HAYSTACK PROJECT
The Voices of Rare & Ultra Rare

July 16, 2021

Dear Representatives DeGette and Upton:

The Haystack Project appreciates your continued leadership in devising a legislative framework to accelerate the discovery, development, and delivery of medical innovations. Our patient communities look to specialists, diagnostics, and the emergence of new, innovative therapies that target specific disease mechanisms for renewed hope that treatment options, and even a cure, might be on the horizon to address the life-limiting and life-threatening conditions they face. We are pleased to provide comments on the discussion draft of your "Cures 2.0 Act."

Haystack Project (Haystack) is a 501(c)(3) non-profit organization enabling rare and ultra-rare disease patient advocacy organizations to highlight and address systemic obstacles to patient access. Our core mission is to evolve health care payment and delivery systems to make innovative quality treatments, diagnostics, and specialists accessible to the patients they were meant to reach. 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 comments focus on provisions of the discussion draft that are particularly relevant to the rare and ultra-rare disease community.

Sec. 306. Establishment of Additional Intercenter Institutes at the Food and Drug Administration (FDA). Haystack Project supports FDA infrastructures that focus on the unique challenges associated with developing treatments and curative therapies for rare diseases. We ask that you ensure that the rare disease intercenter positions more rare disease experts, including patients and their clinicians, to have an active role in the FDA's review process. The new rare disease intercenter should focus on:

- Ensuring that Rare Disease Program staff are included in all reviews of drugs to treat rare diseases, regardless of the division to which an application is assigned;
- Facilitating direct consultation throughout the structured benefit risk assessment and post approval safety monitoring for a rare disease application with
    - (i) experts in the science of small population studies,
    - (ii) experts in the specific disease referenced in an application, and,
    - (iii) patients --
- Making sure that experts in rare diseases are included in FDA Advisory Committee panels as a voting member, or as a non-voting member accompanied by a voting member who has expertise in the science of small population studies when reviewing any rare disease drugs.

Sec. 305. Improving FDA-CMS Communication Regarding Transformative New Therapies: establish an automatic communication requirement between FDA and CMS for Breakthrough Therapy. Haystack Project generally supports inter-agency communication strategies devised with a clear goal of improving patient access to therapies. We do, however, have significant concerns that the well-intended mechanism for intra-agency communication in Section 305 will have an unintended, and significant, impact on development of and access to therapeutic innovations in rare and ultra-rare diseases, and among subpopulations historically under-represented in clinical trials.

Rare disease treatments, particularly those in disease states without FDA-approved options, are almost always designated as breakthrough therapies. Clinical trials are often single-arm studies in relatively small study populations; existing policy balances inherent uncertainties in emerging treatments with the near-certainty of poor outcomes for patients with life-threatening and progressive chronic rare diseases. We strongly believe that the separation and independence of FDA and CMS decisions is essential to accelerate research and development in rare and ultra-rare diseases while also ensuring that patients have access to the treatment options most likely to reduce disease burden and, ultimately, lead to a disease cure. A coordinated approach to either FDA-approval or CMS-driven patient access would, almost inevitably, lead to delays in both, something our patients cannot afford.

Haystack Project would appreciate the opportunity to discuss alternative approaches and/or guardrails that would be needed to ensure that individuals with rare and ultra-rare diseases are not disproportionately and adversely impacted by FDA-CMS communication and collaboration.

Sec. 304. Increase Use of Real-World Evidence. Haystack Project supports HHS initiatives to "outline approaches to maximize and expand the use of RWE; and establish a task force to develop recommendations on ways to encourage patients to engage in real world data generation." We believe that this data would be particularly useful in satisfying post-approval commitments for drugs approved with Breakthrough Therapy status or under the Accelerated Approval pathway. Natural history information collected within patient advocacy organizations, either through patient survey instruments or patient registries, would enhance information developed within the clinical trial context and provide early evidence of the efficacy of new therapies.

In addition, increased use of real-world evidence can be an important tool in reducing health disparities and inequities if data collection is representative and its analysis considers racial and ethnic subpopulations and differential disease burden, progression, and/or treatment responses.

Sec. 204. Patient Experience Data. Haystack Project supports collection and use of patient experience data for rare and ultra-rare diseases so long as the data is meaningful with respect to patient priorities within the context of the specific disease state. We urge caution, however,

in requiring a uniform set of patient experience data elements and in requiring that the data be collected in each clinical trial. Specifically, we are concerned that:

- Unless the data elements are disease-specific and derived from patient priorities and preferences, FDA determinations could be skewed by information that is not relevant to the disease or the patients seeking treatment;
- Rare and ultra-rare disease clinical trials are, by necessity, often designed as single-arm studies. For these studies, it is essential to have access to a historic baseline for each patient experience data element. Unless that baseline is available, patient experience data would not be a meaningful indicator of either safety or efficacy and should not be used in FDA determinations;
- Patient experience data that does not capture the impact of a disease and emerging treatments in underserved patient populations could perpetuate and even expand health disparities.

Haystack Project member organizations have also noted that, while the discussion draft augments the information-gathering aspect of patient experience data, the legislation could be improved with more emphasis on how that data would be used. Haystack Project would like to work with your offices toward greater clarity on FDA use of this data, including:

- How closely related to the clinical trial does the experience have to be for it to be reportable?
- What about infantile and children experiences that are so common in rare and ultra-rare conditions? Should the parental and extended family experience be included?
    - Does patient experience include travel to enable access to therapy, family/sibling life disruption or separation, impact on working parents employment as they enable their other child/loved ones therapy.
    - What about the need to travel outside the US to access treatments in the FDA regulatory pipeline?
- How can/should/will the patient experience data be evaluated, summarized, used, and included in the scientific analysis by the FDA?
- How can patient experience data be used to assess the balance between risks and benefits for new therapeutic options. For example, patients and families struggling with a rare terminal disease with limited therapies may place high value on options with lower efficacy/benefit thresholds than they would accept in other conditions.

Finally, Haystack Project members noted the inherent challenge presented for rare and ultra-rare disorders due to the excessively high standards for consideration of patient experience data. Rare disease advocacy organizations are increasingly focusing on collecting data outside clinical trials, including through registries, surveys, and natural history studies. Many of these initiatives are conducted under IRB review and with carefully validated survey questions. However, given both our small numbers and the extreme heterogeneity of many of our

populations, this data is routinely rejected as not sufficiently reliable for publication or for consideration by FDA.

Section 407. Expanding Access to Genetic Testing. Haystack Project strongly supports increased access to genetic testing. Individuals with rare and ultra-rare diseases often face long, complex journeys from onset of symptoms to a presumptive or definitive diagnosis. For many conditions, each delay in receiving a diagnosis can be associated with medications that are not effective and are potentially harmful, and further disease progression. Early detection and diagnosis reduces the chances of patient harms and ensures that the patient is seeing the right specialists and receiving the treatment most likely to lead to positive outcomes.

Sec. 404. Coverage and Payment for Breakthrough Devices Under the Medicare Program. Haystack Project appreciates that the discussion draft declined to incorporate the definition of "reasonable and necessary" included in the CMS rule on coverage and payment for breakthrough devices. We generally support expedited coverage for breakthrough devices, but are concerned that requiring that devices be used according to FDA approved or cleared indication for use would foreclose access to off-label uses that could be covered under existing mechanisms. Individuals with rare and ultra-rare diseases often manage disease symptoms through off-label use of products approved for more common conditions as part of the practice of medicine within subspecialties caring for these patients. These evolving uses are frequently developed without manufacturer involvement to address symptoms of a rare disease that are in common with other diseases.

An explicit or implied proscription of coverage for off-label uses of breakthrough devices would make it all but impossible for beneficiaries to obtain coverage, even if the device were the best, or only, option for reducing disease burden associated with a very rare disease. Medicare appeals processes would not permit inquiry beyond verifying that the use was off-label and within the regulatory coverage prohibition. The only mechanism for access would be a challenge to the statutory provision itself.

Haystack urges an approach that facilitates early, predictable coverage of breakthrough devices for on-label uses while preserving existing mechanisms for coverage of off-label uses on a claims-specific basis or at the local contractor level.

Sec. 403. Extending Medicare Telehealth Flexibilities. Haystack Project supports extension of Medicare telehealth flexibilities. For rare and ultra-rare disease patients, broadening access to telehealth beyond the PHE may offer value to patients, clinicians, and the Medicare program so long as the decision on whether or not face-to-face clinician visits should be used is based on the patient's condition, needs and preferences. Ideally, telehealth would function as an adjunct to in-person visits that would, for individuals with rare conditions, enable broader access to a continuity of coordinated care that includes disease-specific expertise from local specialists as

well as those outside the patient's geographic area. We recommend that telehealth flexibilities include:

- Allowing physicians to use telehealth to supervise rural non-physician providers;
- Allowing practitioners to satisfy supervision requirements virtually using the appropriate level of technology to meet the needs of direct or general supervision;
- Ensuring provider payment mechanisms to enable participation of American Sign Language (ASL) or tactile sign interpreters in telemedicine visits; and
- Ensuring that the geographic and site of service flexibilities for telehealth service originating sites are permanently adopted.

In the early months of the pandemic, several Haystack member organizations reached out to patients with a survey assessing the patient experience with telehealth services during the PHE. The majority of patients responding to the survey were able to access telehealth with relative ease and felt that the telehealth service flexibilities helped protect them from COVID-19 exposure. For individuals with rare conditions, the increased ease in accessing specialist care underscores the need to continue many of these flexibilities permanently. For example, one patient noted the care they have received through telehealth during the PHE:

> Medication changes, local tests were ordered, met with neurosurgeon to determine surgery is needed. We live in Alaska and frequently have to fly to Seattle for care. We have been able to visit with specialists via telehealth and it's saved us considerable money and provided us with additional opportunities to see experts regarding care.

Many patients expressed concerns that the ability to receive remote care from out-of-state providers could be restricted once again after the PHE resolves.

Haystack has also heard from patients and caregivers regarding the barriers individuals with hearing and/or visual impairments face in seeking care. Usher Syndrome, for example, is a very rare (approximately 25,000 US patients) inherited disease causing combined hearing loss and vision loss from retinitis pigmentosa. For these patients, it is essential that remote care includes access to an ASL interpreter if they have sufficient remaining vision, or a tactile sign interpreter if they do not.

The PHE underscored the need -- and temporarily provided -- Haystack Project's ultra-rare community of patients with access to specialists across state lines and out of network. It eased the burden on physicians having to justify to payers the need to see patients outside their local area. And importantly, it also eliminated the burdensome process payers impose on our patients to justify seeking out of network care. This burden on patients is daunting, and adds to the already tremendous "full time job" of being a patient or caregiver and often has the effect of deterring patients from seeking treatment. Pending legislation to address these barriers

tend to focus solely on provider burden, when in fact the burden on the patient and caregiver is relentless.

Sec. 103. Pandemic Preparedness Rare Disease Support Program. Haystack strongly supports development of a pandemic preparedness plan focused on the unique needs of rare disease patients. In the first several months of the COVID-19 pandemic, Haystack and other rare disease advocacy organizations scrambled to respond to the diverse sets of urgent needs in our patient communities. For many rare diseases, patients were forced to choose between the social distancing measures needed to avoid a potentially fatal exposure to the coronavirus and maintaining life-sustaining treatment regimens. We recommend that you:

- Ensure that the preparedness plans developed under this section, and the level of threat required to trigger their implementation, are subject to notice and comment with the goal of adopting one or more for implementation as needed; and
- Provide that grant funding be awarded to patient advocacy organizations and/or entities working in partnership with patient advocacy organizations, to ensure that the key learnings from the COVID-19 pandemic are fully captured.
- One critical issue, that continues to undermine CMS' PHE flexibilities is the very real lack of in-home administration options for Part B drugs. Self-interested stakeholders in the distribution channels continue to force patients to switch to Part D for their care when it could and should be provided without interruption under Part B. This is taking place without regard to patient out of pocket costs and the fact that many patients responsibly planned and bought supplemental coverage in Part B that is not available to them in Part D.

Suggested new section. Haystack Project would like to work with your offices to limit the impact that value frameworks can have on access to care for extremely rare conditions. Much has been written about limitations on use of the QALY generally, and those limitations become increasingly pronounced when applied to rare conditions that are progressive and/or life-threatening. We are deeply concerned about protecting patients as payers increasingly seek to use value frameworks and QALY-driven assessments to curtail or deny access. We have several suggested guardrails for consideration in this package and welcome a discussion.

Haystack appreciates this opportunity to offer its comments and suggestions in connection with the Cures 2.0 Act. We look forward to working with you to ensure that all patients have access to the care they need, no matter how rare their disease or condition.

If you have questions or need further information, please contact Jim Caro, CEO, Haystack Project, at jim.caro@haystackproject.org