

# FEDERAL EXPERTS SECURITY ADVISORY PANEL



July 2016

Summary of Findings and Recommendations of the Federal  
Security Advisory Panel on the Biennial Review of the  
Select Agents and Toxins List

**Summary of Findings and Recommendations of the Federal Experts Security Advisory  
Panel on the Biennial Review of the  
Select Agent List**

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**EXECUTIVE SUMMARY**

The mission of the Federal Experts Security Advisory Panel (FESAP) is to make technical and substantive recommendations concerning the appropriate safeguards and security standards for persons possessing, using, or transferring biological select agents and toxins (BSAT). The recommendations shall be commensurate with the risk that such agents or toxins pose to public health and safety, to animal and plant health, and to animal and plant products, including the risk of their use in domestic or international terrorism.

On July 2, 2010, President Obama signed Executive Order 13546 “Optimizing the Security of Biological Select Agents and Toxins,” which created the FESAP and tasked it with addressing policy issues relevant to the security of BSAT.

On January 19, 2016, the Departments of Health and Human Services (HHS) (81 FR 2805) and Agriculture (USDA) (81 FR 2762) published Federal Register Notices of proposed rulemaking regarding the select agents and toxins regulations. The Notices announced that HHS and USDA are considering amending the BSAT list by removing several biological agents.

The FESAP was tasked to consider the following six select agents currently on the BSAT list:

*Coxiella burnetii* (HHS only)<sup>A</sup>  
*Rickettsia prowazekii* (HHS only)  
*Brucella abortus* (Overlap)<sup>B</sup>  
*Brucella suis* (Overlap)  
*Brucella melitensis* (Overlap)

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<sup>A</sup> A HHS-only agent or toxin is listed only at 42 CFR § 73.3, and is regulated only by HHS.

<sup>B</sup> An Overlap agent or toxin is listed at both 42 CFR § 73.4 and 9 CFR § 121.4, and is jointly regulated by HHS and USDA.

*Bacillus anthracis* Pasteur strain (Overlap)

The FESAP was tasked to consider whether the proposal to remove *C. burnetii*, *R. prowazekii*, *B. abortus*, *B. suis*, and *B. anthracis* Pasteur strain should be finalized and whether to amend the HHS select agent list by removing *B. melitensis*, which means this select agent would be identified as “USDA-only” select agent.

The FESAP convened several meetings in April and May 2016 to discuss the proposed amendment of the HHS and USDA BSAT lists. The FESAP heard presentations from a wide range of experts and discussed both technical and policy considerations relevant to the six agents.

In order to address the charge, the FESAP utilized appropriate federal subject matter experts (SMEs) from its members’ departments and agencies. The FESAP drew from the expertise of its membership, information from presentations by several federal department and agency SMEs, and technical input from the Federal Select Agent Program (FSAP) Directors to develop recommendations. The recommendations presented in this report represent the view of the members of the FESAP and not necessarily the views of their respective departments, agencies, or offices.

There were differing perspectives among departmental SMEs regarding characteristics of the agents, host response to the agents, and disease modeling assumptions. These differences of opinion remain unresolved. Additional research studies could provide scientifically-based information to help to address the differing perspectives.

The FESAP recommended de-listing *B. abortus* and *R. prowazekii* from the select agent list:

The following agents did not receive the percentage of votes from FESAP members required to recommend removing these agents from the Select Agent list at this time: *B. anthracis* Pasteur strain, *B. suis*, *B. melitensis*, and *C. burnetii*.

There was disagreement among members of the FESAP regarding whether to de-list or retain the agents. Some departments or agencies did not concur with the majority opinion of the FESAP that resulted in recommendations to de-list *B. abortus* and *R. prowazekii* from the select agent list. Other FESAP members favored de-listing agents that the FESAP ultimately recommended to retain. Some FESAP members thought scientific and technical review of data and classified analyses suggest that there is reasonable doubt about some of the parameters that informed the Intragovernmental Select Agents and Toxins Technical Advisory Committee (ISATTAC) conclusions about risk and therefore the basis for de-listing them. Other concerns, beyond those focused on security, also motivated some departments or agencies to non-concur with the majority opinion of the FESAP.

## BACKGROUND

On June 12, 2002, the "Public Health Security and Bioterrorism Preparedness and Response Act of 2002" (Public Law 107-188) was signed into law. This Act was designed to improve the ability of the United States to prevent, prepare for, and respond to bioterrorism and other public health emergencies. Section 201(a) of the Act amends the Public Health Service Act by adding section 351A (Enhanced Control of Dangerous Biological Agents and Toxins) (42 U.S.C. 262a). This section requires all persons possessing, using or transferring those biological agents or toxins designated by the HHS Secretary as having the potential to pose a severe threat to public health and safety (i.e., HHS BSAT) to register with the HHS Secretary and meet biosafety and security standards and procedures established by the HHS Secretary. The Centers for Disease Control and Prevention (CDC) is designated as the HHS agency responsible for promulgating and implementing regulations and providing guidance concerning HHS select agents and toxins. The HHS select agents and toxins regulations can be found in Part 73 of Title 42 of the Code of Federal Regulations (42 CFR Part 73).

Title II, Subtitle B, Sections 211-213 of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (cited as the "Agricultural Bioterrorism Protection Act of 2002," 7 U.S.C. § 8401) requires all persons possessing, using or transferring those biological agents or toxins designated by the USDA Secretary as having the potential to pose a severe threat to animal or plant health or to animal or plant products (i.e., USDA select agents and toxins) to register with the USDA Secretary and meet biosafety and security standards and procedures established by the USDA Secretary. The USDA select agents and toxins regulations covering threats to animals and animal products can be found at Part 121 of Title 9, Code of Federal Regulations (9 CFR Part 121) and the regulations covering threats to plants and plant products in Title 7, CFR Part 331. The Animal and Plant Health Inspection Service (APHIS) is designated as the USDA agency responsible for promulgating, implementing, and providing guidance on 9 CFR Part 121 and 7 CFR Part 331. APHIS is designated as the USDA agency responsible for promulgating and implementing regulations, as well as for providing guidance on 9 CFR Part 121 and 7 CFR Part 331. The current list of select agents and toxins can be found at 42 CFR §§ 73.3, 73.4, 9 CFR §§ 121.3, 121.4, and 7 CFR § 331.3.

In determining whether to include an agent or toxin on the HHS BSAT list, the HHS Secretary shall consider:

- The effect on human health of exposure to the agent or toxin;
- The degree of contagiousness of the agent or toxin 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 any illness resulting from infection by the agent or toxin; and
- Any other criteria, including the needs of children and other vulnerable populations, that the HHS Secretary considers appropriate.

The HHS Secretary shall also consult with appropriate federal departments and agencies and with scientific experts representing appropriate professional groups, including groups with pediatric expertise (42 U.S.C. 262a (a)(1)(B)(ii)). The Secretary shall review and republish the list biennially, or more often as needed, and shall by regulation revise the list as necessary.

In determining whether to include an agent or toxin on the USDA BSAT list, the USDA Secretary shall consider:

- The effect of exposure to the agent or toxin on animal or plant health, and on the production and marketability of animal or plant products;
- The pathogenicity of the agent or the toxicity of the toxin and the methods by which the agent or toxin is transferred to animals or plants;
- The availability and effectiveness of pharmacotherapies and prophylaxis to treat and prevent any illness caused by the agent or toxin; and
- Any other criteria that the USDA Secretary considers appropriate to protect animal or plant health, or animal or plant products.

The USDA Secretary shall also consult with appropriate federal departments and agencies and with scientific experts representing appropriate professional groups (7 U.S.C. 8401 (a)(1)(B)(ii)). The Secretary shall review and republish the list biennially, or more often as needed, and shall by regulation revise the list as necessary.

On January 19, 2016, HHS and USDA published Federal Register Notices of proposed rulemaking regarding the select agents and toxins regulations ([HHS Notice of Proposed Rulemaking \(81 FR 2805\)](#); [USDA Notice of Proposed Rulemaking \(81 FR 2762\)](#)) with a 60-day comment period. The Notices announced that HHS and USDA are considering amending the BSAT list by removing biological agents, including the following:

- *C. burnetii* (HHS only)
- *R. prowazekii* (HHS only)
- *B. anthracis* Pasteur strain (Overlap)
- *B. abortus* (Overlap)
- *B. suis* (Overlap)
- *B. melitensis* (Overlap)

HHS is considering whether to amend the select agent list by removing *B. melitensis*, which means this select agent would shift from an overlap agent to a “USDA-only” select agent if the agent is removed from the HHS list. The same regulatory oversight would be maintained for the agent.

USDA/APHIS considered whether the following agents should be removed from the list of select agents and toxins.

- *Peronosclerospora philippinensis* (*Peronosclerospora sacchari*) (USDA-Plant Protection and Quarantine (PPQ) only)<sup>C</sup>
- *Phoma glycinicola* (formerly *Pyrenochaeta glycines*) (USDA-PPQ only)
- *Sclerophthora rayssiae* (USDA PPQ only)
- *B. anthracis* Pasteur strain (Overlap)
- *B. abortus* (Overlap)
- *B. suis* (Overlap)

## CHARGE

The FESAP was charged to provide policy and technical input for the biennial review of the BSAT list. The Biological Select Agents and Toxins Interagency Policy Committee (BSAT IPC) provided technical criteria and policy factors to inform the FESAP’s deliberations.

The FESAP was charged to consider technical and policy factors related to the following select agents:

- *C. burnetii* (a bacterium that causes Q fever),
- *R. prowazekii* (a bacterium that causes epidemic typhus),
- *B. anthracis* Pasteur strain (an attenuated strain of the anthrax bacterium),
- *B. abortus* (a bacterium that causes brucellosis),

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<sup>C</sup> A USDA-PPQ-only agent or toxin that threatens plants or plant products, is listed only at both 7 CFR § 331.3, and is regulated only by USDA.

- *B. melitensis* (a bacterium that causes brucellosis), and
- *B. suis* (a bacterium that causes brucellosis).

The FESAP was tasked to consider whether the proposal to remove *C. burnetii*, *R. prowazekii*, *B. abortus*, *B. suis*, and *B. anthracis* Pasteur strain should be finalized and whether to amend the HHS select agent list by removing *B. melitensis*, which means this select agent would be identified as an “USDA-only” select agent.

## METHODS

The FESAP convened several meetings in April and May 2016 to discuss the proposed amendment of the HHS and USDA BSAT lists. The FESAP heard presentations from a wide range of experts and discussed both technical and policy considerations relevant to the six agents.

In order to address the charge, the FESAP utilized appropriate federal subject matter experts (SME) from its members’ departments and agencies. The FESAP drew from the expertise of its membership, information from presentations by several federal department and agency SMEs, and technical input from the FSAP Directors to develop recommendations. The recommendations presented in this report represent the view of the members of the FESAP and not necessarily the views of their respective departments, agencies, or offices.

## FESAP FUNCTION

The duties of the FESAP are solely advisory and shall extend only to the submission of advice or recommendations.

## BIENNIAL REVIEW OF THE BSAT LIST

### HHS Biennial Review

- Subtitle A of Title II, Section 201, of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (42 U.S.C. 262a), requires the HHS Secretary to establish by regulation a list of each biological agent and toxin that has the potential to pose a severe threat to public health and safety.
- CDC has the primary responsibility for implementing the provisions of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 within HHS.
- In determining whether to include an agent or toxin on the list, the HHS Secretary considers broad categories:
  - The effect on human health of exposure to an agent or toxin;
  - The degree of contagiousness of the agent or toxin 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
  - Any other criteria including the needs of children and other vulnerable populations.
- Overlap select agents and toxins are those biological agents and toxins that have been independently determined by HHS to have the potential to pose a severe threat to human health and independently determined by USDA to have the potential to pose a severe threat to animal health or animal products. Overlap select agents and toxins are subject to regulation by both HHS and USDA.
- The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 requires that the HHS Secretary consult with federal departments and agencies.

- The Public Health Security and Bioterrorism Preparedness and Response Act of 2002 requires that the HHS Secretary review and republish the HHS list of select agents and toxins on at least a biennial basis.
- The HHS Secretary last republished the HHS BSAT list in the Federal Register on October 5, 2012.
- On February 27, 2015, HHS published in the Federal Register (80 FR 10656) an advance notice of proposed rulemaking (ANPRM) and request for comments in order to announce the HHS intention to review the BSAT list. HHS solicited comments regarding potential additions and deletions from the list of select agents and toxins for 60 days ending April 28, 2015.

### **USDA Biennial Review**

- Subtitle B of Title II of the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 (the “Agricultural Bioterrorism Protection Act of 2002”) provides for the regulation of certain biological agents that have the potential to pose a severe threat to animal health, to plant health, or to animal and plant products.
- APHIS has the primary responsibility for implementing the provisions of the Agricultural Bioterrorism Protection Act of 2002 within USDA.
  - Veterinary Services (VS) select agents and toxins are those biological agents and toxins that have been determined to have the potential to pose a severe threat to animal health or animal products.
  - PPQ select agents and toxins are those biological agents and toxins that have the potential to pose a severe threat to plant health or plant products.
- Overlap select agents and toxins are those biological agents and toxins that have been independently determined by HHS to have the potential to pose a severe threat to human health and independently determined by USDA to have the potential to pose a severe threat to animal health or animal products. Overlap select agents and toxins are subject to regulation by both HHS and USDA.
- In determining whether to include an agent or toxin on the list, the USDA Secretary considers broad categories:
  - The effect of exposure to the agent or the toxin on animal and plant health, and on the production and marketability of animal or plant products;
  - The pathogenicity of the agent or the toxin and the methods by which the agent or toxin is transferred to animals or plants;
  - The availability and effectiveness of pharmacotherapies and prophylaxis to treat and prevent any illness caused by the agent or toxin; and
  - Any other criteria that the Secretary considers appropriate to protect animal or plant health, or animal or plant products.

- The Agricultural Bioterrorism Protection Act of 2002 requires that the USDA Secretary review and republish the USDA list of select agents and toxins on at least a biennial basis.
- The Secretary is also required to consult with federal departments and agencies in determining whether to include an agent or toxin on the list.
- The USDA Secretary last republished the USDA BSAT list in the Federal Register on October 5, 2012.
- On February 27, 2015, USDA published in the Federal Register (80 FR 10627) an advance notice of proposed rulemaking (ANPRM) and a request for comments in order to announce the USDA intention to review the BSAT list. USDA solicited comments regarding potential additions and deletions from the list of select agents and toxins for 60 days ending April 28, 2015.

## **FESAP RECOMMENDATIONS**

After careful consideration of the technical and policy factors, the FESAP developed recommendations related to the proposed removal of six agents from the select agent list.

### **Recommendation to De-list Biological Agents From the Select Agent List**

The FESAP recommended de-listing the following agents from the select agent list:

#### *B. abortus*

*B. abortus* is endemic in wildlife (bison and elk) in the western United States. It can spread from wildlife to cattle, impacting agriculture and commerce. The FESAP recommended de-listing *B. abortus* from the select agent list due to the following factors:

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

- Maintaining *B. abortus* as a select agent severely impacts the ability of USDA to develop a vaccine for wildlife populations, and to conduct the *Brucella* eradication and control programs efficiently.

### *R. prowazekii*

*R. prowazekii* causes epidemic typhus. Epidemic typhus is a potentially lethal, louse-borne, disease. The FESAP recommended de-listing *R. prowazekii* from the select agent list due to the following factors:

- *R. prowazekii* is readily treated with antibiotics.
- The risk of mass casualties is low because *R. prowazekii* can be treated with a single dose of doxycycline when symptoms are present.
- Transmissibility from person-to-person is low due to the fact that *R. prowazekii* is usually transmitted by infected human body lice via contamination of the bite site with louse feces, although it can be spread through inhalation of louse feces.
- The agent has poor environmental stability.
- It is difficult to grow and purify substantial quantities of this agent *in vitro*.

### **Recommendation to Retain Biological Agents on the Select Agent List**

The following agents did not receive the percentage of votes from FESAP members required to recommend removing these agents from the Select Agent list at this time:

#### *B. anthracis Pasteur strain*

*B. 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. To cause anthrax disease, a strain must contain two plasmids: plasmid pXO1 encoding the toxin genes, and plasmid pXO2 encoding the capsule genes. The Pasteur strain contains pXO2, but lacks pXO1, making it unable to produce toxic factors. Therefore, the Pasteur strain is not considered harmful to humans. Although *B. anthracis* Pasteur strain does not cause disease, the FESAP recommended retaining it on the select agent list to:

- Maintain security control and prevent restricted experiments and potential misuse;
- Address concerns about the potential for sampling confusion if both *B. anthracis* Pasteur strain and *B. anthracis* Sterne strain (which contains pXO1 but lacks pXO2) were released in combination; and
- Prevent introduction of the plasmid pXO2 from the *B. anthracis* Pasteur strain into the commercially-available live-attenuated *B. anthracis* Sterne strain, which is used as an

agricultural vaccine strain in the United States. 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 the Pasteur strain with the Sterne strain could occur to produce *de novo* the wild type phenotype *B. anthracis*. A recent study indicates that bacterial transformation of *B. subtilis* with plasmid DNA (e.g., transferring pXO1 into *B. anthracis* Pasteur strain) is inefficient, indicating that transformation with bacteria such as *B. anthracis* would also be inefficient. Concerns remain over the possibility of transformation.

#### *B. suis* and *B. melitensis*

*B. melitensis* and *B. suis* bacteria cause brucellosis, a disease that can spread from animals to humans. *Brucella* species were major agents in both the U.S. and Soviet biological weapons programs. Although it is acknowledged that *Brucella* species have a low mortality rate in humans and are readily treatable with antibiotics, the FESAP recommended retaining *B. melitensis* and *B. suis* on the select agent list based on the bacteria's:

- Ease of growth and production;
- High infectivity via the aerosol route;
- Low infectious dose; and
- Potential for mass disruption.

*Brucella* species, particularly *B. suis*, can persist in soil, outdoor building materials, untreated water, paper, and host carcasses, organs, and blood. *B. melitensis* is a foreign animal disease agent not currently found in the United States. Therefore, the effect of exposure to the agent on animal health, and on the production and marketability of animal products, warrants a recommendation to retain *B. melitensis* as a select agent.

#### *C. burnetii*

*C. burnetii* causes a disease called Q fever. Q fever is an acute febrile rickettsial disease that varies in severity and duration. Although Q fever is not easily transmitted from person-to-person and has a low mortality rate with antibiotic treatment, the FESAP recommended retaining *C. burnetii* as a select agent.

The recommendation to retain *C. burnetii* on the HHS list of select agents and toxins is based on multiple factors, including its:

- Environmental stability;
- Ease of transmission to humans;
- Extremely low inhalational infectious dose;

- High morbidity;
- Ability to incapacitate large numbers of people and potential for mass disruption; and
- Prior history of weaponization and extensive development of this agent as an incapacitating weapon.

### **Rationale for Dissenting From the FESAP Recommendation**

There was disagreement among members of the FESAP regarding whether to de-list or retain the agents. Some departments or agencies did not concur with the majority opinion of the FESAP that resulted in recommendations to de-list *B. abortus* and *R. prowazekii* from the select agent list. Other FESAP members favored de-listing agents that the FESAP ultimately recommended to retain. Some FESAP members thought scientific and technical review of data and classified analyses suggest that there is reasonable doubt about some of the parameters that informed the ISATTAC conclusions about risk and therefore the basis for de-listing them. Some of the non-concurring departments and agencies also had concerns beyond the security focus that motivated other departments' or agencies' votes. Some of the rationales for dissention from the FESAP recommendation in this report are summarized below:

- Although the mortality rate of brucellosis is low (approximately one percent), some concerns remain regarding these agents due to their relative ease of growth. In addition, some believe that *B. abortus* may still be a hazard to abattoir and meatpacking workers, large-animal veterinarians, and laboratory workers. While natural disease is easily treated with available antibiotics, chronic, system-wide symptoms can last as long as the infection persists. It is difficult to determine exactly when an exposure happened, especially among at-risk workers. Some of the objections to removing *Brucella* species from the BSAT list could be overcome if a mechanism were implemented to ensure that institutions and individuals with regular access to isolated, identified cultures of *B. abortus* or *B. suis* were subjected to background investigations and maintained minimum standards of security.
- Concerns remain about the low infectious dose of *R. prowazekii*, its considerable mortality rate (10-40 percent without treatment), increasing mortality with age, and potential for unrecognized aerosol exposures that could lead to infections that might not be treated effectively in time to prevent significant health effects or death. The inhalational infectious dose of the organism for humans is unknown and uncertain. Some objections to removing this agent from the BSAT list could be overcome with additional experimental data conclusively showing a higher infectious dose in a non-human primate model with pathology similar to that seen in humans.
- Although the mortality rate of Q-fever is low (approximately one percent), concerns remain about the low inhalational dose of *Coxiella burnetii*.

- The Pasteur strain has been historically controlled as a Select Agent to prevent unvetted individuals from acquiring both required virulence plasmids and being able to recreate a virulent strain of *B. anthracis*. Some concerns remain that removing the Pasteur strain of *B. anthracis* from the BSAT list increases the risk that an unknown and untrusted individual could acquire a virulent strain of *B. anthracis*.
- *C. burnetii* and *Brucella* species were researched and developed for use as incapacitating agents by the historical offensive biological weapons programs of the United States and the former Soviet Union. *R. prowazekii* was researched by the historical offensive biological weapons programs of Japan, the United States, and the former Soviet Union.
- All six of the agents proposed for removal from the BSAT list are controlled by the United Kingdom and Canada in their versions of select agents lists—Schedule 5 of the Anti-Terrorism, Crime and Security Act, and Schedule 3 of the Human Pathogens and Toxins Act, respectively. Japan also maintains five of the six proposed agents, with the exclusion of *C. burnetii*, in its Pathogen Control Scheme amendment to the Infectious Disease Control Act. France has a comprehensive list of human pathogens, and all six are included at the second highest restriction level. Control of these disease agents by other nations varies widely.
- Concern with voting as an agreed method of decision-making for developing the FESAP recommendations, as well as concern with the 60 percent majority vote required for the FESAP to recommend removal of agents from the BSAT list.
- Three of the four agents that the FESAP recommended maintaining on the list were actually voted to be removed by 50 percent or more of voting FESAP members (but fewer than the 60 percent majority required to recommend removal). Concerns remain about the detrimental impacts to scientific research and public health preparedness that accrue from continuing to maintain pathogens on the select agent list that many scientific and policy experts believe can be removed without compromising safety or security.