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DEPARTMENT OF HEALTH & HUMAN SERVICES

Laboratory of Intracellular Parasites
Rocky Mountain Laboratories
National Institute of Allergy and Infectious Diseases
National Institutes of Health
903 South 4th Street
Hamilton, MT 59840

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Centers for Disease Control and Prevention
Division of Select Agents and Toxins
1600 Clifton Rd, MS A-46
Atlanta, GA 30333

RE: Comments on changes to the list of Select Agents and Toxins

I am writing in response to the request for comments on changes to the list of Select Agents and Toxins as announced in the Federal Register/Vol. 75, No. 139/42363. I am Ph.D. microbiologist with over 25 years of experience with biosafety level-3 bacteria including the Select Agent pathogen *Coxiella burnetii.* I am currently vice chair of the NIAID's Rocky Mountain Laboratories Institutional Biosafety Committee. It is from this perspective that I recommend that *Coxiella burnetii*, the agent of human Q fever, be removed from the list of Select Agents.

The six criteria used by the HHS Secretary when listing a pathogen as a Select Agent are 1) the effect on human health upon exposure to the agent or toxin, 2) the degree of contagiousness of the agent, 3) the methods by which the agent or toxin is transferred to humans, 4) the availability and effectiveness of pharmacotherapies and immunizations to treat and prevent illnesses resulting from the agent or toxin, 5) the potential for the agent or toxin to be used as a biological weapon, and 6) the needs of children and other vulnerable populations.

Q fever typically manifests as a self-liming flu-like illness. Nearly 50% of infections result in asymptomatic seroconversion. In rare instances, chronic infections can occur. Acute Q fever generally resolves without long-term sequelae, even in the absence of antibiotic therapy (doxycycline). Chronic infections are now effectively treated with combination doxycycline-hydroxychloroquine therapy. Q fever is not considered contagious; person-to-person transmission is extremely rare. Both acute and chronic infections are effectively treated with antibiotics. Whole cell killed vaccines are 100% efficacious although they are currently not licensed in the US. Q fever is transmitted by aerosol; however, the threat posed by *C. burnetii* as a biological weapon it is unclear. The "weaponization" of *C. burnetii* referenced in the literature was simply aerosolization of yolk sac slurries from infected eggs. Immunocompromised states (e.g., pregnancy) represent risk factors as does heart valve abnormalities for chronic Q fever (4)

Because Q fever is not contagious, effectively treated with antibiotics, and generally a self-limiting infection with potential control by vaccination, I believe it is questionable

whether *C. burnetii* should remain on the Select Agent list. The ubiquitous nature of *C. burnetii* should also be considered in discussions of regulation. In fact, the extensive environmental reservoirs of the agent are one reason APHIS, USDA in 2008 chose to no longer regulate *C. burnetii*. For example, in the Rocky Mountain region, 44% of random environmental samples (post offices, stores, schools, etc.) contain *C. burnetii* DNA, and cultures can be started from this material (2). Furthermore, 42% of unpasteurized (raw) milk samples acquired from 12 states contain viable *C. burnetii* (3). Finally, Q fever seroprevalence rates can exceed 20% in some populations (5). Thus, regulatory oversight by the Select Agents program, while burdening well-meaning scientists, does nothing to prevent the easy acquisition of *C. burnetii* from environmental sources.

The ready availability of *C. burnetii* from the environment also makes one question the effectiveness and procedures for maintaining inventories, considered one of the more cumbersome Select Agent rules. In testimony before congress last year on the Federal Oversight of High Containment Biolaboratories, Dr. Ronald Atlas, past president of American Society for Microbiology, stated:

"The select agent regulations should be revised to change the requirements for inventory of vials of select agents. Given the intrinsic biological properties of microbes, the actual counting of vials is meaningless, ineffective, misleading and should not be required. Rather, laboratories should be accountable for which agents they possess and where these agents are located."

I strongly agree with Dr. Atlas. Discussions with colleagues indicate a growing reluctance to embark on projects that will significantly increase vial counts, such as characterization of large isolate collections and generation of mutant libraries. Thus, inventory requirements are having the unintended consequence of pushing investigators towards working with attenuated, exempt strains, where inventories are not required. Advances in Q fever forensics, diagnostics, and strain-specific virulence factors are being sacrificed as a result.

I believe that biosecurity is important. Physical security, restricted access, adequate biosafety laboratories and practices, FBI background checks, and adequate training are necessary procedures. However, the specific rules and regulations of Select Agent program should be restricted to Category A agents capable of rapid spread and high morbidity and mortality. This is not the case with *C. burnetii.* Indeed, the Netherlands is currently successfully managing a large outbreak of dairy goat-caused Q fever (>3000 cases) without public panic and socioecomonic crises (1).

Sincerely,

Robert A. Heinzen, Ph.D.
Chief and Senior Investigator
Coxiella Pathogenesis Section
Laboratory of Intracellular Parasites
Rocky Mountain Laboratories, NIAID, NIH
Hamilton, Montana
59840

phone: 406-375-9695
email: rheinzen@niaid.nih.gov

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