated that, due to the high tenacity of spores, inhalation of even a single infective spore can initiate infection; though they admit that this is highly unlikely.[7]
Transmission Chain	Animal-animal (enzootic); Animal-human (zoo-anthroponotic); Human-human transmission (anthroponotic) has been documented though extremely rarely (thought to be impossible in inhalational anthrax cases)
Transmission Route	Indirect (vehicle): Air: aerosolized soil, wool, animal products such as drums and rugs Food: contaminated Water: contaminated Environment: soil particle Direct: Physical (skin, mucousa) contact Ingestion of animal food
Transmission Mode	**Zoo-anthroponotic - Indirect** Vehicle transmission **Air** Inhalation of anthrax spore aerosols, most commonly the context of poorly-ventilated industrial settings where potentially infected animal products are processed **Environment/Fomites** *Skin contact* with spore-containing wool or other animal products; drums, rugs *Skin cont*act with spore-containing soil or bone meal (used in gardening+ animal feed) **Food** *Ingestion* of undercooked meat that has been contaminated during processing/ preparation (gastrointestinal form) - less frequently *Ingestion* of undercooked meat from an infected animal

	Water *Ingestion* of contaminated drinking water - less frequently Vector transmission Occasional transmission can occur via being bitten by a fly that has fed on a diseased animal[8] **Zoo-anthroponotic - Direct** Physical (skin, mucousa) contact- Contact with the tissues, blood, hide of animals (cattle, sheep, goats, horses, pigs, etc.) dying from the disease; most commonly spores enter through very small skin lesions on exposed body parts such as the face, arms, and neck (Cutaneous form)
Transmission Risk	Depends greatly on the number of spores to which the exposed persons have potentially come into contact with, and on the type of contact involved (inhalation, ingestion, physical contact, etc.) Values for the two largest investigated inhalational anthrax outbreaks were 0.10% and 0.16% (The US and Sverdlovsk cases, respectively). Transmission risks have not been investigated for exposures via ingestion or physical contact.
Lethality	Inhalational form: in the past, estimated between 90 and 100%; a recent outbreak in the US showed a lethality of around 45%[9] Cutaneous form: between 5 and 20%[10] Gastrointestinal form: 25 to 75%; rarely diagnosed during life except in the setting of an epidemic
Curative therapy	Antimicrobial therapy is effective against the Cutaneous form and has potential to help in inhalational cases provided that treatment is started before or very soon after the onset of symptoms. When toxins have been produced in the body at high levels, antimicrobial therapy becomes nearly obsolete; at this point, treatment with specific human gamma globulin may be somewhat effective. Penicillin has shown to be effective in the treatment of Cutaneous anthrax. Tests in non-human primates have shown that penicillin, doxycycline and ciprofloxacin are effective for prophylaxis and for early treatment of inhalational anthrax.[11]
Chemoprophylaxis	Those who suspect that they have been exposed to anthrax spores should be prophylactically treated with antibiotics for an extended period of around 60 days due to the unpredictable and potentially long incubation period.[12] Penicillin has shown to be effective in the treatment of Cutaneous anthrax. Tests in non-human primates have shown that penicillin, doxycycline and ciprofloxacin are effective for prophylaxis and for early treatment of inhalational anthrax.[13]
Vaccine (pre and/or post-exposure)/ Immunglobulin	Active vaccine- An active cell-free vaccine made from a culture filtrate containing the bacteria's protective antigen is made by the Bioport Corporation and is given mainly in the US and UK to certain military personnel and to people with high exposure professions.[14] Live spore vaccines based on attenuated strains are produced for human use in China and in the Russian Federation. This vaccine must be administered over the course of several months—three subcutaneous injections given 2 weeks apart, followed by three additional subcutaneous injections given at 6, 12, and 18 months with annual booster injections thereafter. Passive vaccine- New developments are being made to develop a passive vaccine which will potentially produce human immunity within 24 hours of vaccination. However, this passive vaccine produces only short-term immunity (ca. a few weeks). Post-exposure vaccination (cell-free active version) has been suggested in combination with chemoprophylactic antimicrobial

	treatments.[15]
Vaccine production/availability status	Major international manufacturers of the anthrax vaccine include the BioPort Corporation (US), the Health Protection Agency (UK), and certain manufacturers in the Russian Federation (in collaboration with American Biogenic Scientists-ABS).
Immunity	Different animals show varying levels of natural resistance to disease; thus, infectious doses vary according to these parameters. Vaccination with the active cell-free version produces long-term immunity. The passive vaccination will potentially produce immunity lasting only a few weeks.[16]
Risk of transmission	See Attack rate
Reproduction Number (R0)	Not given due to extreme rarity of human-human transmission
Outbreak attack rate	Extensively investigated outbreaks have calculated values of 0.25%[17] and 0.66%[18]; these percentages seem to be highly influenced by the intimacy and frequency of exposures of susceptible persons.[19]
Consequences of spread to the human environment	Contamination of wide areas: "bad fields"; unhabitable
Bioterroristic threat priority	CDC priority category A A number of countries have already made attempts to weaponise anthrax, focusing on development for airborne dispersal, which would lead to inhalation of the organism. A deliberate release of anthrax spores occurred in 2001 in the USA; letters containing the spores were sent through the postal system, and resulted in 22 human cases of anthrax. Out of the 11 inhalational cases (others were cutaneous), 5 people died yielding a case-fatality rate of 45%. The threat of a deliberate release of this agent is considered serious because: The organism is relatively easy to cultivate from environmental sources. The inhalation form of disease has a high mortality rate[20]
Germ Warfare Modes of Transmission	Anthrax disease can be transmitted via a powder or aerosol. A germ warfare attack would be most effective in an unventilated area with a large number of people. The spores remain stable for a long period of time; they release bacteria when they find a suitable environment, such as the human body.
Germ warfare characteristics	Anthrax is an effective low-cost method of producing a large number of fatalities through inhalation. It is extremely difficult to work with as a bioterrorism agent. For effective use the bacteria would have to be modified from the form found in animals to make it more virulent and resistant to antibiotics. Then it would have to be milled into a form small enough to be inhaled, but not so small that it would immediately be exhaled again. Terrorists would probably elect to attack indoors, thereby avoiding effects of even a slight wind, which would disperse the spores before they have much effect. It has been estimated that 50 kg of B. anthracis spores released over an urban population of 5 million would sicken 250.000 and kill 100.000. In a WHO model of a hypothetical dissemination of 50 kg of agent along a 2 km line upwind of a large population center, anthrax and tularemia were shown to cause the highest level of disease and death and the greatest downward spread.

2 Biological agent	Variola Virus
Microbiology	DNA enveloped virus; Variola major, Variola minor
Forms of Disease	Smallpox
Reservoir	Humans are the only known host for the virus. The eradication of smallpox was officially endorsed by the World Health Assembly in 1980.
Incubation Period	7 to 19 days; usually 10 to 14 days[21]
Environmental Stability	Variola virus is relatively stable in the natural environment. In aerosolized form, it can remain infective for at least several hours if not exposed to sunlight or ultraviolet light.[22] In ordinary natural conditions (e.g. ambient temperature, ordinary levels of humidity and exposure to sunlight), Variola will not likely survive for more than 48 hours. When contained in the dry scabs that result from smallpox lesions, variola virus can survive for long periods (13 years has been documented). It can also survive in refrigerated cultures (up to 39 years has been documented for variola, and longer for vaccinia strains). [23]
Infectious Dose	This infectious dose is thought to be very low, in the range of 10-100 infectious virus particles
Transmission Chain	Human-Human (anthroponotic)
Transmission Route	Direct or Indirect
Transmission Mode	**Indirect:** Vehicle transmission- **Air:** via aerosols of respiratory secretions, skin lesions exudates **Fomites:** clothing, bedding which are contaminated with infective secretions of saliva or nasal exudates may also present a risk of infection **Direct:** Droplet transmission- most common form of transmission is direct face-to-face contact via the deposit of droplets of saliva or respiratory secretions from infected persons (from coughing, sneezing, etc.) onto the oropharyngeal, nasal or respiratory mucosa of a susceptible person occasionally, the conjunctivae Diaplacentar transmission placenta are sufficient portals of entry for the virus[24]
Infectious Period	A patient is infective starting from the formation of the first lesions to the point when all scabs have disappeared; this is usually around 3 weeks. Transmission risk (via droplet spread) showed to be highest around the time of early lesion formation. Exposure to patients during the late stages of the disease is much less likely to produce infection.[25]
Lethality	Variola major: 20-50% or more[26] Variola minor: less than 1%[27]
Curative therapy	Curative therapy: The management of symptoms is currently the only treatment currently available. Several compounds are under investigation as possible chemotherapeutic agents. One of these, Cidofovir, a broad-spectrum inhibitor of viral DNA polymerase, has shown some positive results in laboratory studies.[28]
Chemoprophylaxis	**Preventive therapy** Methisazone appears to be useful as preventive therapy following exposure but is poorly tolerated.
Vaccine (pre and/or post-exposure)/ Immune globulin	Pre Exposure- **Vaccinia virus** was the immunizing agent used to eradicate smallpox. This consisted of pulp scraped from vaccinia virus-infected animal skin, mainly calf or sheep, with phenol added in order to

	weaken the bacteria. Currently it is not advised that the general public be vaccinated because the risk of accidental inoculation (1 in 1,000.000 doses) is greater than the known risk of contracting the disease naturally.[29] Post Exposure- Vaccination within 3 days of exposure will, in the vast majority of cases, completely prevent or significantly modify the onset of the disease. Vaccination 4 to 7 days after exposure will likely offer some degree of protection against the disease or may modify the severity of its onset.[30] In light of this, the epidemiologic response to a case of smallpox would be the mass vaccination of possible contacts. Vaccinia immune globulin (VIG) is also effective for post exposure prophylaxis without the side effects of methisazone.[31]
Vaccine production/ availability	Yes
Immunity	After infection, one has strong life-long acquired immunity protecting them against reinfection.[32] Vaccination usually prevents smallpox for at least 10 years and, even if symptoms appear, they are milder and mortality is less than in non-vaccinated persons.
Attack Rate	Based on investigations of past outbreaks in Asia and Africa, the secondary attack rate in households varied from 0.37 to 0.96. These calculations varied according to factors of sanitary deprivation and crowding, as well as to strain variation among variola viruses.[33]
Reproduction Number (R0)	Historical data are available only from periods with substantial population immunity either from vaccination or from having survived natural infection. These records indicate that index cases often produced less than 5 secondary infections. Records of a 1972 outbreak in Yugoslavia report a R0 value of around 12 or more. It is very likely that in the absence of significant vaccination programs and/or substantial immunity among the population, an outbreak today would produce substantially higher R0 values.[34] Different estimates from current literature range from 3-6 and 10-20.[35]
Outbreak Attack Rate	See transmission risk
Consequences of spread to the human environment	Not viable out of the host
Bioterrorismus relevance	CDC priority category A The WHO Orthopoxvirus Committees meeting in 1994 and 1999 have recommended that no one other than the two WHO collaborating centres in the United States and the Russian Federation may have in possession at one time more than 20% of the viral DNA for variola virus.[36] Research samples of variola are contained in: -The CDC in Atlanta, GA, USA Level 4 high-security laboratory -Vector State Research Centre of Virology and Biotechnology Koltsovo, Novosibirsk Oblast, Russia Raised concern about smallpox has emerged with regard to its potential as an agent of bioterrorism because it can be transmitted in an aerosol, can be produced in large-scale, and can be transmitted person-to-person. The variola virus measures 260 by 150 nanometers and contains a molecule of double-stranded DNA coding for some 200 different proteins, one of the largest viral genomes known. The relatively huge size and complexity of the variola's genome makes it exceedingly difficult to create synthetically.[37] For this reason there is widespread controversy regarding the

	continued storage of variola specimens in select laboratories around the world.
Germ warfare characteristics	The Variola virus, the agent of smallpox, is considered to be naturally extinct. Supposedly only two well-guarded stocks of the smallpox virus remain in the world, in a Russian and an American lab. However, there are reports that Russia stockpiled Variola virus as a BW and the fate of these supplies is uncertain in many people's minds. Further, other nations (e.g. China) were suspected of producing stocks of this virus and the status of these programs is not public knowledge. Since routine smallpox vaccination is no longer carried out, the bulk of the world's population is susceptible to this highly communicable pathogen. The smallpox virus is a prime candidate for a BW because of the following characteristics: ▪ It is a DNA virus whose genetic code whose has been sequenced. ▪ It is easily (for a virus) cultivated and large quantities of the virus could be produced in a relatively short period of time. ▪ It is a prime candidate for genetic engineering. ▪ It is easy to engineer it so that the current vaccines are no longer effective and to add virulence factors to the smallpox genome (e.g. botox gene) that would make it virtually 100% fatal. ▪ It is highly infectious, being spread by close human contact. ▪ It can be contracted by inhaling the virus. ▪ It is extremely hardy; surviving on fomites for days or weeks. Most of the world's population is susceptible to this virus as routine vaccination was stopped when the WHO declared its eradication in 1979. The mortality rate is strain dependant, however the mortality rate of the variola major strain is ~50%. It is likely that any BW-strain would have an even higher mortality rate. There is no known treatment to abate the course of the disease other than routine medical care. Smallpox could be dispersed in aerosolized form or perhaps via suicide carriers mixing in crowds. After initial transmission the disease would pass from person to person easily. An outbreak of smallpox in any population would most probably indicate a terrorist attack.
	As an outbreak caused by terrorists would probably show up after 10 to 12 days, the source or site of the attack would not be immediately evident. The later symptoms are severe and unusual enough that most victims would quickly seek medical treatment, and it is at that point that the attack would be recognized. The risk of a terrorist attack with smallpox is reduced by the great technical skill required to culture the virus, to make it into powder or liquid form for aerosol use, and to transport it.

3 Biological agent	Yersinia pestis
Microbiology	Enterobactereaceae family; gram-negative, facultative anaerobe
Forms of Disease	Primary pneumonic form Secondary pneumonic form Bubonic and septicaemic form
Reservoir	Wild rodents (ground squirrels, rats, etc.), some lagomorphs (rabbits, hares, etc.), wild carnivores and domestic cats.[38]
Incubation Period	Primary pneumonic form: usually only 1-4 days (maximum 6 days) Bubonic and septicaemic form: generally 2-8 days.[39]
Environmental Stability	*Y. pestis* is capable of both growth in the presence or absence of oxygen-containing environments. It can remain viable for days when contained in water or moist soil and is resistant to drying if protected by mucus, dried blood and secretions or other substances. It remains viable for about an hour after an aerosol release. The pathogen can only survive for a few hours (ca. 3-4) however, when being directly exposed to sunlight. [40, 41]
Infectious Dose	When inhaled in aerosol form, the infectious dose is approximately 100-500 organisms.[42]
Transmission Chain	Animal-Animal (enzootic); animal-human (zoo-anthroponotic); human-human (anthroponotic)
Transmission Route	Direct or indirect
Transmission Mode	**Indirect:** **AIR** In the case of deliberate use of plague in the context of a bioterrorist attack, the pathogen would likely be release as an aerosol causing the highly virulent pneumonic form (which is also transmissible from human to human)[43] **Indirect:** animal-vehicle-human Vehicle transmission- **FOOD** Consumption of infected animal tissues or, possibly, contaminated soil Rodents coming from non-infected areas can become infected when they dig burrows in previously infected areas[44] Vector transmission: animal-vector-human The most common form of the disease affecting humans (known as bubonic plague) is usually spread by the bites of infected fleas as they regurgitating plague bacteria from infected rodents; the pathogen can also gain entry when passed from an infected flea through a skin lesion[45] Humans are infected when they become "accidental" hosts in a natural disease transmission cycle (sylvatic plague) that occurs between rodents and their fleas. Vector transmission: human-vector-human Vector transmission from human to human via *Pulex irritans* ("human flea") is considered an important transmission factor in some regions where this vector is prevalent (e.g. Andean region, South America)[46] **Direct: Human-Human** Droplet contact- With the pneumonic form of plague, a much more virulent form in which the lungs become infected, transmission can occur directly from person to person by droplet infection[47] Physical Contact: Sin-Skin contact For the bubonic form to be transmitted person to person there must be direct contact with pus from the suppurating buboes of an

	infected person—this is thought to happen only very rarely **Direct: Animal-Human** Droplet contact- In rare cases, droplets can also be passed to human via droplet from pneumatically infected household cats[48]
Infectious Period	Pneumonic plague is transmissible to other people as long as there are viable organisms in the sputum. If effective antimicrobial treatment is started at the early stages of infection, this period will last for about 72 hours.[49] Fleas can remain infective for months under suitable conditions of temperature and humidity.[50]
Duration of Disease	Expected Duration With proper antibiotic treatment, most symptoms of uncomplicated bubonic plague will subside within two to five days, although swollen buboes can remain for several weeks. Recovery from more severe septicemic plague and pneumonic plague usually takes longer, depending on the severity of the patient's bleeding problems, respiratory failure and other potentially life-threatening symptoms.
Lethality	Pneumonic form: Untreated primary septicemic or pneumonic cases are almost invariably fatal (90-100%).[51] Bubonic form: In the absence of therapy, estimated at more than 50% [52]
Curative therapy	**Curative therapy** Antimicrobial curative therapy is effective if begun early in the disease and continued for at least 3 days after body temperature returns to normal. Streptomycin is the historical drug of choice but is not immediately available everywhere. Commonly used alternatives which are considered effective are Gentamicin, Tetracyclines, Doxycycline (preferred for oral treatment because of its ready gastrointestinal absorption), Chloramphenicol, Fluoroquinolones, Ciprofloxacin.
Chemoprophylaxis	**Preventive therapy** Persons in close contact with pneumonic plague patients or who are likely to have been exposed to infected fleas, have had direct contact with body fluids or tissues of an infected mammal, or for any other reason are suspected to have been exposed to the pathogen should receive antimicrobial prophylaxis for a week after the last suspected exposure. Doxycycline and ciprofloxacin are recommended for such use. [53] **Curative therapy** Antimicrobial curative therapy is effective if begun early in the disease and continued for at least 3 days after body temperature returns to normal. Also, several sulfonamides (sulfathiazole, sulfadiazine, sulfamerazine and trimethoprim - sulfamethoxazole) have been used successfully for the treatment and prophylaxis of plague.
Vaccine (pre and/or post-exposure) / Immune globulin	Plague vaccines are available but are not recommended for immediate protection in outbreak situations. It is rather only recommended for high-risk groups, e.g. health workers and laboratory personnel who are constantly exposed to the risk of contamination. Preventive vaccination with killed or live attenuated *Y. pestis* is moderately effective against bubonic but not against pneumonic plague.[54]

	With killed vaccine, protection is relatively short-lived (3 - 12 months) and periodic revaccination is necessary. As with various other pathogens, massive infection can overcome vaccine-conferred immunity. Vaccination would be of little use during a plague outbreak, as at least a month is needed for immunity to build up and recommendations for administration of killed bacteria vaccines include an initial injection and two booster injections over a period of 6 months.
Transmission risk	Available data suggest that the risk of person-to-person spread of pneumonic plague is relatively low. Transmission is via respiratory droplet, and appears to require close contact.[55] While there has been much discussion concerning the transmissibility of primary pneumonic plague, no quantitative estimates could be found in published literature[56]
Reproduction Number (R0)	Around 1.3 (variance = 3.1) for the pneumonic form.[57]
Outbreak Attack Rate	Pneumonic form (human-human transmissible): One study, which simulated a large scale release of aerosolized *Y. Pestis,* estimated an attack rate of about 70%. This was determined taking into account the simulated release method and the hypothesized person-person communicability of the disease. It also considered the better-known attack rates of diseases such as pertussis and chicken pox, which have person-person modes of transmission similar to that of pneumonic plague.[58] Bubonic form: This is very closely associated with specific climatic and environmental conditions in relation to how they affect the interaction between animal host, the fleas they carry, and humans.
Bioterrorismus relevance	CDC priority category A There is increasing concern about the threat of an aerosol release of *Y. pestis.* This threat is serious because when inhaled, plague can lead to rapidly fatal pneumonic infections, secondary cases via human-human spread, and the fact that the historical reputation of the disease would surely cause panic.[59] Multidrug resistant strains of the bacilli have been engineered in laboratories via alteration of plasmids - this has lead to streptomycin resistance in certain strains.[60]
Germ warfare modes of transmission:	The pathogen can be administered as an aerosol in either dry or wet form. After the initial administration, the disease would pass from person to person easily. Because the pneumatic form of plague occurs only rarely in nature (1.000-3.000 cases per year world-wide), an outbreak would probably indicate a terrorist attack.
Germ warfare characteristics	Rapidly advancing and deadly sickness. Initial outbreaks would likely be misidentified or left untreated until too late, contributing to high early death rates and quick spread.

4 Biological agent	Hantaan virus
Microbiology	Family: Bunyaviridae non-enveloped single strand RNA –virus; spherical, about 100 nm in diameter
Forms of Disease	Hantavirus pulmonary syndrome Hemorrhagic fever with renal syndrome (HFRS) Nephropathia
Relevant disease manifestation	Hemorrhagic fever with renal syndrome (HFRS)
Reservoir	Field rodents; humans are accidental hosts
Incubation Period	From 3-60 days; average 14-30 days
Environmental Stability	Sensitive to drying; viral isolates from immunocytomas have remained viable for 2-8 years; infectivity of *Hantavirus* has been reported to persist in neutral solutions for several hours at 37 C and for several days at lower temperatures as well as in dried cell cultures for up to 2 days; virus suspensions have been stored at -60°C in balanced salt solution + 1% bovine albumin for over 5 years and remain infectious.
Transmission Chain	Animal-human (zoo-anthroponotic); human-human (anthroponotic) though extremely rare
Transmission Route	Direct or indirect
Transmission Mode	**Indirect:** Vehicle transmission **Air** Inhalation of **aerosolised** infected rodent excreta. **Food** Ingestion of infected animals **Direct:** Physical contact- Contact between infectious materials (animal faeces, urine, feces, saliva) with mucous membranes, broken skin; Animal bites (rodent to human transmission via bites has been documented) Person-to-person transmission is extremely rare
Infectious Period	Not well defined, person to person transmission is thought to be very rare.[61]
Lethality	5-15%[62]
Curative therapy	Ribavirin given iv has shown to be effective during the early phase of the HFRS illness[63]
Chemoprophylaxis	Not available
Vaccine (pre and/or post-exposure) / Immune globulin	Not available
Vaccine production/ availability	n.a.
Transmission Risk	-
Reproduction Number (R0)	Not given
Outbreak Attack Rate	Not given
Consequences of spread to the human environment	no
Bioterrorismus relevance	CDC priority category **C**
Germ warfare modes of transmission:	Hantavirus was studied as a biological weapon by the Japanese before and during WWII. It was isolated (1978), propagated in the laboratory and produced in volume (1981). An effective treatment was tested (1985) and aerosol transmission was demonstrated

	(1988).
Germ warfare characteristics:	Although hantaviruses cannot be grown to sufficient titers in a practical substrate at this time, there have been laboratory infections, particularly from laboratory animals. Hantavirus-containing particles in the one-to-five-micron range, are inhaled, pass successfully through the nose, and move down into the bronchi. About half of the particles are deposited in terminal respiratory bronchioles or alveolar sacs, resulting in the possibility of infection in humans. Hantaviruses are infectious in aerosols and may be spread on the wind, making them a potential weapon in biological warfare

5 Biological agent	Brucella suis, melitensis, abortus
Microbiology	Gram-negative rod-shaped bacteria
Forms of Disease	Brucellosis; Fever and chills, headache, loss of appetite, mental depression, extreme fatigue, aching joints and sweating
Relevant disease manifestation	Can cause a range of symptoms that are similar to the flu and may include fever, sweats, headaches, back pains, and physical weakness; severe infections of the central nervous systems or lining of the heart may occur. Brucellosis can also cause long-lasting or chronic symptoms that include recurrent fevers, joint pain, and fatigue.
Reservoir	Diverse domesticated and wild mammals, especially cattle, goats, sheep, pigs, camels, buffaloes and marine mammals. Preferred hosts exist for each species: *-B. abortus* commonly infects cattle *-B. suis* commonly infects pigs *-B. melitensis* commonly infects goats, sheep and camels *-B. canis* – dogs Only these four of the six *Brucella* spp. are known to cause brucellosis in humans; *B. melitensis, B. suis* are considered more virulent for humans than *B. abortus* or *B. canis*. [64, 65]
Incubation Period	Typically 5-30 days, but may be up to 6 months.[66]
Environmental Stability	Brucella species can survive for a long time in both hot and cold environments, particularly in moist conditions. Pastures and animal accommodation on farms may remain contaminated for prolonged periods, with survival for up to two years being reported. However, the organisms are very sensitive to direct sunlight, and can be destroyed by pasteurization or cooking.[67] The organism can survive: -in carcasses and organs - up to 135 days -paper - 32 days -soil - 125 days -blood at 4°C - 180 days[68]
Infectious Dose	This is dependent on organism type, virulence, and host resistance. Based on data from laboratory-acquired infections, the dose is probably <500 organisms, and may be as low as 10-100 organisms.[69]
Transmission Chain	Animal-human (zoo-anthroponotic) Person-to-person (anthropootic-anthroponotic) spread is rare
Transmission Route	Indirect/ direct

Transmission Mode	**Zoo-anthroponotic** **Direct:** Physical contact- direct contact of broken skin and the conjunctiva with materials from infected animals (animal tissues, faeces, urine, blood, placenta, vaginal discharge, aborted fetus, milk or milk products)[70] **Indirect:** Vehicle transmission **Air** Inhalation of aerosolised products of conception in infected animals, aerosols generated in laboratory accidents, aerosols from droplets and dust in abattoirs **Food** Ingestion of unpasteurised milk or milk products, including cream and soft cheeses acidified milk products (yoghurts, buttermilk, labna, lassi etc) from infected animals **Anthropootic-anthroponotic** Person-to-person transmission is extremely rare, by sexual contact, vertical transmission
Infectious Period	The infection may persist for several months without causing any symptoms.
Duration of Disease	Onset may be gradual or acute, with variable symptoms, consisting most frequently of undulating fever, chills, exhaustion, depression, back and leg pains, sweating, headaches and loss of appetite. Cutaneous and soft tissue manifestations may include contact lesions, rash and soft tissue abscesses. Splenomegaly and hepatomegaly with associated organ tenderness occur in some patients. Without treatment, patients usually recover within 2–3 months but there may be cycles of relapse and remission extending over years, accompanied by liver, spleen, bone, genito-urinary, central nervous system and cardiac complications.
Lethality	Rarely fatal in humans. Less than 2% of infections result in death, primarily due to untreated endocarditis caused by *B. melitensis*.[71]
Curative therapy	Brucellosis is usually treated with a combination therapy of doxycycline and rifampicin for a minimum of six weeks. Follow-up for a minimum period of a year is essential to encourage patient adherence to the chemotherapy regimen and to detect relapse.[72]
Chemoprophylaxis	No chemoprophylaxis available
Vaccine (pre and/or post-exposure)/ Immune globulin	No human vaccine is available.[73]
Vaccine production/ availability	n.a.
Immunity	Infection with *Brucella* spp. leads to acquired immunity, but the duration of the response is not known.[74]
Outbreak Attack Rate	Not given
Consequences of spread to the human environment	
Bioterrorismus relevance	CDC priority category B
Germ warfare modes of transmission:	*Brucella* is highly infectious by the airborne route and could be used in an aerosolised form or as a contaminant of food, milk and water. The organism survives well in the environment and widespread contamination is possible.
Germ warfare characteristics:	Human infection is rarely fatal but brucellosis can be a protracted debilitating illness often requiring prolonged antibiotic treatment and there are no effective human vaccines, although animal vaccines are available.[75]

6 Biological agent	Francisella tularensis
Microbiology	*Francisella tularensis* subsp. *tulasrensis* (Jesllison type A), *Francisella tularensis* subsp. *holarctica* (Jesllison type B)
Forms of Disease	Oculoglandular tularaemia Orpharyngeal tularaemia Ulceroglandular tularaemia Pulmonal tularaemia Intestinal tularaemia Typhoidale tularaemia
Relevant disease manifestation	Pulmonal tularaemia, Typhoidale tularaemia
Reservoir	Wild animals, particularly rabbits, hares, voles, muskrats, beavers, some domestic animals and various hard ticks.[76]
Incubation Period	Usually 3-5 days with a range of 1-14 days; varies relative to the size(s) of the organism(s) introduced.[77]
Environmental Stability	The organism can survive in water, mud, and straw or animal carcasses for weeks to months. The organism remains viable in tissues for long periods giving it a tendency to cause relapse after treatment.[78]
Infectious Dose	Only 10 to 50 organisms are required to produce clinical illness.
Transmission Chain	Animal-human (zoo-anthroponotic); Animal-Animal (enzootic)
Transmission Route	Direct or indirect
Transmission Mode	Indirect: Vehicle transmission- Food (Ingestion or handling of insufficiently cooked meat from infected animals; Drinking contaminated water) Air (Inhalation of contaminated aerosolized dust particles from soil, grain or hay[79]) Vector transmission- Transmission can occur via arthropod bites including those of infected wood ticks, dog ticks, lonestar ticks, less commonly deer flies, and various mosquito species (mostly observed in the Sweden and the Russian Federation).[80] Direct: Physical contact- Inoculation through the skin (not necessarily with lesion), conjunctival sac, orpharyngeal mucosa with tissues, blood, or water (liquids) passed via direct contact with infected animal carcasses (during skinning, dressing, etc.) or handling contaminated pelts and/or paws[81]
Infectious Period	Person to person transmission does not occur; however, flies can remain infective for 14 days, ticks for their entire lifespan, and infected frozen meats (rabbit especially) up to 3 years.[82]
Duration of Disease	Ulceroglandular tularaemia lasts 2–4 weeks, with a convalescent period of up to 3 months.
Lethality	*Francisella tularensis* subsp. *tulasrensis* (Jesllison type A): 5-15% *Francisella tularensis* subsp. *holarctica* (Jesllison type B): few fatalities even without treatment[83]
Curative therapy	The main preferred antimicrobials include streptomycin or gentamycin; given for a course of 10 days. Streptomycin is given as a 1 gram dosage intramuscularly twice daily. Gentamicin may be more readily available and is given as a 5 mg/kg intramuscular or intravenous dosage once daily.[84]
Chemoprophylaxis	Ciprofloxacin, Doxicyclin
Vaccine (pre and/or post-exposure) / Immune globulin	Live attenuated vaccines injections have proven to prevent or attenuate infection that occurs through cutaneous and inhalatory routes. These vaccines have been administered to high risk populations living in endemic regions of the former Soviet Union and

	in the US to at-risk employees at Fort Detrick, Maryland.
Vaccine production / availability	The vaccine is not yet approved for general usage or sale in the US. Tularemia vaccine supplies are only in the Russian Federation. Attempts to develop improved vaccines are under way in several countries.[85] Vaccine is not available in Austria
Immunity	Because the incubation period for tularemia is usually 3 to 5 days and immunity following vaccination takes about 2 weeks to develop, postexposure vaccination is not considered a viable public health strategy to prevent disease in the event of a mass exposure.
Transmissions-Risk (Kontagionsindex)	Inhaled form: estimated to be nearly 1 (nearly everyone expose becomes ill) due to the extremely low infectious dose
Bioterrorismus relevance	CDC priority category A
Germ warfare modes of transmission:	Release of the agent via aerosol is regarded most hazardous mode of transmission and would affect the most people. According to WHO study done in 1970, very little *F tularensis* (50 kilograms) disseminated throughout an densely populated urban area via aerosolization would be needed to cause substantial casualties, including thousands of deaths.[9]
Germ warfare characteristics	In recent years, Fracicella tularensis (and tularaemia) has gain increased attention because of the potential for its use as an agent of biological warfare or terrorism. It has an extremely high infectivity (as few as 10 inhaled organisms have shown to cause the respiratory form of the disease), it is easily disseminated, and produces symptoms that make it difficult to reach a diagnosis at early stages (when treatment is crucial[86]). For these reasons, tularemia cases are reportable to public health authorities. Unusual patterns of disease must be investigated for both conventional and bioterrorist sources.[87] A primary downfall to using this agent for biological warfare is not transmitted for person to person.

7 Biological agent	Coxiella burnetti
Microbiology	Obligat intracellulare gram-negative bacteria
Forms of Disease	Q-fever
Relevant disease manifestation	Acute cases: sudden onset of one or more of the following: high fevers (up to 104-105°F), severe headache, general malaise, myalgia, confusion, sore throat, chills, sweats, non-productive cough, nausea, vomiting, diarrhea, abdominal pain, and chest pain. Fever usually lasts for 1 to 2 weeks. Weight loss can occur and persist for some time. 30%-50% of patients with a symptomatic infection will develop pneumonia. Additionally, a majority of patients have abnormal results on liver function tests and some will develop hepatitis. In general, most patients will recover to good health within several months without any treatment. Only 1%-2% of people with acute Q fever die of the disease. Chronic Q fever: persists for more than 6 months. Patients who have had acute Q fever may develop the chronic form as soon as 1 year or as long as 20 years after initial infection. A serious complication of chronic Q fever is endocarditis. Most patients who develop chronic Q fever have pre-existing valvular heart disease or have a history of vascular graft.
Reservoir	*C. burnetii* infects a wide range of animals, including mammals, birds, and ticks. Cattle, sheep, and goats are primary reservoirs along with ungulates and pets (cats and dogs) which are the most common sources of the disease. Mammals may shed *Coxiella* in feces, urine, milk, and birth products.[88, 89]
Incubation Period	Most commonly 2-3 weeks. This period varies depending on the number of organisms that initially infect the patient. Infection with greater numbers of organisms will result in shorter incubation periods.[90]
Environmental Stability	*C. burnetii* are resistant to heat, drying, and many common disinfectants.[91] They can survive in dust and animal litter for many weeks and in dried blood for at least 6 months at room temperature.[92] The organism has potential to be carried very large distance via wind.[93]
Infectious Dose	The infectious dose can be as low as a single organism.[94]
Transmission Chain	Animal-human (zoo-anthroponotic); human-human (anthroponotic) extremely rare
Transmission Route	Direct or indirect
Transmission Mode	**Animal-human (zoo-anthroponotic)** **Indirect:** Vehicle transmission – **Air** Inhalation of aerosolised organisms from barnyard dust contaminated by dried placental material, birth fluids, and excreta of infected herd animals[95] **Environment** Effective contact (through cuts or abrasions in the skin, or through the conjunctiva[96]) with surfaces, most commonly bedding or litter (hay or straw) contaminated with parturient fluids of infected livestock. **Food** Less commonly, ingestion of contaminated milk, followed by regurgitation and inspiration of the contaminated food Vector transmission- Very rarely, tick bites **Direct:** Physical contact-

	Infection has also resulted from intradermal inoculation, from blood transfusions[97] Effective contact (through cuts or abrasions in the skin, or through the conjunctiva[98]) with parturient fluids of infected livestock, coats of newborn animals, or the placenta. **Human-human (anthroponotic)** Person-to-person transmission is extremely rare; from transplacental transmission (causes congenital infection)
Infectious Period	Not well defined, person to person transmission is thought to be very rare.[99]
Lethality	Very low
Curative therapy	Doxycycline is the treatment of choice for acute Q fever. Antibiotic treatment is most effective when initiated within the first 3 days of illness. A dose of 100 mg of doxycycline taken orally twice daily for 15-21 days is a frequently prescribed therapy. Quinolone antibiotics have demonstrated good in vitro activity against *C. burnetii* and may be considered by the physician. Therapy should be started again if the disease relapses.[100]
Lethality	None available
Vaccine (pre and/or post-exposure)/ Immune globulin	An effective whole-cell vaccine for Q fever has been developed and has successfully protected humans in occupational settings in Australia. However, this vaccine is not commercially available in the United States[101, 102] and not in Austria. Individuals who have previously been exposed to *C. burnetii* should not receive the vaccine because severe reactions, localized to the area of the injected vaccine, may occur.[103]
Immunity	Those who recover fully from infection may possess lifelong immunity against re-infection.[104] Cell-mediated immunity against *C. burnetii* appears to last longer than humoral immunity and may be a more important factor in long-lasting immunity. NIAID
Bioterrorismus relevance	CDC priority category B
Germ warfare modes of transmission	The agent could be used as a biological weapon in an aerosolised form or as a contaminant of food, water, mail or other items. An aerosol would be the most efficient form of release; a single organism can cause disease if inhaled by a susceptible individual, and there is good evidence as to the role of wind transmission. Its ability to form resistant spore-like forms, remain viable in the environment for long periods after release, and its stability under production, storage and transport conditions also make it a suitable biological weapon.[105]
Germ warfare characteristics	Due to *Coxiella burnetii's* high infectivity, its resistance to heat and drying, and its ability to become airborne and inhaled by humans, this agent is seriously considered as a threat in terms of its potential use for biological warfare.[106] The WHO estimated that dissemination of 50 kg of *Coxiella burnetii* over a major population center would result in 500 deaths and 125.000 incapacitated over 20 km downrange.[107]

8 Biological agent	Botulinum Neurotoxin
Microbiology	These rod-shaped organisms grow best in low oxygen conditions. Bacteria form spores; there are seven types of botulism toxin designated by the letters A through G; only types A, B, E and F cause illness in humans.
Forms of Disease	Botulism = serious paralytic illness; The classic symptoms of botulism include double vision, blurred vision, drooping eyelids, slurred speech, difficulty swallowing, dry mouth, and muscle weakness. Infants with botulism appear lethargic, feed poorly, are constipated, and have a weak cry and poor muscle tone. These are all symptoms of the muscle paralysis caused by the bacterial toxin. If untreated, these symptoms may progress to cause paralysis of the arms, legs, trunk and respiratory muscles. In foodborne botulism, symptoms generally begin 18 to 36 hours after eating a contaminated food, but they can occur as early as 6 hours or as late as 10 days.
Reservoir	Soil
Environmental Stability	High; Bacteria form spores which allow them to survive in a dormant state until exposed to conditions that can support their growth
Lethal dose	To be completed
Transmission Chain	n.a.
Transmission Route	n.a.
Transmission Mode	There are three main kinds of botulism. Foodborne botulism is caused by eating foods that contain the botulism toxin. Wound botulism is caused by toxin produced from a wound infected with *Clostridium botulinum*. Infant botulism is caused by consuming the spores of the botulinum bacteria, which then grow in the intestines and release toxin.
Duration of disease	24-72h; until months
Lethality	high
Vaccine production / availability	An investigational pentavalent (ABCDE) botulinum toxoid vaccine to protect laboratory workers and military personnel is available in the U.S. Vaccine is not available in Austria
Curative therapy	Yes; breathing machine (ventilator) plus intensive medical and nursing care. After several weeks, the paralysis slowly improves. If diagnosed early, foodborne and wound botulism can be treated with an equine antitoxin which blocks the action of toxin circulating in the blood. This can prevent patients from worsening, but recovery still takes many weeks. Wounds should be treated, usually surgically, to remove the source of the toxin-producing bacteria followed by administration of appropriate antibiotics.
Bioterrorismus relevance	CDC Priority Category A
Germ warfare modes of transmission:	Botulinum toxin is the most poisonous substance known. An aerosolized or foodborne botulinum toxin weapon would cause acute symmetric, descending flaccid paralysis with prominent bulbar palsies such as diplopia, dysarthria, dysphonia, and dysphagia that would typically present 12 to 72 hours after exposure. A single gram of crystalline toxin, evenly dispersed and inhaled, would kill more than 1 million people, although technical factors would make such dissemination difficult. It is estimated that a point-source aerosol release of Botulinum toxin could incapacitate or kill 10% of persons within 0.5 km downwind (William C. Patrick, unpublished data, 1998). Effective response to a deliberate release of botulinum toxin will depend on timely clinical diagnosis, case reporting, and epidemiological investigation. Persons potentially exposed to botulinum toxin should be closely observed, and those with signs of

	botulism require prompt treatment with antitoxin and supportive care that may include assisted ventilation for weeks or months. Treatment with antitoxin should not be delayed for microbiological testing.
Germ warfare characteristics	The known disadvantages are that botox is unstable in the air if exposed to sunlight and dry conditions and is destroyed by brief boiling, thus effective exposure is limited by a small window of lighting and humidity conditions. Even though botox is highly toxic it would still take a large quantity to reach a lethal concentration in a large city's water supply.

9 Biological agent	Rickettsia prowazekii
Microbiology	Gram-negative, obligate intracellular bacteria
Forms of Disease	Endemic foci exist in certain regions where louse infestation is common, including parts of Mexico, central and south America, central and east Africa and various regions of Asia. Epidemics may reappear during times of war or famine.
Relevant disease manifestation	Endemic Louse-borne B Typhus Fever
Reservoir	Humans are the reservoir during epidemic periods. Occasional cases are found in flying squirrels although these do not cause human infection.[108]
Incubation Period	1-2 weeks; commonly 12 days[109]
Environmental Stability	Rickettsiae have an obligate relationship with eukaryotic their possession of "leaky membranes" that require the osmolarity and nutritional environment supplied by an intracellular habitat.[110]
Infectious Dose	<10 rickettsial particles[111]
Transmission Chain	Vector born human-human (vectorborn anthroponotic)
Transmission Route	Indirect (vector borne)
Transmission Mode	**Indirect:** Vehicle transmission- **Air** Inhalation of infected lice feces in dust can account for some infections Vector transmission- **Vector – body louse** The disease is spread by the workings of specific body lice, *Pediculus humanus corporis.* Lice become infected with *Rickettsia prowazekii* when feeding on the blood of a human with an acute febrile typhus infection. The organism is the passed through the louse's feces and often incidentally rubbed into (via scratching, etc.) the site where the bite took place, other skin abrasions or mucosal surfaces[112]
Infectious Period	Not transmittable directly from person to person. People can infect lice during the period of febrile illness (ca. 2 weeks) and likely for 2-3 days after high temperatures subside. Lice defecate 2-6 days after the infective blood-meal but are infectious earlier if crushed and in contact with a sufficient portal of entry. Although lice generally die around 2 weeks after infection, *Rickettsia prowazekii* can remain viable in dead lice for weeks.[113]
Lethality	10-40% in the absence of fever; lethality increases with age[114] Infections are rarely fatal in children less than 10 years old; in people over 50 years old, the mortality rate can be as high as 60% without treatment.
Curative therapy	The initial reference treatment of any suspected typhus case is 200 mg of doxycycline.[115] Use of insecticide powers and other media for killing vectors is advised to prevent the spread of possible infectious lice.
Chemoprophylaxis	None available
Vaccine (pre and/or post-exposure)/ Immunglobulin	Studies performed over 20 years ago showed that an inactivated vaccine provided a moderate degree of protection against experimental *R. prowazekii* infection. However, because of licensing concerns and additional concerns that spontaneous reversion of live E-strain may revert to a more virulent strain, the E-strain vaccine is not currently available or in use in any field studies. Although no commercial vaccines have been licensed, experimental vaccines are produced by military sources in the United States and may be available for high-risk situations.
Vaccine production/ availability status	See above

Immunity	Immunity following recovery from infection *R. prowazekii* is lifelong in most cases. *R. prowazekii* can establish a latent infection, however, that can reactivate after years or decades. Cell-mediated immunity is also required for the ultimate clearance of rickettsial infections. NIAID
Reproduction Number (R0)	Not given due to the lack of human to human transmission. However, it should be noted that epidemics of typhus usually occur where louse populations are high—i.e. in populations living in unsanitary, crowded conditions or under conditions of war, famine, floods and other disasters. The ability for potentially infective lice to thrive will greatly contribute to how many vectors will be successful in producing secondary cases.[116]
Outbreak attack rate	According to the WHO s estimate, if 50 kg of aerosolized *R. prowazekii* were released into a major population center, the result would be >100.000 casualties (19.000 deaths and 85.000 incapacitated individuals)[117]
Consequences of spread to the human environment	No
Bioterrorismus relevance	CDC Priority Category B
Germ warfare modes of transmission:	*R. prowazekii* was produced as a bioweapon and used before World War II. It is infectious by aerosol and has a very high lethality.[118]

10 Biological agent	Rickettsia rickettsii
Forms of Disease	Rocky Mountain Spotted Fever
Reservoir	Maintained in nature among ticks via transovarial and transstadial passage. Can be transmitted to dogs, rodents, and other animals although these infections are usually sub-clinical.[119] The principal vectors of *Rickettsia rickettsii* are *Dermacentor variabilis* (the American dog tick) and *Dermacentor andersoni* (the Rocky Mountain wood tick). Principal vectors vary regionally.[120] Examples are: East and South USA - dog tick, *Dermancentor variabilis* Northwest USA - wood tick, *D. andersoni* Southwest USA - Lone Star tick, *Amyblyomma americanum* Latin America - *A. cajennense*[121]
Incubation Period	2-14 days
Environmental Stability	Organism is stable in tick tissues or blood under ambient environmental conditions, surviving up to 1 year; sensitive to drying infected tick feces; organisms quickly lose their infectivity on drying.[122]
Infectious Dose	< 10 organisms Transmission is unlikely when the tick feeds for less than 20 hours.[123]
Transmission Chain	Vector-human
Transmission Route	Direct (only rarely) or indirect
Transmission Mode	Direct: Physical contact- Transmission occurs only rarely via infective tick tissues or feces coming into contact with conjunctival or transcutaneous tissues or via inhalation (eg, after crushing blood engorged ticks) Indirect: Vector transmission- Humans in, in the great majority of cases, results from being bitten by an infected tick when infected saliva gains an effective entry portal[124]
Reproduction Number (R0)	Not given due to lack of human-human transmission
Infectious Period	Person-person transmission does not occur; ticks remain infectious for life, commonly as long as 18 months.[125]
Lethality	Found to be highest in the very young (4 years, 3 to 4 percent) and the elderly (60 years, 4 to 9 percent).[126] A 4-year national study in the US estimated the overall lethality to be 2.4 %.[127] Untreated cases can reach levels as high as 13-25%.[128]
Curative therapy	Early antibiotic treatment with Doxycycline is best for patients suffering from Rocky Mountain Spotted Fever (RMSF) caused by *R. rickettsii* . It should be prescribed in any suspected cases in both children and adults but not in pregnant women and allergic patients. In other rickettsioses a single-day treatment with doxycycline (200 mg) is efficient, but this has not been studied so far for RMSF. For pregnant women, chloramphenicol is the only available alternative to doxycycline.[129]
Vaccine (pre and/or post-exposure)	None licensed; but may be available as killed experimental product from U.S. CDC.[130]
Immunity	One attack probably confers lasting immunity.[131]
Bioterrorismus relevance	EU Threat Category II

11 Biological agent	Venezuelan equine encephalitis virus
Microbiology	Family: *Togaviridae* Genus: *Alphavirus* positive-sense, single-stranded RNA virus
Forms of Disease	**Influenza Like Disease;** Most infections are fairly mild, with symptoms usually lasting 3–5 days.Clinical manifestations of the naturally occurring disease: influenza like, with abrupt onset of severe headache, high fever, chills, myalgia in the legs and lumbosacral area and retro orbital pain. There may also be photophobia, sore throat, nausea, diarrhoea and vomiting. Conjunctival and pharyngeal congestion are the only external signs. Most infections are fairly mild, with symptoms usually lasting 3–5 days. The overall casefatality rate in the 1962–1963 epidemic in Venezuela, among some 30.000 cases, was approximately 0.6%. In some patients there is a second wave of fever and, particularly in children, CNS involvement ranging from somnolence and disorientation to personality change, convulsions, paralysis and death.
Reservoir	The virus is maintained in a rodent - mosquito - rodent cycle. During major outbreaks affecting humans, the disease is transmitted in a cycle involving mosquito vectors and horses or other equines as hosts. For this reason, natural outbreaks are normally preceded by equine epizootics. Humans also may develop sufficient viraemia to serve as hosts in human - mosquito - human cycles.[132]
Incubation Period	Usually 2-6 days; can be as short as 1 day
Environmental Stability	There is no published data on the environmental stability of VEE viral subtypes
Infectious Dose	Although is rare and seen exclusively in laboratories, primary aerosol infection is well known and inhalation of only a few infective organisms is sufficient to cause a significant likelihood of infection. WHO
Transmission Chain	Animal-vector-animal Animal-vector-human Human-vector-human
Transmission Route	Indirect (vector-borne)
Transmission Mode	**Zoo-anthroponotic** **Direct:** There is no evidence of direct transmission from horses to humans. **Indirect:** Vector transmission- Humans become infected from the bite of infected mosquitoes. The major species of mosquito that transmit epidemic VEE are *Psorophora confinnis*, *Aedes sollicitans*, *Aedes taeniorhynchus* (recently revised to *Ochlerotatus taeniorhynchus)* and *Deinocerites pseudes*. [Cecil] Vehicle transmission- **Air** AEROSOL Although **natural aerogenic transmission is not documented** in humans, primary aerosol infection in laboratories is well known and inhalation of only a few infective organisms is sufficient to cause a significant likelihood of infection. The VEE virus can initiate infection via **the nasal mucosa and the olfactory epithelium of the upper respiratory tract**.

	AIRBORN DROPLETS Virus-containing airborne droplets too large to penetrate more deeply into the respiratory system can therefore constitute a hazard. **Anthroponotic** **Direct:** There is no evidence of direct person-to-person transmission. Person-person spread via droplet spread and/or contact with infected pharyngeal excretions of human patients is theoretically possible, however, they are not epidemiologically important. Cecil **Indirect:** Vector transmission- Humans also may develop sufficient viraemia to serve as hosts in human - mosquito - human cycles.[133]
Infectious Period	Infected humans and horses are infectious for mosquitoes for up to 72 hours; infected mosquitoes probably transmit virus throughout their lifetime.
Lethality	4% of children develop encephalitis among which the case-fatality rate is around 35%. Only about 0.5% of adults develop encephalitis among which the case-fatality rate is les than 10%. [Cecil]
Curative therapy	No specific therapy is available, and treatment of encephalitis cases is supportive. [Cecil]
Chemoprophylaxis	Not available
Vaccine (pre and/or post-exposure)/ Immune globulin	An attenuated cell-culture propagated live vaccine TC-83, produced but not licensed in the USA is moderately effective against both natural infection and **aerosol challenge** but is somewhat reactogenic and fails to induce a minimum neutralizing antibody response in approximately one-fifth of persons receiving it, presumably leaving them unprotected. Two other attenuated live virus vaccines, strains 15 and 230, reported to offer good protection **against aerosol challenge**, were developed in the Russian Federation. An inactivated vaccine designated C-84, prepared by formalin-inactivation of the TC-83 strain, is currently used to immunize TC-83 non-responders and as a booster for individuals who have declining titres after TC-83 vaccination. [134]WHO However, there is no licensed human vaccine or effective antiviral treatment for human or equine disease.
Immunity	Mild infections and subsequent immunity occure frequently in endemic areas. Children are at greater risk for developing CNS infection.
Bioterrorismus relevance	**CDC Priority Category B**
Germ warfare modes of transmission	Methods of transmitting the VEE virus as a biological warfare agent were developed in the 1960s; an epidemic of VEE, especially if humans and horses become ill simultaneously, could represent an attack rather than naturally occurring illness. [Cecil]. VEEV remains a naturally emerging disease threat as well as a highly developed biological weapon. The virus can be produced in large amount by unsophisticated methods. Methods of transmitting the VEE virus as a biological warfare agent were developed in the 1960s; an epidemic of VEE, especially if humans and horses become ill simultaneously, could represent an attack rather than naturally occurring illness. [Cecil]

12 Biological agent	**Lassa virus**
Forms of Disease	Hemorrhagic Fever
Reservoir	The animal reservoir of Lassa virus is a rodent of the genus Mastomys, commonly known as the "multimammate rat." Mastomys infected with Lassa virus do not become ill, but they can shed the virus in their excreta (urine and faeces). WHO. *Mastomys* breed very frequently and produce large numbers of offspring. Once infected, rodents continue to shed virus throughout their life. These rodents are numerous in the savannas and forests of West, Central, and East Africa. In addition, *Mastomys* generally readily colonize human homes. All these factors together contribute to the relatively efficient spread of Lassa virus from infected rodents to humans.[135]
Incubation Period	The incubation period for Lassa fever is usually between 7 and 10 days, although a range of 3-21 days has been reported. Lassa virus infection causes only mild or no symptoms in approximately 80% of those infected.[136]
Environmental Stability	No specific studies have been undertaken, but Lassa virus, like all other viral hemorrhagic fever-causing (VHF) pathogens, is an RNA virus with a lipid envelope. This renders the organism relatively susceptible to detergents as well as to low pH environments. Conversely, they are quite stable at neutral pH, especially in the presence of protein.[137]
Infectious Dose	Infectious dose is unknown.[138]
Transmission Chain	Person-to-person (anthroponotic) , animal-person (zoo-anthroponotic)
Transmission Route	Direct or Indirect
Transmission Mode	Direct: <u>Physical contact</u>- Person to person transmission occurs through exchange of infected bodily fluids, such as blood, saliva, urine or semen. This can happen either in the laboratory, in a healthcare setting or via sexual or other close contact Person-to-person transmission occurs in both community and health care settings, where the virus may be spread by contaminated medical equipment, such as re-used needles. Sexual transmission of Lassa virus has been reported.[139] Indirect: <u>Vehicle transmission-</u> Consuming infected rats (they are considered a delicacy and are eaten by up to 90% of people in some areas)[140] Effective contact with droppings from infected rodents or through touching objects or eating food contaminated with these materials, (virus commonly enters through cuts or sores); Inoculation with infected needles and or with other materials contaminated with infected patients' pharyngeal secretions or urine[141] Inhalation of tiny particles soiled with rodent urine or saliva can also cause infection[142]

Transmission Risk	A recent case series showed low admission rates and high case fatality rates for people aged less than 18 years (who make up 51% of the total population (United Nations Development Programme)) compared with older people (see table A on bmj.com). During pregnancy, high rates of maternal death (29%) and fetal and neonatal loss (87%) have been recorded (uterine evacuation improves outcome significantly), with 25% of all maternal deaths in Sierra Leone being due to Lassa fever.16 An estimate of the case fatality rate in the general population is 1-2%, much lower than in hospitalised cases, possibly as a consequence of differences in severity[143] People of all ages are susceptible [144], [145], [146]
Infectious Period	The virus is excreted in urine for three to nine weeks from infection and in semen for three months. The extent of sexual transmission is unknown.[147]
Lethality	Pregnant women suffer more severe infection, particularly in the third trimester, and up to 95% of fetuses of infected mothers die; Untreated: 76 %. Treated: 9 %.
Chemoprophylaxis	An antiviral drug called Ribavirin has been used for treatment and is effective if given early in the illness, preferably within 6 days after the start of symptoms.
Vaccine (pre and/or post- exposure)	There is no vaccine.
Immunity	The duration of immunity following infection is unknown[148]
Bioterrorismus relevance	CDC Priority Category A
Germ warfare modes of transmission:	VHF agents are known to be readily capable of person-to-person spread. If aerosolisation does occur, there would be a serious threat of widespread infection. A human outbreak of this type has never been recorded. The threat of infection from Lassa and other VHF viruses is considered serious because: They can cause severe, rapidly fatal infection. Secondary cases may arise from contact with primary cases. The reputation of these diseases is such that they can induce public anxiety and disrupt everyday life in the population. Laboratory testing on animal models shows that some agents may be transmitted by aerosol, although this has not been seen in the human outbreaks studied.
Germ warfare characteristics:	**Hemorrhagic Fever Viruses** Weapons disseminating a number of HFVs could cause an outbreak of an undifferentiated febrile illness 2 to 21 days later, associated with clinical manifestations that could include rash, hemorrhagic diathesis, and shock. The mode of transmission and clinical course would vary depending on the specific pathogen. Diagnosis may be delayed given clinicians' unfamiliarity with these diseases, heterogeneous clinical presentation within an infected cohort, and lack of widely available diagnostic tests. Initiation of ribavirin therapy in the early phases of illness may be useful in treatment of some of these viruses, although extensive experience is lacking. There are no licensed vaccines to treat the diseases caused by HFVs (JAMA, May 8, 2002 - Vol 287, No. 18). Several studies have demonstrated successful infection of nonhuman primates by aerosol preparations of Ebola, Marburg, Lassa, and New World arenaviruses. Since 1967, when the first outbreak of VHF caused by Marburg virus occurred in Germany and Yugoslavia, there have been 18 reports of human outbreaks of VHF secondary to Ebola or Marburg viruses, resulting in approximately 1.500 cases to date.

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