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DEPARTMENT OF HEALTH AND HUMAN SERVICES

42 CFR Part 73

Docket No. CDC-2015-0006

RIN 0920-AA59

Possession, Use, and Transfer of Select Agents and Toxins; Biennial Review

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

ACTION: Advance notice of proposed rulemaking and request for comments.

SUMMARY: In accordance with the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, Subtitle A (Department of Health and Human Services) of Title II (Enhancing Controls on Dangerous Biological Agents

and Toxins) of Public Law 107-188 (June 12, 2002) (the Bioterrorism Response Act), the Centers for Disease Control and Prevention (CDC) located within the Department of Health and Human Services (HHS) has initiated the review of the HHS list of biological agents and toxins that have the potential to pose a severe threat to public health and safety. We are considering whether to propose amending the HHS list by removing six biological agents.

DATES: Comments should be received on or before [Insert date 60 days after date of publication in the Federal Register].

ADDRESSES: You may submit comments, identified by Regulation Identifier Number (RIN), 0920-AA59 or Docket Number CDC-2015-0006 in the heading of this document by any of the following methods

- Federal eRulemaking Portal: http://www.regulations.gov. Follow the instructions for submitting comments.

- Mail: Centers for Disease Control and Prevention, Select Agent Program, 1600 Clifton Road NE., Mailstop A-46, Atlanta, Georgia 30329, ATTN: RIN 0920-AAxx.

Instructions: All submissions received must include the agency name and RIN for this rulemaking. All relevant comments received will be posted without change to http://www.regulations.gov, including any personal information provided.

Docket Access: For access to the docket to read background documents or comments received or to download an electronic version of the ANPRM, go to http://www.regulations.gov. Comments will be available for public inspection Monday through Friday, except for legal holidays, from 9 a.m. until 5 p.m. at 1600 Clifton Road, N.E., Atlanta, GA, 30329. Please call ahead to 1-866-694-4867 and ask for a representative in the Division of Select Agents and Toxins to schedule your visit. Please be aware that comments and other submissions from members of the public are made available for public viewing without changes.

FOR FURTHER INFORMATION CONTACT: Robbin Weyant, Director, Division of Select Agents and Toxins, Centers for Disease

Control and Prevention, 1600 Clifton Road N.E., Mailstop A-46, Atlanta, Georgia 30329. Telephone: (404) 718-2000.

SUPPLEMENTARY INFORMATION:

The Preamble to this notice of proposed rulemaking is organized as follows:

I. Public Participation

Interested persons or organizations are invited to participate in this rulemaking by submitting written views,

recommendations, and data. Comments are invited on any topic related to this rulemaking.

In addition, HHS/CDC invites comments specifically as to whether there are biological agents or toxins that should be added or removed from the HHS list of select agents and toxins based on the following criteria, or any other appropriate criteria:

1) The effect on human health of exposure to the agent or toxin;
2) The degree of contagiousness of the agent or toxin and the methods by which the agent or toxin is transferred to humans; and
3) The availability and effectiveness of pharmacotherapies and immunizations to treat and prevent any illness resulting from infection by the agent or exposure to the toxin.
4) The needs of children and other vulnerable populations.

Comments received, including attachments and other supporting materials, are part of the public record and subject to public disclosure. Do not include any information in your comment or supporting materials that you consider confidential or inappropriate for public

disclosure. HHS/CDC will carefully consider all comments submitted in preparation of a proposed final rule.

II. Background

The Bioterrorism Response Act requires the HHS Secretary to establish by regulation a list of biological agents and toxins that have the potential to pose a severe threat to public health and safety. In determining whether to include an agent or toxin on the list, the HHS Secretary considers criteria such as the effect on human health of exposure to an agent or toxin; the degree of contagiousness of the agent and the methods by which the agent or toxin is transferred to humans; the availability and effectiveness of pharmacotherapies and immunizations to treat and prevent illnesses resulting from an agent or toxin; and the needs of children and other vulnerable populations. The current list of HHS select agents and toxins can be found at 42 CFR 73.3 (HHS select agents and toxins) and 42 CFR 73.4 (Overlap select agents and toxins). The list of HHS and Overlap select agents and toxins is available at: http://www.selectagents.gov/Select%20Agents%20and%20Toxins%20List.html.

The HHS Secretary last republished the list of HHS select agents and toxins in the Federal Register on October 5, 2012 (77 FR 61084). The list of HHS select agents and toxins is divided into two sections. The select agents and toxins listed in § 73.3 (HHS select agents and toxins) are those regulated only by HHS under the authority of the Bioterrorism Response Act (42 U.S.C. 262a). The select agents and toxins listed in § 73.4 (Overlap select agents and toxins) are those regulated by HHS under the authority of the Bioterrorism Response Act and regulated by the U.S. Department of Agriculture under the authority of the Agricultural Bioterrorism Protection Act of 2002 (7 U.S.C. 8401).

The Bioterrorism Response Act requires the HHS Secretary to review and republish the list of select agents and toxins on at least a biennial basis. Using government subject matter experts, HHS/CDC conducts the biennial review process in consultation with the HHS/CDC Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC). The ISATTAC recommends changes to the list of HHS select agents and toxins. The ISATTAC is comprised of Federal government employees from CDC, Biomedical Advanced Research and Development Authority (BARDA) within the Office of the Assistant Secretary for

Preparedness and Response, the National Institutes of Health (NIH), the Food and Drug Administration (FDA), the Department of Homeland Security (DHS), the Department of Defense (DOD), the USDA/Animal and Plant Health Inspection Service (APHIS), USDA/Agricultural Research Service (ARS), and USDA/CVB (Center for Veterinary Biologics). Based on the criteria outlined in the Bioterrorism Response Act, the ISATTAC used the following measures in its review: the degree of pathogenicity (ability of an organism to cause disease), communicability (ability to spread from infected to susceptible hosts), ease of dissemination, route of exposure, environmental stability, ease of production, ability to genetically manipulate or alter, long-term health effects, acute morbidity (illness), acute mortality (death), available treatment, status of host immunity, vulnerability of special populations, and the burden or impact on the health care system.

III. Proposed changes to 42 CFR part 73, modifications to the list of select agents and toxins being considered

The purpose of this advanced notice of proposed rulemaking is to seek public comment on the appropriateness of the current list of HHS and Overlap select agents and

toxins. Specifically, we are providing an opportunity for interested persons to submit comments, research data, and other information that will better inform us as to whether: 1) there are any other biological agents or toxins that should be added to the list because they have the potential to pose a severe threat to public health and safety; 2) there are any other biological agents or toxins currently on the list that should be removed because they no longer have the potential to pose a severe threat to public health and safety, and/or 3)the biological agents specifically listed in the following paragraphs should be removed or remain on the list.

HHS/CDC is also seeking comments on the following considerations regarding the list of HHS and Overlap select agents:

A. Coxiella burnetii

Coxiella burnetii causes a disease called Q fever. Q fever is an acute febrile rickettsial disease that varies in severity and duration. Should *Coxiella burnetii* be removed or retained as a HHS select agent? Are there other reasons or research data to support the removal besides the following reasons?

- It is not easily transmitted from person to person (1);
- It has a low mortality rate with antibiotic treatment (2); and
- There is an investigational new drug (IND) vaccine available for at-risk personnel (3).

B. Rickettsia prowazekii

Rickettsia prowazekii causes epidemic typhus. Epidemic typhus is a potentially lethal, louse-borne, disease caused by *R. prowazekii*. Should *Rickettsia prowazekii* be removed or retained as a HHS select agent? Are there other reasons or research data to support the removal besides the following reasons?

- It is readily treatable with antibiotics (4);
- The risk of mass casualties is low because *R. prowazekii* can be treated with a single dose of doxycycline when symptoms are present (4); and
- Transmissibility from person to person is low due to the fact that *R. prowazekii* is usually transmitted via blood, although it can be spread through inhalation of louse feces.

C. *Bacillus anthracis* Pasteur strain

Bacillus anthracis is the bacterium that causes anthrax, an acute disease in animals and humans. However, different strains of *B. anthracis* have different abilities to cause disease. The Pasteur strain, for example, is unable to produce toxic factors and is not considered harmful to humans. Should *B. anthracis* Pasteur strain be removed or retained as an Overlap select agent? Are there other reasons or research data to support the removal besides the following reasons?

- *B. anthracis* Pasteur strain lacks the plasmid that encodes the toxin genes causing disease (6);
- *B. anthracis* Sterne strain, which lacks the plasmid that encodes for the capsule, was excluded from the requirements of the regulations effective on February 27, 2003 (7-8); and
- Historically, the *B. anthracis* Pasteur strain has been retained as a select agent to allow for continued oversight of laboratories in which the accidental (or intentional) combination of this strain with the Sterne strain could occur to produce de novo the wild type phenotype *B. anthracis*. However, a recent study indicates that bacterial transformation of *B. subtilis*

with plasmid DNA (e.g. pXO1 into *Bacillus anthracis* Pasteur strain) is inefficient; indicating that transformation with bacteria such as *B. anthracis* would also be inefficient(9).

D. *Brucella abortus, B. melitensis, and B. suis*

Brucella abortus, B. melitensis, and B. suis bacteria cause brucellosis, a disease that can spread from animals to humans. Should *B. abortus, B. melitensis, and B. suis* be removed or retained as select agents? Are there other reasons or research data to support the removal besides the following reasons?

- *B. abortus* has a low human mortality rate (10);
- *B. abortus, B. melitensis, and B. suis* are readily treatable with antibiotics (10); and
- Human-to-human transmission is extremely rare, and wildlife carriers in the United States often come into contact with humans without significant transmission (10).

IV. References

1. T.J. Marrie. Q fever. In: Marrie TJ, editor. Q fever. Vol. 1. Boca Raton, FL: CRC Press; 1990. (The disease).
2. M. Maurin and D. Raoult. Q fever. Clin Microbiol Rev. Oct. 1999;12(4):518-53.
3. Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th Edition, http://www.cdc.gov/biosafety/publications/bmbl5/BMBL5_sect_VIII_d.pdf.
4. D. Raoult, J.B. Ndihokubwayo, H. Tissot-Dupont, V. Roux, B. Faugere, R. Abegbinni, and R.J. Birtles. Outbreak of epidemic typhus associated with trench fever in Burundi. The Lancet. Aug. 1998; 352 (3125):353-358.
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7. Centers for Disease Control and Prevention, National Center for Emerging and Zoonotic Infectious Diseases "Anthrax Sterne strain (34F2) of Bacillus anthracis,"

http://www.cdc.gov/nczved/divisions/dfbmd/diseases/anthrax_sterne/.

8. Federal Select Agent Program, "Select Agents and Toxins Exclusions," http://www.selectagents.gov/SelectAgentsandToxinsExclusions.html.

9. C. Johnston, B. Martin, G. Fichant, P. Polard, and J.P. Claverys. Bacterial transformation: distribution, shared mechanisms and divergent control. Nature Rev. Microbiol. 2014; 12: 181-196.

10. Center for Food Security and Public Health, "Brucellosis Technical fact sheet," http://www.cfsph.iastate.edu/Factsheets/pdfs/brucellosis.pdf.

Dated: February 5, 2015.

Sylvia M. Burwell

Secretary

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