February 23, 2015

The Honorable Lamar Alexander
Chairman,
Senate HELP Committee
428 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Patty Murray
Ranking Member,
Senate HELP Committee
428 Dirksen Senate Office Building
Washington, DC 20510

The Honorable Richard Burr
217 Russell Senate Office Building
Washington, DC 20510

Submitted electronically via Innovation@help.senate.gov

RE: Innovation for Healthier Americans: Identifying Opportunities for Meaningful Reform to Our Nation’s Medical Product Discovery and Development

Dear Chairman Alexander, Ranking Member Murray and Senator Burr:

Thank you for your recent endeavors to examine efforts in which Congress can provide additional direction to Federal agencies to accelerate the discovery, development, and delivery of innovative new treatments and cures, creating more jobs, and maintaining our nation’s role as the innovation capital of the world. The Immune Deficiency Foundation looks forward to being a partner with you in developing the appropriate legislative framework in the next several months.

The Immune Deficiency Foundation (IDF) is the national patient organization, founded in 1980, dedicated to improving the diagnosis, treatment and quality of life of persons with primary immunodeficiency (PI) disease through advocacy, education and research. To provide you with our perspective, we strive to answer the questions most relevant to our patient population below.

BACKGROUND ON THE STATE OF CURES AND TREATMENTS FOR PRIMARY IMMUNODEFICIENCY (PI) DISEASES

Primary immunodeficiency (PI) diseases represent a group of more than 250 rare disorders. Many patients with PI depend on lifelong immunoglobulin replacement therapy (Ig therapy) to replace the antibodies their bodies do not produce. Besides the obvious importance of the safety and efficacy of Ig therapy, people with PI continue to seek therapeutic options that allow them to lead a more normal life while maintaining good outcomes. Improved product choices will benefit patients. We have been pleased that there have been recent new Ig products that have been directed towards more convenient presentations (liquid as opposed to lyophilized,
subcutaneous as well as intravenous), higher concentrations (10% and 20% solutions) and products that have greater theoretical assurance of viral safety (additional methods of viral removal or inactivation).

However, we recognize that patients want and deserve additional options in order to minimize existing burdens of their treatment.

- Patients can be limited in the product or routes of administration, which can be used to effectively treat their PI.
  - In a 2008 IDF survey of patients with PI, just one-third of intravenous immunoglobulin (IVIG) users and 28% of subcutaneous immunoglobulin (SCIG) users report that they tolerate all immunoglobulin products similarly.
  - In some patients, it is difficult to achieve appropriate IgG-trough levels despite increased SCIG and IVIG doses.

- For patients whose compliance is optimized with self-administration, SCIG provides an option. Sometimes however, limitations can arise due to the inability to infuse large quantities of Ig into the subcutaneous site in a timely manner. Such limitations include:
  - Frequency of dosing and number of needle sticks.
    - Some patients would prefer less frequent dosing.
    - Some patients require multiple needle sticks per infusion.
    - A number of patients would prefer to reduce the number of needle sticks per infusion.
  - Frequency of local site reactions.
  - Decreased bioavailability can result in increased use in Ig.

- For patients whose compliance is optimized with less frequent administration, IVIG provides a good option. However, limitations do exist, which include:
  - Significant supervision during administration is required by a health care professional.
  - Receiving infusions in a doctor’s office or outpatient hospital setting may not be ideal due to the potentially increased risk of exposure to infections.
  - Many patients have difficulty with venous access, which may affect therapy choice and increase discomfort during infusion.
  - IVIG can be less tolerable for some patients due to the increased risk of systemic adverse reactions, which may create additional morbidity or pose additional significant risk.

In summary, some PI patients would have more favorable treatment outcomes with choices that could alleviate some of the issues outlined above. The Immune Deficiency Foundation is always looking for new and innovative ways to help our patients receive the Ig therapy they need in the least restrictive treatment environment, recognizing that no one treatment or setting is appropriate for all patients.

In addition to the need for products that can make the lives of patients more normal and avoid some adverse reactions, we continue to be concerned with antibody efficacy and
diversity for patients with PI, all of whom depend on Ig therapy as replacement, rather than immune modulation.

Additionally, IDF continues to have an issue with insurers who treat Ig therapies as generic. IDF hopes that the FDA could help clarify that Ig therapies are, indeed, unique products, and that patients do react differently and have distinctive needs.

V. FROM BENCH TO BEDSIDE: THE ROLE OF BASIC RESEARCH IN NEW MEDICAL PRODUCTS

How can we improve the appropriate sharing of data and information and enhance the impact of our biomedical research dollars?

IDF encourages the Committee to support investment in patient-centered data and information that enhance clinical research and are demonstrated in patient populations.

IDF provides administrative support for the United States Immunodeficiency Network (USIDNET), a research consortium established to advance scientific research in the field of primary immunodeficiency diseases, focusing on a primary immunodeficiency disease registry. USIDNET, a program of the IDF, is funded in part by the National Institute of Allergy and Infectious Diseases (NIAID) and the National Institutes of Health (NIH). NIAID supports research to advance the understanding of transplantation and to prevent, diagnose and treat infections and Immune-mediated illnesses.

The USIDNET Registry is a national patient consented registry of individuals with PI diseases. The goals are to advance research in the field and to improve the quality of life of patients. It is managed by leading immunologists and administered by IDF.

In addition, IDF also created for its patients an electronic personal health record (IDF ePHR) to enable patients to track their own medical information, improve communication with their providers, and ultimately, to improve their health. In December 2013, IDF was awarded a contract from the Patient-Centered Outcomes Research Institute (PCORI) to create a Patient Powered Research Network, which we are calling PI Connect that will share patient entered information from IDF ePHR with the clinical information in the USIDNET Registry.

VII. WHAT DOES THE “GOLD STANDARD” LOOK LIKE IN THE 21ST CENTURY AND BEYOND?

Should standards be updated to reflect how they are being applied today for both drugs and devices? How certain do we need to be that a drug is safe and effective, and does that differ for different diseases, populations, or circumstances?

IDF urges the Committee to include biological products, and especially biosimilars, in its consideration of this question as it is imperative to our patient population that these products
are deemed safe and effective. IDF is a member of the Patients for Biologics Safety & Access (PBSA), a national coalition representing more than 20 patient advocacy organizations working to ensure that the voices and interests of patients are heard as the FDA considers approval of a new category of drugs known as biosimilars. It is critical that the FDA have clear review standards and processes in place to protect patient safety and ensure efficacy of biosimilar medicines prior to making decisions about these applications. It is also vital that the process used to develop these standards is transparent so that patients and the public have a full and fair opportunity to review and comment upon these standards before they are finally adopted. **We urge the Committee to exercise its oversight role of implementation of the biosimilars pathway and schedule a hearing on this topic as part of the Innovations process.**

As you know, biologics are far more complex and much more difficult to develop and manufacture than traditional chemical drugs. The advent of sophisticated biologic medicines such as immunoglobulin, clotting factor and monoclonal antibodies has saved and transformed the lives of Americans who have been diagnosed with many life-threatening diseases.

People living with PI diseases, for example, rely on lifelong use of biologics for long-term management of their conditions. Without biologics, many primary immunodeficient individuals are unable to fight off even minor infections and viruses, including the common cold.

When Congress passed the Affordable Care Act (ACA), it gave the FDA regulatory authority to review and approve a new group of biologic drugs known as biosimilars. A biosimilar is a medicine that is highly similar, but not identical to a reference biological medicine. Because of the uniqueness and complexity of biologics, biosimilars are not generic copies of biologic medicines.

As biosimilars are developed and approved in the United States, IDF urges the FDA to take steps that uphold patient safety above all else. FDA should recognize that there are tremendous variations in the complexity of biologics and there are substantial differences in therapeutic responses to biologics from patient to patient. Even a minor difference between a biosimilar drug and the innovator biologic could have a significant adverse health impact for a patient. **Consequently, a one-size-fits-all approach to the approval of biosimilars could threaten patient safety.**

IDF implores the Committee to recognize that safety and efficacy do differ based on disease, population or circumstances. **Therefore, IDF urges the Committee to follow the example set by the European Medicines Agency (EMA) and exempt immunoglobulin (Ig) therapies from the biosimilar pathway.** Current science cannot demonstrate that two products will provide the exact same clinical results for a large number of patients or that switching patients from one product to another will pose no additional risks. At minimum, biosimilar products intended for our patient population should undergo clinical trials to determine whether a proposed interchangeable therapy will offer patients the same clinical outcome.
Are today's regulatory pathways sufficient to ensure a predictable pathway for innovators as they bring forward medical products for review by the agency? Are today's pathways achieving their intended purpose? Are they being fully leveraged on behalf of patients?

Individuals with PI diseases are vulnerable to infection since they lack antibodies to fight these infections. Therefore, resistant pathogens are of great concern to our patient population. IDF believes Congress can incentivize basic research on the most troubling resistant pathogens by addressing current regulatory burdens to antibiotic development. **IDF urges the Committee to advance the bipartisan Promise for Antibiotics and Therapeutics for Health (PATH) Act, S. 185**, introduced by Senators Hatch and Bennet, which would establish a new FDA approval pathway to incentivize the study of new antibiotics to treat serious or life-threatening infections for which there is an unmet medical need. It is critical to stay ahead of antibiotic resistance which threatens our patients and the general public every day.

**FINANCIAL BURDEN OF CHRONIC DISEASE**

IDF urges the Committee to consider that one of the biggest obstacles to care for our patients as well as many (if not most) other patients who have a rare and chronic disease is the increasing use of co-insurance cost-sharing policies of insurers. Payers are moving more and more specialty drug treatments, which are primarily used by patients with rare and chronic diseases, out of drug tiers with co-payment arrangements to specialty tiers which require patients to pay a percentage of the cost of treatment. According to a study by Avalere Health of such arrangements in the Affordable Care Act (ACA) Marketplaces, over 20% of plans reviewed require patients to pay at least 40% of the treatment costs. The monthly cost of treatment for our patients with PI can range between $5,000 and $10,000 per month for the rest of their lives. For other diseases, the cost of treatment can even be higher.

The annual out-of-pocket (OOP) costs limitation of the ACA is beneficial for most people. However, in conjunction with high co-insurance requirements it is being used to keep people from getting their treatments because all of the costs are front loaded. It is not unusual for payers to require those patients with high cost drug treatments to pay the annual cost cap ($12,750) plus any applicable deductibles at the time of the first (or maybe 2nd) treatment of the year. For those with life-long treatments as our patients with PI, the cost is staggering. How many Americans can afford to pay premiums, deductibles, co-payments and co-insurance and come up with nearly an additional $13,000 per year – every year? The use of coinsurance for the most sick in our population with the most expensive treatments is tantamount to economic and health discrimination.

These policies encourage people to forego treatment. There is ample evidence of this behavior by patients if costs are too high. The irony of this situation is that studies show that when patients with PI do not have their treatments, they will get sick many times in a given year, requiring payers to cover the costs of symptomatic treatments while patients incur a fraction of the costs. One study indicated it cost payers twice as much to treat sick patients with PI who
are not on Ig replacement therapy as it would if they had received the prophylactic benefit of the drug therapy.

IDF urges the Committee to include provisions from the *Patients’ Access to Treatment Act* which would restrain high cost-sharing for specialty medications, thereby enabling more patients with chronic, disabling, and life threatening conditions to access the treatments they need. It would limit cost-sharing requirements applicable to medications in a specialty drug tier (typically Tier IV or higher) to the dollar amount applicable to drugs in a non-preferred brand drug tier (typically Tier III). It would enable patient access to treatments, reduce disability and constrain health care costs.

Again, we strongly appreciate your efforts in this area, and we look forward to continuing to work with you toward the introduction of legislation. If you have any questions or would like to discuss our recommendations further, please feel free to contact me at 443-632-2552 or llamotte@primaryimmune.org.

Sincerely,

Lawrence A. La Motte
Vice President, Public Policy