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March 30, 2015

Dr. Gerald L. Epstein
Deputy Assistant Secretary for Chemical, Biological, Radiological, and Nuclear
Policy
U.S. Department of Homeland Security
245 Murray Lane, SW; Mail Stop #0315
Washington, DC, 20528

[Submitted Via Electronic Submission to SAReview@hq.dhs.gov]

Re: Request for Public Comment: Impact of Select Agent Regulations

Dear Dr. Epstein:

The Infectious Diseases Society of America (IDSAs), representing over 10,000 infectious diseases physicians and scientists devoted to patient care, disease prevention, public health, education, and research in the area of infectious diseases (ID), is pleased to comment on the Office of Science Technology Policy's (OSTP) request for information (RFI) concerning the impact of select agent regulations (SAR).

IDSAs strongly believes that research conducted with select agents and toxins require the highest level of biosafety and biosecurity measures to mitigate their risk to public health and safety. The SAR were developed to ensure that this vital research is indeed performed in a safe and responsible manner. However, we are also concerned that the SAR, as currently conceived, unduly restricts the public health community's capacity to quickly respond to emerging ID threats; ID researchers' efforts to advance our scientific understanding of select agent and toxin list (SATL) pathogens; and medical countermeasure (MCM) developers' ability to ensure the availability of lifesaving vaccines, therapeutics, and diagnostics. Our comments are organized with reference to select questions proposed in the RFI, as applicable.

Question # 9: Describe how the overall costs of the SAR are or are not appropriately balanced with their overall benefits.

The overall U.S. government costs to inspect laboratories registered with the Select Agent Program (SAP) is more than \$2 million annually, with part of the cost burden due to duplicative inspections by more than one government department. Additionally, the direct personnel costs to each inspected entity are approximately \$15,000 per inspection¹. The initial capital outlay to bring a laboratory into SAP compliance is unknown as is the annual cost of maintaining that compliance. The direct and indirect costs, in governmental, academic and private sector laboratories will invariably result in reduced productivity. These expenses are not reimbursed by the government and must be underwritten by the inspected entity, making

participation in research and development with a SAP covered agent untenable to some researchers. This can have a critical impact on the advancement of scientific knowledge about the pathogen as well as delaying the development of needed MCMs. Therefore, we believe the overall costs of implementing the SAR/SAP could be lessened by decreasing the scope of pathogens listed (see Recommendation # 1 below).

Question # 10: Is designing the regulations around a list of agents advantageous or disadvantageous?

The current design around a list of agents is disadvantageous based upon its scope. IDSA affirms that the use of a threat list like the SATL causes undue attention to be directed to specific agents at the cost of a lack of scrutiny to other possible biothreats. Within the SATL itself, its broad scope incurs heavy regulatory burden on lower-risk agent research while hindering focused oversight towards agents whose research may pose a higher risk to the public. The process of select agent listing and de-listing also remains inconsistent and opaque, creating both uncertainty and undue regulatory burden for SATL efforts. In some cases, the rationale for why certain agents have been included has not been publically disseminated. A transparent, standardized review process examining the risk and benefit of research for agents is sorely needed.

Inclusion in the SATL is also primarily based on the taxonomy of an organism, a problematic approach given that recent genetic surveys have revealed uncertain boundaries between microbial species historically considered separate. For example, *Bacillus cereus* is difficult to distinguish from its close relative *Bacillus anthracis*, and can cause anthrax-like disease when it obtains the required virulence factors. This raises the question of whether these strains are distinct, or simply variations of the same species. The SATL inclusion criteria should be updated to more accurately delineate what agents fall under SAR.

IDSA Recommendation # 1: Re-evaluate the scope of the SATL and improve the consistency of listing and de-listing through a standardized, transparent review process.

In certain cases, a rapid public health response to combat a SATL threat may require an alteration or suspension of SAR. In November 2004, the investigation responding to a novel US outbreak of soybean rust was significantly hindered because the causative agent, *Phakopsora pachyrhizi*, was on the SATL. As a result, the U.S. Department of Agriculture moved to remove the agent from the SATL. In anticipation of future outbreaks of novel and emerging infections like ongoing 2014-2015 Ebola Virus Disease (EVD) outbreak in West Africa, measures should be in place to quickly modify the SAR as needed to address critical public health needs.

IDSA Recommendation #2: Develop a simple and rapid process by which the Secretary of HHS could suspend the SAR either in toto or with regard to a specific pathogen as in the case of EVD.

The SAR, as currently drafted, does not have a standardized approach to distinguish between high and low virulence isolates of a given select agent, such as attenuated vaccine and research strains. While the SATL has taken steps to discern between such strains, decisions are made on

¹ Government Accountability Office. Overlap and Duplication: Federal Inspections of Entities Registered with the Select Agent Program. GAO-13-154 Jan 2013.

a case-by-case basis that requires researchers to argue that their lower-risk agent warrants exemption. This could have the serious unintended consequence of delaying pandemic responses by weeks to months.

For example, highly pathogenic H5N1 influenza (HPAI) virus can be predictably attenuated by standard genetic methods for use in vaccine development, with 27 such attenuated strains having been developed and distributed by the World Health Organization thus far. However, if a novel HPAI pandemic occurs, its attenuated vaccine strain would remain under SAR until research is conducted to verify it is not a select agent, creating lengthy delays. Should manufacturers move forward with vaccine production while the strain remains on the SATL, they would be forced to “harden” manufacturing facilities normally used to make seasonal influenza vaccines, a cost-prohibitive measure with no commensurate benefit for public safety.

IDSA Recommendation # 3: Ensure that rapid development of vaccines and other medical countermeasures is not compromised by SATL.

Question # 12: Are the SAR appropriately configured to accommodate changes in science and technology?

The SAR primarily act to lower risk to the public by criminally prosecuting those with unauthorized access to select agents and toxins. Unfortunately, the rapid pace of molecular biology has significantly lowered barriers to researchers using recombinant engineering to increase an organism’s virulence or synthesizing a select agent organism *de novo*. With the recent efforts to improve disclosure and sharing of research data, the information needed to conduct this research is easier than ever to acquire. While the SAR primarily addresses biosafety risks, this misuse of molecular techniques raises large biosecurity risks that the SAR is not currently able to address.

IDSA Recommendation# 4: Design regulations to address concerns about recombinant engineering.

We welcome the OSTP’s careful review of the SAR and its commitment to improving them to appropriately balance the benefits of SATL research against their public health risk. Should you have any questions about these comments, please contact Greg Frank, PhD, IDSA Program Officer for Science and Research Policy, at gfrank@idsociety.org or 703-299-1216.

Sincerely,

A handwritten signature in purple ink that reads "Stephen B. Calderwood". The signature is written in a cursive, slightly slanted style.

Stephen B. Calderwood, MD, FIDSA
IDSA President