Congress of the United States
Washington, DC 20515

October 9, 2026

Secretary Robert F. Kennedy Jr.
U.S. Department of Health and Human Services
Hubert H. Humphrey Building
200 Independence Avenue S.W.
Washington, D.C., 20201

Acting Commissioner Kyle Diamantas
U.S. Food and Drug Administration
White Oak Bldg 1, Room 2217
10903 New Hampshire Ave,
Silver Spring, MD 20993

Dear Secretary Kennedy and Acting Commissioner Kyle Diamantas:

We write to express our concern regarding the lack of clear, consistent standards, advice or methodologies from the U.S. Food and Drug Administration on how to define, measure, and document patient populations for rare diseases. As scientific innovation and diagnostic capabilities have advanced, the absence of standardized expectations for determining how the agency defines patient populations— and how prevalence data should be generated and submitted — is creating uncertainty across the research, regulatory, and patient communities.

Today, advances in genomics and precision medicine have enabled clinicians and researchers to identify increasingly specific disease subtypes and patient populations. However, there remains limited clarity from the FDA on how these populations should be evaluated for regulatory purposes. This ambiguity complicates efforts by sponsors to design clinical trials, identify appropriate patient cohorts, and demonstrate unmet medical need in a consistent and transparent manner. In addition, whether a disease is considered rare by FDA can have significant implications with respect to, among other things, support for natural history studies and clinical trials, availability of incentives to promote innovation to address unmet needs, and access to increased engagement with FDA to help move products forward.

In particular, we are concerned by the lack of uniform standards for collecting and submitting prevalence data. Stakeholders currently rely on a range of methodologies — including point prevalence, period prevalence, population that requires treatment and incidence-based estimates — often with significant variation in data sources, geographic scope, and diagnostic criteria. Without clear FDA guidance on acceptable methodologies and evidentiary standards, these inconsistencies can lead to unpredictable regulatory outcomes and may discourage investment in therapies targeting small or complex patient populations.

Alarmingly, several diseases such as Sarcoidosis, which were once considered rare diseases, are now slightly over the threshold of 200,000 of prevalence based on one of the many ways a

disease can be submitted to the FDA for prevalence based on some prevalence estimates.[1] While a few of the prevalence data place roughly 204,000 people are diagnosed with Sarcoidosis other prevalence data places it lower. Furthermore only about 60,000 patients require treatments and development of new therapies. This means if the FDA considers prevalence rate with the higher estimate as the prevailing rate, diseases like Sarcoidosis are no longer capable of receiving crucial rare disease funding to find cures even though the patient population that needs treatment is well below the current FDA standard for rare.

Additionally, several diseases at risk of losing rare disease status under the current criteria include: Multiple Myeloma, Charcot-Marie-Tooth disease, Trigeminal Neuralgia, Scleroderma, Immunoglobulin A Nephropathy, Neuroendocrine Tumors (NETs), Hereditary Angioedema, and Pulmonary Hypertension. These conditions represent serious, often life-altering illnesses where continued innovation and access to treatment through rare disease-specific funding options remain critical.

There is limited direction on how to account for evolving scientific understanding, including the use of biomarkers, genetic stratification, and real-world evidence to define patient populations. As diseases are increasingly segmented into narrower subtypes, developers need greater clarity on how to justify population definitions and how those definitions will be evaluated during the regulatory review process.

We know that there are more than 10,000 rare diseases that affect an estimated 25 million to 30 million Americans.[2] These challenges are not merely technical — they have real implications for patients. Uncertainty in how populations are defined and how prevalence must be demonstrated can delay or deter the development of therapies for individuals with serious and often life-threatening conditions. Clear and consistent regulatory expectations are essential to ensuring that innovation keeps pace with scientific progress and that patients are not left behind. When 95 percent of rare diseases do not have cures, we cannot risk discouraging innovation in areas where scientific progress is rapidly outpacing regulatory adaptation.[3]

Accordingly, we urge the Department of Health and Human Services and the U.S. Food and Drug Administration to undertake a comprehensive review and clarity on the rare disease definition. Specifically, we recommend consideration of the following actions:

1. Establish clear, standardized definitions and expectations for how patient populations should be delineated, including the role of genetic, biomarker, and clinical criteria.

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1 American Lung Association. (n.d.). *Learn about sarcoidosis*. https://www.lung.org/lung-health-diseases/lung-disease-lookup/sarcoidosis/learn-about-sarcoidosis#:~:text=Patients%20of%20any%20Scadding%20stage%20can%20have%20involvement%20of%20other%20organs%20from%20sarcoidosis.&text=Join%20over%20700%2C000%20people%20who%20receive%20the%20latest

2 *Our Impact on rare Diseases | National Center for Advancing Translational Sciences*. (n.d.). https://ncats.nih.gov/research/our-impact/our-impact-rare-diseases

3 PCH-HSC--Healthy and Safe Communities--8400. (n.d.). *Rare diseases*. Washington State Department of Health. https://doh.wa.gov/you-and-your-family/genetic-services/rare-diseases

2. Issue guidance on acceptable methodologies for calculating and submitting prevalence data, including preferred data sources, timeframes, and analytic approaches that capture nuances for prevalence based on subpopulations most relevant for drug development in the population.
3. Clarify how different forms of epidemiological evidence — including real-world data and registry-based studies — should be incorporated into regulatory submissions.
4. Provide greater transparency into how population definitions and prevalence estimates are evaluated during the review process.
5. Clarify the role of the population size of diagnosed patients requiring treatment and FDA approved therapies compared to those who are asymptomatic or require no drug development as consideration for rare disease status.
6. Engage stakeholders, including patient groups, researchers, and industry, to develop consensus-driven best practices for population identification and data submission.

Patients living with rare diseases often face significant barriers, including delayed diagnoses, limited treatment options, and high out-of-pocket costs. Providing this clarity will help reduce uncertainty, support more efficient drug development, and ultimately improve access to therapies for patients with serious and underserved conditions.

We look forward to your response outlining how your agencies plan to evaluate and provide clarity in the rare disease framework to better reflect the realities of today's healthcare landscape.

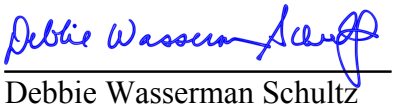
Sincerely,

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Member of Congress

Max L. Miller
Member of Congress

Madeleine Dean
Member of Congress

Mark Pocan
Member of Congress



Debbie Wasserman Schultz
Member of Congress



Rashida Tlaib
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Henry C. "Hank" Johnson, Jr.
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Member of Congress



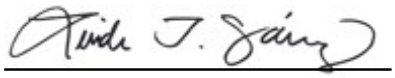
Steve Cohen
Member of Congress



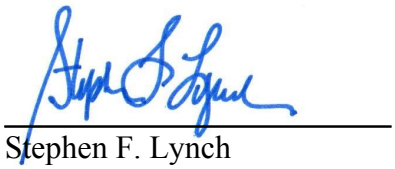
Darin LaHood
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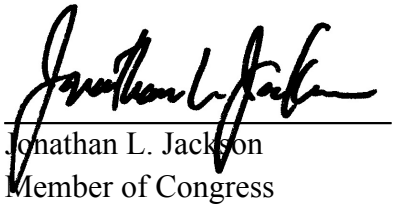
Shri Thanedar
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Linda T. Sánchez
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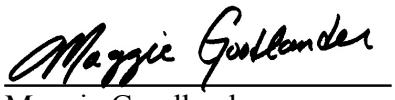
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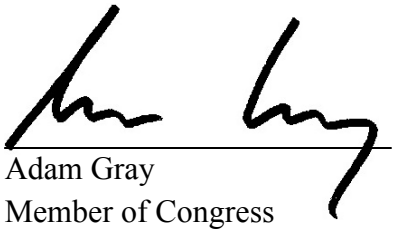
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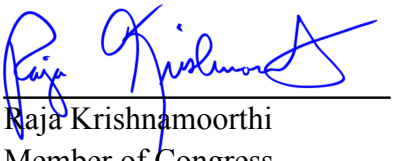
Brian K. Fitzpatrick
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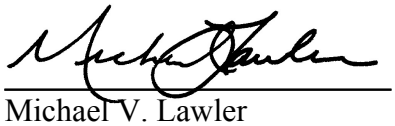
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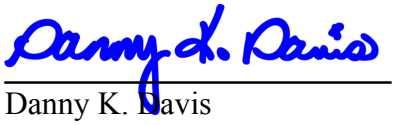
Raja Krishnamoorthi
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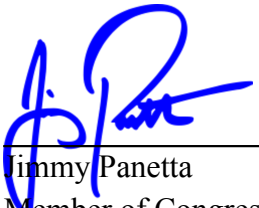
Michael V. Lawler
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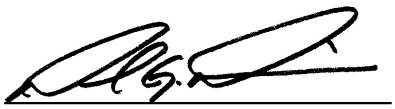
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