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November 26, 2018

Tickborne 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 Tickborne Disease Working Group,

The Infectious Diseases Society of America (IDSAs) is writing to provide feedback on the Working Group report as well as the processes the Group undertook to produce the report. We wish to highlight significant concerns with the working group having a lack of transparency and minimal opportunities for meaningful public input. While we are pleased to support many of the recommendations, we must stress that some key recommendations, if implemented, would cause significant harm to patients and public health. We urge you to ensure that the federal government response to tick-borne diseases is solidly rooted in the best available scientific evidence.

We have a sincere appreciation of both 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.

IDSAs is the largest infectious diseases medical society in the United States, representing more than 11,000 physicians, health care professionals and scientists. Our members care for patients of all ages with serious infections, including tick-borne diseases. IDSAs is committed to giving patients 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 would be happy to serve as a resource for any issues surrounding tick-borne diseases.

Working Group Practices and Composition

IDSAs comments are based on the draft report released at the July 24, 2018 Working Group meeting. We are deeply troubled that there was no opportunity to submit comments to the Working Group on this draft for consideration before the final iteration. Until the July 24 release of the draft report, the only information made available about the contents were high-level recommendations voted upon by the Working Group. These recommendations constitute a small minority of the actual content of the draft report. 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 only a few days to review and to respond to the Working Group materials.

Further, several of the Working Group subcommittees excluded participants whose viewpoints aligned with scientific evidence and the mainstream medical community, despite many qualified volunteers submitting applications. The makeup of the Working Group skewed to individuals with perspectives that do not align with the overwhelming majority of scientific evidence regarding the diagnosis and treatment of Lyme disease. We do not believe that the Working Group composition and practices align with congressional intent and we are extremely concerned that the non-evidenced based approach favored by the Working Group has produced a report containing irresponsible recommendations that run counter to quality scientific and clinical information. If implemented, these would cause significant harm to patients and public health.

Epidemiology and Ecology Chapter

IDSA supports recommendations for enhanced funding to study 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.

We also agree with the Working Group 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. As clinicians depend on the knowledge of whether tickborne diseases occur in their community, a proper diagnosis will be impaired if they do not have access to accurate information detailing the burden of disease in their communities. We emphasize that any new approaches for expanding surveillance of tick-borne diseases must meet rigorous, evidence-based standards to ensure accuracy.

While 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, as the draft report seeks to do, would cause unnecessary confusion among clinicians and may lead to higher numbers of 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 receiving misdiagnoses with Lyme disease; being subjected to unnecessary, unhelpful, and potentially harmful antimicrobial treatments; and losing the opportunity for accurate diagnoses and appropriate treatment of their genuine problems.

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. IDSA also believes further research into vaccines that target the disease reservoirs and vectors would be highly beneficial to prevention efforts.

We also support the Working Group recommendation to conduct studies of effective interventions for reducing the incidence of tick-borne diseases in humans, including novel approaches to vector control. Vector control for ticks is not nearly as well understood as vector control for mosquitos. Education of at-risk populations is another vital 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 mechanism 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 unable to distinguish active versus past infections, which is true of many antibody-based tests.

Federal research funding should be geared toward such studies that will genuinely 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 in all but the rarest of cases. In the setting of patients who have symptoms persisting beyond six months after initial antibiotic therapy, six prospective, randomized, placebo-controlled studies have failed to document sustained or significant benefit. These studies serve to counter observational studies that are cited by some as a basis for using long-term antibiotics in patients labeled as suffering from Lyme disease. The scientific method based on prospective study indeed informs clinicians with the highest-quality evidence. Therefore it is easy to state that there is no robust scientific evidence supporting the use of long-term antibiotic therapy in patients with Lyme disease as an approach to help with chronic symptoms such as pain, fatigue, sleep difficulties or subjective neurocognitive complaints.

IDSA agrees with the Working Group that effective therapeutics for symptoms that persist after Lyme disease treatment would be beneficial. We support further research that would develop a better understanding of why some patients do not improve after antibiotic therapy.

The inflammatory state of Lyme arthritis deserves further study. It 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 adequately 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 sound scientific evidence and should not attempt to undermine medically appropriate diagnostic practices. Except in rare cases as is 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, thus 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 be rooted in the best currently available evidence.

Diagnosis Chapter

IDSA greatly appreciates the Working Group 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 been infected for at least two to four weeks as this is the typical response time for the human immune system to make antibodies against a bacterial pathogen, such as *Borrelia burgdorferi*. In patients who are just infected, the diagnosis is best made if the characteristic rash, erythema migrans, is present as patients are frequently seronegative—the human antibody-based immune response is not mounted with high efficiency in the first weeks of infection. Current, clinically-validated FDA tests are the best available tests for diagnosis of Lyme disease when the characteristic rash 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 increased funding to derive more accurate and specific diagnostics. Progress in this area would significantly reduce misdiagnosis and link patients to effective treatments more quickly.

Significant 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

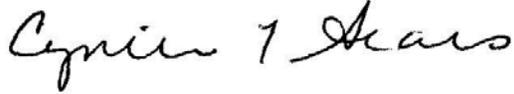
IDSA has grave concerns about the content in the Access to Care chapter. If the recommendations were implemented as written, they would essentially remove any accountability for physicians providing unproven treatments to patients who may or may not have Lyme disease. These treatments can be harmful, and the recommendations in this chapter would remove patients' opportunity for redress and prohibit state medical boards from censuring these doctors or preventing them from harming additional patients.

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 evidence-based to ensure patients receive the highest level of care possible. Increased federal funding for responses to tick-borne diseases is vital, but this funding cannot come at the expense of funding for other diseases, including HIV. We must sustain efforts to respond to infectious diseases or risk severe and potentially deadly outbreaks, as we have already seen recently with new HIV infections arising from the opioid epidemic.

IDSA supports patient access to evidence-based, medically-appropriate diagnosis and treatment of Lyme disease including persistent symptoms that are safe and effective. The recommendations and policies outlined in this chapter would subject patients to faulty diagnostic procedures and dangerous, 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 apprehensive about the potential impact of the recommendation to provide protections for doctors who follow "recognized guidelines." The term is exceedingly broad and could easily be applied to guideline recommendations that lack sufficient evidence or are based mainly on patient preference such as the ILADS guidelines that give physicians broad latitude regardless of documented efficacy or safety. This recommendation was adopted by a margin of only one vote, by far the most contentious vote of the Working Group, yet due to the composition of the writing group, the report will contain no minority opinion on this issue. This is a highly significant oversight and defect. Broad protection for physicians who subject patients to substandard or even dangerous therapies will likely increase 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,

A handwritten signature in black ink that reads "Cynthia Sears". The signature is written in a cursive, flowing style.

Cynthia Sears, MD, FIDSA
President, IDSA