IDSA Headquarters
1300 Wilson Boulevard
Suite 300
Arlington, VA 22209
TEL: (703) 299-0200
FAX: (703) 299-0204
EMAIL ADDRESS:
info@idsociety.org
WEBSITE:
www.idsociety.org

IDSA
Infectious Diseases Society of America

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[By Electronic Submission to www.regulations.gov]

Robbin Weyant, PhD
Director, Division of Select Agents and Toxins
Centers for Disease Control and Prevention
1600 Clifton Road, NE; Mailstop A–46
Atlanta, Georgia 30333

Re: RIN 0920–AA34: Possession, Use, and Transfer of Select Agents and Toxins; Biennial Review; Proposed Rule

To whom it may concern:

The Infectious Diseases Society of America (IDSA) is pleased to have this opportunity to comment on the Centers for Disease Control and Prevention's (CDC) proposed rule entitled, "Possession, Use and Transfer of Select Agents and Toxins: Biennial Review" ("Proposed Rule"). IDSA represents nearly 10,000 infectious diseases physicians and scientists devoted to patient care, prevention, public health, education, and research in the area of infectious diseases.

The need for enhanced biosafety in the conduct and in support of research involving special agents and toxins is clear—biosafety must be mandatory for all involved in such research. The issue of biosecurity also is an important matter, one in which the realistically achievable biosecurity must be weighed alongside the amount of effective and timely research that must be conducted.

Background

CDC published the Proposed Rule in accordance with the Public Health Security and Bioterrorism Preparedness and Response Act of 2002 requiring a biennial review of the list of select agents and toxins, as well as in response to Presidential Executive Order (EO) 13546, July 2, 2010, entitled "Optimizing the Security of Biological Select Agents and Toxins in the United States". EO 13546 called for:

- Designating a subset of select agents and toxins, so-called "Tier 1", which present the greatest risk of deliberate misuse with the greatest potential for mass casualties or devastating impact on the U.S. economy, critical infrastructure or public confidence;
- Exploring options for graded protection for Tier 1 agents and toxins to permit tailored risk management practices;
- Considering reducing the overall number of select agents and toxins on the current Select Agents and Toxins List (SATL); and
- Establishing the Federal Experts Security Advisory Panel to advise the Department of Health and Human Services (HHS) and the United States

Department of Agriculture (USDA) on these matters, as well as to establish suitability standards for those with access to select agents and toxins and physical and information security standards for these Tier 1 agents and toxins.

IDSA appreciates the aspects of the Proposed Rule that provide greater clarification for managing select agents and toxins. However, there are a number of issues that are not adequately addressed in the Proposed Rule. The Society recommends that CDC and HHS:

- Reconsider the overarching regulatory impact on this essential research community, including administrative burden, financial resources and morale;
- Consider standardizing the process by which select agents are listed and de-listed to avoid inconsistencies and arbitrariness;
- Consider the neutralizing impact of rapid advances in molecular and cellular biology upon the biosecurity aspects of the Proposed Rule;
- Consider the need to provide guidance towards managing timely and appropriate study of new agents and toxins; and
- Consider removing all well-accepted vaccine strains of select agents from the SATL.

Reconsider the overarching regulatory impact on this essential research community

The Proposed Rule will add substantial administrative and technical burdens on the scientific and supporting workforce. As an example, on page 61219, CDC proposes to add, on top of existing regulations, additional forms which are estimated to take 10, 947 total hours annually, or roughly 28.4 hours per respondent annually. This equates to time not spent on research critical to our nation's security. Furthermore, no mention is made of any incremental administrative funding to support such form-filling, which suggests that the burden lies directly upon the people doing and supporting this research.

Other examples of the measures proposed include creation of detailed record-keeping processes and designating Responsible Officials and Alternate Responsible Officials at local institutions for such record-keeping, with new mandatory training with annual refreshers (page 61219). It is not clear what qualifications such responsible officials or their alternates will require and such positions create new challenges for which academic laboratories have no experience or capability. Additionally, the Proposed Rule recommends creation of an occupational health monitoring system to ensure the suitability of individuals, based on their health profile, to Tier 1 access (page 61217), as well as shortening re-approval of individual access to Tier 1 agents and toxins from every 5 years to every 3 years (page 61215), creating additional administrative burden on institutions.

CDC also proposes to add a requirement that the security plan include procedures for the Responsible Official to immediately notify the Federal Bureau of Investigation (FBI) of suspicious activity, including through "network connectivity monitoring", that may be interpreted as criminal in nature and related to the entity, its personnel, or its select agents or toxins (page 61215). The vagueness of such terms as "suspicious activity", and requiring local institutions to probe individuals via "network connectivity monitoring" and other methods, stands to create an atmosphere of paranoia, mistrust, and suspicion. Network security to prevent intrusion and infiltration is entirely appropriate. However, when these new requirements are added on to the numerous existent security measures within each laboratory, it is easy to imagine a much slower pace of research, as well as the possibility of discouraging talented researchers. It is difficult to

imagine how research could be conducted in an emergency setting such as during a bioterror attack or a new emerging infectious disease outbreak.

IDSA strongly supports the concept of securing select agents and toxins, as well as the corresponding research and support, in a uniform and regulated manner. We also recognize that the need for processes leading to successful prevention, or at least attribution, of misuse and crimes is important. However, currently established scientists who want to conduct meaningful scientific research with select agents and toxins critical to our national security are very likely to be excessively burdened by the scope of the Proposed Rule, possibly incenting them to leave this field of study. Further, these same burdens will likely serve as a barrier to new scientists interested in these areas. The Proposed Rule suggests that these changes will not have a significant impact on the personnel to which this is directed (e.g., page 61219); we do not believe the real impact has been fully appreciated and appropriately assessed.

Consider standardizing the process by which select agents are listed and de-listed to avoid inconsistencies and arbitrariness

Identifying threat lists both creates the illusion that such lists define a boundary to the biothreat problem and focuses undue amounts of resource and attention on specific agents. It has been argued that such lists may hinder and degrade security through inappropriate attention to listed agents, as opposed to other possible threats. Nonetheless, this has been mandated and needs addressing. In order for EO 13546 to have a positive effect, we agree that there should be a major overall reduction in the length of the list. However, removal of six agents and addition of two, for a net reduction of four (from a total of more than 80) from the SATL, while identifying 11 Tier 1 select agents and toxins, does not constitute a meaningful change in the scope of coverage. Maintaining such a large list prevents any possible gain in focus or re-distribution of resources and attention towards the top tier.

Moreover, managing all such select agents and toxins under expanded regulatory scrutiny not only increases the local institution's burden, without providing any incremental resources, it also increases barriers to conducting research into natural infectious diseases associated with the listed agents and toxins. As a specific example, Drs. Arturo Casadevall and David Relman have published their concerns that the ten-fold greater number of toxin-related vs. capsule-related *Bacillus anthracis* articles is almost certainly due to the fact that capsule-related research must be carried out within the SATL-associated regulations (*Nat Rev Microbiol* 2010;8:149-54). They write, "If, in fact, these regulations are hindering capsule-related research, such hindrance has direct biodefense and preparedness implications, given that capsule components have been shown to be effective vaccines."

Other potential concerns arise: it is not clear whether the increasing use of botulinum toxins (e.g., BoTox) for numerous human therapeutic uses might also be covered by the Proposed Rule. Another serious concern is that the additional attention generated by the new top tier of 11 will come at the cost of resources and energies diverted from research in other important areas. Close study of the notice does not reveal any consistent decision pattern for the retention of certain agents, other than preserving as large a list as possible for reasons related to biosecurity (but see next paragraph).

Consider the neutralizing impact of rapid advances in molecular and cellular biology upon the biosecurity aspects of the Proposed Rule

The fundamental need for creating a large list of select agents and toxins, as well as a smaller Tier 1 list is built in part on the premise that access thus will be denied to those outside the affected institutions, and misuse and crimes will be prevented from being committed by personnel within these institutions. In light of many factors not within the purview of the Proposed Rule, the degree to which the proposed regulations' effectiveness actually adds to our national security may not be so clear. Many of these select agents and toxins exist in the wild around the world and within the U.S. "Virus hunters" regularly make the news as they search for new pathogens in Africa and other places. Major advances over the past few years in synthetic DNA/RNA chemistry and reverse recombinant engineering using novel molecular biology techniques have made possible the creation *de novo* of existent, chimeric or possibly new life forms from inanimate starting materials. The internet also has resulted in dissemination of these advances far faster than could have been conceived a decade ago. Our concern here is that while biosafety is well-covered within the Proposed Rule, relying primarily on the SATL for biosecurity should be viewed akin to closing barndoors after some of the horses have escaped.

Consider providing guidance towards managing timely and appropriate study of new agents and toxins

Interestingly, while the SATL is actually growing as new agents and toxins are discovered, the Proposed Rule does not discuss how to manage new agents and toxins as they are detected. These agents could result from natural or bioterror-associated sources. Even without bioterror-related events, the probability of new agents and toxins being identified is high—and the American people deserve a system that can respond rapidly to assess the impact of these new agents and toxins. Our related concern is that the administrative burden created by the Proposed Rule may in fact slow down information flow, especially in an emergent setting (e.g., a highly contagious, previously unknown viral outbreak). In the interest of ensuring appropriate and timely research, should an unknown agent or toxin emerge, having an overarching approach toward managing this challenge should be considered as important as any list of known agents and toxins.

Consider removing all well-accepted vaccine strains of select agents from the SATL

The SATL already exempts several vaccine strains, especially those that are licensed in the U.S. However, vaccine strains that have been developed and well-accepted in other countries are treated in the same manner as the fully virulent select agent. For example, the Pasteur vaccine strain of *B. anthracis* is a select agent subject to the same restrictions as wild-type strains. By de-listing vaccine strains, the CDC will make available numerous new strains that will allow important basic research to be done with attenuated organisms outside of the very cumbersome SATL regulatory framework.

CONCLUSION

IDSA appreciates the CDC undertaking this important review of the Select Agent regulations. Key issues, including the impact of regulations on the individuals involved; the pace of advances in molecular biology, synthetic DNA, and new agent/toxin discoveries; and the probabilities that new agents and pathogens can be expected to emerge at any time, should be included in any decision-making regarding the content and implementation of the Proposed Rule. It is otherwise

simply too easy to keep adding more select agents and toxins to an already large list, as it is to keep adding new regulations around the list.

Thank you for the opportunity to comment on this Proposed Rule. Should you have any questions about these comments, please contact Audrey Jackson, PhD, IDSA's program officer for science and research, at ajackson@idsociety.org or 703-299-1216.

Sincerely,

Thomas G. Slama MD

Thomas G. Slama, MD, FIDSA
President