



June 13, 2014

The Honorable Fred Upton, Chairman
U.S. House of Representatives
Committee on Energy & Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Upton,

On behalf of the 30 million men, women, and children affected by one of the nearly 7,000 known rare diseases, the National Organization for Rare Disorders (NORD) thanks Chairman Upton and the Energy & Commerce Committee for their continuing support of the rare disease community. We are excited to participate in the 21st Century Cures Initiative, a bi-partisan effort within the House Committee on Energy & Commerce aimed at improving the treatment discovery, development, and delivery process in the United States.

NORD is a unique federation of voluntary health organizations dedicated to helping people with rare "orphan" diseases and assisting the organizations that serve them. NORD is committed to the identification, treatment, and cure of rare disorders through programs of education, advocacy, research, and patient services.

We welcome the opportunity to comment on the 21st Century Cures Initiative's third white paper titled, "Patients". This white paper poses the question of how we can close the gap between the number of diseases and the number of treatments. Obviously, this is an extremely important topic for NORD, as the vast majority of diseases without a treatment are rare.

In order to address this question, we have developed the following proposals to accelerate the pace of medical innovation, and ensure that all rare disease patients receive the treatment they deserve. We look forward to discussing these ideas with the Energy & Commerce Committee as the 21st Century Cures Initiative continues.

1. Ensure Sufficient and Consistent Funding for the National Institutes of Health (NIH)

To assure that the basic, translational and clinical research system remains strong in the United States, Congress must provide sufficient and consistent funding for the NIH. The NIH is currently vastly underfunded, as yearly appropriations have largely remained stagnant since

2005. The recently proposed funding level for the NIH in the FY 2014 budget is actually lower than what the NIH received in 2012.¹

Not only is the NIH sorely underfunded, but the cyclical unpredictability of NIH funding is detrimental to medical research. Funding interruptions or alterations can derail projects, resulting in the loss of potentially valuable medical research. This also turns promising early career investigators away from research careers, a problem that then has long-lasting effects on the next generations of researchers.

The NIH operates several programs and initiatives that are critical to rare disease research. The National Center for Advancing Translational Sciences (NCATS) conducts various initiatives that advance innovation in rare disease research. NCATS collaborates with industry partners and academia to find new therapeutic uses for existing molecules, many of which may be effective in treating rare diseases.²

NCATS operates the Clinical and Translational Science Awards (CTSA) program which funds and coordinates clinical and translational research in over sixty research institutions across the United States.³ NCATS also operates the Therapeutics for Rare and Neglected Diseases (TRND) program which collaborates with academic researchers, patient organizations, and industry to speed the development of therapies for rare diseases.⁴

Finally, the Office of Rare Diseases Research (ORDR) within NCATS supports the Rare Diseases Clinical Research Network (RDCRN) and operates a rare disease database with nearly 7,000 diseases included.⁵

If the 21st Century Cures Initiative is to succeed in strengthening the medical research framework of this country, it must strengthen NIH funding and then remove the unpredictability of funding levels each year.

2. Create Incentives for Researchers to Enter the Rare Disease Research Field

Funding the NIH at an appropriate level will be effective in accelerating the pathway to cures only if we have talented and well-trained researchers to conduct the research. As proposed in NORD's previous 21st Century Cures Initiative Comments, Congress should create incentives to medical professionals in training for entering the rare disease field.

¹ Johnson, Judith A. "Brief History of NIH Funding: Fact Sheet" *Congressional Research Service*, 23 Dec. 2013 Web. 13 June 2014

² "Discovering New Therapeutic Uses for Existing Molecules" *National Center for Advancing Translational Sciences*, May 2014 Web. 13 June 2014

³ "About the CTSA Consortium" *Clinical Translational Science Awards*, Web. 13 June 2014

⁴ "Therapeutics for Rare and Neglected Diseases" *National Center for Advancing Translational Sciences*, Web. 13 June 2014

⁵ "The Rare Diseases Clinical Research Network" *Office of Rare Diseases Research*, Web. 13 June 2014

Within the NIH, Congress could create incentives, such as further fellowship funding or student loan repayment for entering rare disease research. Not only will this accelerate the pace of rare disease research, it will also accelerate innovations in treating common diseases, as many medical breakthroughs for common diseases originated with research into rare diseases.

Finally, with targeted incentive programs, Congress can assist in supporting early career rare disease research investigators by encouraging NIH to enlarge the presence of clinical investigator expertise, and the science of small clinical trials, throughout its grant review process.

By expanding the pool of researchers who focus on rare diseases, Congress will accelerate the pace of medical discovery for both rare and common diseases.

3. Commission a “National Plan for Rare Diseases”

The U.S. needs a consensus document that sets for a National Plan for Rare Diseases. This agenda would address many of the questions that the “Patients” white paper asks.

First, Congress should examine the Institute of Medicine’s (IOM) 2010 report titled “Rare Diseases and Orphan Products: Accelerating Research and Development”.⁶ This report aims to implement an overarching national strategy for rare disease research and product development.

After examining existing recommendations on how to improve the nation’s rare disease research system, Congress should commission a comprehensive agenda that evaluates the entire rare disease healthcare ecosystem, and makes recommendations on how to improve the discovery, development, and delivery of treatments to rare disease patients. Congress can follow the precedent of other National Plans it has commissioned, such as the National Plan to Address Alzheimer’s.⁷

This plan must be entirely comprehensive and cover the entire spectrum of the rare disease landscape. It should address the duties of each public agency involved in rare disease treatment discovery, development, and delivery. This plan must also address how these public agencies can collaborate with private entities to improve the rare disease ecosystem.

Within this National Plan, Congress should specifically commission the following:

- **National Rare Disease Research Recommendations**

Congress can strengthen the basic and translational rare disease research ecosystem by requesting the Orphan Products Board (see NORD’s comments on the 21st Century Cures’ first white paper) to publish a yearly agenda with recommendations for rare disease research and products development.

⁶ “Rare Diseases and Orphan Products” Institute of Medicine, Oct. 2010, Web. 13 June 2014

⁷ “National Plan to Address Alzheimer’s Disease: 2014 Update” U.S. Department of Health & Human Services Web. 13 June 2014, <<http://aspe.hhs.gov/daltcp/napa/NatlPlan2013.shtml>>

The Orphan Products Board will work, in consultation with the NIH and FDA, to recommend advances in innovative clinical trial designs for orphan therapies. The Orphan Products Board will also work with the Centers for Disease Control and Prevention (CDC) on epidemiological techniques and advances.

In developing this agenda, the Orphan Products Board will consult with government, medical, and academic researchers. The Orphan Products Board will also consult with sponsors on how to facilitate bringing products to market. Finally, the Orphan Products Board will consult with patients on priorities in developing new treatments.

- **The Benefits of Rare Disease Research on the Economy and Healthcare System**

Rare diseases are generally costlier to treat, per capita, than more common diseases, because rare diseases often take between five and ten years to diagnose, orphan therapies are often more expensive, and the vast majority of rare diseases are chronic, thus leading to a life-time of healthcare costs.

As part of this National Plan, Congress should commission a study on how better funding and coordination of rare disease research will benefit the economy and the healthcare system, as well as lower the Federal government's healthcare expenditures. Greater coordination of research will foster a more efficient use of public and private resources.

- **National Agenda on Rare Disease Registries and Natural History Studies**

Natural history studies and registries play a critical role in the drug discovery and development process. Patient registries represent one of the best resources to collect prevalence, demographic, natural history, and comparative effectiveness data on rare diseases. Standardized natural history registries, tied to tissue banking, facilitate the generation of research leads, and accelerate studies examining associations between phenotype (disease-related physical and mental characteristics) and genotype. Currently, very few rare disease patient registries exist and where they do, they are often limited in their usefulness.

In collaboration with the NIH and FDA, NORD is currently in the process of building a rare disease patient registry program to ensure rare disease patients have adequate natural history information in order to spur drug discovery and development.

We cannot do it alone, however, and with nearly 7000 diseases without a treatment, Congress should commission a plan to coordinate rare disease patient registries and

natural history studies in order to catalyze drug discovery and development for these diseases.

- **National Agenda for the Collection of Rare Disease Data**

While there have been great advancements in our collective knowledge on rare diseases, there is still far much more we need to learn in order to find treatments and cures for the nearly 7,000 diseases with no treatment.

Congress can start to address this knowledge gap by mandating that rare disease information, including prevalence, length of diagnosis, off-label prescription use, and many others, be included within the already existing data collection efforts undertaken by various government agencies. With this information, we will better understand the challenges facing the rare disease patient, and will be better able to address these challenges.

4. Ensure All Current Laws that Increase the Patient's Involvement are Implemented Fully

While NORD believes that the patient's voice must be strengthened in the drug development and approval process (see #5), we first need to assure that current laws addressing patient involvement are being implemented fully. The Food and Drug Administration Safety and Innovation Act (FDASIA) made groundbreaking strides in encouraging that patients play a greater role during the drug approval process. The FDA has implemented many of these changes admirably but there are various other measures contained within FDASIA that are not being implemented to the fullest extent, or not at all.

First, the FDA must include a patient or patient representative on the drug review committee as mandated by section 903 of FDASIA.⁸ While the FDA has increased patient involvement in other aspects of the drug approval process, such as in Advisory Committee Hearings, the FDA has yet to include patients on a review panel. The FDA should be required to fulfill this mandate.

Second, while the FDA has conducted several patient-focused drug development meetings, it has yet to demonstrate how it intends to use the collected information to inform the drug review process. While NORD appreciates the FDA's efforts in implementing the patient-focused drug development initiative, we are particularly eager for the findings from these meetings to be incorporated within the drug review process.

Finally, NORD requests that the FDA develop a guidance advising patient organizations on how they can administer their own patient-focused drug development meetings and provide data that

⁸ Food and Drug Administration Safety and Innovation Act § 903

will be useful to the drug approval process. Under current law, the FDA is to hold twenty patient-focused drug development meetings. The information derived from these meetings can be broadened substantially if FDA provides guidance on how patient organizations can independently conduct their own patient-focused drug development meetings in a manner that would enable the FDA to use the findings of these meetings to enhance the drug review process.

5. Expand Patient Partnerships Within the FDA

We advocate that patients be regarded and treated as partners with the FDA in the drug review process. At present, despite progress, patients are regarded as outside participants who are asked to occasionally consult on drug efficacy and effectiveness, usually under the auspices of the drug companies.

We urge FDA to standardize patient input within the drug review process. Currently, the level of patient involvement varies among review divisions. Patient contribution at regular and predictable times must be built into the process.

Rare disease patients, their families, and their caregivers can be most useful for the FDA when assessing the benefit-risk of a therapy. In its “Patients” white paper, the 21st Century Cures Initiative asks, “How should regulators evaluate benefit-risk? How do you work with regulators regarding benefit-risk? Can this process be improved?”

It is NORD’s opinion that patients can make significant contributions in helping to evaluate the benefit-risk of a drug. Patients must be equal partners with the FDA and companies in making this assessment.

6. Ensure Sufficient and Consistent Funding for the Food and Drug Administration

Much like the NIH, the FDA is also drastically underfunded for the wide array of regulatory responsibilities it maintains. The FDA is continually charged by Congress with additional oversight responsibilities, not to mention the drastic expansion of existing responsibilities due to globalization and increasingly diverse scientific innovations.

It is NORD’s belief that the FDA desires to undertake and complete many, if not all, of the reforms NORD has called for within our responses to the 21st Century Cures White Papers. However, they simply do not have the means to do so.

It is time for Congress to recognize the importance of the FDA and dramatically increase the yearly appropriations the FDA receives. The 21st Century Cures Initiative can accelerate the pace at which treatments reach the patient by giving the FDA the resources they need to utilize the expedited review pathways for all treatments that qualify. Appropriate funding will also allow the FDA to ensure its review staff is well trained in the newest scientific breakthroughs, and will allow them to engage the patient community at every opportunity.

7. Ensure Reimbursement for “Non-Conventional” Rare Disease Therapies

In NORD’s comments on the 21st Century Cures Initiative white paper titled, “A Call to Action”, we highlight the issue of high cost-sharing within drug formularies for specialty drugs, many of which treat rare diseases. We also discuss off-label reimbursement issues, and the importance of off-label use of therapies for rare disease patients.

These are several of many reimbursement issues facing patients with rare diseases, including lack of coverage of orphan therapies under the Medicare and state Medicaid programs.

While reimbursement problems exist for all orphan therapies, we are particularly concerned about issues surrounding “non-conventional” treatments, especially the lack of reimbursement for such products.

For the purposes of this paper, NORD defines non-conventional therapies as treatments that are not the standard “small-molecule” drug or “large-molecule” biologic. Instead, “non-conventional” therapies are treatments such as medical foods for Inborn Errors of Metabolism (as well as various other rare diseases), medical devices (particularly humanitarian use devices), bio-engineered treatments, and more.

NORD is concerned that the reimbursement model that the Federal, State, and private health insurance plans utilize often ignores the importance of these therapies, and how critical they are to the survival of many rare disease patients. As Congress addresses the discovery, development, and delivery of treatments for rare disease patients, NORD requests that Congress stay particularly mindful of diseases that require therapies, such as medical foods and humanitarian use devices that do not fall within the common categories of drugs and biologics.

Thank you again for the opportunity to engage in this exciting and much-needed initiative. We look forward to working with Chairman Upton and the Energy & Commerce Committee as the 21st Century Cures Initiative continues, and we are grateful for the Chairman’s recognition of these extremely important issues within the rare disease community.

For questions regarding NORD or the above comments, please contact Diane Dorman, Vice President of Public Policy, at ddorman@rarediseases.org or (202) 588-5700 ext. 102.

Sincerely,



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NORD President and CEO