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IDSA
Infectious Diseases Society of America

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Tick-Borne Disease Working Group
Office of the Assistant Secretary for Health
US Department of Health and Human Services
200 Independence Avenue, SW
Washington, DC 20201

Dear Members of the Tick-Borne Disease Working Group:

The Infectious Diseases Society of America (IDSA) appreciates the opportunity to submit comments to the Tick-Borne Disease Working Group and commends the group for addressing the important issue of vector-borne infections. IDSA is the largest infectious diseases medical society in the United States, representing more than 11,000 physicians and scientists. Our members care for patients of all ages with serious infections, including tick-borne diseases. IDSA is committed to ensuring that patients receive the highest quality care for infectious diseases, including Lyme disease. Society members focus on the epidemiology, diagnosis, investigation, prevention, and treatment of infectious diseases in the U.S. and abroad.

We have great sympathy for patients—and their loved ones—who suffer from both short- and long-term effects of Lyme disease or other conditions. Our goal as infectious diseases physicians, public health practitioners, and scientists is to have all patients achieve the best possible outcomes.

To positively impact federal policy with regard to the prevention, surveillance, diagnosis, treatment, and research of tick-borne diseases, it is important that this working group solicit input from relevant experts. In fact, this is required by the statute that established the working group. Unfortunately, the working group's efforts to solicit such input have been uneven. Infectious diseases physicians and scientists who understand widely accepted, evidenced-based findings regarding the diagnosis and treatment of Lyme disease were excluded from several of the subcommittees that developed draft recommendations for the working group. Further, the public has been provided with fewer than two business days to provide comments on hundreds of pages of subcommittee reports, with comments due on Mother's Day. Therefore, with such a tight turnaround time, we cannot comment sufficiently on a large number of recommendations or their bases. Such practices do not appear to reflect an earnest attempt by the working group to solicit input, nor are they in keeping with congressional intent. Perhaps most troubling, the exclusion of scientific input has resulted in some recommendations that, if implemented, could severely harm patients and public health.

IDSA is pleased that some of the subcommittees offer important recommendations that can strengthen the federal response to tick-borne diseases, and we are pleased to offer our support for these recommendations in our comments below. We also express concern about several recommendations that would weaken our rigorous scientific approach to the diagnosis and treatment of tick-borne diseases and subject patients to substandard, ineffective and even dangerous care. We urge the working group to exclude such recommendations from its report. We would welcome the opportunity for ongoing dialogue with the working group to help ensure that its recommendations best serve the interests of patients and public health.

Disease Vectors, Surveillance, and Prevention
IDSA supports the subcommittee's call for more research to determine effective interventions for reducing the incidence of tick-borne diseases in humans, including novel approaches to vector control, and comprehensive vector control programs that encompass both mosquitos and ticks. Vector control for ticks is not nearly as well understood as vector control for mosquitos and would greatly benefit from further study. IDSA agrees that CDC regional Centers of Excellence in Vector-borne Disease need additional funding and should be utilized and leveraged for their knowledge and expertise in these areas. We also support further studies on geographic and ecological studies on tick-borne diseases, as well as the factors that are causing changes and expansions in endemic areas. Education of at-risk populations is another important prevention strategy that should be better used in endemic areas.

We also agree with the subcommittee that additional surveillance and epidemiology are required to understand the burden of tick-borne infections, particularly as the endemic area for some disease-bearing tick species is expanding. Proper diagnosis of a tick-borne illness can be hampered if clinicians do not have access to accurate information detailing the burden of disease in their area. While the IDSA acknowledges that the CDC case definition for Lyme disease is intended for use as an epidemiological tool, it is incorrect to promulgate somehow the notion that the components of the surveillance definitions should not be used for clinical diagnosis. To further popularize such a statement would confuse clinicians from understanding that the clinical diagnosis of Lyme disease rests on the foundations of either objective clinical findings and/or laboratory testing. The language used by the subcommittee appears to have the intent of inappropriately broadening the definition of Lyme disease to include patients with only fatigue, pain or other subjective conditions. We emphasize that any new approaches for expanding surveillance of tick-borne diseases must meet rigorous, evidence-based standards to ensure accuracy.

Access to Care Services and Support to Patients
IDSA supports the subcommittee's recommendations for increased education on the prevention of tick-borne diseases and removal of ticks. It is essential that all educational materials include only evidence-based information and do not promote over-diagnosis or misdiagnosis of Lyme disease or unsafe or ineffective treatments, including long-term antibiotic use.

IDSA supports patient access to evidence-based, medically appropriate diagnosis and treatment of Lyme disease and post-Lyme disease treatment syndrome that is safe and effective. We oppose policies that would subject patients to faulty diagnostic procedures or dangerous or unproven treatments. We also oppose recommendations or laws designed to protect clinicians who provide harmful treatments. In addition, we oppose any attempts by the working group to undermine widely accepted medical guidelines for the treatment of Lyme disease that are rooted in scientific evidence or to promote clinical guidelines that are lacking in evidence-basis.

While IDSA supports increased federal funding for research on tick-borne diseases, this funding cannot come at the expense of funding for other diseases, including HIV. Pitting one disease against another, is counter productive and costly. As has been evidenced repeatedly, we must sustain our efforts in responding to infectious diseases or risk serious and potentially deadly outbreaks, as we have already seen recently for HIV due to the opioid epidemic.

Other Tick-Borne Diseases and Co-Infections
There are many other serious and potentially fatal tick-borne diseases such as Powassan virus, babesiosis, anaplasmosis, ehrlichiosis, tularemia, Rocky Mountain Spotted Fever and other spotted fever group rickettsioses, anaplasmosis, and others. These diverse infections may present with symptoms and signs somewhat similar to early Lyme disease including fever, aches, and rashes. Some of these diseases are also expanding into new geographic areas. Thus, increased surveillance and epidemiology, as well as additional research into these diseases would be greatly beneficial. While ticks feed on animals infected

with Bartonella there is no convincing evidence that it is a tick-transmitted human pathogen. The working group appears to highlight Bartonella as a known tick pathogen for humans while this is not the case. We appreciate the subcommittee's attention to these diseases.

Pathogenesis, Transmission, and Treatment

IDSA acknowledges that some patients who are successfully treated for Lyme disease continue to suffer from persistent symptoms after treatment. Further research into the exact causes of these symptoms is vital to developing safe and effective treatments for these patients. IDSA supports additional research to discover better indicators of active Lyme disease infection to help clinicians and patients understand microbiological cure. Currently available serology inherently is not able to distinguish active versus past infections.

It is important that federal research funding be geared toward such studies that will truly enhance our understanding of Lyme disease. Conversely, there is not a pressing need for additional federally supported research on antibiotic treatment for Lyme disease. There is clear, widely accepted scientific evidence indicating that a 10-28 day course of antibiotics, depending on the stage of Lyme disease, will kill the Lyme disease bacterium in humans. Despite multiple clinical trials on this subject, there is no robust scientific evidence supporting the use of long-term antibiotic therapy in patients with Lyme disease that gains them sustained benefit either as initial therapy or prolonged treatment for long-term symptoms. Persistence of *Borrelelia burgdorferi* in humans should not be acknowledged as recommended in the subcommittee report while the facts are not supportive of this view. In fact, there is evidence that long-term antibiotic therapy for patients can lead to serious and life-threatening complications and can accelerate the development of antibiotic-resistant bacterial infections in patients. Patients who have been on long-term antibiotic therapy after diagnoses of chronic Lyme disease have later developed *Clostridium difficile, Pseudomonas aeruginosa, Acinetobacter,* and other infections. Some of these patients developed septic shock and died.

It is essential that research on tick-borne diseases meet established standards for scientific rigor to ensure that study results are meaningful and can safely and effectively guide patient care. Attempts to make clinical trials more inclusive or pragmatic must not override the need to ensure that enrolled patients have Lyme disease based on widely accepted standards. While the tick microbiome deserves further investigation, to widely popularize basic scientific information as something that clinicians should routinely understand inappropriately leaps over the required steps to understand if such pathogens are a cause of human infections.

Clinical education on the diagnosis and treatment of tick-borne diseases must continue to rely upon robust scientific evidence and should not attempt to undermine medically appropriate diagnostic practices. Except in rare cases as true with all infectious diseases, Lyme disease causes well-characterized presentations. Over-testing and over-diagnosis of Lyme disease can lead to patients who do not have Lyme disease receiving unnecessary and potentially harmful treatments. While IDSA continues to call for more research to improve diagnostic tools for Lyme disease, it is essential that clinical education is rooted in the best currently available evidence.

The subcommittee's recommendation that peer-reviewed reports be created by clinicians and scientists that represent a wide spectrum of medical opinions on the treatment of Lyme disease is of great concern. Approximately 20 clinical and scientific organizations in North America and Europe and numerous scientific and public health bodies agree with the IDSA perspective regarding the lack of efficacy and significant danger of long-term antibiotic therapy for treating Lyme disease. Medical opinions that lack the foundation of rigorous scientific evidence should not be held in equal regard in the working group's recommendations, and doing so would be greatly detrimental to patients and public health.

Testing and Diagnostics

IDSA greatly appreciates the subcommittee's recommendations for increased research to improve Lyme disease diagnostics. Lyme disease is diagnosed by a combination of medical history, physical exam, and if needed, diagnostic testing. The current FDA-approved serologic tests work best for patients who have

symptoms beyond the first two to four weeks as this is the typical response time for the human immune system to make antibodies against a pathogen, such as *Borrelelia burgdorfer*i. In patients who are just infected, the diagnosis is best made if the characteristic rash, erythema migrans is present as patients are frequently seronegative. Currently, clinically-validated FDA tests are the best available tests for diagnosis of Lyme disease when the characteristic rash or history is not present. Scientific advances are needed to improve testing strategies for the earliest phases of Lyme disease.

As serologic tests may remain positive for decades after successful treatment of Lyme disease, development of a test that provides supportive evidence that a patient has been microbiologically cured of infection would be of great benefit. Particularly for a patient who has persistent symptoms after antibiotic therapy, this would assist in guiding their clinician to avoid unnecessary additional antimicrobial therapy. IDSA has long advocated for more funding and research into more accurate and specific diagnostics. Progress in this area would greatly reduce misdiagnosis and link patients to effective treatments more quickly.

Important strides have been made to support the development of new diagnostic testing procedures. The NIH and CDC initiated a Serum Reference repository in 2008 and, at the end of 2011, began making standardized Lyme disease cases with serum samples available to the scientific community on a broad basis for testing and comparison of new diagnostic tests. The repository enables comparison of newly developed and existing diagnostic tests under identical conditions using the same panel of well-characterized reference specimens. CDC is also developing next-generation direct diagnostic tests (e.g., biomarkers) to improve upon current serological tests. However, the development, validation and commercial distribution of new tests can take years and millions of dollars.

Vaccines and Therapeutics

IDSA greatly appreciates the work done by the vaccine and therapeutics subcommittee, and supports many of the recommendations made in its report. A new vaccine that is safe and effective in humans would be an excellent tool for the prevention of Lyme disease. We also appreciate the acknowledgment of the barriers to acceptance of a new Lyme disease vaccine from the public and industry perspectives and hope the working group can more explicitly detail strategies for overcoming these challenges. IDSA also believes further research into vaccines that target the disease reservoir and vector would be greatly beneficial to prevention efforts. It is unclear to IDSA why recommendations regarding a Lyme disease vaccine are not addressed by this phase of the working group. An effective vaccine would be a key to prevention and thereby critically reduce the public health threat of Lyme disease.

IDSA agrees with the subcommittee that therapeutics for symptoms that persist after Lyme disease treatment would be greatly beneficial. We support further research that would develop a better understanding of why some patients do not improve after antibiotic therapy. We also support the conclusion that the efficacy of antimicrobials for treatment of acute Lyme disease in well-defined patient populations is well documented, and add that additional long-term antibiotic treatments have not demonstrated any clinical benefits.

IDSA thanks the working group for its attention to tick-borne diseases and looks forward to the opportunity to help inform and advance evidence-based policy that will best serve the interests of patients and public health. If the working group acknowledges the need for more time to develop detailed responses, we would like the opportunity to amend this letter.

Sincerely,

Paul G. Auwaerter, MD, MBA, FIDSA
President, IDSA