



DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 73

Select Agent Determination concerning *Coxiella burnetii* Phase II, Nine Mile Strain, plaque purified clone 4 with reversion to wildtype *cbu0533*

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

ACTION: Determination.

SUMMARY: The Centers for Disease Control and Prevention (CDC), located within the Department of Health and Human Services (HHS), has determined that an excluded attenuated strain, *Coxiella burnetii* Phase II, Nine Mile Strain, plaque purified clone 4, has, in one instance, been shown to spontaneously mutate when passaged *in vivo*. The resulting mutant, *C. burnetii* Phase II, Nine Mile Strain, plaque purified clone 4 with reversion to wildtype *cbu0533*, has enhanced pathogenicity and virulence. Therefore, *C. burnetii* Phase II, Nine Mile Strain, plaque purified clone 4 with reversion to wildtype *cbu0533* is not an excluded strain but is a select agent and subject to the HHS select agent and toxin regulations.

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

FOR FURTHER INFORMATION CONTACT: Samuel S. Edwin Ph.D., Director, Division of Select Agents and Toxins, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Mailstop H21-4, Atlanta, Georgia 30329, Telephone: (404) 718-2000.

SUPPLEMENTARY INFORMATION: *Coxiella burnetii* is a select agent that is regulated pursuant to the HHS select agent and toxin regulations (42 CFR part 73). *C. burnetii* is a gram-negative intracellular bacterium that causes Q Fever. Q Fever is a zoonotic disease that causes flu-like symptoms in humans, including fever, chills, fatigue,

and muscle pain. Humans become infected when they are in close contact with infected animal fluids and products.

The HHS select agent regulations (42 CFR part 73) 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 regulations. On October 15, 2003, *C. burnetii* Phase II, Nine Mile Strain, plaque purified clone 4 was excluded from HHS select agent regulations as it does not pose a significant threat to public health and safety (<https://selectagents.gov/sat/exclusions/hhs.htm>).

As set forth under 42 CFR section 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. On March 20, 2023, an entity informed CDC of a reversion whereby *C. burnetii* Phase II, Nine Mile Strain, plaque purified clone 4 spontaneously mutated. The *C. burnetii* Phase II, Nine Mile Strain, plaque purified clone 4 with reversion to wildtype *cbu0533* displayed increased pathogenicity and virulence. The entity stated that after the excluded strain was injected into guinea pigs, a spontaneous reversion occurred that resulted in a mutant strain of the agent and the guinea pigs subsequently exhibited elevated fever and weight loss. The genetic mutation that led to the mutant strain was the reversion and restoration of a deletion in the *cbu0533* gene. CDC subject matter experts have determined that this reversion in *cbu0533* restored virulence and pathogenicity. Therefore, *C. burnetii* Phase II, Nine Mile Strain, plaque purified clone 4 with reversion to wildtype *cbu0533* is determined to be a select agent and subject to 42 CFR part 73.

Xavier Becerra

Secretary,

Department of Health and Human Services.

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