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Robert J. Beall, Ph.D.
President and CEO
Cystic Fibrosis Foundation
6931 Arlington Road
Bethesda, MD 20814

Answers to Questions for the Record for the hearing:
"21st Century Cures: Incorporating the Patient Perspective"
Committee on Energy and Commerce, Subcommittee on Health

The Honorable Leonard Lance

- 1. In the first panel I questioned Dr. Woodcock on the effectiveness of ClinicalTrials.gov. I would like to get your thoughts on the effectiveness of ClinicalTrials.gov. Is it something any of you use as a resource? What can be done to improve the site, and what role can it play in modernizing clinical trials?**

Yes, the Cystic Fibrosis Therapeutics Development Network uses ClinicalTrials.gov as a resource. All trials that are posted to the Cystic Fibrosis Foundation website contain a link to ClinicalTrials.gov, and the descriptions used for trials on this site are the basis for the descriptions we post.

ClinicalTrials.gov could be improved greatly by posting plain language descriptions of the studies. The majority of the descriptions posted on ClinicalTrials.gov are at a college reading level or above. Half of adults in the country read at an 8th grade level or below, which makes the material on the site difficult for non-researchers to use.

The website could also utilize more robust educational tools to explain clinical trials, and the jargon used in the descriptions to the public could be communicated in a more user-friendly way by using pictures and illustrations to demonstrate complex concepts.

- 2. It was clear from our discussion that more needs to be done to increase patient engagement in the clinical trial process. Will you walk me through the process for recruiting and selecting patients for clinical trials? What information is provided to patients? How can researchers and physicians make patients more comfortable with participating in clinical trials?**

Generally, patients are notified that they are eligible to participate in a study by the Research Coordinator (RC) or Principal Investigator (PI) at the site conducting the study. The cystic fibrosis Patient Registry helps to identify patients that meet eligibility criteria. Patients also can find out about studies through a variety of sources including the cff.org website, ClinicalTrials.gov, or advertising from the

center conducting the study that allows the patients to contact the RC personally. To be selected they have to pass the screening criteria set up in the research protocol.

The Cystic Fibrosis Foundation has produced a lot of information for patients and families about clinical trials. We aim to establish a culture of research through our network of accredited cystic fibrosis care centers so that patients are familiar with what is being done in CF research and are educated in what it means to participate in a clinical trial. This material includes:

- Videos from people with cystic fibrosis who have participated in a clinical trial,
- Webcasts with researchers about what it is like to participate in a clinical trial,
- Educational material on the web and in print about clinical trials (in English and Spanish),
- Awareness and educational materials that are passed out in the clinic to familiarize patients with CF research, including brochures that were written by a person with CF who is active in clinical research,
- Newsletters and educational sessions provided by care centers with updates on research at their center and nationally, and
- Searchable material on clinical trials and the drug discovery process at cff.org.

We believe it is important to create a culture of research from the start of care. This means talking with all cystic fibrosis patients about CF clinical research, not just those who are eligible for a particular study.

It is also important to involve patients in the clinical research process. To do this we have an adult with cystic fibrosis and parent of a child with CF on our protocol review committee to help review and give input on the study design and feasibility for the participant. We also encourage cystic fibrosis care centers to conduct surveys on participant experiences in clinical research.

Clinical trials should have a customer service approach where patient needs are at the forefront. This includes providing services in off hours, having weekend visits, and ensuring that center personnel and patients are communicating through the medium in which the patient feels most comfortable.

Engaging patients more deeply in the clinical trial process is a top priority for the Cystic Fibrosis Foundation, and we are currently working to increase the scope of our efforts in this area.

The Honorable Gus Bilirakis

- 1. The CF Foundation operates and fully funds the CF registry and seems to have captured the entire CF population in their registry. How can other groups successfully establish their own registry and how can they successfully grow it?**

The Cystic Fibrosis Foundation is nationally known for its comprehensive Patient Registry, established in 1966 to track data on the health of cystic fibrosis patients in the United States. This robust collection of quality data has played an essential role in the improvement of care quality and disease outcomes for those with cystic fibrosis, and provides important natural history data for researchers. It also provides information to foster medication adherence programs and policy initiatives to encourage better coverage and payment for life-saving CF therapies.

One of the Foundation's most important lessons learned in its decades of administering the Patient Registry is that of continual growth and improvement. The CF Foundation consistently seeks to improve the Patient Registry, the data collected and stored in the Registry, and the optimal uses of these data.

For example, in 1995, the Foundation expanded the collection capabilities of the Registry from the documentation of basic demographic and disease characteristics and outcomes to include quarterly measures of growth and lung function, as well as more detailed data on complications and treatment. This provided epidemiologists a resource to better understand the pathogenesis of CF and the opportunity to identify risk factors that may be associated with patient-level variations in disease course and outcome. Another example came about in 2003, when the Registry transformed its data collection from paper-based year-end summary to a more dynamic web-based data entry tool called PortCF, which allows greater access to raw data and the implementation of tools to better track and study care quality and health outcomes.

A notable, major milestone in the evolution of the Patient Registry was in 2006, when CFF became the first and only rare disease organization to publicly release comparative health outcomes of care for its nationwide network of accredited CF care centers. CFF began to examine care center variations in practice and outcomes in the late 1990s, and making this data publicly available enables the CF community to identify and adopt best treatment practices and improve overall patient care.

2. Section 903 of FDASIA was the Expert Act, which encourages FDA to proactively engage with specific rare disease experts on an individualized, case by case basis. This is an important provision because many times FDA may lack the expertise on a disease, especially a rare disease. How is the Expert Act being implemented by the FDA? How can FDA take advantage of the Expert Act to move treatments to patients quickly?

The Cystic Fibrosis Foundation commends the Food and Drug Administration for moving quickly to implement a number of important provisions of the Food and Drug Administration Safety and Innovation Act (FDASIA) that seek to incorporate the patient perspective and encourage greater efficiency in drug review. However, we have not seen evidence that the FDA is implementing Section 903 to the fullest extent possible, and the Cystic Fibrosis Foundation urges the agency to make the most of this important tool as it considers innovative new treatments and confronts the challenges ahead.

The CF Foundation strongly supported the inclusion of section 903 in the user fee reauthorization. This type of case-by-case consultation with external experts, initiated by FDA reviewers, is different from other provisions of FDASIA. It is not tied to drug sponsors, and it is not part of a pre-scheduled public meeting or workshop. There are 7,000 rare diseases, each with their own demographics, consideration of unmet medical need and disease severity. At times, the challenges inherent in the review of a drug for a rare disease must be articulated and clarified by someone who specializes in that disease or that challenge, on an individualized basis. Section 903 encourages such collaboration.

We know this type of collaboration works. For example, the FDA approved Kalydeco, a groundbreaking genetically-targeted treatment for CF, in only three months. Its review time was one of the fastest in the FDA's history. Throughout Kalydeco's review, the Cystic Fibrosis Foundation and renowned CF experts worked closely with Vertex Pharmaceuticals and the FDA, providing valuable insight on specific issues related to CF, clinical research on CF treatments, and other issues related to the product and its review. We believe this contributed to a more efficient evaluation and is a testament to what can be achieved

when stakeholders collaborate across sectors to ensure a swift review of critical drugs for patients. Section 903 would help make this best practice a standard practice.

In particular, Section 903 requires the agency to ensure that opportunities exist for FDA consultation with rare disease experts. Specifically, it states, “The Secretary shall develop and maintain a list of external experts who, because of their special expertise, are qualified to provide advice on rare disease issues...The Secretary may, when appropriate to address a specific regulatory question, consult such external experts on issues related to the review of new drugs and biological products for rare diseases and drugs and biological products that are genetically targeted.” To our knowledge this list has not been developed.

We urge the FDA to develop this list thoughtfully and transparently, and include a skilled, diverse group of individuals that specialize in the wide range of rare disease issues outlined in the law. Furthermore, this list will only create a meaningful impact if the agency commits to taking full advantage of the expertise of the individuals it identifies for consultation. It is critical that FDA personnel meaningfully and proactively take advantage of this important resource and utilize the unique knowledge of those who specialize in particular diseases and rare disease issues.