



May 5, 2023

Victor Dzau, MD
President
National Academy of Medicine
500 Fifth Street, NW
Washington, DC 20001

Dear Dr. Dzau,

Haystack Project looks forward to the implementation of the rare disease provisions of the Consolidated Appropriations Act. In particular, we are closely following implementation of the HEART Act, contained in Section 3202 of the bill.

Haystack Project is a 501(c)(3) non-profit organization enabling its membership of rare and ultra-rare disease advocacy organizations to highlight and address systemic access barriers to the therapies they desperately need. We strive to amplify the patient and caregiver voice in disease states where unmet need is high, and treatment delays and inadequacies can be catastrophic. Our core mission is to evolve health care payment and delivery systems, spurring innovation, and quality in care toward effective, accessible treatment options for Americans living with rare or ultrarare conditions. Haystack Project is committed to educating policymakers and other stakeholders about the unique circumstances of extremely rare conditions with respect to product development, commercialization, and fair access to care.

Haystack Project's member organizations have expressed ongoing and growing frustration with FDA, which is what led us to conceive of, draft, and work with Congress to pass the HEART Act. The experiences and frustrations expressed by Haystack Project members guided the content of the HEART Act; our involvement in the bill means that we can help the National Academies understand and FDA implement Section 3202, consistent with its intent.

The HEART Act requires that the National Academies conduct a study on processes for evaluating the safety and efficacy of drugs for rare diseases or conditions in the United States and the European Union. In addition to issues around trial design and enrollment, our patient groups have had numerous concerns with FDA's understanding of how patients and caregivers' approach and perceive the balance of benefit and risk as well as how FDA analyzes data gathered from small trials. Further, we have heard that different divisions provide different advice to drug developers, meaning that FDA's standard for approval can vary widely between divisions. We look forward to discussing these issues with NASEM as it undertakes its assessment.

The National Academies is asked to consult relevant stakeholders. We look forward to working with the National Academies to share our rare patient and caregiver communities' experience and the deficiencies in FDA policies and practices those experiences reveal.

One example is the use of natural history data as a control arm in trials for rare disease treatments. FDA's Draft Guidance, Rare Diseases: Common Issues in Drug Development speaks to the importance of natural history studies. However, ultra-rare disease groups that have natural history studies, which is uncommon, have told us that FDA does not accept the data from those hard-won and likely irreproducible databases. Like many apparent policies and practices in rare diseases, this is applied inconsistently from division to division.

Another concern our members have raised is the risk-benefit calculus patient and caregivers make. As most rare diseases do not have a treatment, much less a cure, patients are often willing – and even eager -- to face a different risk-benefit balance than FDA typically assumes. For example, the risk that patients, families, and doctors would gladly assume for a chance at more time, slowed progression, or a cure in a rare, fatal, degenerative disease should not be, but reportedly is, overridden by the guesses of FDA staff who may be more familiar with chronic diseases in the same body system.

We respectfully request to meet with National Academies leadership and staff to discuss these, and other issues, we have encountered in FDA's review of treatments for rare and ultra-rare diseases. We can also provide further information about the genesis of the bill. Please contact me or our policy consultant, Cara Tenenbaum, at cara@strathmorehealth.com for any questions. We'll also plan to reach out to you promptly to schedule a meeting.

Sincerely,

A handwritten signature in blue ink, appearing to read "Chevese Turner".

Chevese Turner, CEO
Haystack Project

Cc:

J. Michael McGinnis, Leonard D. Schaeffer Executive Officer of the National Academy of Medicine

Monica N. Feit, Executive Director, Health and Medicine Division