DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 73

Select Agent: Determination that Vaccine Strain, TC-83(A3G) of Venezuelan Equine Encephalitis Virus (VEEV) is a Regulated Strain of VEEV

AGENCY: Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (HHS).

ACTION: Regulatory determination.

SUMMARY: The Centers for Disease Control and Prevention (CDC), located within the Department of Health and Human Services (HHS), has determined that a modification to the attenuated, excluded strain Venezuelan Equine Encephalitis Virus (VEEV) TC-83 has been shown to increase its virulence. The modified VEEV strain TC-83(A3G) demonstrated increased pathogenicity and lethality. Therefore, the modified VEEV strain TC-83(A3G) is not an excluded strain but is a select agent and is subject to regulation.

DATES: This action is effective [INSERT DATE OF PUBLICATION IN THE FEDERAL REGISTER].

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SUPPLEMENTARY INFORMATION: VEEV is a member of the genus *Alphavirus* in the family *Togaviridae*, and is a small, enveloped virus with a genome consisting of a single strand of positive-sense RNA. VEEV is a mosquito-borne virus that causes encephalitis or encephalomyelitis in all equine species and humans.

The select agent regulations (42 CFR Part 73) established a process by which an attenuated strain of a select biological agent or toxin that does not pose a severe threat to public health and safety may be excluded from the requirements of the select agent regulations. On February 7, 2003, VEEV strain TC-83 was excluded from select agent regulations because mice vaccinated subcutaneously with the VEEV strain TC-83 rapidly developed immunity to subcutaneous or airborne challenge with virulent VEEV (https://www.selectagents.gov/sat/exclusions/overlap.htm). As such, CDC determined that the attenuated strain did not have the potential to pose a severe threat to public health and safety.

As set forth under 42 CFR 73.4(e)(2), if an excluded attenuated strain is subjected to any manipulation that restores or enhances its virulence, the resulting select agent will be subject to the requirements of the regulations. Based on review by subject matter experts, CDC has determined that a modification to the excluded

attenuated VEEV vaccine strain TC-83 has been shown to increase its virulence and pathogenicity. An adenine (A) at position 3 in TC-83 has been shown to contribute to the attenuation of VEEV. In TC-83(A3G), the A has been changed to a guanine (G), which is found in all wild-type isolates of VEEV. The reversion of this nucleotide mutation to the wildtype nucleotide resulted in increased lethality in mice when compared to mice inoculated with the vaccine strain TC-83. Additional data determined that the pathogenic effects of TC-83(A3G) are more pronounced in young mice. As such, the modification of the excluded, attenuated VEEV vaccine strain TC-83 to create VEEV strain TC-83(A3G) restores the virus's virulence and therefore, VEEV strain TC-83(A3G) is subject to 42 CFR Part 73.

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