Rare Disease Company Coalition

BY ELECTRONIC DELIVERY

August 2, 2024

The Honorable Diana DeGette
United States House of Representatives
2111 Rayburn House Office Building
Washington, DC 20515

The Honorable Larry Bucshon, M.D.
United States House of Representatives
2313 Rayburn House Office Building
Washington, DC 20515

RE: Response to 21st Century Cures Act and Cures 2.0 Request for Information

Dear Congresswoman DeGette and Congressman Bucshon:

The Rare Disease Company Coalition (RDCC) appreciates the opportunity to provide comments on the experience to-date with implementation of 21st Century Cures and Cures 2.0. RDCC applauds your longstanding leadership in developing and advancing policy solutions on behalf of the 1 in 10 Americans living with a rare disease.

The RDCC represents 24 life science companies committed to discovering, developing, and delivering treatments for patients living with rare diseases. RDCC member companies are leaders in rare disease innovation. Collectively, RDCC members invested more than $17 billion in research & development (R&D) in 2023, and continue to reinvest over half of annual expenditures back into R&D. Coalition members have brought nearly 50 treatments to market, and are currently working on more than 200 rare disease development programs, many of which would be the first ever FDA-approved therapy for their respective patient communities.

RDCC respectfully submits the following comments regarding the 21st Century Cures initiative, and recommendations for policy improvements to facilitate the discovery, development, and delivery of treatments for people living with a rare disease. We look forward to working with you to advance legislation to accomplish these goals.

Do the policies included in Cures 2.0 that have advanced through legislation or executive action meet the needs that the original Cures 2.0 bill aimed to address?

RDCC commends Congress for its significant strides in advancing regulatory reform for rare diseases, including through the Cures 2.0 Achieved Objectives. The recent Food and Drug Administration (FDA) guidance on Cures 2.0 topics – including gene and cell therapy, expedited approval, and the inclusion of real-world evidence in regulatory decision-making – is very helpful to sponsors of rare disease treatments. Additional guidance that is applicable across FDA's Centers, including on key topics such as the development and acceptance of novel biomarkers for rare diseases, is needed to advance the timely availability of new treatments.

Recommendation 1: We recommend that Congress build on the progress of Cures 2.0 and require the promulgation of guidance (to be applicable across FDA's Centers) to clarify the scientific rationale that underpins the Agency's acceptance of a new biomarker or intermediate clinical endpoint to support accelerated approval. We look forward to reviewing the Center for Biologics Evaluation and Research (CBER)'s forthcoming guidance, *Expedited Program for Serious Conditions – Accelerated Approval of Drugs and Biologics*.

What additional reforms, support mechanisms, or incentives are needed to enhance or improve the effectiveness of the steps already taken, including any structural reform to agencies, offices, or programs involved?

While 21st Century Cures and Cures 2.0 yielded notable progress in advancing the development and availability of treatments for rare diseases, there is a critical need for further action to address the unmet needs associated with rare disease. For people living with a rare disease who are fortunate to have an FDA-approved treatment for their condition, there are several ways to improve the facilitation of timely access to ensure patients can have the opportunity to benefit from safe and effective treatments as soon as they are approved. To that end, RDCC urges Congress to prioritize the following initiatives:

I. Implement a coordinated rare disease framework

RDCC acknowledges and commends FDA's recent announcement to establish a Rare Disease Innovation Hub (the Hub), which will work across rare diseases, serve as a single point of contact for matters that intersect the Center for Drug Evaluation and Research (CDER) and CBER, and enhance inter-center collaboration. The RDCC looks forward to working with the FDA as it implements the Hub. It is critical that the FDA partner with a wide range of rare disease stakeholders to realize the full potential of the Hub's vision. To fully realize the intent of the Rare Disease Innovation Hub, RDCC urges that Congress:

Recommendation 2: Provide oversight of the newly announced Rare Disease Innovation Hub to ensure that FDA establishes both a clear process for stakeholder participation in development and operation of the Hub and metrics for success. RDCC is supportive of efforts to advance a shared vision across the Agency to facilitate rare disease product development and applauds efforts to increase center coordination across the FDA. However, it is imperative to monitor the progress and achievements of the Hub to ensure that it accomplishes its objectives. Congress should direct the FDA to issue a report detailing the successes and learnings from the Hub, due one year from its launch.

II. Preserve and enhance the pillars that support the health of the rare disease ecosystem

Rare disease drug development has unique challenges that are further exacerbated in pediatric populations. At the same time, children are disproportionately affected by rare diseases. 1 in 2 patients diagnosed with a rare disease are children, and a third of those children won't live to see their fifth

birthday.[1] There are proven policies that help de-risk innovation for pediatric rare disease programs and increase the availability of treatments for children living with rare diseases.

Recommendation 3: RDCC urges that Congress permanently reauthorize the rare pediatric disease priority review (PRV) program. The rare pediatric disease PRV program is a critical tool to encourage rare disease drug development. The program has resulted in new treatments across 47 distinct rare disease indications benefitting more than 220,000 Americans with rare disease.[2] While the program has received strong bipartisan support in its reauthorization efforts since its original implementation in 2012, the risk that the program may lapse every few years can minimize the impact of the program. To realize the value of the PRV program and ensure the availability of new treatments for children with rare disease, the RDCC urges Congress to permanently reauthorize the rare pediatric disease PRV program.

III. Encourage and support FDA to leverage existing authorities and flexibilities to ensure that safe and effective rare disease products are available to patients in a timely manner

For rare disease drug development, one size does not fit all. Rare diseases involve unique challenges, such as small, heterogeneous patient populations; diagnostic delays; and slow rates of progression for some diseases. Over the past several decades, Congress has enacted laws and FDA has issued regulations and policies that together comprise a rare disease "toolkit." However, the flexibilities provided in this toolkit are not always consistently applied. In 2023, the Congressional Rare Disease Caucus urged FDA to "improve policy and uniformity across the Agency for the review of rare disease therapy and product applications" citing "significant, uneven application of rare disease policies, guidance, and expertise, even, at times, for the same product application.[3]" To address these concerns, the RDCC urges Congress to:

Recommendation 4: Maintain oversight authority of FDA's approach to rare disease drug development and review. In order to ensure that the FDA is adhering to directives via Prescription Drug User Fee Act (PDUFA) agreements and other Congressional activities, Congress should continue to conduct oversight informed by congressionally mandated reports. These reports help to ensure FDA is on-track to meet its goals, and also helps sponsors better understand the FDA's approach to and understanding of rare disease issues.

Recommendation 5: Continue to encourage FDA to exercise its existing authorities to the fullest extent throughout the development and review of rare disease treatments. Congress has established important regulatory authorities and flexibilities – including innovative trial designs, use of real-world evidence, and

[1] Delivering Hope for Rare Diseases. NIH National Center for Advancing Translational Sciences. https://ncats.nih.gov/sites/default/files/NCATS_RareDiseasesFactSheet.pdf
[2] Impact of the Priority Review Voucher Program on Rare Pediatric Disease Drug Development. Rare Disease Company Coalition. May 2024. https://www.rarecoalition.com/wp-content/uploads/Impact-of-the-Priority-Review-Voucher-Program-on-Rare-Pediatric-Disease-Drug-Development-1-1.pdf
[3] Letter from Rare Disease Congressional Caucus to FDA Commissioner Robert Califf. May 2023. https://www.klobuchar.senate.gov/public/_cache/files/8/6/86568676-ebfc-4416-a714-27a249fa34a2/B40F79902D4A9B717A210312961E17CA.05032023-letter.pdf

the accelerated approval pathway – to ensure that safe and effective rare disease products are available to patients in a timely manner.

IV. Enact legislative reforms that enhance regulatory science and enable progress

Congress and FDA have made significant progress, including through the implementation of 21st Century Cures initiatives, to advance new innovations for people with rare disease. However, there remains significant and urgent unmet medical need for new and better treatments. RDCC strongly supports new approaches to ensure that FDA is positioned and resourced to exercise its scientific and regulatory leadership, and to build a rare disease ecosystem that meets the needs of patients. Specifically, RDCC urges that Congress:

Recommendation 6: Enact the Better Empowerment Now to Enhance Framework and Improve Treatments (BENEFIT) Act (S. 373/H.R. 4472) to require FDA to include patient-centric data in its assessment of benefit and risk. RDCC applauds Congress for promoting the importance of patient experience data including through Cures and the Consolidated Appropriations Act of 2023. FDA should be further empowered to include patient experience data in the assessment of benefit and risk throughout the rare disease product lifecycle.

Recommendation 7: Establish a mechanism to ensure FDA's access to clinical and scientific expertise and timely scientific exchange by authorizing the Externally-Led Science Focused Drug Development (SFDD) meeting. SFDD represents a new forum to facilitate earlier discussion and education about specific rare diseases or groupings of rare diseases between FDA leaders, reviewers, scientific & medical experts, industry, and patient representatives. While helpful forums exist among FDA's current suite of meeting types, gaps remain in ability to educate FDA on scientific and development considerations for rare diseases. Like the format of Externally-Led Patient Focused Drug Development (PFDD) meetings, SFDD meetings would be organized and funded by external stakeholders, with no cost to the FDA beyond participation. SFDD meetings promote cross-training of Agency and sponsor teams and provide a meaningful opportunity for collaboration, knowledge sharing, and scientific alignment earlier in the development process. Similar ad-hoc workshops are currently embraced by scientific and medical experts, patient groups and developers. Congress should create the Science Focused Drug Development meeting to ensure that regulatory approaches keep pace with rapidly evolving science.

V. Enable rare disease patient access to accelerated approval therapies

The accelerated approval pathway (AAP) is a critical tool that can address the unique challenges of rare disease drug development and provide rare disease patients with earlier access to treatment based initial evidence of safety and effectiveness, while confirmatory studies required to verify clinical benefit are ongoing. However, some federal proposals have shown a willingness by public and private payers to modify coverage protocols based on arbitrary conditions of a drug's effectiveness in certain populations, which would limit patient access to life-saving treatments. A recent study found that these types of

changes to accelerated approval would put therapies that have the potential to address the needs of 3.6 million patients at risk of withdrawal.[4]

Any future policy reforms to the AAP should protect patient access, build upon Congress' recent steps to boost FDA oversight of accelerated approval products, leverage and enhance its existing authorities, and protect the integrity of this critical pathway. As such, we urge Congress to:

Recommendation 8: Protect FDA's regulatory authority and reject proposals that arbitrarily limit patient access to safe and effective therapies. The FDA is the sole authority to approve drugs for human use and evaluate their safety and effectiveness. Congress should reinforce FDA's regulatory authority and ensure that CMS, state Medicaid, and commercial payers do not undermine FDA's determination of a product's safety and efficacy by re-adjudicating FDA's decision. Congress should also prohibit any federally funded health care program from using payment as leverage to modify or counter FDA's evaluation of the safety and effectiveness of a rare disease treatment.

VI. Modernize newborn screening to enable earlier diagnosis

Rare disease diagnosis is uniquely complex. With over 10,000 known rare diseases, it can be challenging to pinpoint a diagnosis, especially when patient populations are as small as just a few dozen. Furthermore, the very nature of the rare disease means that physicians may not have the specialized knowledge needed to achieve an accurate diagnosis. Without an accurate diagnosis, patients living with a rare disease are less likely to receive transformative therapies that could slow, stop, or even reverse their symptom progression.

Newborn screening (NBS) is a vital and proven public health program that screens approximately four million U.S. newborns each year. In the first 24 to 48 hours of a baby's life, a small blood sample is taken to detect serious, often fatal, genetic conditions that can be treated if diagnosed early. We believe equitable access to newborn screening can ensure that all babies have the best chance for a healthy life. However, limitations of the current NBS system can cause significant delays between the availability of transformative therapies and comprehensive screening, putting children at risk for preventable- injury or death. There is an urgent need to modernize and advance newborn screening to ensure that all babies have access to a timely diagnosis.

To address these challenges, RDCC urges that Congress:

Recommendation 9: Establish a new stream of federal funding for the implementation of newborn screening. Currently, the majority of states do not screen for all conditions included on the Recommended Uniform Screening Panel (RUSP)[5], a list of disorders that the Secretary of the Department of Health and Human Services (HHS) recommends for states to screen as part of their state programs. Targeted funding

[4] Calculating the Value and Impact of Accelerated Approvals. Vital Transformation. November 2022. https://vitaltransformation.com/wp-content/uploads/2022/11/AA-Project_FINAL_2022_11_11.pdf
[5] Baby's First Test. https://babysfirsttest.org

is necessary to incentivize national harmonization among states, accelerate review of a greater number of conditions each year, and enable states to support and improve their patient/family and pediatrician/provider follow-up programs. The RDCC recommends increasing state funding so that state newborn screening programs are equipped to more quickly implement newborn screening of new conditions.

Recommendation 10: Pass S.350/H.R.482, the Newborn Screening Saves Lives Reauthorization Act. This bill would renew critical federal grants and programs that assist states in improving and expanding their newborn screening programs; support parent and provider education; and ensure laboratory quality and surveillance for newborn screening.

VII. Advance the availability and accessibility of new testing technologies

Innovation in revolutionary treatments has dramatically improved Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES), which help identify genetic variations or provide incidental findings. By identifying genetic causes, patients can begin treatments and interventions earlier and potentially alter the course of a condition. RDCC recommends that Congress:

Recommendation 11: Ensure that patients have equitable access to new diagnostics methods such as WGS, WES, phosphate regulating endopeptidase homolog X-linked (PHEX) genetic testing and other gene panels. RDCC supports the newly- proposed Transitional Coverage for Emerging Technologies (TCET) procedural notice, and additional efforts to streamline the coverage of new technologies by reducing the time between the FDA approval of new diagnostic testing tools and coverage by public payers. RDCC urges regulators to facilitate the inclusion of new technologies applicable to rare disease patients in these new coverage/approval paradigms.

Recommendation 12: Preserve regulatory paradigms to allow new testing innovation: Currently, many newborn screenings utilize laboratory-developed tests (LDTs). These tests, regulated under the Clinical Laboratory Improvement Amendments (CLIA), have included several technologies designed to meet unmet medical needs and to address and track rare disease diagnoses and progression. RDCC supports continued patient access to high-quality, accurate tests that promote innovation and keep pace with discovery in rare disease diagnosis and treatment. Any regulatory or legislative activity in this area should avoid disruption of patient access to such testing.

Recommendation 13: Pass the Precision Medicine Answers for Kids Today Act. This bill would help eliminate barriers, such as lack of insurance coverage and the inability to see relevant health professionals, to allow better access to genetic and genomic testing. Previously included in Cures 2.0, this critical legislation will make testing tools more accessible and affordable, thereby improving the lives of children living with rare genetic diseases.

VIII. Accelerate access to newly available therapies

Even the most innovative and effective rare disease treatments are only as valuable as they are accessible. For rare disease patients who are fortunate to have an FDA-approved treatment for their condition, it is important to advance policies that facilitate timely access so patients can benefit from treatments as soon as they are available.

Ultimately, policy must ensure that both public and private payers uphold the FDA's statutory authority—including for drugs approved through expedited development and review programs—in determining a medical product's safety and efficacy. This includes preventing payers from adopting pricing and reimbursement policies that would disincentivize the use of FDA's expedited development and review programs, and other regulatory tools to overcome barriers to rare disease drug development and speed patient access. To ensure that rare disease innovations are available to patients in a timely manner, we urge Congress to:

Recommendation 14: Reinforce timely access to treatment and remove administrative barriers that delay access. Patients living with rare diseases in the U.S. can experience a range of financial barriers to diagnosis, care, and treatment depending on their type of health insurance. Medicaid is a critical resource for Americans living with a rare disease and coverage decisions have significant consequences for timely access. Restrictive policies and barriers to coverage impose disproportionate and often insurmountable burdens on vulnerable patient populations, who may have no other path to diagnosis and treatment.

In Medicaid, for example, although states are required to cover drugs as long as the manufacturer enters into a Medicaid Drug Rebate Program Agreement,[6] Medicaid agencies have imposed access barriers more restrictive than the FDA-labeled indication, particularly for rare disease therapies due to concerns around cost and budget impact.

When an age limit or specific disease milestone is included in the FDA-approved indication statement, it is imperative that patients receive access to that treatment before the age limit or milestone is reached. Otherwise, patients suffering from a rare disease may further and irreversibly deteriorate. In approving a therapy and determining the indication statement, FDA relies on totality of data, scientific expertise, and risk-benefit profile. Therefore, the population included in the FDA-approved indication is the population that should be the foundation of a payer's coverage policy and, therefore, drive authorization. Inappropriately applying clinical trial criteria as the coverage criteria and basis for prior authorization undermines FDA's scientific authority.

Federal law requires that FDA-approved drugs subject to a rebate agreement be covered by each state Medicaid program upon availability.[7] In some states, lengthy pharmacy and therapeutics (P&T) Committees or Drug Utilization Review Boards (DURB), an entity that authorizes and reviews the prescribing, distribution and use of medication, carry out proceedings to generate and implement formal

[6] Sec. 1927. [42 U.S.C. 1396r–8], Social Security Act (SSA), https://www.ssa.gov/OP_Home/ssact/title19/1927.htm
[7] Sec. 1927. [42 U.S.C. 1396r–8], Social Security Act (SSA), https://www.ssa.gov/OP_Home/ssact/title19/1927.htm

coverage criteria that contradict such a requirement and can hinder access to newly available therapies for patients in need. Each state P&T Committee or DURB follows its own new-drug review law and policy, which in many states permits or even mandates extended review timelines. Such delays can result in unreasonable access restrictions on new drugs.

Congress should work with the Centers for Medicare & Medicaid Services (CMS) to ensure timely patient access to treatment and to achieve shorter, streamlined drug coverage approval processes. This includes enforcing existing Medicaid outpatient drug coverage obligations for state fee-for-service and contracted managed care organizations (MCOs) to ensure that when a drug is prescribed for its medically accepted FDA-approved indication, and a manufacturer has a signed Medicaid drug rebate agreement, the patient is promptly approved for treatment. CMS should instruct state Medicaid programs (including its MCOs) to reduce burdensome and unnecessary prior authorization processes to facilitate timely access to medicines.

IX. Facilitate cross-state Medicaid access

Rare disease patients often see providers in multiple states as there may be a limited number of specialists/experts for their given disease or condition. Yet, rules for credentialing providers are complex, and disincentivize coverage for out-of-state providers. This results in a patchwork system that discourages patient access to care. To simplify and expedite access to out-of-state coverage, we encourage Congress to:

Recommendation 15: Pass the Accelerating Kids' Access to Care Act (S. 2372/H.R.4758).[8] This bill provides a framework that policy makers should consider to ensure timely access to treatment across state lines. The Accelerating Kids' Access to Care Act would streamline the complicated and lengthy Medicaid provider screening and enrollment process

Recommendation 16: Mandate coverage for interstate telehealth. Both in-person and telehealth visits for patients with a rare disease should be covered when clinically appropriate. When out-of-state medical assistance is required due to the nature of a patient's symptoms or diagnosis, a plan should immediately recognize the out-of-state provider as a participating provider.

Recommendation 17: Establish a federal safe harbor to provide more certainty for manufacturers to offer travel support programs. This would help enable patients who need financial support to travel to treatments sites to receive care.

Recommendation 18: Instruct CMS to launch a Medicaid demonstration project to promote access for patients living with rare diseases. This demo would evaluate the impact of the payment of a quarterly separate furnishing fee to States to cover budget shortfalls resulting from payment to out-of-state providers for certain telehealth services, and the acquisition and administration of certain drugs.

[8] S. 2372, 118th Congress (2022-2023): Accelerating Kids' Access to Care Act, https://www.congress.gov/bill/118th-congress/senate-bill/2372

X. Ensure protections for rare conditions in employee health plans

Specialty drugs have the potential to transform and cure patients with devastating diseases, saving patients, and employers costs in the long-term. However, many employer-sponsored health plans fail to see the long-term savings that these specialty drugs can deliver.

Many self-insured employee health plans are not subject to the Affordable Care Act Section 1557, which prohibits discrimination in health care plans and activities. However, there is evidence that such plans are restricting coverage for rare disease patients through discriminatory policy designs based upon protected characteristics such as age and disability.[9] In order to prevent discrimination against rare disease patients, we encourage Congress to:

Recommendation 19: Increase transparency within the self-insured employer ecosystem. Health plans should be required to clearly disclose which FDA-approved drugs and their respective rare diseases are included in and which are excluded from the benefit packages made available for employers to select from in the upcoming plan year. This transparency will ensure all employers are educated and understand the benefit packages to inform the right health plan for their employees.

Recommendation 20: Prohibit the use of Alternative Funding Vendors (AFVs). Congress should amend ERISA to prohibit common practices of AFVs, including requiring patients to apply for financial assistance from charities before providing coverage for a drug; requiring beneficiaries assign legal powers to AFVs before providing coverage; and conditioning coverage of a prescription drug based on financial assistance available for the drug from non-profit organizations.

Recommendation 21: Mandate enhanced monitoring and oversight of Third-Party Administrators. Third-party administrators (TPAs) act as a consultant or company that provides recommendations and or health benefits management for insurance companies or businesses with self-funded health plans. While some services provided by TPAs can be beneficial, they have become complicit in aiding the uptake and increased prevalence of AFVs in the self-insured market governed by ERISA.

XI. Streamline value-based payment methodologies for rare disease therapies

Some policies and proposals turn to value assessments as a way to determine how much to pay for medicines and other treatments. Yet assessments often use a "one-size-fits-all" approach when considering the value of treatments that can undermine access for people living with rare diseases. State Prescription Drug Affordability Boards (PDABs) and similar groups may use value assessments to set upper limits on drug prices, leverage and improve state purchasing power. Depending on the methodologies and inputs they use, their assessments could be based on false standards and inequitable criteria and limit patients' access to needed treatments. We urge Congress to:

[9] Quality-Adjusted Life Years and the Devaluation of Life with a Disability. National Council on Disability. November 2019. https://nmqf.org/wp-content/uploads/2023/09/DisparitiesandValueAssesssmentWhitePaper.pdf

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Recommendation 22: Eliminate the use of one-size-fits-all value assessments and ensure that value assessments for rare disease therapies are patient-centered. Value assessments for rare disease treatments should reflect the available evidence for rare disease treatments including both the direct and indirect benefits of a treatment, particularly those most important to the patient. They can do so by accounting for measures the progression of disease, symptom control, a treatment's impact on productivity, ability of a patient to participate in activities of daily living, impact on caregiver burden, improvement over alternative treatments, impact on public health, and the value of hope.

Conclusion

We appreciate the opportunity to provide comments on the ongoing Cures initiative, and we thank Congresswoman DeGette and Congressman Bucshon for their continued commitment to improving the lives of Americans living with rare diseases. Should you have any questions, please feel free to contact me at stacey@rarecoalition.com. We look forward to working with you.

Sincerely,

Stacey Frisk
Executive Director
Rare Disease Company Coalition