Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
CHAPTER 3

Viral Biothreat Agents

Kevin Anderson
National Biodefense Analysis and Countermeasures Center, Science and Technology Directorate, U.S. Department of Homeland Security, Frederick, MD, USA

OUTLINE
Introduction
The Spectrum of Biological Threats
Viruses of Concern

Preparedness
Conclusions

ABSTRACT

The risk posed by viruses as biological threat agents is discussed primarily from a public health perspective, with the potential occurrence of significant morbidity and mortality as a result of infection via natural or intentional exposure. Parameters of risk associated with the spectrum of viruses considered as biological threat agents are discussed, to include examples of intentional use. In consideration of the threat posed by viruses, mitigating illness and preventing death are the principal goals of medical countermeasure development efforts. The existence of safe and efficacious vaccines is critical to establishing a robust posture of preparedness to address the spectrum of viral threat agents.

INTRODUCTION

Given the primary focus of this text is on vaccines, the term biological threat will be defined primarily from a public health perspective. Therefore, viruses as biological threat agents are defined as those that cause harm to public health as manifested by significant morbidity and/or mortality, which can occur via natural or intentional exposure.

Natural exposure to viruses that cause human disease can occur via direct or indirect contact. Direct
contact would include person-to-person spread, such as with community-acquired viral infections; animal-to-person spread, as with viral zoonoses; and spread to an unborn child from its mother, also known as vertical transmission. Also, viruses can be transmitted directly by vectors, such as mosquitoes and ticks. Indirect contact would include environmentally acquired viral infections (via food, water, air, or fomites) that are not spread by close contact. Infectious viral diseases can be spread through the air either by direct or indirect contact via droplet or particle transmission, respectively.

Intentional exposure to viruses resulting in human disease would include biowarfare, bioterrorism, and biocrimes (Swearengen, 2006). Biowarfare is defined as the military use of biological agents, where targets of agents are predominately military personnel, government officials, or resources that might hinder a nation’s ability to attack and/or defend itself. Bioterrorism is defined as the threat or use of biological agents by individuals or groups motivated by political, religious, ecological, or other ideological objective. Viruses of concern from a biowarfare or bioterrorism perspective represent a major theme of this chapter. A biocrime is defined as the threat or use of biological agents for individual objectives such as revenge or financial gain. Use of viruses in biocrimes against people have been documented, with sources limited primarily to clinical samples containing viruses such as HIV-1 and hepatitis A (Carus, 2001). Viruses have also been used to reduce animal populations unlawfully and by definition, such action would be categorized as a biocrime (Carus, 2001).

The extent to which particular viruses are considered as biological threats is largely dependent on the risk they pose. The risk posed by a virus is defined as the probability of it causing infections of significant consequence, with high morbidity and mortality, as a result of either naturally occurring epidemic or pandemic disease, or malevolent intent, in the case of biocrime, bioterrorism, or biowarfare.

Viruses as credible, high-impact threats are defined by the properties or characteristics of the virus, the vulnerability of those subject to exposure and also, in the case of malevolent use, the capability and intent of perpetrators. Credible, high-impact threats include viruses that could inflict harm by either natural exposure, in which parameters of risk include agent characteristics and vulnerabilities, or intentional exposure, in which adversary capability and intent also become factors to consider (Fig. 3.1). Parameters of risk associated with properties or characteristics of viruses would include high infectivity, high morbidity and mortality, environmental stability, airborne transmissibility, and high contagiousness. Parameters associated with vulnerabilities include limited or unavailable medical countermeasures, such as vaccines and therapeutics, with cost and increasing public resistance to vaccination as contributing factors, limited or unavailable means to detect and identify viruses, and the ability of a virus to cause disease that is difficult to treat. Parameters of risk associated with adversary capability and intent include ease of acquisition, production, and dissemination of viral agents; and evidence of prior research and development as a biological weapon (Center for Biosecurity, UPMC, 2008).

In human history, the consequences of natural exposure to viruses have been much greater with respect to morbidity and mortality than those realized by intentional release, as depicted in Fig. 3.1. With the exception of smallpox, which some experts speculate is responsible for more deaths throughout modern history than all other infectious diseases combined, the greatest human and economic consequences derived from virus infections via natural exposure have been realized from emerging diseases, all of which have been derived from infected animals via zoonoses. For example, influenza pandemics that occurred in 1918 (H1N1), 1957 (H2N2), and 1968 (H3N2) resulted in approximately 40 – 50, 2, and 1 million deaths worldwide, respectively (World Health Organization, 2008). It is thought that the 1918 H1N1 virus was an avian virus that was introduced into pigs, and subsequently transmitted to human carriers, which spread the virus along trade routes and shipping lines resulting in a global pandemic (Taubenberger and Morens, 2006). In the past 25 years, approximately 60 million people have been infected by HIV-1, resulting in greater than 25 million deaths (Avert, 2008). HIV-1 most likely originated in wild chimpanzees living in...
tropical rain forests of equatorial Africa, with infection of humans likely occurring during the French colonial period from 1919 to 1960 (Keele et al., 2006).

**THE SPECTRUM OF BIOLOGICAL THREATS**

Although the societal effects of emerging infectious diseases continue to shape the landscape of medical preparedness, the proliferation of biological materials, technologies, and expertise has increased the potential for adversaries to use viruses for biological attacks. Not only does society have a need for developing vaccines, therapeutics, and diagnostics to counter naturally occurring and emerging infectious diseases, but countermeasures must keep pace with potentially devastating adversarial efforts to subvert developing or existing biomedical technologies. Moreover, caution must be exercised to prevent biomedical advances that benefit mankind from being applied to create enhanced or advanced viral threat agents generated through the use of these technologies (Petro and Carus, 2005).

The spectrum of viruses considered as biological threat agents resulting from intentional exposure encompasses four categories as shown in Fig. 3.2, each of which presents unique challenges and significant opportunities for development of medical countermeasures (Bush, 2007). Traditional agents would include viruses that could be disseminated to cause mass casualties in susceptible populations. Although risk posed by traditional viral agents is significant, a finite number of viruses fit in this category. Of particular concern are variola virus (smallpox) and viruses that cause hemorrhagic fever such as filoviruses (Lake Victoria marburgvirus and ebola viruses), arenaviruses (Lassa, Junin, Machupo, Guanarito, and Sabia viruses), bunyaviruses (hantaviruses, Rift Valley fever virus, and Crimean-Congo hemorrhagic fever virus), and flaviviruses (yellow fever virus, tick-borne encephalitis virus, and dengue viruses) (NIAID, 2008). These viruses can be easily disseminated or transmitted from person-to-person, resulting in high case-fatality rates and have the potential for major public health impact (Peters, 2002); might cause public panic and social disruption; and require special action for public health preparedness (Centers for Disease Control and Prevention, 2008; WHO, 2005). Therefore, the development or existence of targeted medical countermeasures against these agents will reduce the current risk posed or the likelihood of mass casualties resulting from intentional use.

Emerging agents would include those viruses which undergo rapid co-evolution with their hosts and the environment. Emerging viruses are for the most part, zoonotic in nature and spillover via natural exposure to humans as incidental hosts: examples of which are SARS coronavirus and avian influenza virus. Improved disease surveillance, to include early detection, is essential for containing the spread of an outbreak and is dependent on strong, flexible public health systems at local, state, and federal levels (Centers for Disease Control and Prevention, 2008).

Enhanced agents would include selection of naturally occurring viruses to enhance their virulence or host range or to facilitate their delivery beyond parameters that define natural exposure. For example, viruses used in an aerosol attack may exhibit altered patterns of infectivity, resulting in a different outcome than that observed in naturally occurring outbreaks. Enhanced viral agents may also be capable of producing disease with a more rapid onset of symptoms, making timely diagnosis, treatment, and containment more difficult (Schmaljohn and Hevey, 2005). Increasingly, medical countermeasure development

---

**FIGURE 3.2** The spectrum of biological threats.

| Traditional | Enhanced | Emerging | Advanced |
|-------------|----------|----------|----------|
| Naturally occurring microorganisms (e.g., viruses) or toxins with the potential to be disseminated to cause mass casualties. | Traditional agents that have been modified or selected for enhanced ability to harm human populations or circumvent current countermeasures. | Previously unrecognized pathogens that might be naturally occurring and present a serious risk to human populations. | Novel pathogens or other materials of biological nature that have been artificially engineered to bypass traditional countermeasures or produce a more severe or enhanced spectrum of disease. |

---

**I. BIOTHREATS AND EMERGING INFECTIOUS DISEASES**
strategies should include protection against agent enhancements, such as aerosol exposure as mentioned above.

Advanced agents would include viruses that have been artificially engineered in the laboratory to circumvent countermeasures or produce a more severe or enhanced spectrum of disease. Of particular concern have been examples of viruses engineered to contain host biological response modulators, which in animal models have demonstrated an ability to circumvent levels of protective immunity obtained from prior vaccination, a primary example being ectromelia virus engineered to express IL-4 (Jackson et al., 2001).

Given the challenges of developing medical countermeasures against enhanced, emerging, and advanced agents, which are confounded to a great extent by unknowns, a posture of preparedness is largely based on the ability to rapidly identify and characterize the agent, understand the extent of exposure, and to evoke appropriate levels of patient care and social distancing to limit the spread of infection (World Health Organization and Robinson, 2004).

## VIRUSES OF CONCERN

Several lists of threat agents, which include viruses, have been generated by groups or agencies within governments for a variety of purposes, including relative risk, biosecurity, and export control (select agents), as shown in Table 3.1. Although all of the agents listed represent traditional or emerging agents, the likelihood of their use for intentional exposure is a key consideration for prioritizing development of biodefense medical countermeasures, including vaccines.

Smallpox is a bioterrorism threat due to its potential to cause severe morbidity in a nonimmune population and because it can be transmitted via inhalation, ingestion, abrasion, or injection (Darling et al., 2005). A single confirmed case of smallpox identified anywhere in the world would be considered a public health emergency (Saks and Karras, 2006).

The first documented attempt to use variola virus as a biological weapon occurred during the French and Indian Wars (1754–1767) in North America. Blankets from smallpox victims were given as gifts to susceptible North American Indians, resulting in epidemics among native populations leading to case-fatality rates approaching 50% in some areas. During World War II, the Japanese Military conducted experiments with variola virus for use as a biological weapon. The former Soviet Union conducted biological weapons programs to include large-scale industrial production of variola virus that was stable in an aerosol and was claimed to be deliverable in warheads (Alibek and Handelman, 1999).

Subsequent to the World Health Organization (WHO) declaration of the eradication of smallpox in 1980, member nations agreed to destroy all laboratory stocks of the virus and/or provide them to one of the two officially sanctioned WHO reference laboratories: The Centers for Disease Control and Prevention in Atlanta, GA, or the Institute of Virus Preparations in Moscow, Russia. Although remaining stocks at these laboratories were scheduled to be destroyed in 1996, the World Health Assembly subsequently accepted a recommendation to retain the remaining stocks and to review a decision to destroy them on a periodic basis. Should the existing repositories be destroyed, other potential sources of smallpox may exist. Conceivably, sources of the variola virus may include unknown stores, cadavers in permafrost, and recreation of the viral genome or strains in laboratories utilizing genetic engineering, recombination, and data from published genomic sequences as a basis for design (Darling et al., 2005).

In addition to variola virus, a number of other viruses have been weaponized or studied for possible use as biological weapons against humans by state programs, including Lake Victoria marburg-virus, Venezuelan equine encephalitis virus, ebola viruses, Junin virus (Argentinian hemorrhagic fever), Machupo virus (Bolivian hemorrhagic fever), yellow fever virus, Lassa virus, Japanese encephalitis virus, and tick-borne encephalitis virus (Alibek and Handelman, 1999). Most of these viruses can be readily acquired from naturally occurring outbreaks and can be grown in the laboratory to high titers. The hemorrhagic fever viruses associated with this group are notorious for causing aerosol-mediated laboratory infections with case-fatality rates as great as 30% (Peters, 2002).

A number of viruses of concern are viewed primarily as threats to agriculture and their introduction to domestic livestock would have devastating effects such as reduced food production, economic loss in food and farm sectors, export embargoes, destabilization of markets, and loss of public confidence in the safety of the food supply (CIDRP, 2008). Such viruses would include foot-and-mouth disease, Rift Valley fever, Venezuelan equine encephalitis, and other viruses that may employ invertebrate hosts as vectors, from which virus can be subsequently amplified in animal hosts and also can be transmitted to humans. In addition, Nipah and Hendra viruses have been transmitted from domestic animals or livestock to
| List        | African horse sickness virus | African swine fever virus | Akabane virus | Alcelaphine herpesvirus type 1 | Andes virus | Bluetongue virus | Caliciviruses | California encephalitis virus | Camel pox virus |
|-------------|-----------------------------|---------------------------|--------------|--------------------------------|-------------|-----------------|---------------|-----------------------------|----------------|
| Australia Group | Yes                        | Yes                       | No           | No                             | No          | Yes             | No            | No                          | No             |
| HHS         | No                         | No                        | No           | No                             | No          | No              | No            | No                          | No             |
| USDA        | Yes                        | Yes                       | Yes          | Yes                            | Yes         | Yes             | Yes           | No                          | Yes            |
| WHO         | No                         | No                        | No           | No                             | No          | No              | No            | No                          | No             |
| NATO        | No                         | No                        | No           | No                             | No          | No              | No            | No                          | No             |
| NIAID       | No                         | No                        | No           | Yes                            | Yes         | Yes             | Yes           | Yes (B)                     | No             |

| List        | Cercopithecine herpesvirus | Chikungunya virus | Classical swine fever virus | Crimean-Congo hemorrhagic fever virus | Dengue viruses | Dobrava virus | Eastern equine encephalomyelitis virus | Ebola viruses | Flexal virus |
|-------------|---------------------------|------------------|-----------------------------|--------------------------------------|---------------|--------------|----------------------------------------|---------------|-------------|
| Australia Group | No                       | Yes              | No                          | Yes                                  | Yes           | Yes          | Yes                                    | Yes           | Yes         |
| HHS         | Yes                       | No               | No                          | Yes                                  | No            | No           | Yes                                    | Yes           | Yes         |
| USDA        | No                        | No               | Yes                         | No                                   | No            | Yes          | No                                    | No            | No          |
| WHO         | No                        | Yes              | No                          | Yes                                  | Yes           | No           | Yes                                    | No            | No          |
| NATO        | No                        | Yes              | No                          | Yes                                  | Yes           | No           | Yes                                    | No            | No          |
| NIAID       | No                        | Yes (C)          | No                          | Yes (C)                              | Yes (A)       | Yes (C)      | Yes (B)                                 | Yes (A)       | No          |

| List        | Foot and mouth disease virus | Goat pox virus | Guanarito virus | Hantaan virus | Hendra virus | Hepatitis A virus | Herpes virus (Aujeszky's disease) | Hog cholera virus | Influenza viruses |
|-------------|-----------------------------|---------------|----------------|--------------|--------------|--------------------|---------------------------------|------------------|-------------------|
| Australia Group | Yes                       | Yes           | Yes            | Yes          | No           | No                 | Yes                            | Yes              | No                |
| HHS         | No                         | No            | Yes            | No           | Yes          | No                 | No                             | No               | Yes               |
| USDA        | Yes                        | Yes           | No             | No           | Yes          | No                 | No                             | No               | Yes               |
| WHO         | No                         | No            | No             | Yes          | No           | No                 | No                             | No               | Yes               |
| NATO        | No                         | No            | No             | Yes          | No           | No                 | No                             | No               | Yes               |
| NIAID       | No                         | No            | Yes (A)        | Yes (A)      | Yes (C)      | Yes (B)            | No                             | No               | Yes (C)           |

(Continued)
## TABLE 3.1 (Continued)

| List         | Japanese encephalitis virus | Junin virus | Kyasanur Forest disease virus | LaCrosse virus | Lake Victoria marburgvirus | Lassa virus | Louping ill virus | Lumpy skin disease virus | Lympohytic choriomeningitis virus |
|--------------|-----------------------------|-------------|--------------------------------|----------------|-----------------------------|-------------|------------------|-----------------------------|-----------------------------------|
| Australia Group | Yes                          | Yes         | Yes                            | No             | Yes                         | Yes         | Yes              | Yes                         | Yes                               |
| HHS          | No                           | Yes         | Yes                            | No             | Yes                         | Yes         | No               | No                          | No                                |
| USDA         | Yes                          | No          | No                             | No             | No                          | No          | No               | Yes                         | No                                |
| WHO          | Yes                          | No          | No                             | No             | Yes                         | No          | No               | No                          | No                                |
| NATO         | No                           | Yes         | No                             | No             | Yes                         | No          | No               | No                          | No                                |
| NIAID        | Yes (B)                      | Yes (A)     | Yes (B)                        | Yes (A)        | Yes (A)                     | No          | No               | Yes (A)                     | Yes (A)                           |

| List         | Lyssavirus                   | Machupo virus | Menangle virus | Monkey pox virus | Murray Valley encephalitis virus | Newcastle disease virus | Nipah virus | O'nyong-nyong virus | Omsk hemorrhagic fever virus |
|--------------|-----------------------------|---------------|----------------|------------------|----------------------------------|------------------------|-------------|---------------------|-----------------------------|
| Australia Group | Yes                          | Yes           | No              | Yes               | Yes                              | Yes                    | Yes         | No                  | Yes                          |
| HHS          | No                           | Yes           | No              | Yes               | No                               | No                     | Yes         | No                  | Yes                          |
| USDA         | No                           | No            | Yes             | No                | No                               | Yes                    | No          | No                  | No                           |
| WHO          | No                           | No            | No              | No                | No                               | Yes                    | No          | No                  | No                           |
| NATO         | No                           | Yes (A)       | No              | No                | No                               | No                     | No          | Yes                 | No                           |
| NIAID        | No                           | Yes (A)       | No              | Yes (A)           | No                               | Yes (C)                | No          | Yes (C)             | Yes (C)                      |

| List         | Oropouche virus              | Peste des petits ruminants virus | Porcine enterovirus virus type 9 | Powassan virus | Puumala virus | Rabies virus | Rift Valley fever virus | Rinderpest virus | Rocio virus |
|--------------|------------------------------|----------------------------------|----------------------------------|----------------|--------------|--------------|------------------------|-----------------|-------------|
| Australia Group | Yes                          | Yes                              | Yes                              | Yes             | Yes          | No           | Yes                    | Yes             | Yes         |
| HHS          | No                           | No                               | No                               | No              | No           | Yes          | No                     | No              | No          |
| USDA         | No                           | Yes                              | Yes                              | No              | No           | Yes          | Yes                    | Yes             | No          |
| WHO          | No                           | No                               | No                               | No              | No           | Yes          | Yes                    | Yes             | No          |
| NATO         | No                           | No                               | No                               | No              | No           | Yes          | No                     | No              | No          |
| NIAID        | No                           | No                               | Yes (C)                          | Yes (C)         | Yes (A)      | No           | No                     | No              | No          |
### List of Viruses of Concern

| List   | Sabin virus | SARS corona virus | Seoul virus | Sheep pox virus | Sin Nombre virus | St. Louis encephalitis virus | Swine vesicular disease virus | Teschen disease virus | Tick-borne encephalitis virus |
|--------|-------------|--------------------|-------------|-----------------|------------------|-----------------------------|------------------------------|------------------------|-------------------------------|
| Australia Group | Yes | No | Yes | No | No | Yes | No | Yes | Yes |
| HHS    | Yes | No | No | No | No | No | No | No | Yes |
| USDA   | No | No | Yes | Yes | No | No | Yes | No | No |
| WHO    | No | No | Yes | No | No | No | No | No | Yes |
| NATO   | No | No | Yes | No | No | No | Yes | No | Yes |
| NIAID  | Yes (A) | Yes (C) | Yes (A) | Yes (C) | No | No | No | Yes | Yes (C) |

| List   | Variola virus | Venezuelan equine encephalomyelitis virus | Vesicular stomatitis virus | West Nile virus | Western equine encephalomyelitis virus | White pox agent | Yellow fever virus |
|--------|---------------|------------------------------------------|---------------------------|-----------------|----------------------------------------|----------------|-------------------|
| Australia Group | Yes | Yes | Yes | No | Yes | Yes | Yes |
| HHS    | Yes | Yes | No | No | No | No | No |
| USDA   | No | Yes | Yes | No | No | No | No |
| WHO    | Yes | Yes | Yes | No | Yes | No | Yes |
| NATO   | Yes | Yes | No | No | No | Yes | Yes |
| NIAID  | Yes (A) | Yes (B) | No | Yes (B) | Yes (B) | No | Yes (C) |

**Notes:** (A) NIAID Category A Priority Pathogen; (B) NIAID Category B Priority Pathogen; and (C) NIAID Category C Priority Pathogen.
humans leading to high case-fatality rates and therefore, are of concern from both an agricultural and a public health perspective.

PREPAREDNESS

Biodefense vaccine development represents, in part, a defensive strategy to protect the public from biological terrorism through the development of safe and effective countermeasures to mitigate illness and death, protect critical infrastructure, and minimize economic consequences (Gay et al., 2007). The need to accelerate and expand development of current and new vaccines to prepare for intentional introduction or natural occurrence of catastrophic human and zoonotic diseases is reflected by the list of vaccines shown in Table 3.2. In summary, licensed vaccines exist for only a few viruses of concern and are of limited supply in case of catastrophic need (Schmaljohn and Hevey, 2005). For other viruses, vaccines are available under investigational new drug (IND) status, which have not been licensed for a variety of reasons, primarily the lack of market incentive to develop through to licensure (Schmaljohn and Hevey, 2005). In light of the paucity of medical countermeasures effective against viruses of concern, subsequent chapters of this text are devoted to review of vaccine development efforts against biodefense, emerging and neglected diseases.

Adoption of a national strategy to rapidly develop effective biodefense countermeasures, which includes safe and efficacious vaccines, requires periodic threat and risk assessments to understand the evolving biological threat (Bush, 2002). Such assessment must be performed to define gaps in knowledge or vulnerabilities in our preparedness posture, thus guiding prioritization of investments in biodefense-related research, development, planning, and overall preparedness. Vaccines represent a necessary component of biodefense countermeasure development to prepare for and to minimize the consequences of a biological attack. Risk assessments have provided a means of identifying and prioritizing vaccine research and development efforts for biological agents capable of being used in biological attacks. In support of vaccine research and development, current biodefense strategies include the development of an enduring infrastructure to test and evaluate existing, proposed, or promising countermeasures, assess their safety and effectiveness, expedite their development, and ensure rapid licensure (Gronvall et al., 2007c; NIAID, 2008; U.S. Department of Health & Human Services, 2008).

Response to bioterror events involves rapid agent detection and diagnosis, implementation of exposure control measures, and use of vaccines, when appropriate, to minimize consequences to human and animal health (Gronvall et al., 2007b). Current approaches to biodefense vaccine development include use of existing applications for development and manufacturing, and development of new technologies to rapidly design, test and evaluate, and manufacture desired products. Given the urgency with which vaccines designed to minimize consequences of bioterror events are needed, new technologies and infrastructure are mandated to shorten timelines for their development. New technologies applicable to the design of vaccines would include rapid methods for the identification and selection of protective immunogens, and the development of vaccines that allow for differentiation of vaccinated hosts from those infected by exposure to virus, with options to employ improved adjuvants that stimulate innate immune responses and/or promote adaptive immune responses (Capua, et al., 2004). New infrastructure would include biocontainment facilities to increase current capacities for vaccine testing and evaluation, to optimize vaccine dosage and delivery in conjunction with routes of exposure, and enhance manufacturing capacities to ensure availability of a minimum number of doses for intervention and reduce average cycle times to manufacture vaccine lots. Rapid deployment of biodefense vaccines will require both infrastructures, to include facilities for storage of vaccine stockpiles, and technologies that ensure validated storage conditions for such stockpiles (Gronvall et al., 2007a).

CONCLUSIONS

Programs to develop better medical countermeasures against viruses must increasingly reflect the potential use of enhanced, emerging, or genetically engineered viruses as biological weapons and scenarios that require countermeasures to provide broad-spectrum coverage to prevent illness postexposure. Support for research and development of biodefense countermeasures, including vaccines, should result in improved methods for vaccine discovery and development, and enhance preparedness against viruses, as biological threats, to the benefit of public and animal health.

ACKNOWLEDGMENTS

Many thanks to David Hodge, Sara Klucking, and Jens Kuhn for critical review and to Ed Marino and Cynthia Sheffield for exceptional technical assistance in preparation of this chapter.

I. BIOTHREATS AND EMERGING INFECTIOUS DISEASES
TABLE 3.2 Available countermeasures against viruses considered as biological threat agents

| Virus                                | Countermeasure(s)                        |
|-------------------------------------|-----------------------------------------|
| Alphavirus                          |                                         |
| Venezuelan equine encephalitis virus | Live attenuated and killed vaccines (IND)|
| Eastern equine encephalitis virus   | Killed vaccine (IND)                     |
| Western equine encephalitis virus   | Killed vaccine (IND)                     |
| Chikungunya virus                   | Live attenuated vaccine (IND)            |
| Arenavirus                          |                                         |
| Lassa virus                         | No vaccine, Ribavirin                    |
| Junin virus                         | Live attenuated vaccine (IND), Ribavirin |
| Machupo virus                       | No vaccine, Ribavirin                    |
| Bunyaviridae                        |                                         |
| Crimean-Congo hemorrhagic fever virus| No vaccine, Ribavirin                    |
| Hantaan, Seoul, Puumula, Dobrava viruses | No vaccine, Ribavirin                      |
| Sin Nombre, Andes viruses           | No vaccine, Ribavirin                    |
| Rift Valley fever virus             | Killed vaccine (IND)                     |
| Flaviviridae                        |                                         |
| Tick-borne encephalitis virus       | Killed vaccine (licensed Europe)         |
| Yellow fever virus                  | Live attenuated vaccine (licensed)       |
| Japanese encephalitis virus         | Killed vaccine (licensed)                |
| Dengue viruses                      | Live attenuated vaccine (IND),           |
| Filoviridae                         |                                         |
| Ebola viruses                       | None                                     |
| Lake Victoria marburgivirus         | None                                     |
| Henipavirus                         |                                         |
| Nipah and Hendra viruses            | None                                     |
| Orthopoxivirus                      |                                         |
| Variola virus                       | Live attenuated vaccine (licensed),      |
| Monkeypox virus                     | Ribavirin                                |

References

Alibek, K., and Handelman, S. Biohazard: the Chilling True Story of the Largest Covert Biological Weapons Program in the World, Told From the Inside by the Man Who Ran It. 1st ed. xi, 319 p, [8] p of plates vols. New York: Random House, 1999.
Avert. Worldwide AIDS & HIV Statistics Including Deaths. Apr. 13, 2008. http://www.avert.org/worldstats.htm.
Bush, G.W. Biodefense for the 21st Century: Homeland Security Presidential Directive/HSPD-10. Apr. 13, 2008. 2002. http://www.whitehouse.gov/news/releases/2004/04/20040428-6.html.
Bush, G.W. Medical Countermeasures against Weapons of Mass Destruction: Homeland Security Presidential Directive/HSPD-18. Apr. 13, 2008. 2007. http://www.whitehouse.gov/news/releases/2007/02/20070207-2.html.
Capua, I., Cattoli, G. and Marangon, S. DIVA: a vaccination strategy enabling the detection of field exposure to avian influenza. Dev. Biol. (Basel) 2004; 119:229–233.
Carus ,W.S. Bioterrorism and Biocrimes. The Illicit Use of Biological Agents Since 1900. Apr. 13, 2008. 2001. National Defense University http://stinet.dtic.mil/oai/oai?verb=getRecord&metadataPrefix=html&identifier=ADA402108.
Center for Biosecurity. Agents and Diseases Background Information: Categorization and Ongoing Assessment of Biological Agents. Apr. 13, 2008. http://www.upmc-biosecurity.org/website/focus/agents_diseases/background.html.
Centers for Disease Control and Prevention. Public Health Emergency Response: The CDC Role. Apr. 13, 2008. http://www.bt.cdc.gov/.
CIDRP. Overview of Agricultural BioSecurity. Apr. 13, 2008. http://www.cidrap.umn.edu/cidcont/content/biosecurity/ag-biosec/biofacts/agbiooview.html.
Darling, R.G., Burgess, T.H., Lawler, J.V. and Endy, T.P. Smallpox as a biological weapon. Biological weapons defense infectious diseases and counterbioterrorism. In: Infectious Disease (L.E. Lindler, F.J. Lebeda, and G. Korch, Eds.), xix, 597 p vols, pp. 99–120. Totowa, NJ: Humana Press, 2005.
Gay, C.G., Richie, T.L., Pastoret, P.P., Minguiez-Tudela, L., de Baetselier, P., Gobel, T., Goddeeris, B., Kaiser, P., Morrison, I., Sanchez-Vizcaino, J.M., Anderson, K., Baille, L.W., Brown, W.C., Estes, D.M., Herrera, E., Nara, P.L., Ockenhouse, C.F., Roth, J.A. and Sotein, M.B. Advances in immunology and vaccine discovery report of the United States-European Commission workshop. Vaccine 2007; 25(41): 7007–7011.
Gronvall, G.K., Fitzgerald, J., Chamberlain, A., Inglesby, T.V. and O’Toole, T. High-containment biodefense research laboratories: meeting report and center recommendations. Biosecur. Bioterror. 2007a; 5(1):75–85.
Gronvall, G.K., Matheny, J., Smith, B.T., Main, M., Chamberlain, A., Deitch, S., Borio, L., Inglesby, T.V. and O’Toole, T. Flexible defenses roundtable meeting: promoting the strategic innovation of medical countermeasures. Biosecur. Bioterror. 2007b; 5(3):271–277.
Gronvall, G.K., Smith, B.T., Matheny, J., Main, M., Chamberlain, A., Deitch, S., Borio, L., Inglesby, T.V. and O’Toole, T. Biomedical Advanced Research and Development Authority (BARDA) roundtable. Biosecur. Bioterror. 2007c; 5(2):174–179.
I. BIOTHREATS AND EMERGING INFECTIOUS DISEASES