

*Cystic Fibrosis Foundation
Subcommittee for Labor, Health and Human Services, Education and Related Agencies
National Institutes of Health*

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 2010 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 which 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 six years in 1955 to 37 years in 2007. 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 is 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 more rapidly and efficiently discover and develop new CF treatments aimed at controlling or 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 FY1999 and FY2003 as well as the significant investment provided by the American Recovery and Reinvestment Act (ARRA). 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 that the doubling and the infusion of funds from ARRA generated.

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 increasing the budget for all health discretionary spending by 13 percent in FY2010, or \$7.4 billion over the FY2009 Omnibus. This increased investment will help maintain the NIH's ability to fund essential biomedical research today that will provide tomorrow's care and cures. 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 peoples' lives.

STRENGTHENING OUR NATION'S RESEARCH INFRASTRUCTURE

Because CF is a disease that impacts several systems in the body, several institutes at the NIH share responsibility for CF research. We urge the NIH to pay special attention to advances in treatment

methods and mechanisms for translating basic research across institutes into therapies that can benefit patients across institutes. The Cystic Fibrosis Foundation has been recognized for its own research approach that encompasses 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 that are being examined to treat people with CF.

The Clinical and Translational Science Awards (CTSA)

The Clinical and Translational Science Awards (CTSA) program was a key component of the NIH's Roadmap initiative. The program is designed to transform how clinical and translational research is conducted, ultimately enabling researchers to provide new treatments more efficiently to patients. Tremendous effort brought institutions together to rally around this program, yet current funding levels make it difficult for the 39 programs (out of a planned 60) to succeed.

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 such as inpatient stays, lab tests, nursing staff, was made available at no additional cost. Today, individual investigators must provide funds for clinical care cost-sharing from grants funded from other NIH institutes. As research becomes more expensive and private capital dries up, it becomes even more critical to ensure support for translational research, that is, research that moves a potential therapy from development to the market. In order to maximize the potential of the CTSA, multiple institutes within the NIH must be able to provide financial resources for this critical program.

Supporting Clinical Research

A significant discrepancy persists between the funding awarded to clinical and basic laboratory investigators for first awards. 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.

FACILITATING CLINICAL RESEARCH AND DRUG DEVELOPMENT

The Cystic Fibrosis Foundation applauds the NIH's efforts to encourage greater efficiency in clinical research. The Foundation has been a leader in creating a clinical trials network to achieve greater efficiency in clinical investigation. Because the CF population is so small, a more significant portion 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. Research conducted by the Foundation is more efficient than ever before and we are a model for other disease groups.

The Model of the Cystic Fibrosis Therapeutics Development Network

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 its centralization of data management and analysis and data safety monitoring in the TDN will be useful in designing clinical trial networks in other diseases. We urge the Committee to direct the NIH and other agencies to allocate additional funds for innovative therapeutics development models like the TDN. The Cystic Fibrosis Foundation urges the Committee to allocate additional resources for clinical research in order meet the demand for testing the promising new therapies for cystic fibrosis and other diseases.

Alternative Models for Institutional Review Boards

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. We urge the Committee to direct the Social Security Administration to disregard any compensation to an individual who is participating in a clinical trial testing rare disease treatments that has been reviewed and approved by an institutional review board and meets the ethical standards for clinical research for the purposes of determining that individual's eligibility for the SSI program.

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.

Exploring Protein Misfolding & Mistrafficking

We applaud the National Heart, Lung and Blood Institute (NHLBI), and the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) for their initiatives that target research on protein misfolding, and urge an aggressive commitment to facilitate continued exploration in this area to build upon promising discoveries. We urge the NIH to continue to devote special attention to research in protein misfolding and mistrafficking, an area which could yield significant benefits for patients with CF and other diseases where misfolding is an issue.

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, cause an intense inflammatory response. The Cystic Fibrosis Foundation enthusiastically supports investments by the NIH to gain a greater understanding of inflammatory signaling and inflammatory cascades, 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 the NIH Roadmap suggestions. 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. Several companies developing CF treatments have used SBIR grants to fund their development process.

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.

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.