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On behalf of the Cystic Fibrosis Foundation and the 30,000 people with cystic fibrosis (CF), we are pleased to submit the following testimony regarding fiscal year 2011 appropriations for cystic fibrosis-related research at the National Institutes of Health (NIH) and other agencies.

**ABOUT CYSTIC FIBROSIS**

Cystic fibrosis is a life-threatening genetic disease for which there is no cure. People with CF have two copies of a defective gene, known as CFTR, which causes the body to produce abnormally thick, sticky mucus that clogs the lungs and results in fatal lung infections. The thick mucus in those with CF also obstructs the pancreas, making it difficult for patients to absorb nutrients from food.

Since its founding, the Cystic Fibrosis Foundation has maintained its focus on promoting research and improving treatments for CF. More than thirty drugs are now in development to treat CF; some treat the basic defect of the disease, while others target its symptoms. Through the research leadership of the Cystic Fibrosis Foundation, the life expectancy of individuals with CF has been boosted from less than 6 years in 1955 to 37 years today. This improvement in the life expectancy for those with CF can be attributed to research advances and to the teams of CF caregivers who offer specialized care. Although life expectancy has improved dramatically, we continue to lose young lives to this disease.

The promise for people with CF lies in research. In the past five years, the Cystic Fibrosis Foundation has invested over \$660 million in its medical programs of drug discovery, drug development, research, and care focused on life-sustaining treatments and a cure for CF. A greater investment is necessary, however, to accelerate the pace of discovery and development of CF therapies. This testimony focuses on the investment required to rapidly and efficiently discover and develop new CF treatments aimed at controlling and curing CF.

**SUSTAINING THE FEDERAL INVESTMENT IN BIOMEDICAL RESEARCH**

This Subcommittee and Congress are to be commended for their steadfast support for biomedical research and their commitment to the National Institutes of Health (NIH), particularly the effort to double the NIH budget between FY 1999 and FY 2003 as well as the significant investment provided by the American Recovery and Reinvestment Act (ARRA) in 2009. These increases in funding brought a new era in drug discovery that has benefited all Americans. Congress must adequately fund the NIH so that it can capitalize on scientific advances in order to maintain the momentum generated by the doubling of funds and the infusion from ARRA.

The flat-funding of the NIH since 2003 has decreased purchasing power, limiting the pursuit of critical research. The Cystic Fibrosis Foundation joins the Coalition for Health Funding to recommend all health discretionary spending be increased \$67.1 billion in FY 2011, or \$9.3

billion over the FY 2010 levels. This increased investment will help maintain the NIH's ability to fund essential biomedical research today that will provide the care and cures of tomorrow. If the Committee is not able to recommend funding at this level, Congress should advise the NIH to focus on contributing funds to research partnerships that will accelerate therapeutic development to improve people's lives.

### **STRENGTHENING CLINICAL RESEARCH AND DRUG DEVELOPMENT**

The Cystic Fibrosis Foundation has been recognized for its unique research approach which encompasses everything from basic research through Phase III clinical trials, and has created the infrastructure required to accelerate the development of new CF therapies. As a result, we now have a pipeline of more than thirty potential therapies which are being examined to treat people with CF. As a prime example, in February 2010, Cayston<sup>®</sup> a new much-needed antibiotic that combats recurrent lung infections, arrived in the hands of people with CF. This new treatment is a direct result of the Foundation's innovative research agenda, advancing from bench to bedside through the Foundation's research program which speeds the creation of new CF therapies. Our successes, and specifically our Therapeutics Development Network discussed below, can serve as a map for the development of new treatments for other diseases.

The Foundation is a leader in creating a clinical trials network to achieve greater efficiency in clinical investigation. Because the CF population is small, a higher proportion of people with the disease must partake in clinical trials than in most other diseases. This unique challenge prompted the Foundation to streamline our clinical trials processes. As a result, research conducted by the Foundation is more efficient than ever before and we are a model for other disease groups.

We applaud the efforts by the nation's health agencies to encourage greater efficiency in clinical research and we are hopeful that the Committee will direct the national health agencies to pay special attention to advances in treatment methods and mechanisms for translating basic research across institutes into therapies that can benefit patients.

#### **Development of Rare Disease Research Networks**

The Committee should direct the NIH and other agencies to allocate additional funds for innovative therapeutics development models including the Therapeutics for Rare and Neglected Diseases (TRND) and Cures Acceleration Network (CAN) programs as well as for clinical research to meet the demand for testing promising new therapies for cystic fibrosis and other diseases. Support should also be directed toward the continuation of other rare disease research networks, such as the NIH's pediatric liver disease consortium.

The CF Foundation's established clinical research program, the Therapeutics Development Network (TDN), plays a pivotal role in accelerating the development of new treatments to improve the length and quality of life for cystic fibrosis patients. Lessons learned from the TDN's centralization of data management and analysis and data safety monitoring in the TDN will be useful in designing clinical trial networks for other diseases. Dr. Francis Collins, director of the NIH, has specifically cited the TDN as an exemplar for TRND. Coupled with the newly established CAN, the time between discovery and development of drugs and therapies can be accelerated if these programs are fully funded.

### **Providing for the U.S. Food and Drug Administration (FDA)**

We urge the Committee to increase funding for the FDA to ensure that the Agency has the necessary resources and funding to effectively evaluate new and emerging treatments. In order to be effective, the FDA needs not only an adequate number of reviewers of new treatments, but also those with the appropriate skills and expertise, particularly for rare diseases like cystic fibrosis. Additional support for the FDA through increased funding not only assures that the nation has a safe and effective supply of drugs and devices, but also that the agency can give the necessary attention to reviewing treatments that treat small populations but serve specific unmet medical needs, such as Cayston<sup>®</sup>.

The CF Foundation applauds the appointment of Dr. Anne Pariser as the new Associate Director for Rare Diseases in the FDA's Center for Drug Evaluation and Research's Office of New Drugs. We are pleased to see this new position held by such a capable and competent administrator. Similarly, we applaud the regulatory science initiative formed by the NIH and the FDA with the goal of accelerating the development and use of new approaches to evaluate drug safety, efficacy and quality and urge the Committee to strongly support this type of collaboration. Support for coordination between new programs like TRND and CAN throughout the national health agencies leverages the federal investment in new research, facilitating swifter development and delivery of new medical treatments.

### **Supporting Translational Research and Investigators**

A significant discrepancy persists between the first award funding granted to clinical laboratory investigators and that granted to basic laboratory investigators. The difference is even greater for second awards and prolonged funding of clinical investigators. The NIH must maintain support for translational research and the investigators piloting those projects. Without this support, the NIH stands to lose an entire generation of clinically trained individuals committed to clinical research. The "generation gap" that would be created by the loss of these clinical researchers would affect the ability of the NIH to conduct world-class clinical investigation and jeopardize the standing of the United States as the world's premiere source for biomedical research.

### **The Clinical and Translational Science Awards (CTSA)**

We urge the NIH to enhance the Clinical and Translational Science Awards (CTSA), a program designed to transform the way in which clinical and translational research is conducted. Such an increased emphasis on clinical translation can enable researchers to provide new treatments more efficiently to patients. For example, at Seattle Children's Hospital, a CTSA program has been instrumental in identifying best practices for efficient clinical trial participation and improving clinical outcomes in care for cystic fibrosis. Tremendous effort has brought institutions together to rally around this program and similar programs at other institutions, yet current funding levels make it difficult for the full complement of programs to be funded. Additionally, key to the success of the CTSA is the development of cost-sharing for use of infrastructure services. An example of this mechanism is the General Clinical Research Centers (GCRC), which allowed institutes to reduce their research budgets by having investigators use the GCRC when clinical care was made available at no additional cost. In order to maximize the potential of the CTSA, multiple institutes within the NIH must be able to provide financial resources for critical programs such as this.

### **Alternative Models for Institutional Review Boards (IRB)**

We are pleased that the Department of Health and Human Services has encouraged the exploration of alternative models of IRBs, including central IRBs, by the CTSA. We encourage

Congress to urge the Department to demonstrate more aggressive leadership in persuading all academic institutions to accept review by a central IRB—without insisting on parallel and often duplicative review by their own IRB—at least in the case of multi-institutional trials in rare diseases. Such oversight could help provide greater expertise to improve trial design and enable critical research to move forward in a timelier manner without undermining patient safety.

### **Research Compensation for Supplemental Security Income**

An additional impediment in our effort to accelerate the development of new therapies is the Social Security Administration's current Supplemental Security Income (SSI) rules, which count research compensation for participation in a clinical drug study as income for determining SSI. This policy creates an unnecessary barrier to clinical trial participation for a significant number of people with CF, and thus severely limits efforts to develop new therapies. H.R. 2866, the Improving Access to Clinical Trials Act of 2009, would allow the Social Security Administration to disregard any income received from compensation for clinical trials when determining eligibility for programs like SSI. Support from the Committee on resolving this disincentive toward clinical research is appreciated.

### **Partnership with the National Center for Research Resources (NCRR)**

The CTSA program, administered by the NCRR, encourages novel approaches to clinical and translational research, enhances the utilization of informatics, and strengthens the training of young investigators. The Cystic Fibrosis Foundation has enjoyed a productive relationship with the NCRR to support our vision for improving clinical trials capacity through its early financial support of the TDN. Recently, however, the NCRR decided to reject funding for disease-specific networks in favor of those without a disease focus. As a result of this policy, some of the best clinical research consortia are prohibited from competing for NCRR grants, including but not limited to the CF TDN. We urge the NCRR to reverse this decision.

### **SUPPORTING DRUG DISCOVERY**

The Cystic Fibrosis Foundation's clinical research is fueled by a vigorous drug discovery effort—early stage translational research of promising strategies to find successful treatments for this disease. Several research projects at the NIH will expand our knowledge about the disease, and could eventually be the key for controlling or curing cystic fibrosis.

### **Opportunities in Animal Models**

The Cystic Fibrosis Foundation is encouraged by the NIH's investment in a research program at the University of Iowa to study the effects of CF in a pig model. The program, funded through research awards from both NHLBI and the Cystic Fibrosis Foundation, bears great promise to help make significant developments in the search for a cure. While a company has been established to produce the animals, the infrastructure and extensive animal husbandry required to keep the animals alive and conduct research on them is available at few academic institutions. We urge additional funding to create a facility that would enable researchers from multiple institutions to conduct research with these models.

### **Facilitating Scientific Data Connections**

An explosion of data is emerging from "big science" projects such as the Human Genome Project and the International HapMap Project. We encourage investments by NIH into the development of systems that permit the linkage of gene expression, protein expression and protein interaction data from independent laboratories. While construction of such an interface

would be difficult, it would undoubtedly facilitate generations of new ideas and open new areas of medically important biology.

### **Increasing Investment in Inflammatory Response Research**

Cystic fibrosis, like diseases such as inflammatory bowel disease, chronic bronchitis, and rheumatoid arthritis, causes an intense inflammatory response. The Cystic Fibrosis Foundation enthusiastically supports investments by the NIH to gain a greater understanding of neutrophil-driven inflammatory responses, which would lead to improved methods of safely interfering with the inflammatory process and contributing to the health and wellbeing of the US population.

### **Supporting High Throughput Screening**

The committee should urge the NIH to continue to fund high throughput screening initiatives in keeping with Common Fund priorities. Support for the follow-up and optimization of compounds identified through this type of screening can help to bridge the development gap and bring about more drugs that can make it to patients' bedsides.

### **Funding Systems Biology Platforms**

In order to rapidly accelerate the identification of potential biomarkers and understand the mechanisms of action of CFTR function, data generated from multiple laboratories and scientific centers must be integrated. To address this, the Cystic Fibrosis Foundation has partnered with a systems biology company called GeneGo to generate a cystic fibrosis-focused systems biology platform to illustrate the various effects of CFTR dysfunction in multiple cell systems. The CF Foundation urges NIH to provide additional funding to support research efforts aimed at leveraging systems biology platforms to integrate multiple disciplines within the CF research community in order to accelerate drug development and biomarker validation for cystic fibrosis.

### **Small Business Innovation Research Program at NIH**

Small Business Innovation Research (SBIR) program grants allocated by the NIH have helped many small biotechnology and pharmaceutical companies to develop vital treatments for a variety of diseases. The SBIR program could provide further support by directing that a portion of all grants awarded be used for rare disease research. With such a small portion of the population likely to purchase the drugs, research to produce drugs to treat rare diseases is often considered too large a financial risk to take on. It is important to note, however that there are over 25 million Americans with a rare disease. By directing even small dollar grants to develop drugs for these diseases, Congress can eliminate some of the risk that keeps biotechnology and pharmaceutical companies from developing drugs for rare diseases.

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The NIH has wisely focused on translational research as a touchstone for ensuring the relevance of the agency to the American public. The CF Foundation is the perfect example of this notion, having devoted our own resources to developing treatments through drug discovery, clinical development, and clinical care. Several of the drugs in our pipeline show remarkable promise in clinical trials and we are increasingly hopeful that these discoveries will bring us even closer to a cure. Encouraged by our successes, we believe the experience of the CF Foundation in clinical research can serve as a model of drug discovery and development for research on other orphan diseases and we stand ready to work with NIH and Congressional leaders. On behalf of the Cystic Fibrosis Foundation, we thank the Committee for its consideration.