August 2, 2024

Honorable Diana DeGette
2111 Rayburn House Office Building
Washington D.C. 20515

Honorable Larry Bucshon
2313 Rayburn House Office Building
Washington D.C. 20515

RE: 21st Century Cures Request For Information

Submitted electronically to *cures.rfi@mail.house.gov*

Dear Representatives DeGette and Bucshon:

On behalf of the United Mitochondrial Disease Foundation (UMDF), a national non-profit organization dedicated to promoting research and education for the diagnosis, treatment, and cure of mitochondrial disorders, we are pleased to provide suggestions on ways in which the *21st Century Cures Act* can be strengthened in response to the Request for Information (RFI).

Mitochondrial disease generally refers to a group of disorders attributable to malfunctioning mitochondria – mitochondria that cannot efficiently or effectively generate energy. This results in a lack of cellular energy to perform various functions and an accumulation of byproducts that impair or destroy the cell. Symptoms are extremely diverse and progressive, and the result can be the manifestation of any number of rare diseases, which often can be fatal. There are no known treatments or cures. In addition to dozens of primary mitochondrial diseases, mitochondrial dysfunction has been linked to many severe secondary illnesses, including Alzheimer's disease, Autism, Parkinson's disease, ALS, Gulf War Illness, diabetes, and others.

For the mitochondrial disease community, and the rare disease community more broadly, the *21st Century Cures Act* was a monumental piece of legislation that modernized federal law to conform to a rapidly changing healthcare landscape while also providing substantial resources to new and innovative programs designed to facilitate discovery in drug development, precision medicine, cancer treatment, and other areas. Indeed, the *21st Century Cures Act* has already sparked significant forward progress in the mitochondrial disease community by strengthening the FDA's efforts on patient-focused drug development, providing additional resources for the development of breakthrough therapies for rare diseases, including mitochondrial disease, and enhancing FDA's research capabilities by promoting the use of innovative clinical trial designs, real-world evidence, and data extrapolation. These provisions have helped and will help our community's search for treatments, and hopefully cures, for mitochondrial diseases.

UMDF is strongly supportive of a next-generation *Cures* initiative that builds off of these successful initiatives and provisions to ensure that patients, families, caregivers, researchers, and others in the mitochondrial disease community have access to the best medical treatment and are empowered to contribute to the development of treatments and cures for their disease.

Please see UMDF's specific comments below.

Long COVID Research

There is increasing evidence connecting impaired mitochondrial function to so-called "long haul" COVID-19. Several recently published studies and reports have noted this relationship.[1] Mitochondria plays a central role in the host response to viral infection and immunity by acting as a platform for immune signaling. Research suggests that SARS-CoV-2 hijacks the mitochondria and uses them for protection and viral replication, diverting resources from supporting normal cellular function to serving as a viral factory.[2] It is believed that this then leads to impaired functioning and the extreme fatigue seen in long haul COVID. This is very consistent with similar relationships being identified between mitochondrial function and illnesses such as Chronic Fatigue Syndrome.

This new learning reinforces the central role that the mitochondria play in numerous diseases and disorders, including primary mitochondrial disease, underscoring the need for the National Institutes of Health (NIH) to make a more concerted effort to expand research in this field, including developing therapeutics to address primary mitochondrial disease.

As Congress allocates significant resources to Long COVID, we urge Congress to continue advocating for better mitochondrial therapeutics for those plagued by Long COVID and the many others with impaired mitochondria functionality resulting from primary or secondary disease.

Coverage and Payment for Medical Nutrition

Uncertainty surrounding the coverage of needed health care services is pervasive and stress-inducing amongst mitochondrial disease patients, their families, and caregivers. For instance, given that mitochondrial disease patients are energy-compromised, high-dose supplemental nutrition is frequently necessary for mitochondrial disease patients to function. Most manage these complex nutritional needs by consuming specialized formulas – medical nutrition – because failure to maintain the required diet puts them at risk for brain damage, repeated hospitalizations, inability to grow, or even death. However, medical nutrition for mitochondrial disease patients, and rare disease patients in general, is expensive, typically costing between $400 and $1,000 out-of-pocket per patient per month. Currently, only TRICARE covers medical nutrition at the federal level. A current piece of legislation, the *Medical Nutrition Equity Act* (H.R. 3783), would provide coverage for medical nutrition under Medicare, Medicaid, and private insurance, increasing access to these lifesaving formulas.

Telehealth

We applaud the efforts through Cures 2.0 to improve guidelines for innovative digital health technologies, eliminate geographic and originating site restrictions in Medicare coverage of telehealth services, and allow the Health and Human Services Secretary to expand the list of healthcare providers who could use telehealth and the types of services covered by Medicare.

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[1] A good overview of several of these studies can be found in this article: https://www.everydayhealth.com/coronavirus/mitochondrial-dysfunction-may-be-to-blame-in-long-covid-19/#:~:text=But%20now%2C%20several%20recent%20studies,produce%20energy%20for%20cellular%20metabolism

[2] Decoding SARS-CoV-2 hijacking of host mitochondria in COVID-19 pathogenesis - PubMed (nih.gov)

Telehealth has become an essential component of our healthcare system, proving crucial for mitochondrial disease patients who require care in their homes and access to specialists regardless of their location. This is particularly vital given the limited number of specialists with expertise in mitochondrial diseases and the complexity of care coordination across various providers.

Unfortunately, these important telehealth flexibilities are set to end on December 31, 2024, unless Congress takes further action. Despite previous extensions, telehealth access will revert to being limited to rural areas only, and Medicare patients will have to visit an "originating" site, such as a hospital, to receive most telehealth services. They will no longer be able to access most telehealth services from home.

We strongly support the passage of H.R. 7623, the *Telehealth Modernization Act of 2024*, which would extend the removal of geographic originating site restrictions for two years and continue the hospital-at-home program for an additional five years.

Real-World Evidence

UMDF applauds the FDA's final 2023 guidance (as a result of the *21st Century Cures Act*) on the use of real-world data and real-world evidence. We support additional provisions to strengthen the FDA's ability to incorporate real-world evidence into the drug development process. For many mitochondrial diseases, known patient populations are extremely small, and clinical researchers are frequently confounded by small study populations when trying to collect robust data for therapy development. Real-world evidence provides a mechanism for greater data collection from these populations, which is crucial in the search for cures. UMDF supports additional federal resources to build off the *21st Century Cures Act*'s original provisions around real-world evidence.

Closing

We thank you for the opportunity to comment on this important initiative for the mitochondrial disease community. Should you have any questions, please get in touch with Andy Dearth at andy.dearth@umdf.org.