



DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 73

Select Agent: Modified Junín Virus Vaccine Strain

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

ACTION: Notification of determination.

SUMMARY: The Centers for Disease Control and Prevention (CDC), located within the Department of Health and Human Services (HHS), has determined that a previously excluded attenuated strain, Junín virus vaccine strain Candid No.1, has key attenuating mutations in the glycoprotein envelope at GP1 T168A and GP2 F427I. Revertants at either of these positions have increased pathogenicity and virulence. Therefore, Junín virus vaccine strain Candid No. 1 containing GP1 168T and/or GP2 427F is a select agent and is subject to the select agent and toxin regulations.

DATES: This determination is applicable as of May 3, 2024.

FOR FURTHER INFORMATION CONTACT: Daniel A. Singer, MD, MPH, FACP, Acting Director, Division of Regulatory Science and Compliance, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mailstop H21-4, Atlanta, Georgia 30329, Telephone: (404) 718-2000.

SUPPLEMENTARY INFORMATION: Junín virus is a negative sense, double stranded RNA virus and is the causative agent of Argentine hemorrhagic fever. Junín virus causes chronic infection in *Calomys musculinus*, the Drylands vesper mouse. Humans can become infected upon exposure to infected animals or infected animals' waste. Human-to-human spread is rare but can occur upon contact with an infected person's bodily fluids.

In accordance with the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (Bioterrorism Response Act), HHS regulates biological agents and toxins that have the potential to pose a severe threat to public health and safety (42 U.S.C. 262a(a)(1)). The list of HHS select agents and toxins is provided in the HHS select agent and toxin regulations (42 CFR part 73) and Junín virus, a South American hemorrhagic fever virus, is included as a select agent (42 CFR 73.3(b)).

The HHS select agent and toxin regulations established a process by which an attenuated strain of a select biological agent that does not have the potential to pose a severe threat to public health and safety may be excluded from the requirements of the select agent and toxin regulations (42 CFR 73.3(e)). On February 7, 2003, Junín virus vaccine strain Candid No.1 was excluded from the regulations as it does not pose a significant threat to public health and safety (McKee KT Jr, Oro JG, Kuehne AI, Spisso JA, Mahlandt BG. “Candid No. 1 Argentine hemorrhagic fever vaccine protects against lethal Junín virus challenge in rhesus macaques” *Intervirology*. 1992; 34(3):154-63). This exclusion was granted based on the historically safe use of this strain as a vaccine against Argentine hemorrhagic fever for agricultural workers at risk of occupational exposure in Argentina.

As set forth under 42 CFR 73.3(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. CDC’s Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC), which comprises federal government subject-matter experts from HHS, the U.S. Department Agriculture, the Department of Homeland Security, the Environmental Protection Agency, and the Department of Defense, reviewed the data published in the study, “Restoration of virulence in the attenuated Candid No.1 vaccine virus requires reversion at both positions 168 and 427 in the envelope glycoprotein GPC” (published in the *Journal of Virology*

[<https://doi.org/10.1128/jvi.00112-24>] on March 20, 2024). The ISATTAC concluded that the modified strains (Candid No.1 containing GP1 168T and/or GP2 427F) showed an increased virulence compared to the parental excluded Candid No.1 strain when injected into guinea pigs and huTfR1 mice. CDC concurred with the ISATTAC's assessment and, on May 3, 2024, CDC determined that given the restoration of virulence, Junín virus vaccine strain Candid No.1 containing GP1 168T and/or GP2 427F is a select agent and is subject to the select agent and toxin regulations in accordance with 42 CFR 73.3(e)(2).

Dated: December 18, 2024.

Xavier Becerra,

Secretary,

Department of Health and Human Services.

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