DEPARTMENT OF HEALTH & HUMAN SERVICES **Public Health Service**

Office of the Director
Tel: 404-639-3788
Fax: 404-639-3039

Centers for Disease Control and Prevention
National Center for Emerging & Zoonotic Diseases
1600 Clifton Road NE
Atlanta, Georgia 30329

November 20, 2019

Dear Mr. Fries and Ms. Ahern,

We have reviewed your Information Quality Appeal: Request for Reconsideration related to antimicrobial prophylaxis for the prevention of Lyme disease, which appears on CDC's website, publications, and presentations. This request is listed as #64 on the HHS website on Information Quality Requests at: https://aspe.hhs.gov/information-requests-corrections-and-hhs-responses. For your information, an independent review of the information in your Request for Reconsideration was conducted by my office. My office provides scientific leadership that oversees the Division that provided the CDC response to your initial Request for Correction.

Upon further review, we do not believe that the evidence supports the removal of the antimicrobial prophylaxis information on CDC's website, publications, and presentations or a subsequent publication of a notice in CDC's Morbidity and Mortality Weekly Report.

The original request for correction referred to a study published in the New England Journal of Medicine (NEJM) that evaluated the efficacy of single dose doxycycline for preventing Lyme disease after tick bite. Endpoints in the study included erythema migrans (EM), isolation of *Borrelia burgdorferi* in culture, or seroconversion. The study design was randomized, double-blind, and involved over 450 human subjects.[1]

In your Request for Reconsideration, you reiterate your concern that the primary and secondary endpoints in this trial are inadequate to detect infection with *B. burgdorferi*. As evidence, you reference a study by Embers and colleagues in which only one in 10 monkeys exposed to infected ticks developed EM at the site of a tick bite.[2] However, the full endpoints in this study included EM, isolation of *B. burgdorferi*, and seroconversion; these are the same endpoints used in the NEJM study. Using these criteria, Embers and coauthors found that fully 90% of exposed monkeys had objective evidence of *B. burgdorferi* infection. Results of the Ember's study confirm rather than refute the utility of the endpoints used in the NEJM study.

The two remaining sources cited as evidence do not support your above claim. First, MyLymeData[3] is a web-based registry of patients who are self-identified as having chronic Lyme disease. The registrants represent a distinct subset of patients. There is no reason to believe that the frequency of erythema migrans reported by these patients is representative of the general population presenting with early Lyme disease, nor is it clear if or how infection with *B. burgdorferi* was confirmed in many of the registrants. Secondly, the *Tick-Borne Disease Working Group 2018 Report to Congress*[4] states, "Readers should not consider the report or any part of it to be guidance or instruction regarding the diagnosis, care, or treatment of tick-borne diseases or to supersede in any way existing guidance." The report to Congress cited above does not constitute a primary data source and therefore should not be used as the basis for making scientific claims.

Your letter expresses concern that the data supporting antimicrobial prophylaxis for the prevention of Lyme disease has been judged to be of very low quality by an advocacy-based review group, despite being a collected through a blinded, randomized trial. Instead, you propose endorsement of a regimen set forth in Cameron *et al*.[5] that recommends 100-200 mg of doxycycline, twice daily for 20 days, despite its being backed by low-quality evidence and a statement that, "The evidence supporting use of 20 days of antibiotics is limited to the previously mentioned murine trials." The murine trials[6,7] cited by Cameron et al. do not evaluate the use of doxycycline over a period of 20 days, but rather a single injection of sustained-release doxycycline.

Finally, we refer you back to content from our last letter that was not included in this Request for Reconsideration regarding bias toward the null. Regardless of the endpoints used, if the NEJM study had excluded half the cases of Lyme disease as claimed, the effect would be to reduce the likelihood of finding a significant difference between treatment arms. The fact is that a significant difference between treatment arms was detected nevertheless. In this respect, the findings of the doxycycline study are more robust, not less.

Best Regards,

/S/

Elise M. Beltrami, MD, MPH
Associate Director for Epidemiologic Science
National Center for Emerging and Zoonotic Infectious Diseases
Centers for Disease Control and Prevention

References

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3. MyLymeData. https://www.mylymedata.org/.
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5. Cameron DJ, Johnson LB, Maloney EL. (2014) *Expert Rev Anti Infect Ther*. 2014;12(9):1103–1135.
6. Zeidner NS, Brandt KS, Dadey E, *et al*. *Antimicrob Agents Chemother*. 2004 Jul; 48(7): 2697–2699.
7. Zeidner NS, Massung RF, Dolan MC, *et al*. *J Med Microbiol*. 2008 Apr;57(Pt 4):463-8.