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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
U.S. 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. 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 for all patients to achieve the best possible outcomes.

IDSA comments below reflect our understanding of the contents of the Working Group's draft report based upon the discussion at the Working Group's June 20 meeting. We are deeply troubled that we have only 7 business days following that meeting to submit comments in time to inform the Working Group's report. We are further concerned that there is no plan to provide an opportunity for the public to review and comment upon the draft report before it is finalized. Unfortunately, this is consistent with a pattern of behavior by the Working Group to limit public feedback on its work and, particularly, to stifle the voices of physicians who use sound, evidence-based science to direct care for their patients. Previous comment periods have provided extremely limited time to review Working Group materials.

Further, several of the Working Group's subcommittees completely excluded volunteers with evidence-based scientific viewpoints, and the makeup of the Working Group itself is skewed in favor of individuals whose perspectives do not align with the overwhelming bulk of scientific evidence regarding the diagnosis and treatment of Lyme disease. We do not believe that the Working Group's composition and practices align with congressional intent and we are extremely worried that the biased approach favored by the Working Group may produce a report containing recommendations that, if implemented, would cause significant harm to patients and public health.

IDSA is pleased that some of the draft report's chapters offer important recommendations that can strengthen the federal response to tick-borne diseases. We 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.

Epidemiology and Ecology Chapter
IDSA supports the recommendations for more funding and studies on the ecology and surveillance of ticks, particularly in regions where the burden of disease may be changing or is not well understood. More funding is also necessary to keep pace with the discovery of novel tick-borne pathogens. According to the Centers for Disease Control and Prevention since 2004 there have been seven new human pathogens discovered in ticks, and it is necessary to characterize these novel infections as quickly and accurately as possible.

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 will 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 the notion that the components of the surveillance definition should not be used for clinical diagnosis. To further popularize such a statement would cause unnecessary confusion among clinicians and may lead to more inaccurate diagnoses. The clinical diagnosis of Lyme disease rests on the foundations of objective clinical findings and/or laboratory testing. The language used by the Working Group appears to have the intent of inappropriately broadening the definition of Lyme disease to include patients with only fatigue, pain or other subjective conditions. Such a change would likely lead to many more patients being inaccurately diagnosed with Lyme disease; being subjected to unnecessary, unhelpful, and potentially harmful treatment; and losing the opportunity for accurate diagnoses and appropriate treatment of other healthcare problems. We emphasize that any new approaches for expanding surveillance of tick-borne diseases must meet rigorous, evidence-based standards to ensure accuracy.

Prevention Chapter
IDSA greatly appreciates and supports many of the recommendations made in the prevention chapter. 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 we hope the Working Group can more explicitly detail strategies for overcoming these challenges. IDSA also believes further research into vaccines that target the disease reservoirs and vectors would be greatly beneficial to prevention efforts.

We also support the Working Group recommendation to conduct studies 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. Education of at-risk populations is another important prevention strategy that should be better used in endemic areas.

Causes and Treatment Chapter

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. The FDA-approved *B. burgdorferi* serologic test inherently is not able to distinguish active versus past infections, which is true of many antibody-based tests.

It is important that federal research funding is 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.

IDSA agrees with the Working Group 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.

One area does deserve consideration of further treatment study. The inflammatory state of Lyme arthritis often takes weeks or months to resolve; however, patients are often subject to multiple additional courses of antibiotic that are of unclear worth. Late Lyme arthritis, classically causing a swollen knee, has not been subject to a large, well-designed clinical trial to determine the appropriate type and duration of antibiotic therapy. Moreover, the 10-15% of patients who experience antibiotic-refractory Lyme arthritis have not been subject to prospective trials to determine the best anti-inflammatory strategies to resolve their condition. A multi-center study to address the best antibiotic treatment for Lyme arthritis would significantly help answer these fundamental questions and also lead to identifying patients who do not fully respond to antibiotics and could enter a subsequent study for antibiotic-refractory arthritis.

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.

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. This practice can also cause clinicians to overlook and fail to diagnose other conditions, such as multiple sclerosis, cancer, or fibromyalgia, those robbing patients of the opportunity to receive appropriate therapies. 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.

Diagnosis Chapter

IDSA greatly appreciates the Working Group'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. Current, 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.

Access to Care Chapter

While IDSA supports creating a federal repository of information on Lyme and other tick-borne diseases, it is critical that all of the information be science- and evidence-based to ensure patients receive the highest level of care possible. Increased federal funding for tick-borne diseases is vital, but this funding cannot come at the expense of funding for other diseases, including HIV. Pitting one disease against another is counterproductive and costly. As has repeatedly been evidenced, 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.

IDSA supports patient access to evidence-based, medically appropriate diagnosis and treatment of Lyme disease and persistent symptoms 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 not evidence-based. We are extremely worried about the potential impacts of the recommendation to provide protections for doctors who follow "recognized guidelines." The term is exceedingly broad and could easily be applied to guidelines that lack sufficient evidence. This recommendation was adopted by a margin of only one vote, by far the most contentious vote of the meeting, yet due to the composition of the chapter's writing group, the report will contain no minority opinion on this issue. This is a significant oversight, and we strongly encourage the addition of a minority opinion on this issue. Broad protection for physicians who subject patients to substandard or even dangerous therapies will likely result in an increase in the number of patients who are harmed.

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. Below we are pleased to offer a compilation of the published evidence that has informed our comments. We hope these resources will be of use as the Working Group prepares its report.

Sincerely,

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President, IDSA

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