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Thomas R. Frieden, MD, MPH
Director
Centers for Disease Control and Prevention
Division of Select Agents and Toxins
1600 Clifton Road, NE., MS A-46
Atlanta, GA 30333

Re: Comments on the changes to the list of select agents and toxins

Dear Director Frieden:

The Executive Council of the American Committee on Arthropod-Borne Viruses (ACAV) in conjunction with the American Society for Tropical Medicine and Hygiene (ASTMH) has compiled the following comments in reference to the Advance Notice of Proposed Rulemaking (ANPR) request for comments on the biennial review of the HHS and USDA lists of select agents. ASTMH is a worldwide organization of scientists, clinicians, and program professionals whose mission is to promote global health through the prevention and control of infectious and other diseases that disproportionately afflict the global poor. As a special interest committee within ASTMH, ACAV is the only national group devoted exclusively to the study of vector-borne viruses (arboviruses); as such, we are including comments only on the select agent arboviruses including Japanese encephalitis virus, Akabane virus, Bluetongue virus, Vesicular stomatitis virus, enzootic strains of Venezuelan equine encephalitis virus (Subtypes ID and IE) and South American strains of Eastern equine encephalitis virus.

The ACAV supports the comments of the American Society for Microbiology (ASM) regarding tiering of the select agent pathogens. We strongly believe that the highest tier should only include those pathogens which pose the most severe risk to human or animal populations. This would include no arboviral pathogens. The next tier should be limited to pathogens that can be easily disseminated or transmitted from person to person, result in high mortality rates, have the potential for major public health impact, or require special action for public health preparedness. The only arbovirus which fits these criteria is Crimean-Congo hemorrhagic fever virus. All remaining select agent arboviruses should be tiered lower or removed from the select agent list as noted below.

The ACAV respectfully recommends the removal of several viruses from the USDA select agent list. In particular, we believe that Japanese encephalitis virus, Akabane virus, Bluetongue virus, vesicular stomatitis virus, enzootic strains (subtype ID and IE) of Venezuelan equine encephalitis virus, and South American strains of Eastern equine encephalitis virus should be removed. All of these viruses have low epidemic potential combined with low morbidity and mortality. The zoonotic potential of these viruses is equally low with a limited potential for the viruses to spread to a large number of animals or to cross species barriers. Because the likelihood of any large outbreaks or rapid spread of these viruses is extremely small, the economic and trade impact that could arise due to outbreaks of these viruses is equally minimal. All of these pathogens can be readily detected by laboratories trained by the USDA and/or CDC using specific and sensitive tests that can distinguish these pathogens from other agents causing similar clinical signs.

The most serious of these arboviruses, Japanese encephalitis virus (JEV) is a flavivirus present predominantly in Southeast Asia. In this region, there are an estimated 50,000 human cases annually. However, a vaccine is available which virtually eliminates risk to humans and could further limit any possible transmission of the virus if an outbreak were to occur. Note that JEV is not on the CDC select agent roster. Pigs may serve as amplifying hosts, but are not the principal vertebrate reservoirs of the virus. Pigs do not develop encephalitis due to infection with the virus but may abort if infected during pregnancy. However, even in areas where the virus is endemic in Southeast Asia, researchers have demonstrated that JEV infection in pig farms decreases as more modern, large farms are utilized. Furthermore, the vaccine protects the female pigs thus preventing abortions while pregnant and eliminating any economic or trade impact.

Akabane virus is a vector-borne virus distributed in the temperate and tropical regions of Asia, Australia, and parts of Africa and the Middle East yet outbreaks are infrequent and evidence of past infection (antibody prevalence) is low in domestic animals in most endemic areas. Attenuated mutants are frequently recovered from nature indicating that not all lineages of the viruses are even capable of causing animal disease. Transmission of the virus among domestic animals is low as the amount of virus present in oronasal discharge is insufficient to effectively initiate further infections via contact transmission. Vaccines have also been developed for this virus making the possibility of a large outbreak with economic impact relatively minor.

Bluetongue virus is actually a collection of at least 24 distinct viruses within 10 lineages. Most of these do not appear to be associated with clinical illness and it is postulated that the expansion of the viruses will actually reduce the likelihood of disease development as enzooticity is established. This would result in a decrease in trade limitations making select agent status less important.

Vesicular stomatitis virus (VSV) infrequently causes disease in equines, bovines and swine in the U.S. although inapparent infections are more common. Clinically, the disease can mimic FMD; however, advances in the technology and the adoption of diagnostics for VSV can readily distinguish the two pathogens in infected animals. VSV-New Jersey is still endemic in the Southeast, and VSV-Indiana-1 sporadically appears in the Southwest. These types are not designated as select agents. For this reason, we do not feel that exotic types of VSV-Indiana

(Cocal-type 2 and Alagoas-type 3) pose a serious threat to the U.S. and do not warrant select agent status.

The committee also recommends that enzootic subtypes and varieties of Venezuelan equine encephalitis virus (VEEV, subtypes ID and IE) be removed from the select agent list. We believe that inclusion of VEEV subtypes as select agents should be based solely on their ability to cause an epidemic or epizootic following a bioterrorism event. This would require inclusion of only varieties 1AB and 1C VEEV which have been shown to have epidemic/epizootic potential. The reasons for excluding 1D and 1E VEEVs from the select agent list are: 1) No subtype 1D or 1E VEEV have ever caused large equine epizootics; 2) Inclusion of 1D viruses because they might be precursors to 1C viruses is not sufficient for making 1D viruses select agents. Essentially all of this evidence is laboratory based. The possibility of a 1D virus mutating to a 1C virus following a bioterrorism event is unlikely since 1D viruses are unlikely to establish epidemic or epizootic transmission cycles in the US. Natural transmission cycles would likely be needed for any evolution from 1D to 1C to occur in nature; 3) Emergency vaccination of equines with currently approved equine vaccines or humans with IND vaccines (e.g. TC-83) would interdict or greatly dampen a 1D or a 1E epizootic, based on antigenic cross-reactivities of subtype 1 viruses; 4) The currently available humanized or human anti-VEEV monoclonal antibodies that could be produced for emergency use would also have prophylactic, and possibly therapeutic efficacy for all VEEV subtype 1 infections with which they cross react (includes 1D and 1E viruses).

Central and South American strains of Eastern equine encephalitis virus (EEEV) are distinctly different in their geographic, pathogenic, ecologic, genetic, and epidemiologic profiles from North American strains of EEEV. The South American EEEVs are so distinct that it has been proposed that they actually constitute a separate species of virus. The mosquito vectors that transmit the virus in South America are typically limited to tropical forest habitat suggesting there is only focal transmission of these strains of virus. A similar localized pattern of movement exists for the vertebrate reservoirs of these zoonotic strains. Because of the transmission patterns that limit the distribution and epidemic potential of South American EEEV and the lack of pathogenicity of South American strains, we suggest that only North American EEEV be designated as select agents.

ACAV and ASTMH appreciate the opportunity to provide input for the revision of the select agent lists. We hope these comments will be valuable as the lists are reviewed and revised.

Respectfully,

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ACAV Executive Council

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