

IN BRIEF

EVERYWHERE YOU LOOK: SELECT AGENT PATHOGENS

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THE UNITED STATES regulates more than 80 human, animal, and plant pathogens as part of the Select Agent Program,¹ imposing strict controls on access by U.S. researchers and laboratories. However, almost all of these pathogens are also found in nature. The map at the end of this article (see supplementary material at http://www.liebertonline.com/doi/suppl/10.1089/bsp.2011.0321/suppl_file/Supp_Data.pdf) depicts the countries in which select agent pathogens caused disease between January 1, 2009, and October 31, 2010. Although pathogen security measures justifiably have been strengthened since 2001, the widespread natural occurrence of these pathogens indicates an inherent limitation of the regulations.

METHODOLOGY AND LIMITATIONS

To create this map, we searched for reports of animal and human diseases caused by select agents during the 22 months from January 1, 2009, to October 31, 2010. The sources for reports included ProMED Mail archives,² the World Animal Health Information Database (WAHID) of the World Organization for Animal Health (OIE),³ the Global Early Warning and Response System for Major Animal Diseases including Zoonoses (GLEWS),⁴ Euro-surveillance,⁵ and HealthMap,⁶ an automated online infectious disease data aggregating tool. Searches were performed using scientific and common names for agents as well as the diseases they cause.

Although we were able to find cases of disease caused by nearly all of the select agents, this map is almost certainly

incomplete. There are limitations in disease surveillance and reporting, as well as in availability and access to diagnostic tests. Additionally, this map does not describe where diseases are *thought* to be endemic; countries considered to be endemic were not labeled to have a disease if there were no documented cases during our research period. For example, cercopithecine herpes virus (herpes B virus) is generally considered to be endemic in macaque monkeys in Japan, but no cases were reported during the research period.

Another limitation was a lack of information on specific strains of disease. For example, the Indiana subtypes of vesicular stomatitis virus (VSV) are regulated by the select agent program, but other subtypes are not. The causative subtype in reported outbreaks was not always noted. In this map, both untyped reports and Indiana subtypes were included. A similar issue arises with the tickborne encephalitis flaviviruses. These viruses (Central European tickborne encephalitis virus, Far Eastern tickborne encephalitis virus, Kyasanur Forest disease virus, Omsk hemorrhagic fever virus, and Russian spring summer encephalitis virus) are all select agents. However, reports of tickborne encephalitis often did not include a specific subtype, so we grouped tickborne encephalitis viruses together.

The map excludes diseases caused by select agent toxins and plant pathogens. Toxins were not included because of a lack of data and may not generally be reported as the cause of a disease or outbreak. We also excluded plant pathogens, in large part because of a scarcity of outbreak information.

Several other select agents are absent from this map. Variola major and variola minor viruses are the causative agents of smallpox and are select agents, but they have been

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eradicated from the natural world. Likewise, rinderpest virus, which causes a deadly animal disease, is also thought to have been eradicated; no cases were reported during the research period.⁷ Similarly, the 1918 influenza virus is not a currently circulating influenza strain and can be found only in laboratories. Additionally, no specific cases of disease caused by the South American hemorrhagic fever viruses were reported in the sources used, including Junin, Machupo, Sabia, Flexal, and Guanarito. Menangle virus, which was discovered in bats in Australia, also was not reported. Akabane virus, discovered in Japan as the cause of central nervous system abnormalities in ruminants, was not reported. Monkeypox is considered to be endemic in parts of Africa and has caused animal and human outbreaks within the past decade, but no specific cases were observed through the resources used.

SELECT AGENT PROGRAM

The Select Agent Program was launched by the Anti-terrorism and Effective Death Penalty Act of 1996, which required some “select” agents to be registered with the Centers for Disease Control and Prevention (CDC) before they could be transferred from one laboratory to another. The 2001 USA PATRIOT Act and the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 strengthened accountability and restrictions for access to pathogens on the select agent list. The Select Agent Program regulates the possession, use, and transfer of those agents; imposes security requirements for the facility in which the work will be performed; requires inspections; and can impose criminal and civil penalties on those who do not adhere to the law.

The program primarily involves 3 government agencies: the Animal and Plant Health Inspection Service (APHIS) at the Department of Agriculture (USDA); the CDC, at the Department of Health and Human Services; and the Department of Justice. The CDC and APHIS enumerate pathogens that require select agent clearance. Security risk assessments are administered to individuals who work with select agents by the Department of Justice, a process that is renewed every 5 years. There are 3 categories of select agents: those regulated solely by the CDC (primarily human pathogens, such as Ebola virus), those regulated by APHIS (primarily animal pathogens, such as foot-and-mouth disease virus), and “overlap” agents, which are regulated by either agency (such as *Bacillus anthracis*, the causative agent of anthrax, which can infect humans but is generally a livestock disease). All select agents are treated equally under the law and carry the same restrictions, and violators face the same penalties—thus, illegal possession of anthrax is treated as seriously as illegal possession of lumpy skin disease virus, which does not infect humans and is difficult to work with in a research laboratory.

There are inherent limitations to the Select Agent Rule. The first, demonstrated by this map, is that most select agents are naturally occurring and thus are obtainable for legitimate or nefarious use from nonlaboratory, non-U.S. sources. A second limitation is that the program and laws apply only within U.S. borders. Critics of the select agent program have pointed out that this provision of the rule creates difficulties in international scientific collaboration and scientific progress on these pathogens, which, as demonstrated by the map, cause natural outbreaks all over the world. Some have suggested that delineating the select agent list into different tiers of security restrictions, or reducing the number of pathogens on the select agent list, could limit the public health impact of the regulations while still maintaining security benefits.^{8,9} Certainly, the inherent limitations of tracking pathogens, which grow and multiply, suggest that the select agent program can be only one part of U.S. biodefense efforts.

CHANGES MAY BE FORTHCOMING

On July 2, 2010, President Obama issued an Executive Order titled “Optimizing the Security of Biological Select Agents and Toxins in the United States.”¹⁰ The order maintains that select agents are a research priority and that they should be secured “in a manner appropriate to their risk of misuse, theft, loss, and accidental release,” but it recognizes that the efficacy of security measures need to be balanced “with the need to minimize the adverse impact on the legitimate use” of select agents. As part of the order, a Federal Experts Security Advisory Panel (FESAP) was created to evaluate how best to revise the Select Agent Program. A report is expected in February 2011.

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