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February 10, 2015

Congressman Fred Upton
Chair, Committee on Energy and Commerce
2183 Rayburn House Office Building
Washington, DC 20515

Congresswoman Diana DeGette
Committee on Energy and Commerce
2368 Rayburn House Office Building
Washington, DC 20515-4329

Sent via e-mail: cures@mail.house.gov

RE: 21st Century Cures Act Discussion Draft – Subtitle N – Medicare Part D Patient Safety and Drug Abuse Prevention

Dear Chairmen Upton and Congresswoman DeGette,

The Global Healthy Living Foundation (GHLF) is a 501 (c)(3) patient group that works to improve the quality of life for people with chronic disease, often focusing on those least able to advocate for themselves. As a patient advocacy organization, GHLF represents more than 75,000 chronically ill patients, including your fellow Michigan and Colorado residents. Many of these individuals have rheumatoid arthritis and other autoimmune disease, take prescription pain medication, and will be directly impacted by policies included in the recently released 21st Century Cures Act discussion draft.

On behalf of the patient community we represent, I'd like to sincerely thank you for your leadership in this bipartisan effort. Few leaders would have the courage to take on the monumental task of modernizing the discovery, development, and delivery of new therapies for patients. Throughout 2014 we were particularly encouraged by your effort to emphasize the diverse perspectives of patients across the country at several town hall/roundtable meetings. Representatives from our organization attended several of those discussions and continue to be in contact with Energy & Commerce committee staff to share input.

After reviewing the recently released discussion draft, I am writing you today to express our concern for "Subtitle N – Medicare Part D Patient Safety and Drug Abuse Prevention" under Title IV.

We believe this particular provision of the proposed legislation is troublesome because it:

- Restricts access of patients with legitimate chronic pain under the guidance of a physician to essential medications
- Is duplicative of state prescription drug monitoring programs established under the National All Schedules Prescription Electronic Reporting (NASPER) Act

Subtitle N provides Medicare Advantage Part D programs the authority to identify and flag individuals seeking to fill prescriptions of frequently abused class II, III, IV, or V controlled substances. It is our understanding that an alert would be triggered when a patient's prescription activity does not adhere to 'utilization guidelines' established by the Secretary and plan sponsors. We are specifically concerned with language that limits patients to as few as one pharmacy. Many states limit the amount of controlled substances that any single pharmacy is allowed to have on hand, which already forces disabled patients to visit pharmacy after pharmacy to fulfill their prescription. Thus in these states, restricting their access to one pharmacy could eliminate access to their medications. Many of the chronic pain patients in our community rely on these classes of medication to live productive lives, and often times these individuals have been taking class II, III, IV, or V controlled substances for several years and now require high doses to reach clinical effectiveness. If 'utilization guidelines' are not written to take these patients into account, the alert algorithms used to identify abusers will easily confuse them with valid patients and exacerbate already prevalent patient access issues.

Absent, specific details concerning the algorithm that will facilitate the Secretary and plan sponsor's 'utilization guidelines', we are fearful that legitimate chronic pain patients under the guidance of a physician will be labeled as abusers and suffer disenrollment from their Part D plans. While Subtitle N provides an appeals process whereby individuals identified as abusers can challenge the decision, the provision does not provide clarity on the duration of the appeals process or mention a max cap on the time in which a decision must be made. We are concerned that the legitimate chronic pain patient may be forced to languish in agonizing and debilitating pain as a result of being misidentified and forced to navigate a lengthy administrative process. We believe this is immoral and wrong.

Second, Subtitle N is duplicative of state prescription drug monitoring programs established under the National All Schedules Prescription Electronic Reporting (NASPER) Act. NASPER already allows for the collection of information on Medicare beneficiaries, therefore, separate and duplicated efforts are not required. In lieu of including this provision in the final draft of the 21st Century Cures Act, we strongly urge you to reauthorize and fully fund the NASPER Act.

Enacted in 2005, the NASPER Act, passed with overwhelming bipartisan support in both chambers, aimed to stop opioid abuse at the miniscule cost of $60 million over five years. However, Congress never fully funded the bill and the program only received $12 million. How miniscule is $12 million? It is four-cents per person per year saving hundreds of billions of dollars in prescription drug abuse-related costs. The law provides grants to states to create prescription drug monitoring programs – databases that include information about the physician, patient, and prescription.

In fact, 37 states already have fully operational programs. A physician or pharmacist can check the database before writing a prescription and easily identify an abuser who is doctor shopping for drugs, already received prescriptions for pain management, or has tried to fill multiple prescriptions at several different pharmacies. Instead of reinventing the wheel, the 21st Century Cures Act should support this existing program to help the remaining states develop their own prescription monitoring programs.

The Global Healthy Living Foundation and the patients we represent are extremely supportive of the Energy & Commerce committee's 21st Century Cures Act generally. However, we feel Subtitle N under Title IV of the discussion draft is unnecessary and misguided because it will unintentionally restrict access for legitimate patients and is duplicative of existing PDMPs. As the Committee works on this important legislation, we ask that you remove this harmful provision.

We appreciate your thoughtful consideration of our perspective and would be pleased to provide any further information that you may require as the discussion process evolves.

Sincerely,

Seth Ginsberg
President, Global Health Living Foundation

CC: Members, House Energy & Commerce Committee

February 10, 2015

Congressman Fred Upton
Chairman, Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton:

Thank you for the opportunity to submit comments on the 21st Century Cures Initiative. Health IT Now (HITN, www.healthitnow.org) is a diverse coalition of health care providers, patient advocates, consumers, employers and payers who support the adoption and use of health IT to improve health care and to lower costs.

We are convinced technology must play a foundational role in fostering 21st Century cures. Many aspects of our current health care system encourage inefficiency and promote waste aided and abetted by program and data silos. In some instances, federal policy and taxpayer dollars subsidize this waste. Perhaps worse, current technology solutions and data are not being brought to bear on pressing health problems. We thus believe the Committee has substantial opportunities to both address current problems and build a federal framework to encourage the discovery, development, and delivery cycle.

Specific Comments

Sec. 2001. Innovative Cures Consortium. HITN supports this provision of the legislation. Given the importance of technology in innovation, we believe that the consortium should include representation from the health IT industry. We do not support the funding match requirement in the provision [Sec. 281D(b)]. We note that many new and innovative ideas come from small start-up companies who may not have access to matching funds. We are concerned the provision would thus reward larger, better funded companies. We believe federal policy should be neutral in terms of opportunity to participate in this program. We encourage the Committee to devise other ways small companies might participate, such as via loan matching or zero cost, no-interest loans.

Sec. 2021. Medical Product Innovation Advisory Commission. Medical products hold great promise in transforming our health care system. As witnessed over the past decade, the definition of medical products is constantly evolving – largely due to the health IT sector. As a result, we urge the Committee to include representation from the health IT industry on the Commission.

Title II, Subtitle E. Sensible Oversight for Technology which Advances Regulatory Efficiency (Sections 2061, 2062 and 2063). As our February 6 letter to Congressmen Blackburn and Green indicated, HITN believes the Committee has substantial opportunities to promote innovation by clearly defining the products subject to FDA review and those products that are not. The latest draft is the clearest, best written bill on the subject we have seen to date. We have some minor suggested changes to the language outlined below.

Current Language	Recommendation
SEC. 2061. MEDICAL AND HEALTH SOFTWARE DEFINED.	
Subsection (2) "(B) is not intended to provide a diagnosis; and	We suggest changing subsection (2)(B) to "is not intended to provide a **definitive** diagnosis" to ensure that software intended to provide a recommendation for a diagnosis is not unintentionally excluded
"(C) is intended to analyze patient-specific information and other information to recommend to health care professionals a single treatment or course of action—	We suggest changing section (2)(C) to "is intended to analyze patient-specific information **to produce a single recommendation**— in order to cover software intended to provide recommendations for diagnosis are not unintentionally excluded
''(i) without the need for such professionals to perform additional interpretation of, or to independently confirm the means for, such recommendation; and ''(ii) for the purpose of informing or influencing health care decisions in the prevention, diagnosis, prognosis, treatment, cure, or disease management related to any disease or condition in humans.	We suggest changing section (2)(C)(i) to "without the **opportunity** for such professionals" to better represent an amount of time or a situation in which something can be done and "independently **review**" to better reflect the act of looking at or examining the quality or condition of something or someone.
Subsection (3)	The intended use of the terms "data" in subsections (3)(C), (3)(G), and (3)(G) and "information" in subsections (3)(E), (3)(H), and (3)(I) and the relationship between the two terms require clarification.
"(B) is intended for use for clinical, laboratory, or administrative workflow and related record keeping including health records;	We suggest changing section (3)(B) to "is intended for use for clinical, laboratory, or administrative workflow and related record keeping **or informational display**, including health records;
''(C) is intended for use for use aggregation, conversion, storage, management, retrieval, or transmission of data from a device or other thing;	This is unclear. Does the use of "other thing" refer to the emerging definition of the Internet of Things? We suggest clarifying or deleting "other thing" from section (3)(C). There is also ambiguity over whether section (C)(3)(C) is intended to cover MDDS.

"(H) is intended for use to analyze patient-specific information or other information for purposes of presenting patient-specific recommended treatments or courses of action to inform health care professionals' decisions with respect to the prevention, diagnosis, prognosis, treatment, cure, or management of a particular disease or condition, with the opportunity for additional interpretation or an independent confirmation of such treatments or courses of action; or	We suggest changing subsection (H) to "is intended for use to **present or** analyze patient-specific information or other information for purposes of presenting patient-specific recommended treatments**, diagnoses,** or courses of action to inform health care professionals' decisions with respect to the prevention, diagnosis, prognosis, treatment, cure, or management of a particular disease or condition, with the opportunity for additional interpretation or an independent **review** of such treatments, **diagnoses,** or courses of action; or" to account for software providing diagnosis suggestions with any opportunity for independent confirmation.

We believe current regulatory uncertainty stifles healthcare innovation and that there is significant confusion in the market about what technologies may be regulated, by which agencies, and to what standards. Uncertainty creates barriers to the development of technologies that can help clinicians access more evidence-based medicine, provide patients with more individualized care, and generate better caregiver engagement. We believe Congress must act to address this serious problem in the interests of patients and advancing innovation now and in the future.

Sec. 2081. Standardization of Data in Clinical Trial Registry Data Bank on Eligibility for Clinical Trials. HITN applauds the Committee for including such an important provision in the draft legislation and encourages you to retain it as the bill moves forward.

Technology, including electronic health records (EHRs), health information exchanges, and mobile medical apps, is able to securely capture clinical and administrative information to create a vast data pool that can be used for genomics, population health, disease management, and clinical research. Unfortunately, the potential use of these vast data resources remain unemployed. By requiring that clinical trial opportunities posted on ClinicalTrials.gov include eligibility criteria using standardized technical vocabularies, EHR systems will be able to compare relevant trial requirements to a patient's clinical and claims data without exposing the patient's private information. Providers will then be able to easily identify and provide information on relevant trials that may be beneficial to an individual's care. HITN believes that this could help address a large barrier in the discovery of new treatments – low recruitment and retention rates in clinical trials – and the costs that flow with these barriers. We look forward to working with the Committee to ensure passage of this important provision.

Sec. 2082. Clinical Trial Data System. HITN supports the creation of a clinical trial data system to increase data sharing for research purposes. However, we ask that the Committee expand this data system to include clinical data captured by (EHRs) and genomic databases. We believe that making this additional de-identified information available to researchers will be greatly beneficial to bettering health care outcomes by allowing a more longitudinal and comprehensive view of a patient's health care needs. We acknowledge that this may require more security measures; however, we believe the possible reward is worth the effort to address barriers to utilizing highly valuable data. For too long, research efforts have been hindered by data silos. We believe the Committee has a wonderful opportunity to address this long-standing problem.

Sec. 2092. Recommendations for Development and Use of Clinical Data Registries. HITN strongly supports the use of clinical data registries for the improvement of patient care. Despite the promise of registries, we know from real-world experience that these registries are often blocked by the business practices of EHR vendors from reaching their full potential. There is anecdotal evidence of EHR vendors refusing to work with clinical data registries to ensure data sharing between two systems. Congress should not allow these actions, and HITN believes that the Committee should amend the language in Sec. 2092(b)(1) to require EHRs to work with clinical data registries on interoperability standards and to prohibit EHR products that are used in federal programs to continue to be used for MU certification if they block clinical data registries from interfacing with their products.

Sec. 2181. Interoperability. We strongly support including this section in the bill because we are very concerned HITECH is not achieving the goals set out by Congress, namely increased efficiency, improved health outcomes and better access to electronic information. We bleive this is largely because the program has failed to facilitate interoperation across systems and providers. We are likewise concerned that Meaningful Use is becoming more and more of a burden on health care providers with little improvement in patient care quality or health and where the costs of the program may outweigh the program's benefits. There are several reasons for this, including: a process that produces poor results; misaligned time frames; poorly defined priorities; and a lack of focus on achievable short-, mid- and long-term outcomes.

This is unfortunate, because we believe the Meaningful Use program is necessary – even foundational – in efforts to advance innovative payment and delivery models in Medicare and Medicaid that improve outcomes, quality and lower costs. We believe it is important to ensure that every health care provider has access to longitudinal data on their patients to make evidence-based decisions, coordinate care and improve health outcomes. Providers need interoperable systems to treat patients well.

We encourage you to include provisions in this section to:

- Fix the process. Empower the private sector to develop and propose interoperability standards by reforming the current standards process.

- Define the Architecture and Standards. Require the Administration to adopt interoperability standards for certified health IT systems by a date certain, require vendors to publish their interfaces, and prioritize information sharing among clinicians and consumers.

- Enforce Program Rules. Authorize new enforcement tools so that providers know the products they buy will work as advertised, including the ability to de-certify poorly performing products

Sec. 2301. Precision Medicine. HITN strongly supports the Committee's focus on Precision Medicine and look forward to working together to detail exactly what this initiative will entail.

Since the enactment of the HITECH Act in 2009, taxpayers and the medical industry have collectively invested more than $100 billion in an information technology infrastructure to meet America's healthcare needs. These investments hold vast potential for revolutionizing medical science, population health and cost management.

But realizing these promises requires progress on a number of obstacles, many of which are relics of a "pre-data" era.

Nowhere is the potential opportunity costs greater than in genomic medicine—a type of precision medicine that involves mapping and sequencing of genes to discover and create individualized treatments for genetically driven diseases such as cancer and diabetes.

At its core, cancer is a genetic scourge, the result of millions of errors in gene replication. This makes cancer treatment highly individualistic and dependent on each patient's genetic makeup and ever-changing environmental factors.

With incentives, technology and data resources can be leveraged to speed treatments and cures to patients. We appreciate that interoperability, some HIPAA changes and the SOFTWARE provisions will foster precision medicine. We suggest the Committee go further by explicitly investing in a modern data infrastructure. Realizing the potential of genomics and individualized medical treatments will require large investments in data infrastructure coupled with updated privacy laws. When it comes to data, we are falling behind in the international community. The U.S. is vastly behind China, which possesses one-third of the global genomics computing capacity and the jobs that go with it.

Fifteen years into the 21st century is high time for the U.S. to apply data-driven technologies to medicine. The gap between our current data capabilities and future data requirements is vast and growing. We look forward to working with you to more fully develop this proposal.

Sec. 4181. Advancing Telehealth Opportunities in Medicare. As we stated in our January 26 letter, we applaud your efforts to remove current Medicare barriers to beneficiaries receiving telehealth services. We encourage you to mirror steps the private sector payers have taken to incorporate and integrate telehealth into the major medical benefits policies they offer.

To reiterate our concerns outlined in the January 26 letter, we believe the telehealth provisions should be changed to reflect the following:

1. *In General*. HITN does not believe that telehealth visits should automatically be reimbursed at the same amount as in-person visits. We believe that the use of technology in health care can lower costs, and this should be taken into consideration when developing reimbursement rates for services provided via telehealth. We also believe that all limitations on what qualifies as an originating site, any geographic limitation, or any limitation on the type of health care provider who may furnish such services should be lifted, and it should not be left to the discretion of the Secretary.

2. *Payment for Selected Telehealth Services*. HITN believes that the wording on line 19 should be changed to reflect services furnished “electronically,” rather than “via a telecommunications system” to ensure that the language is flexible enough to incorporate varying and always changing technology.

3. *Telehealth Services Defined*. HITN supports a common definition of telehealth that can be used across federal programs. However, we do not support using the definition under section 1834(m)(4)(F). We support the language in The Telehealth Modernization Act of 2013, which was introduced in the 113th Congress by Congresswoman Doris Matsui and Congressman Bill Johnson, and we believe that this should be inserted into the legislation.

4. *Encouraging Greater Access to Telehealth Services in Bundled Payment Models*. HITN supports removing current Medicare reimbursement restrictions on telehealth services in the case of bundled payment projects or models. We also support waiving medical licensure requirements for entities participating in bundled payment models that practice across state lines. This is essential to allow for truly coordinated care.

5. *Store and Forward Technology*. We do not believe that store-and-forward technologies should only be reimbursed under bundled payment demonstration projects or models. We support removing the current restriction on the reimbursement of this technology under Medicare overall.

6. *Reimbursement for Remote Patient Monitoring*. We urge Congress to provide a clear avenue for reimbursement for remote patient monitoring for chronic conditions, either through specific authorization to pay CPT codes on an unbundled basis. Under CMS' definition of telehealth services, remote patient monitoring and many other evidence based technology-enabled care is not a telehealth service, rather it is a physician service. However, only in rare cases has CMS assigned a value to the remote patient monitoring codes. Given the deep and broad evidence base demonstrating that remote patient monitoring for a number of chronic conditions is associated with reduced utilization, lower costs, and improved outcomes, it is essential that ACOs, bundled payment, and fee-for-service (during the transition to risk based models) physicians are permitted to use and receive reimbursement for remote patient monitoring when cost savings and improved health are supported by evidence.

6. *Sense of Congress Regarding State Medical Board Compacts.* We are extremely concerned with the "Sense of Congress Regarding State Medical Board Compacts." This language endorses an approach to addressing a significant barrier to the practice of telehealth services – the outdated state-based medical licensure system – that will only further fragment and complicate the licensure process for doctors who wish to practice telehealth across state lines. The compact only provides for expedited licensing and does acknowledge the transient nature of today's society. Under the compact, a provider must anticipate where their patient may be going, if a need arises for treatment or consultation. Americans travel from coast to coast - vacationing, visiting sick or ailing relatives, to attend business meetings and conferences. With this mobility, patients may need to seek the care of their physician from a location not anticipated in the proposed licensure model.

In addition, state compacts are only effective if a majority states agree to them. Therefore, relying on a compact agreement means some progress in some states for certain beneficiaries, but not others, and only after years of delay. Or worse, it is just as likely that there would never be agreement across states. HITN believes Congress must recognize that Medicare, as a federal program, should be treated like physicians within the DOD and VA programs with regards to licensure and should be able to see patients across state lines without the requirement to obtain multiple state licenses. HITN supports removing this section altogether and we suggest substituting the following language:

> *"It is the Sense of Congress that the current state-based provider licensure process does not support a mobile society nor take advantage of the available technologies to provide care from nearly anywhere to nearly anywhere in the US."*

7. *Report on Barriers to Telehealth*. HITN thinks that a better approach, rather than a Sense of Congress, would be to add a section to the legislation that would require the Secretary to issue a report and recommendations on how to remove barriers to the utilization of telehealth services. We suggest the following language be added:

> *"The Secretary of Health and Human Services shall, within 180 days, issue a report and recommendations on how to remove barriers to telehealth services that impede coordinated care delivery across the nation. The Secretary shall convene relevant stakeholders to provide input into the report, including but not limited to: patients, health care providers, state government officials, health technology developers, telecommunications companies, specialist physician organizations, senior citizens, academic medical centers, insurers, employers, accountable care organizations, community health organizations, and other federal agencies. The recommendations shall specifically address:*
>
> - *Creating a framework for interstate licensure and authorization of providers to deliver care via telehealth services to patients;*
>
> - *Guidance of a common definition of telehealth services for the States to use in conforming their laws to facilitate the delivery of care; and,*

- *Plans to develop and expand current federal health programs through a streamlined and simplified licensure process to provide improved access to telemedicine services for seniors and other federal health program recipient."*

We appreciate the opportunity to share our initial thoughts with you on this important issue and look forward to working with you to ensure the promise of 21st Century Cures are realized for all Americans.

Joel C. White

Chairman Upton and Esteemed Members of the House Committee on Energy and Commerce:

I am offering comments pertaining to the 21st Century Cures Bill, specifically directed to Subtitle E_Sensible Oversight Technology Which Advances Regulatory Efficiency_p 154

Vague Definitions:

The attempt to distinguish between "medical" software and "health" software does not succeed in meeting its intended goal, and only serves to obfuscate the succinct definition of a medical device in the Federal Food Drug and Cosmetic Act.

Unintended Consequences of Rewriting the Federal Food Drug and Cosmetic Act:

To rewrite the F D and C Act to exclude certain software integral to medical devices from oversight in the pre and after market puts patients at high risk.

Risks of Digitized Medical Care:

As a daily user of several vendors' electronic health record (EHR) devices with their integral electronic ordering (CPOE) device and electronic decision support (CDS) device, I bring to your attention widespread adversity and risk to patients wrought by these devices when used with the best of intentions.

The magnitude and incidence of the adverse events, near misses, injuries, and deaths are unknown because there has never been a systematic approach to gathering this data and the users have not had an organization disclosed to them to which to report. CDS is often wrong and inappropriate. CPOE impedes individualization of care and promotes new errors. I am aware of innumerable patients who suffered adversity, including death, from these devices.

Whether they improve overall outcomes or reduce overall costs of the system of health care in the USA is unknown.

The Errorgenicity of EHR Devices:

When my patients' care is being governed by these devices, I must be vigilant 24/7 to protect their safety because of the pervasive and indolent errors they cause and because of the actual flaws and defects in the carrying out of orders due to interface failures and other dysfunctions.

Intellectual Disruption:

Additionally, they are cognitive disruptors resulting in intellectual errors. Nurses do not know their patients and when they call me at 2am regarding a problem and I ask for the vital signs (blood pressure, respiratory rate, temperature, and heart rate), they need to log on to the EHR to get the vital information.

Delays in Care:

Misidentifications resulting in wrong treatments, lab data stored in EHR silos without anyone knowing it is there, and orders not reaching the intended recipient, and/or the recipient not knowing a new order has arrived all put the patient at risk.

The usability of these devices involving human factors is poor and puts patients at risk.

Patient Risks from Devices that are NOT Safe and Effective:

The legislation must direct the Executive to ensure that medical software and the devices it runs is "safe and effective" and for it to require that medical software and the devices it runs should meet all applicable industry standards for software engineering and specify that these should include "good manufacturing process" and "traceability".

Devices Not Fit for Purpose:

The aftermarket oversight and premarket evidence and validation that the devices are fit for purpose, must be included in the Bill and these devices should not be exempt from said oversight.

Attached are 3 scholarly papers representing the tip of the iceberg of the risks and adversity from software driven EHR and medical devices that this Bill would allow to go unfettered.

Linked here are You Tube video examples of the upcoding features of a prominent vendor's EHR device at a prominent medical center, none of which are addressed in the Bill.

Constructing a Macro to maximize billing:

http://www.youtube.com/watch?v=VqqqDkdZe68

Constructing a Precompleted (before the patient shows up (sic) Note (the genre of EHR safety hazard that may have facilitated Ebolagate in Dallas):

http://www.youtube.com/watch?v=cvqKR4CNsXA&feature=youtube_gdata_player

Thus, to exempt these EHR devices, or any other medical devices that are operated with software of varying degrees of complexity puts the patients whose care is governed or affected by them at the highest level of risk.

Thank you for the opportunity to present these comments. I am available to you to meet in person if you desire.

Sincerely,

Dean Kross, MD
CEO, Heart Care Medical Associates

hivma
hiv medicine association

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February 19, 2015

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:

The HIV Medicine Association (HIVMA) appreciates the opportunity to comment on the draft 21st Century Cures legislation that the House Energy and Commerce Committee released in late January, 2015. HIVMA represents nearly 5,000 HIV clinicians and researchers that work on the frontlines of the HIV epidemic across the U.S.

We appreciate the work, stakeholder consultation, and deliberation this undertaking represents. Policy proposals in the draft bill could improve the US biomedical research enterprise, spur medical innovations, and reduce barriers that slow the translation of new discoveries to therapeutics and diagnostics that directly benefit patients and improve health outcomes. We offer comments on a few of these policy proposals below.

1. We generally support provisions of the bill that would assess and evaluate methodologies to streamline clinical trials processes and explore the use of alternate research models to improve efficiencies while maintaining standards of scientific rigor and integrity.

   In this regard, we would like to highlight the work of the National Institute of Allergy and Infectious Diseases (NIAID) HIV/AIDS Clinical Trials Network and the Centers for AIDS Research (C-FARs), which are among the greatest achievements and core infrastructure of the NIH's HIV/AIDS research portfolio. These essential HIV research programs offer lessons for how we can work synergistically to enhance and coordinate high quality research projects through interdisciplinary collaboration –especially between basic and clinical investigators and behavioral scientists — to support translational research.

   The NIAID Network includes the AIDS Clinical Trials Group (ACTG), International Maternal Pediatric Adolescent AIDS Clinical Trials (IMPAACT), Microbicide Trials Network (MTN), HIV Prevention Trials Network (HPTN) and the HIV Vaccines Trials Network (HVTN).

These networks are advancing studies that continue to build on the results of NIH-funded HPTN-052 (named the scientific breakthrough of the year by Science Magazine), which showed that early HIV treatment provides benefits in HIV clinical outcomes as well as dramatically reducing the risk of HIV transmission. NIH also leads the effort around the world to develop an HIV prevention toolkit that includes vaccines, microbicides and pre-exposure prophylaxis using antiretroviral drugs (PrEP) to accelerate achievement of an AIDS-free generation.

The CFAR system provides administrative efficiencies through 19 core facilities across our nation that offer expertise, resources, and services not otherwise readily obtained through more traditional funding mechanisms. The CFAR program also encourages training and mentoring of young investigators as well as inclusion of women and minorities. We encourage the Committee to consider lessons learned from the CFAR and ACTG programs that may be of benefit for design and development of clinical trials research on other diseases.

2. We support proposals to allow expanded patient access to covered investigational drugs. Expanded access programs created for novel HIV treatments played an historic role in the early days of HIV/AIDS therapeutics, by unlocking access to treatments that saved our patients' lives when there were no other treatment options.

3. We support incentivizing drug development in areas of unmet medical need where economic and regulatory barriers persist and discourage drug development. Classes of particular concern are antibiotics and antifungals where development has nearly halted due to low drug prices, shorter treatment durations and restraints on usage to preserve their utility. However, we are concerned that some of the other proposals may not be narrowly targeted enough to have the intended benefit. We see first hand the negative impact that out of control drug pricing can have on access to HIV treatment and more recently curative treatment for hepatitis C for many of our patients. We are concerned that some of the policy proposals may worsen rather than address this issue and hope that the proposals will be carefully reviewed to ensure they will spur development for conditions and diseases where new diagnostics and treatment options are urgently needed.

4. While we support the urgent need to incentivize new and emerging investigators, we would not want to see such initiatives financed at the expense of eliminating funding that supports the Agency for Healthcare Research and Quality (AHRQ), as the draft bill proposes. AHRQ supports the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) that includes more than 200 sites collecting data on 130,000 HIV-infected and 150, 000 HIV-uninfected participants. NA-ACCORD studies are a critical data source for HIV treatment guidelines, including the Department of Health and Human Services' Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents.

5. We are troubled by several provisions throughout the bill that are overly prescriptive in terms of curtailing NIH authority to let the science guide the direction and prioritization of resource allocations across the medical research enterprise. The NIH has sufficient transparent strategic planning processes and reporting requirements in place to allow for judicious and appropriately evolving agenda-setting across the institutes and centers. We have some serious concerns in particular about mandating that 55% of the NIH budget be directed to basic research. In today's drive towards translational research approaches, with some exceptions, "basic research" rarely stands alone but rather is intertwined with inter-disciplinary collaborative approaches with clinical researchers. We also believe it is short-sighted and misguided for the bill to dictate that the NIH as a whole should be limited to "not more than 10" priority focus areas.

   We also strongly urge caution against measures that could lead to increased politicization of the NIH, including proposals to concentrate more authority in the NIH Director's office and allocate additional resources to the Common Fund that could better be used to directly fund more research awards. Similarly, we are concerned that imposition of terms limits (though renewable) on the Directors of the Institutes and Centers could politicize these essential leadership positions.

6. We note that language on NIH travel (Sec. 4003) is "to be supplied." If language addressing this issue is to be developed, we would underscore the importance of supporting and encouraging the participation of federal scientists in scientific meetings and conferences. Such national and international meetings play a critical role in the scientific process and in the implementation of scientific advances by facilitating discussion and interaction between government experts and other physicians and scientists in addition to supporting education and mentoring of junior researchers and physicians.

7. Lastly, we would like to express our support for several Medicare proposals added on to the legislation, including development of reimbursement/coding and payment mechanisms for telemedicine; increased access to Medicare claims data for research purposes; and greater transparency with regard to provider, benefit and cost sharing information for Medicare beneficiaries. Telemedicine, in particular has helped extend HIV and Viral Hepatitis specialty expertise to rural and underserved areas in addition to providing training opportunities for primary care providers and mitigating HIV and Viral Hepatitis medical workforce shortages.

   We have learned much from our experience in the field of HIV/AIDS research, which has greatly benefitted a wide range of diseases, including cancers and viral hepatitis. Yet many challenges remain. It remains absolutely clear that stable and sustained increases in NIH funding will be critical to train the next generation of scientists and support the next breakthrough discoveries that could pave the way for an HIV vaccine and a cure.

Thank you for your consideration of our views. We look forward to engaging with the Committee as this important legislation and its component pieces move forward. Please count on us as a resource if we can be of any assistance. We can be reached through HIVMA Policy officer Kimberly Miller at kmiller@hivma.org or (703) 740-4957.

Sincerely,

Adaora Adimora, MD, MPH, FIDSA
Chair, HIVMA Board of Directors

IKARIA®

February 10, 2015

The Honorable Fred Upton
Chairman
House Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
Ranking Member
Oversight & Investigations Subcommittee
House Committee on Energy & Commerce
2368 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton and Ranking Member DeGette,

Ikaria, Inc. is a biopharmaceutical and medical device company focused on innovative therapies designed to address the significant unmet medical needs of critically ill patients whose complex conditions often lack effective treatment options. Ikaria respectfully submits the following comments to the Committee for consideration in response to the solicitation for feedback on the *21st Century Cures Discussion Draft*. Ikaria appreciates this opportunity to provide our support and opinions on this important legislation. We also thank the Committee for your work with the *Roundtable on Critical Care Policy* and your interest in engaging with the critical care community on ways to improve the policy environment to accelerate treatments for critical care patients.

Policies that bolster research and foster innovation in critical care help improve the health of Americans and reduce the economic burden of disease and illness. Ikaria is very supportive of ***Section 2101, Utilizing Real-World Evidence***. **In areas such as critical care, where traditional clinical trials may be difficult to conduct, the ability to utilize real-world evidence for regulatory decision-making can help bring much-needed innovative treatments to patients.** Real-world data can help more rapidly and effectively develop and deploy new therapies in critical care medicine. These patients are overwhelmingly treated for multiple acute and chronic conditions, and the clinical effectiveness of treatments is most accurately determined through the assessment of real-world data generated in the treatment setting. We appreciate the Committee's understanding and support of provisions to drive use of real-world evidence in regulatory decision making.

Ikaria also supports ***Title I, Subtitle A, Patient-Focused Drug Development*** and the establishment of a structured framework for meaningful incorporation of patient experience data into the regulatory decision-making process. Improving survival remains the focus for much of drug development, but supporting research and development of therapies indicated for use in the Intensive Care Unit (ICU) and Neonatal Intensive Care Unit (NICU) that focus on improving how a patient functions can also be important. Current measures for clinical effectiveness—such as living longer or feeling better—can be difficult to measure and unrealistic for critically ill patients. Efforts to enable the FDA to develop a regulatory review

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process that allows validated patient-reported outcome measures to be included in regulatory decision making can provide immense value for evaluating potential critical care therapies. **For critical care patients, physician-reported outcomes and experiences are vital for these patients from the Intensive Care Unit or Neonatal Intensive Care Unit who could not respond on their own behalf as they may have been unconscious, intubated, anesthetized or simply too young, as in the case of patients in Neonatal Intensive Care Units. We hope that the current draft language can be strengthened to better include the provider perspective for these patients.** From a critical care perspective, there is value in including patient and provider input in the drug development and regulatory decision-making process in a consistent and predictable manner.

Section I, Subtitle H, Facilitating Responsible Communication of Scientific Methods and Medical Developments is important to Ikaria and other stakeholders in critical care. We understand that the Committee is still finalizing the language, but it is important to remove limitations on the ability of biopharmaceutical manufacturers to communicate with health care professionals on truthful and not misleading information for approved uses, or medically accepted alternative uses of approved products. Drug manufacturers like Ikaria -- who continually assess published literature, support ongoing research and capture safety data for FDA reporting about their drugs -- are currently limited in their ability to participate in ongoing scientific and medical dialogues about what may be best for patients. FDA's current interpretation of the law generally restricts or limits proactive communication of even truthful and non-misleading information, even if the information is only presented to physicians and even if the alternative uses reflect the current accepted standard of care. Ikaria is pleased that the Committee recognizes the value that manufacturers of medicines can bring to these discussions about what may be best for patients when information is shared responsibly. We hope the final legislation will enhance beneficial health care communications between industry, physicians and other relevant health care stakeholders.

Ikaria is also very supportive of ***Title I, Subtitle N, Orphan Product Extensions Now.*** The additional six-month extension of existing exclusivity periods for products approved for a new indication to prevent, diagnose, or treat a rare disease or condition could greatly help drive much-needed advances in critical care treatments. The *New England Journal of Medicine* recently editorialized about the inefficiencies in U.S. critical care research, noting that critical care practitioners today face many of the same problems that they did when the field of critical care was first defined in the 1950s. Indeed, the unsurprising result is that relatively few breakthroughs have occurred in critical care medicine in decades as compared to the many breakthroughs in most other areas of medicine. With so many orphan conditions being treated in critical care, these exclusivity provisions could be helpful in driving the discovery of new treatments.

Finally, Ikaria hopes you will also consider measures that would improve the coordination of critical care research. As you look to streamline and strengthen federal research and development efforts, we hope you will recognize the unique challenges of critical care patients. The basic scientific research that occurs at the National Institutes of Health (NIH) can provide

the foundation for the discovery, development and delivery of new cures and treatments for critically ill patients. One barrier towards progress in critical care is likely due to the multidisciplinary nature of the field, resulting in a scattering of critical care related projects throughout the NIH's 27 institutes and across the federal government with very little coordination among the varying entities and researchers. Along with *The Roundtable on Critical Care Policy*, **Ikaria encourages the inclusion of legislative language below that was included in the bipartisan *Critical Care Assessment and Improvement Act* (H.R. 2651 and S. 2966) in the 113th Congress.** This legislative language would create a Critical Care Coordinating Working Group within NIH to help facilitate information sharing among the various Institutes, grantees and affiliates. A Coordinating Working Group, which would add no new cost to the system, would serve to both identify critical care research gaps where resources could be more appropriately allocated, as well as identify duplicative projects. Given the impact of critical care medicine on the nation, we believe that a Coordinating Working Group is necessary to ensure our research dollars are utilized most effectively and yield the greatest result.

NIH CRITICAL CARE COORDINATING WORKING GROUP.

(a) Establishment- The Secretary shall establish a working group within the National Institutes of Health to be known as the Critical Care Coordinating Working Group (in this section referred to as the `Working Group').

(b) Membership- The Secretary shall ensure that the membership of the Working Group includes representatives throughout the National Institutes of Health and any other component of the Department of Health and Human Services, as the Secretary determines appropriate to increase agency coordination on critical care, and based on existing resources, such as --

(1) the National Heart, Lung, and Blood Institute;

(2) the National Institute of Nursing Research;

(3) the Eunice Kennedy Shriver National Institute of Child Health and Human Development;

(4) the National Institute of General Medical Sciences;

(5) the National Institute on Aging; and

(6) the National Institutes of Minority Health.

(c) Duties- The Working Group shall--

(1) serve as the focal point and catalyst across the National Institutes of Health and any other component of the Department of Health and Human Services, as the Secretary determines appropriate for advancing research and research training in the critical care setting;

(2) coordinate funding opportunities that involve multiple components of the Department of Health and Human Services;

(3) catalyze the development of new funding opportunities;

(4) inform investigators about funding opportunities in their areas of interest;

(5) represent the National Institutes of Health in government-wide efforts to improve the Nation's critical care system;

(6) coordinate the collection and analysis of information on current research of the National Institutes of Health relating to the care of the critically ill and injured and identify gaps in such research;
(7) provide an annual report to the Director on the National Institutes of Health regarding research efforts of the Institutes relating to the care of the critically ill and injured; and
(8) make recommendations in such report on how to strengthen partnerships within the National Institutes of Health and between the Department of Health and Human Services and public and private entities to expand collaborative, cross cutting research.

Thank you for your consideration of Ikaria's thoughts on the *21st Century Cures Discussion Draft.* Should you have any questions, please don't hesitate to contact Anne Esposito, Ikaria's Vice President of Government Affairs and Public Policy, at anne.esposito@ikaria.com or 202-393-7427.

Sincerely,

Daniel Tasse
President and CEO

February 13, 2015

SUBMITTED ELECTRONICALLY via cures@mail.house.gov

Chairman Fred Upton
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Ranking Member Frank Pallone
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

RE: Support for the "Ellmers-Butterfield Provision on Disposable Medical Technology" in the 21st Century Cures Discussion Draft

Dear Chairman Upton and Ranking Member Pallone:

The undersigned members of the Independence Through Enhancement of Medicare and Medicaid (ITEM) Coalition write to applaud your efforts to accelerate the pace of cures and medical breakthroughs and to specifically support Subtitle G - Disposable Medical Technologies, authored by Representatives Renee Ellmers (R-NC) and G.K. Butterfield (D-NC), in the 21 Century Cures Discussion Draft. We strongly encourage you to maintain this provision in the final bill.

The ITEM Coalition is a national consumer and clinician-led coalition advocating for access to and coverage of assistive devices and technologies for persons with injuries, illnesses, disabilities and chronic conditions of all ages. Our members represent individuals with a wide range of disabling conditions, as well as the providers who serve them, including such conditions as multiple sclerosis, spinal cord injury, visual impairments, hearing and speech impairments, limb loss, brain injury, stroke, cerebral palsy, spina bifida, myositis, osteogenesis imperfecta, and other life-altering conditions.

As medicine advances and innovation occurs in the treatment of injuries, illnesses, disabilities, and chronic conditions, Medicare beneficiaries are losing access to disposable forms of devices and treatments that traditionally have been covered under the durable medical equipment (DME) benefit. The Medicare program does not recognize the value of disposable technologies in the home because of a conflict with the decades-old definition of DME, which requires longer term durability of the products at issue. These include all sorts of devices and treatments including wound care that is used to treat decubitus ulcers incurred by long-term wheelchair users and others who are non-ambulatory.

These modern, disposable items are commonly covered by private payers, as they are easier to use, less expensive, and provide good outcomes. We therefore urge you to include the Disposable Medical Technologies provision in your 21st Century Cures legislation upon formal introduction to ensure patients have access to disposable medical technologies that would otherwise be covered as DME, but for the fact that, due to advances in medical technology and treatment, they may no longer be considered "durable." As such, we do not view this as an expansion of the DME benefit, but rather, a protection against erosion of what was always intended to be covered under the Medicare DME benefit.

****

Thank you for your consideration of our views and we look forward to working with you and your staff to further legislation that will allow for coverage of disposable medical technology under the Medicare DME benefit. Should you have further questions, please contact the ITEM Coalition Steering Committee, listed below, or Peter Thomas, ITEM Coalition coordinator, via email at Peter.Thomas@ppsv.com or by calling 202-466-6550.

Sincerely,

ITEM Coalition Steering Committee Members

Mark Richert, American Foundation for the Blind (MRichert@afb.net)

Lisa Satterfield, American Speech-Language-Hearing Association (LSatterfield@asha.org)

Laura Weidner, National Multiple Sclerosis Society (Laura.Weidner@nmss.org)

Lee Page, Paralyzed Veterans of America (LeeP@pva.org)

Alexandra Bennewith, United Spinal Association (ABennewith@unitedspinal.org)

ITEM Coalition Endorsing Organizations

ACCSES

Advanced Medical Technology Association

American Academy of Physical Medicine and Rehabilitation

American Association on Health and Disability

American Cochlear Implant Alliance

American Congress of Rehabilitation Medicine

American Foundation for the Blind

American Medical Rehabilitation Providers Association

American Music Therapy Association

American Occupational Therapy Association

American Speech-Language-Hearing Association

American Therapeutic Recreation Association

Amputee Coalition

Association for Education and Rehabilitation of the Blind and Visually Impaired

Association of Assistive Technology Act Programs

Brain Injury Association of America

Caregiver Action Network

Christopher & Dana Reeve Foundation

Easter Seals

Lakeshore Foundation

Myositis Association

National Disability Rights Network

National Multiple Sclerosis Society

National Stroke Association

Paralyzed Veterans of America

Spina Bifida Association

The Arc of the United States

United Spinal Association

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IDSA
Infectious Diseases Society of America

February 9, 2015

Representative Fred Upton
Chairman
Energy and Commerce Committee
2183 Rayburn House Office Building
Washington, DC 20515

Representative Diana DeGette
Ranking Member
Subcommittee on Oversight and Investigation
Energy and Commerce Committee
2368 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton and Representative DeGette:

On behalf of the Infectious Diseases Society of America (IDSA), I write to thank you for the hard work to date by you and your staff in compiling a comprehensive draft to advance the 21st Century Cures Initiative. IDSA appreciates the opportunity to comment on the January 26, 2015 discussion draft and is particularly pleased that this draft represents a strong commitment to advancing the development of urgently needed new antibiotics. Our patients continue to suffer from multi-drug resistant infections that we cannot effectively treat with our current arsenal of antibiotics, and provisions in this draft bill can have a significant impact for such patients. Further, antibiotic research and development (R&D) faces very unique scientific, economic and regulatory challenges that necessitate specific, targeted federal policies. In addition, we appreciate the draft bill's focus on diagnostics and vaccines, and are pleased to offer additional ideas to strengthen the bill in these areas.

More broadly, we greatly appreciate the Committee's commitment to fostering overall research. These are critical priorities worthy of additional investment. We are eager to support policies that will maintain America's status as a leader in biomedical innovation, and to do so, we believe it is critical that our leading federal agencies, such as the National Institutes of Health (NIH), maintain their authority to drive research based upon the best available science and evolving scientific opportunities.

Below please find specific comments on individual sections of the discussion draft. We hope the Committee will find these helpful as you continue working on this important effort.

Title I, Subtitle D—Antibiotic Drug Development

Sec. 1061 Approval of certain drugs for use in a limited population of patients

IDSA enthusiastically supports the creation of a new limited population drug approval pathway for antibacterial and antifungal drugs to treat serious or life-threatening infections where there exists an unmet medical need. We thank the Committee for including this important provision in the Cures discussion draft, and urge you to continue to advance this important component as you work toward bipartisan introduction of the legislation. In September, the President's Council of Advisors on Science and

Technology (PCAST) issued a Report to the President on Combating Antibiotic Resistance that also recommended this approach. Last Congress, multiple stakeholders joined together to express support for this concept as addressed in the bipartisan Antibiotic Development to Advance Patient Treatment (ADAPT) Act. This provision would speed patient access to important antibacterial and antifungal drugs to treat serious or life-threatening infections where there exists an unmet medical need by allowing such drugs to be approved based upon smaller, more rapid clinical trials. As you may know, it is often not feasible for these antibiotics to be developed using traditional, large clinical trials due to the limited numbers of patients in whom the targeted infections currently occur. While IDSA strongly supports advancing this provision and appreciates the committee's work on this provision, we urge the Committee to consider improving this language by addressing the following issues.

Given that this provision would establish a new Food and Drug Administration (FDA) approval pathway, we recognize that there has been interest in clarifying the process that companies wishing to pursue a new drug approval under ADAPT would utilize with FDA, and we appreciate the Committee's efforts to clarify what such a process may look like in this provision. We agree with the goal of fostering productive communications between FDA and drug sponsors and appreciate the committee's and ADAPT Act sponsors' work to clarify this process. However, like you, we want the provision to be feasible to ensure its successful implementation.

- Page 37, lines 4-11 and lines 16-22, and page 38, lines 15-22: We are unclear whether this language could require the FDA to agree upon (1) postapproval commitments, (2) the efficacy or safety data necessary to support expansion of the approval or licensure of the drug beyond use in the limited population, and (3) the clinical development program before a new drug application is even submitted. We agree with the need to hold meetings and discuss such issues as early as possible, but recommend that specific references to making agreements during such early meetings be removed from the discussion draft as we are concerned that asking FDA to make such agreements so early in the process, before reviewing relevant data in the application, could result in this important new pathway not being fully utilized.

In addition, on page 36, lines 12-16, the draft bill specifies timeframes within which FDA must hold particular meetings with drug sponsors. IDSA appreciates efforts to speed this process and ultimately shorten the time it takes for urgently needed new antibiotics to reach patients. However, we also recognize that FDA should have flexibility to respond to unpredictable emergencies, such as the current Ebola outbreak. We encourage the Committee to continue working with FDA to ensure this language provides that necessary flexibility, while still maintaining the inherent goals of this legislation.

It is important that drugs approved under this pathway be used judiciously, particularly given that they will be approved for limited populations, not the broader population of patients with non-serious infections that can be treated effectively with existing drugs. Appropriate use is critical to deliver optimal patient care and limit the development of drug resistance. IDSA strongly supports provisions in the draft legislation to help guide appropriate use, including pre-review of marketing materials and monitoring the use of drugs approved under this pathway, as well as patterns of resistance. We also support the language on page 39, lines 8-16, which would

require the labeling of drugs approved under this pathway to prominently include the following statement: "This drug is indicated for use in a limited and specific population of patients." However, IDSA would like to see the Committee strengthen this language by requiring the labeling of these drugs to also include a prominent visual element to make it simple for the health care community to quickly recognize that these drugs are approved for a limited population and must be used prudently.

Sec. 1062 Susceptibility test interpretive criteria for microbial organisms

IDSA strongly supports this provision to ensure that susceptibility test interpretive criteria (commonly referred to as "breakpoints") for antimicrobial drugs are regularly updated in a timely fashion, and that updated breakpoints are made publicly available via FDA's website. A breakpoint provides information that helps to predict whether a patient infected with a specific pathogen will have a good clinical response to standard doses of a drug (i.e., whether an antimicrobial drug is expected to successfully treat an infection). Prescribers need accurate and up-to-date breakpoints to guide the selection and dosage of antimicrobial drugs to maximize patients' chances for positive clinical outcomes. Breakpoints are used in antimicrobial susceptibility testing (AST) devices, results of which serve as the basis for drug selection by clinicians. Inaccurate (including out-of-date) breakpoints can result in health care providers unknowingly selecting ineffective treatments or incorrect dosing, putting patient safety and lives at risk.

Updated and accurate breakpoint information is crucial not only for individual patient care, but also for the broader public health. Updated and accurate breakpoint information is crucial not only for individual patient care, but also for the broader public health. Inaccurate breakpoints lead to the removal of potentially effective drugs from the clinician's already limited therapeutic options, and possibly the use of drugs with greater toxicity or that are overly broad-spectrum that could further contribute to the development of antimicrobial resistance. Even more troubling, inaccurate breakpoints risk use of a potentially ineffective drug that fails to resolve the infection and may also drive the development of resistance.

Moreover, health care facilities often rely on accurate AST devices to identify patients with dangerous, multi-drug resistant infections for whom certain infection control protocols must be activated to prevent the further spread of the resistant organism. Without updated breakpoints, an AST device may misclassify the susceptibility of infecting pathogens to antibiotic agents, putting patients at risk of misguided and ineffective care, and putting other patients, family members, and others at risk of exposure.

Sec. 1053 Election to convey a portion of extended exclusivity period applicable to qualified infectious disease products

IDSA has long advocated for a variety of economic incentives to spur antibiotic development. Significant unique economic barriers persist that are hampering the development of urgently needed new antibiotics. Antibiotics are typically priced low compared to other new drugs, used for a short duration, and held in reserve to protect their utility, making them far less economically viable investments for companies than other types of drugs. In 1990, there were

nearly 20 pharmaceutical companies with large antibiotic research and development (R&D) programs. Today, there are only 2 or 3 large companies with strong and active programs and a few small companies with more limited programs.

This provision to allow a company developing a new antibiotic to transfer some of that antibiotic's extended exclusivity to a different product would provide an important economic incentive for antibiotic development and we urge the committee to continue to advance this provision as you work toward introduction. As you may know, IDSA recommended a similar approach in our Bad Bugs, No Drugs report in 2004. However, our proposal at that time recommended utilizing patent extension rather than exclusivity. IDSA appreciates that the discussion draft requires that companies electing this transferable exclusivity option be required to donate a portion of their profits to the National Institutes of Health (NIH) for research on antimicrobial resistance. IDSA made a similar recommendation in its 2004 report and believes that this policy will help bolster NIH research in this critical area, which is particularly important given the recent climate of fiscal austerity that has impacted all federal research funding.

Sec. 1064 Encouraging the development and use of new antimicrobial drugs

IDSA supports the inclusion in the discussion draft of this provision to provide increased reimbursement to new antimicrobial drugs that treat a serious or life-threatening infection with high rates of morbidity or mortality and that address an unmet medical need. This narrowly focused incentive is an important complement to the other provisions in this subtitle and will appropriately target limited federal resources toward the development of the drugs that patients most urgently need. Given that these drugs can be even more challenging to develop than the broader set of antibiotics to treat serious or life-threatening infections, it is important to provide additional incentives to ensure that these urgently needed products reach patients. IDSA also appreciates that this provision would allow a company to seek a designation for a product as eligible for this incentive during the drug's development, rather than requiring a company to wait until its new drug has been approved by the Food and Drug Administration (FDA) in order to apply for increased reimbursement. This approach will give companies the predictability they need in order to target their development programs to the areas of greatest patient need and serve as a strong incentive for them to invest in antibiotic research.

In addition to spurring the development of new antimicrobial drugs, it is equally critical that we also take steps to help ensure their appropriate use in order to protect patients and safeguard these precious drugs from rapid development of resistance caused by misuse. We appreciate that this provision would require prescribing hospitals to participate in the Antimicrobial Use and Resistance (AUR) module of the Centers for Disease Control and Prevention (CDC) National Healthcare Safety Network (NHSN) or a similar reporting program to track the use of these important drugs. IDSA continues to work with CDC, health care institutions, and other key stakeholders to improve data collection on antibiotic use and resistance, and we hope that this legislation can help advance this important effort. We are also working with CDC and related stakeholders to help expand the type of data collected to ultimately include use indication, site of infection, organism, basic patient demographics, treatment duration, and outcomes (efficacy and side effects). These data are crucial for evaluating the effectiveness strategies to address

resistance, targeting antimicrobial drug and diagnostic development priorities, and defining clear benchmarks for progress.

Subtitle E—Priority Review for Breakthrough Devices

IDSA is pleased to support this subtitle which would establish priority review for PMA, de novo, and 510(k) breakthrough devices. This provision will speed approval of devices, including diagnostic tests, for which no alternatives exist, as well as tests that offer significant advantages for patients over existing approved or cleared tests. In 2014, the FDA issued draft guidance, which IDSA supported, that would similarly expedite access to PMA devices that address an unmet medical need. By extending priority review to lower risk tests that still meet the breakthrough criteria, this provision could speed patient access to a much wider variety of diagnostic tests that could provide much more rapid and reliable results in patients suffering from infectious diseases. Such tests have tremendous potential to improve patient outcomes and shorten hospital stays by facilitating administration of appropriate treatment much earlier in the course of a disease. These diagnostics may also be extremely useful in identifying patients eligible for antimicrobial drug clinical trials.

Subtitle F—Accelerated Approval for Breakthrough Devices

IDSA supports this subtitle that would provide accelerated approval for PMA, de novo and 510(k) breakthrough devices that have an impact on a surrogate endpoint that is reasonably likely to predict clinical benefit, or on a clinical endpoint that can be measured earlier than irreversible morbidity or mortality, that is reasonably likely to predict an effect on irreversible morbidity or mortality or other clinical benefit. The accelerated approval pathway is already utilized successfully for drug development and approval, and IDSA supports similar efforts to speed patient access to urgently needed diagnostic tests. For a patient with a serious or life-threatening infection that cannot be identified in a sufficiently rapid manner to substantively impact care and outcomes, FDA must appropriately weigh the risk of approving a new diagnostic test based upon a smaller premarket data set against the risk of not having urgently needed new diagnostics. Importantly, this provision provides for the conduct of post-market studies to verify clinical benefit. Post-market data can allow FDA to continue to clarify uncertainties regarding the benefits and risks of the device without inappropriately slowing or blocking patient access to an urgently needed test. We believe this provision is appropriately aligned with draft guidance issued by the FDA in 2014 regarding the balance of premarket and post-market data collection for PMA devices.

This provision will be particularly helpful in developing viral load tests for infections such as cytomegalovirus (CMV) that impacts transplantation patients. These tests can clearly identify and reliably establish viral load in patients, and can also be used to establish the duration of treatment with optimal efficacy, cost-effectiveness, and patient outcome. However, clinical trials for these tests are extremely difficult because clinical endpoints are rarely reached due to preemptive treatment of high risk patients. This provision would allow trials to use a surrogate endpoint like quantification of viral load as related to a comparator test, greatly simplifying the trials process. By allowing accelerated approval of these tests, post-market data can be collected

to better validate the medical benefits of using these tests as guides for treatment response while not unnecessarily delaying patient access to these important tools.

Subtitle G—Expanded Access

IDSA appreciates the Committee's attention to the important issue of providing patient access to experimental therapies outside of a clinical trial. The Expanded Access program can be life-saving for patients with a variety of infectious diseases, including for example emerging infections, Ebola virus disease, and infections caused by multi-drug resistant organisms. IDSA appreciates the inclusion of Qualified Infectious Disease Products (antibiotic or antifungal drugs to treat a serious or life-threatening infection) in this provision. In the field of infectious diseases, we see patients with a variety of infections that are extremely difficult or impossible to treat with existing antimicrobial drugs. In such instances, an experimental therapeutic may be the best option for some patients and this provision seeks to improve the information, metrics and speed by which patients in great need can utilize this option. We do not seek any changes to this provision, but we would like to share with the Committee the unique challenges that infectious diseases present in this area.

First, speed is essential. For serious infections, a delay of even a few hours in effective treatment may significantly impact patient outcomes and even mean the difference between life and death. For some patients who present earlier in the course of a serious infection, access to an experimental treatment within 48 hours may provide a meaningful impact on patient outcome. However, expanded access programs that take several days or weeks to provide an experimental drug to a patient would typically not be useful for most bacterial or fungal infections. We appreciate that the provision seeks more information on the time it takes patients to access such treatments and seeks to improve the overall process to reduce unnecessary delays.

Second, antibiotic and antifungal development is already extremely challenging, and the drug pipeline remains very fragile. The few companies who are trying to develop new antibiotics and antifungals already face significant challenges enrolling patients in clinical trials. Some of the most deadly infections are currently occurring in a relatively small number of patients, which severely limits the number of people eligible for a clinical trial. The lack of rapid diagnostics creates significant difficulty in identifying patients eligible for a clinical trial. For patients who are severely ill, we must often initiate antimicrobial drug therapy before there is time to enroll that patient in a clinical trial. Given these factors, IDSA appreciates that this provision does not alter existing FDA regulation that stipulates that a patient can only get access to an investigational drug through expanded access if the Secretary of Health and Human Services "determines that provision of the investigational drug or investigational device will not interfere with the initiation, conduct, or completion of clinical investigations to support marketing approval."

Title II, Subtitle A—21st Century Cures Consortium Act

IDSA is very encouraged by the inclusion of this provision to establish the 21st Century Cures Consortium in the draft Cures bill and believes it is a necessary step to advance antimicrobial drug and diagnostic research and development in the U.S. IDSA has long urged Congress and

the Administration to establish a complementary effort to the European Union's Innovative Medicines Initiative (IMI), specifically its New Drugs for Bad Bugs (ND4BB) and Rapid Point-of-care test Platforms for Infectious Diseases (RAPP-ID) projects. Such public private partnerships are essential to furthering the R&D process for new antibiotics and diagnostics because they convene the required diverse stakeholders to tackle the complex scientific and economic challenges that currently impede the development of these products. For example, ND4BB brings together government leaders, academia, industry and other experts for an unprecedented sharing of information and multi-disciplinary collaboration. The focus of the overall program is to develop better networks of researchers, create fluid and innovative clinical trial designs and provide incentives for companies to meet the challenges of antibiotic resistance quickly and efficiently. RAPP-ID convenes similar diverse groups of experts to develop fast and reliable point-of-care tests for the detection of various pathogens. RAPP-ID is gathering input from clinicians to focus its activities on areas of greatest need that can most significantly impact patient care. This effort is focused on diagnostics for blood infections, lower respiratory tract infections (including community-acquired pneumonia and ventilator-associated pneumonia) and tuberculosis.

Multiple IDSA leaders have been engaged with the IMI's activities, and we are pleased to offer their expertise as the Committee continues to refine this provision. We would also like to offer specific recommendations to strengthen the current discussion draft.

- Page 183, lines 10-14: The discussion draft would allow the consortium to provide grants to individual non-profits or small businesses. IMI instead provides grants to partnerships that include academic groups, informatics groups, and large and small companies. IDSA recommends that the Committee modify the discussion draft to explicitly provide grants to such partnerships for two key reasons: First, this approach fosters better collaboration across stakeholders by explicitly requiring that they work together in order to receive funding. Other existing public private partnership models in the U.S., such as the Biomedical Advanced Research and Development Authority (BARDA) and the Reagan-Udall Foundation already provide grants to individual entities. Providing grants instead to partnerships would make this new entity unique and allow it to fill a current void in the U.S. Second, providing grants to partnerships that include a variety of stakeholders would allow for participation by large companies. IDSA believes such participation is necessary to stimulate development of urgently needed new antibiotics and diagnostics. In the IMI, large companies do not directly receive government funds, but through the partnerships described above, they actively participate in projects and contribute significantly through "in-kind" resources. For example, large companies donate their researchers' time and provide access to research facilities or resources. Further, in the IMI's ND4BB project, new antibiotics from large pharmaceutical companies are often among those studied. The ND4BB project is allowing these new antibiotics from large companies to be studied when they otherwise would not.

- Page 132, lines 1-5: In describing the purpose of the Consortium, the bill lists "innovative cures, treatments, and preventive measures," as the areas the Consortium should address. IDSA strongly recommends adding "diagnostics" to that list. Similarly, to ensure that

diagnostics are included in this important effort, we recommend the following changes: Sec. 281B Duties, page 132, lines 19-22, add "diagnostics"; Sec. 281D, Grants, Contracts, and Other Assistance, page 137, line 18, add "diagnostics." While it was unclear whether or not the Committee intended for diagnostics to be included in this provision, we strongly urge that the Committee make the above changes to explicitly ensure their inclusion. We urgently need new infectious diseases diagnostic tests that provide rapid results, are easy to use, and accurately identify the pathogen causing an infection and the best drug to use. New and improved diagnostics can significantly improve patient care by giving physicians the information they need to more rapidly provide appropriate treatment. For example, currently, 20-30% of patients with sepsis receive inadequate initial treatment because the cause of the infection can take several days to diagnose. Better diagnostics can also improve public health by identifying patients for whom isolation or other infection control measures are needed, improving the tracking of outbreaks and emerging infectious disease threats. Improved diagnostics can also guide the appropriate use of antimicrobial drugs, and therefore are critical to the campaign to address antimicrobial resistance. Unfortunately significant barriers persist that hamper the development of these new tests, including high research and development costs, difficulty accessing clinical samples and clinical and laboratory expertise, and scientific challenges. Public private partnerships, such as those that could be supported through the new Consortium, are ideal for overcoming these hurdles.

- Page 139, lines 6-13: The draft bill would terminate the Consortium in 2021. IDSA suggests that rather than statutorily terminate the Consortium, the Committee instead include language calling for a reassessment. In the field of infectious diseases, new pathogens are always emerging and mutating, necessitating the need for new drugs, diagnostics and vaccines. In addition, we suggest that the reassessment occur in 2026, rather than 2021 as proposed in the draft bill, as we think that a 10-year timeframe would more appropriately allow the Consortium sufficient time to advance projects and demonstrate an impact.

- Page 139, lines 16-21. We note that the funding amount is left blank in the draft bill. As a point of reference, the IMI has a 3.3 billion Euro budget for 2014-2024, with approximately half of the funding coming from government sources and the remainder from the European Federation of Pharmaceutical Industries and Associations (EFPIA) companies. IDSA recommends that a similar level of funding is needed for the proposed new Consortium to have a similarly significant impact. We recognize that securing new federal funding remains very challenging in the current environment. However, we urge the Committee to consider that the new antimicrobial drugs and diagnostics this Consortium could help develop have the potential to significantly lower health care costs by reducing the administration of ineffective or unnecessary treatment and shortening hospital stays by enabling more rapid administration of effective treatments. Currently it is estimated that antibiotic resistant infections are responsible for an additional 8 million hospital days in the U.S. every year and cost our health care system $21-$34 billion annually.

Title II, Part 2—Improving Clinical Outcomes for Patients and Program Integrity through CMS Data

Sec. 2085 Expanding availability of Medicare data

IDSA welcomes legislative action that would facilitate access to Medicare data for purposes of quality and patient care improvement activities. Whereas there are some limitations to the use of these data, given the lack of granularity due to the limited information captured on the Medicare claim, access to these data will be of great value to medical societies such as IDSA. In the past, IDSA has purchased Medicare data in order to establish the positive impact of an infectious diseases physician's involvement on inpatient stays. This type of research is important in order to confirm the value of ID specialty care as the health care system moves to alternative payment models (bundled payments) in a value-based, integrated delivery system. It is unclear to us what activity might be allowable under this provision regarding the promotion of published literature, based on research resulting from access to Medicare data. IDSA asks the Committee for more clarity on the intent of subparagraph (C) of this provision, pertaining to prohibitions of the use of such data for marketing purposes. Specifically, IDSA hopes that a non-profit organization's promotion of published research would be permissible.

Title II, Part 3, Subtitle L—NIH Federal Data Sharing

IDSA supports this provision, which requires any entity receiving NIH funding to release its findings to the public and share with the public data generated through such research. Improving access to such scientific data in this manner makes sense and may help strengthen and accelerate additional research.

Title II, Part 3, Subtitle M—Accessing, Sharing, and Using Health Data for Research Purposes

IDSA supports this provision, which creates an exception to the Common Rule in cases where clinical data registries, as well as other individuals or entities, are collecting identifiable patient information, but are not engaged in direct human subjects intervention or interaction. IDSA has previously supported improving access to patient information as long as privacy remains appropriately protected.

Improving access to clinical data registries would accelerate critical infectious diseases health care operations research, such as studies regarding the clinical integration of rapid diagnostic tests into patient care settings. New rapid infectious disease diagnostics require improved coordination between laboratories, attending physicians, infectious diseases specialists, antimicrobial stewards, and public health professionals. For example, if a test can yield results in 30 minutes, but the treating physician does not receive the results for several hours, the rapid test's ability to impact patient care is not realized. Further, rapid results must also be communicated swiftly to public health and infection control professionals to allow them to trigger protocols designed to limit the spread of infection. Access to clinical data registries can allow researchers to examine the processes for communicating diagnostic test results between these parties, and how to optimize such processes to realize the patient care and public health benefits of a rapid diagnostic test.

Title III, Subtitle A—Clinical Research Modernization

Sec. 3001 Protection of Human Subjects in Research; Applicability of Rules
Sec. 3002 Use of Institutional Review Boards for Review of Investigational Device Exemptions

IDSA has long supported efforts to streamline the regulatory process while maintaining research participant protections. We are pleased to support both of these sections, which we believe are appropriately aligned with a recently released draft NIH policy on the use of a single institutional review board (IRB) for multi-site research. Currently, duplicative review of multicenter studies by local IRBs delays study initiation, requires substantial resources from local investigators and IRBs and does not improve protocol or human subject protections.

Title IV, Subtitle A—National Institutes of Health

Sec. 4003. NIH Travel

Although the Committee has not yet released draft language for this section, IDSA would simply like to take this opportunity to highlight the importance of federal scientists' participation in scientific conferences, which often require some travel. These meetings allow for analytical discussion and interaction between experts and other physicians and scientists that are crucial to scientific advancements. Further, scientific conferences provide leading federal scientists with the opportunity to educate and mentor junior researchers and physicians—a critical priority as we seek to develop the next generation of innovators. Unfortunately, policies such as sequestration have caused federal attendance at scientific conferences to decline significantly in recent years. We look forward to the Committee's proposals to address this important issue.

Title IV, Subtitle C—Vaccine Access, Certainty, and Innovation

IDSA is pleased that the draft bill includes an extensive subtitle on vaccines. Vaccines are our best tools for preventing infectious diseases, and IDSA supports policies that promote access and stimulate innovation and licensure of new and better vaccines where there is an unmet need. IDSA is pleased to support several of the provisions in this subtitle, further described below. However, we must also raise concerns about a few of the provisions as drafted and offer recommendations that we believe would more effectively advance the goals of this subtitle.

Part 1—Development, Licensure, and Recommendations

Sec. 4041. Prompt Review of Vaccines by the Advisory Committee on Immunization Practices

IDSA appreciates the goal of this section to ensure that the Advisory Committee on Immunization Practices (ACIP) promptly reviews vaccines and makes recommendations with respect to the route of administration, dosage and frequency of administration for specific populations. Quick review subject to a set timeframe may be beneficial for public health planning purposes, including quickly educating parents and patients and distributing vaccines to providers; however, IDSA has strong concerns with this provision as currently drafted.

Several IDSA members currently or have previously served on the ACIP, and we are pleased to offer their expertise as the Committee works to refine this draft legislation. IDSA has a deep appreciation of ACIP's important work as well as the challenges faced by ACIP members to analyze scientific data and make deliberate, well-informed recommendations. For each vaccine recommendation under consideration, ACIP members must review considerable microbiological, clinical, and epidemiological data, typically stretching the committee's workload to capacity.

It is also important to note that unlike FDA, the ACIP does not have a model for expedited approval requiring manufacturers to provide additional funding to support additional staff time to perform an expedited review process. As such, this provision would place strict constraints on ACIP members without providing any additional support to help them meet new requirements. IDSA is deeply concerned that as written, this provision could jeopardize the integrity of ACIP's recommendations by failing to provide sufficient time for a thorough review of relevant data.

Sec. 4042. Review of Transparency and Consistency of ACIP Recommendation Process

IDSA strongly supports measures to ensure that the U.S. government's vaccine recommendation process is transparent and communicated clearly to the public. However, we are unaware of any problems in this area, and as such do not see the need for this provision. As a Federal Advisory Committee, ACIP is governed by federal standards of transparency and public engagement. All regular ACIP meetings are accessible to the public. All working group decisions and accompanying rationale are shared publicly at regular ACIP meetings.

This provision would also require review of the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to the review and analysis of scientific and economic data. There is already extensive literature pertaining to GRADE. Both GRADE and the cost-effectiveness analyses used by ACIP have been presented at CDC in great detail, and have been posted on the internet or otherwise published.

As written, we are concerned that this provision could divert already strained CDC resources from other activities that would have a more significant impact on public health.

Sec. 4043. Guidance on Vaccine Development

IDSA strongly supports this provision to require FDA to issue final guidance to facilitate the use of accelerated and expedited pathways for the development and licensure of urgently needed vaccines, specifically those to prevent emerging, re-emerging or rare infectious diseases and vaccines for infectious diseases for which current vaccines are not addressing the full scope of public health needs. This provision would be helpful for rapidly emerging diseases that currently affect relatively few Americans, such as coccidiomycosis (valley fever) and Chikungunya fever. It would also be helpful for vaccines that need to be improved, such as those for pertussis and influenza.

Clear FDA guidance for vaccine manufacturers is important to ensure clear communication about licensure pathways available for vaccine products, as well as the clinical trial data and

other regulatory requirements with which companies will need to comply. With a better understanding of the licensure pathways and respective regulatory requirements, vaccine manufacturers and their investors will be better able to make informed decisions about vaccine R&D and target their resources to areas of greatest need. FDA guidance will also help to ensure that Biologics License Applications (BLA) meet FDA expectations earlier in the process, thus saving FDA staff time and manufacturer time and expediting public access to vaccines. As with other guidance for industry documents, public comment should be considered before finalizing any draft.

Sec. 4044. Meetings Between CDC and Vaccine Developers

Open communication between public health authorities and vaccine manufacturers is a worthy goal, and we understand that CDC priorities and epidemiological changes over time can significantly impact the potential market for a new vaccine product. However, IDSA has significant concerns with this provision. We believe that requiring CDC to meet with any vaccine manufacturer within 90 days of a request is unreasonable given very limited CDC staff resources. Unlike the FDA, which has access to user fees and designated full time employees to hold meetings with medical product sponsors, the CDC has no such dedicated financial or staff support for these activities. IDSA has consistently advocated for increased CDC funding. We are concerned that requiring CDC to accommodate these activities, without providing the agency with additional resources, may divert CDC resources from other critical priorities.

IDSA strongly supports ensuring that federal policies promote, and do not inhibit, the development of urgently needed new vaccines. As such, we would be interested in working with the Committee to better understand exactly what epidemiological data is currently unavailable to vaccine developers and the public through existing means so that we may better recommend more appropriate policies to ensure its availability. We would also look forward to working with the Committee to explore other more practical ways to facilitate more open communication between CDC and vaccine developers, such as through a regular open forum.

Sec. 4045. Modifications to the Priority Review Voucher Program for Tropical Diseases

IDSA supports this provision. IDSA strongly supported legislation enacted in December 2014 to add Ebola virus to the Priority Review Voucher (PRV) program. That legislation made additional important improvements to the program, and we believe this provision builds upon those efforts by providing more clarity about the process and methodology with which the FDA will determine what diseases will qualify for the program. This language may facilitate the addition of other appropriately qualifying diseases to the PRV program, such as Chagas disease. Chagas disease is a tropical disease caused by the parasite *Trypanosoma cruzi*, which is commonly transmitted to humans by insect vectors. Trypanosomes may also be spread through blood transfusion and organ transplantation, ingestion of food contaminated with parasites, and from a mother to her fetus. It is estimated that as many as 8 million people in Mexico, Central America, and South America have Chagas disease. Chagas disease is a very painful, debilitating disease. As the disease progresses, serious chronic symptoms can appear, such as heart disease and malformation of the intestines. If untreated, the chronic disease is often fatal. Nearly all of the victims of Chagas disease are poor people living in developing countries. There is almost no

private sector research for Chagas disease. IDSA also recognizes that additional improvements to this program may be appropriate to ensure it meets continually evolving needs, and we look forward to working with the Committee and other stakeholders to periodically assess how this program functions and how it may be strengthened.

Sec. 4048. Expanding NIH Research on Vaccines

IDSA strongly supports expanding vaccine R&D programs at NIH, especially in areas where there is an unmet need or where better vaccines are needed, such as pertussis and influenza. Influenza vaccines are currently our best interventions for prevention of seasonal influenza, even when vaccines are less than perfectly matched to the circulating virus strains. The relatively low level of protection offered by this season's vaccine underscores the need for greater research in this area.

Pertussis outbreaks in various U.S. regions in recent years highlight the need for an improved vaccine for this disease. IDSA supports a national research agenda that includes investigation of the pathogenesis of pertussis and modes of protection against *Bordetella pertussis* infection, informed by molecular microbiology, immunology, and epidemiology. We support a comprehensive approach to systemize, coordinate, and strengthen vaccine R&D across all relevant agencies and between the federal government and the private sector.

Title IV, Subtitle C, Part 2—Medicare, Medicaid and Other Provisions

Sec. 4061. Requiring Prompt Updates to Medicare Program upon Issuance of ACIP Recommendations

IDSA supports this provision. We believe that ACIP recommendations, once formally adopted by the CDC, should be implemented as soon as possible to ensure access to the vaccine for the indicated population. For the Medicare population, access to a vaccine depends largely upon whether the Medicare program covers it. These coverage decisions should be made as expediently as possible following the ACIP recommendation. We believe the 60-day timeframe specified in this provision provides the Centers for Medicare and Medicaid Services (CMS) with a reasonable amount of time to update the Medicare Benefit Policy Manual to reflect new vaccine recommendations. In addition, IDSA is eager to work with the Committee and other relevant stakeholders to facilitate greater CMS involvement with ACIP and CDC's vaccine recommendation process to ensure that Medicare officials can adequately anticipate and respond to important new recommendations that impact the Medicare population.

Sec. 4062. Encouraging Health Plans to Establish Programs to Increase Adult Immunization

IDSA has long highlighted the troublingly low rates of adult immunizations, and the resulting burden of vaccine-preventable illnesses. Increasing adult immunization rates is a critical public health priority. We are grateful that the Committee included a provision that explicitly acknowledges the need for greater efforts across the public and private sectors to improve adult immunization rates. Public and private insurance plans have an important role to play in ensuring access to recommended vaccines for adults. Allowing plans to include programs to

increase adult immunization as a quality improvement activity for purposes of calculating the Medical Loss Ratio is a strong incentive. However, programs to increase adult immunization by themselves will not necessarily result in an actual increase in immunization rates. We urge the Committee to explicitly require plans to show an actual immunization increase among their beneficiary population in order to qualify for the MLR benefit.

Given the Committee's strong interest in improving adult immunization rates, we also offer an additional suggestion that we believe will provide an even greater impact. The current discrepancy between Medicare Part B and Part D coverage of important vaccines is a significant barrier to seniors' access to vaccines. Under current law, Medicare Part D plans are responsible for covering vaccines not covered under Medicare Part B, including those protecting seniors from herpes zoster, pertussis, tetanus, and diphtheria. Unfortunately, not all seniors have Part D plans, and even those who do are often subject to prohibitively expensive copays for these vaccines. In addition, the existing fractured coverage imposes significant administrative challenges for patients, physicians, and pharmacists. For example, patients who need the herpes zoster vaccine to prevent shingles must obtain the vaccine from a pharmacist but then have it administered by a health care provider. This policy leads to fewer seniors receiving this vaccine. We strongly recommend that the Committee include in this bill a provision requiring coverage for all ACIP recommended vaccines through both Medicare Part B and D to ensure that no senior falls through the cracks.

Title IV, Subtitle E—FDA Hiring, Travel, and Training

Although the Committee has not yet released draft language for this section, IDSA would simply like to take this opportunity to highlight the importance of federal scientists' participation in scientific conferences, which often require some travel. As we explained above regarding a similar section on NIH travel, we note that scientific meetings allow for analytical discussion and interaction between experts and other physicians and scientists that are crucial to scientific advancements. We look forward to the Committee's proposals to address this important issue.

Title IV, Subtitle I—Telemedicine

Sec. 4181 Advancing telehealth opportunities in Medicare

IDSA greatly appreciates the Committee's recognition of the value that telemedicine can offer with more widespread use of this technology. ID specialists continue to leverage telemedicine to extend timely care to patients who have severe and complex infections. As many infectious diseases physicians practice in or near academic centers, telemedicine has the potential to provide specialty infectious diseases care to patients outside these areas where unmet need exists, including rural areas and correctional facilities. Telemedicine can be used to link patients directly to infectious diseases specialists or to facilitate consultations between primary care providers and specialists. Moreover, telemedicine expansion holds promise for improvements in management of chronic infectious diseases like hepatitis C (HCV) and HIV/AIDS, clinical decision support systems, and disaster preparedness and response. This provision would facilitate the extension of ID specialty care to applications that are not dependent on geographical or health care provider type limitations and that, we believe, will actually result in

improved outcomes with lower costs. We support the plan calling for collaboration through the use of State medical board compacts to create common licensure requirements for telehealth services and to define the terms that may allow such services across state lines.

Subtitle L—Global Surgery Services Rule

IDSA does not support this Subtitle that would prohibit the Secretary from implementing any provision of the Medicare CY2015 Physician Fee Schedule Final Rule with respect to transitioning and revaluing the 10-day and 90-day global surgery services with 0-day global periods. IDSA understands the rationale that CMS has presented in both the proposed and final rules and deems the work involved in carrying this out to be worthwhile to pursue at this point. Already, this change called for in the final rule has led to productive conversations among medical specialty societies as to how to consider a revaluation of the global bundles and candid, general discussions around new methods to explore towards more accurate valuation of physician services. Therefore, we urge the Committee to remove this provision and instead continue to monitor CMS activities in this area to assess their impact.

Subtitle S—Continuing Medical Education Sunshine Exemption

Sec. 4381. Exempting from manufacturer transparency reporting certain transfers used for educational purposes

IDSA is pleased to support this provision, which would ensure that peer-reviewed journals, journal reprints, journal supplements, and medical textbooks are included in existing Sunshine Act reporting exclusion for continuing medical education (CME) activities. The importance of up-to-date, peer reviewed scientific medical information as the foundation for good medical care is well documented. Independent, peer reviewed medical textbooks and journal article supplements and reprints represent the gold standard in evidence-based medical knowledge and provide a direct benefit to patients because better informed clinicians render better care to their patients. In August, 2014, IDSA joined a significant number of national and state medical societies to urge CMS to exempt these materials from Sunshine Act reporting requirements, and we are grateful for the Committee's attention to this important issue.

Additional Recommendations

In addition to the very comprehensive discussion draft that the Committee has compiled, IDSA has a few additional recommendations that we believe are central to the overall goal of this legislation to spur innovation that will benefit patients. The following recommendations specifically focus on fostering the development of new infectious diseases diagnostics. In addition to the summaries below, we are also attaching draft legislative language for the first two proposals, which we hope the Committee will find helpful.

<u>Biorepositories</u>: Direct the National Institute for Allergy and Infectious Diseases (NIAID) to examine opportunities to support the development of virtual biorepositories for viruses, fungi and other pathogens, utilizing samples already being collected under existing NIAID-funded research, similar to the existing bacteria virtual biorespository. Provide incentives and support for institutions to save de-identified specimens and to participate in virtual

biorepository catalogues when possible. A key challenge in clinical trials for new diagnostics is access to clinical samples, particularly those containing rare pathogens. Many clinical laboratories no longer freeze specimens containing novel or unusual organisms for further use. Even when such critical samples are available, the cost of accessing them has, in many cases, become prohibitive. The Antibacterial Resistance Leadership Group (ARLG), a strategic research team funded by NIAID, established a Virtual Biorepository (VB) Catalogue, a web-based system that provides researchers with unique access to clinically well-characterized bacteria for the development of diagnostic tests and other research. The bacteria are already being collected through other ARLG research projects and are housed at multiple locations. This approach requires significantly less resources than traditional physically centralized biorepositories. Researchers are able to search the virtual biorepository catalogue to locate the samples they need. This approach could be very useful in other areas of infectious diseases diagnostics development (e.g. virus, fungi, etc.).

Conflict of Interest: Clarify, through report language, that institutions receiving federal funding should implement conflict of interest (COI) policies that appropriately enable transparent industry/institutional research collaborations. Direct the Food and Drug Administration (FDA) to clarify and revise its COI policy to enable more effective recruitment of subject matter experts while retaining objective regulatory review. Often expert input or independent validation of a potential test is needed during development. Institutional COI policies are often much more strict than the National Institutes of Health (NIH) COI regulatory framework, which was intended to provide guidance to institutions on how to manage COI. Unfortunately, institutional COI policies often bar those best suited for these activities, sometimes even if the expert is willing to work for free on his or her own time. Even when an institution does not explicitly ban such activities, policies are sometimes misinterpreted, resulting in a stifling of collaboration between academic researchers and industry. This forces developers to forgo expert input or use laboratories lacking expertise for independent testing. This loss of expert input and the resources diverted to train and supervise testing at labs lacking expertise can add considerable time and cost to diagnostic development.

Strong educational programs to inform physicians about the utility of new diagnostics: Direct the Agency for Healthcare Research and Quality (AHRQ), specifically through its Center for Evidence and Practice Improvement (CEPI), to conduct or support research to demonstrate the impact of new ID diagnostics on patient care and outcomes, and to disseminate the results of that research to physicians to encourage them to appropriately utilize new diagnostics. Many physicians and other health care providers may be hesitant to use new diagnostic tests, in part because they are often uncertain of how best to integrate them in their practice and how to interpret results. Physicians often look to education, such as clinical guidelines developed by their professional societies, such as IDSA, and government bodies, such as the AHRQ, to suggest the best methods to diagnose and treat an infection. Little guidance currently exists on the use of diagnostic tests for a particular type of infection, or what bundles of tests should be used if a patient has a particular set of symptoms. The ability to construct useful guidelines is hampered by the lack of clearly designed outcomes studies demonstrating patient benefit when tests are used as part of clinical decision making. IDSA is open to this type of research being conducted or supported elsewhere in the federal government. However, CEPI is well-suited to address this need, as the Center is tasked with conducting and supporting research

on health care delivery and improvement and advancing decision and communication sciences to facilitate informed treatment and health care decision making by patients and their health care providers.

Once again, IDSA is grateful to the Committee for the hard work evident in this comprehensive discussion draft. We hope our comments will be helpful as you seek to refine and advance this important effort. We look forward to continue working with you toward policies that will benefit patients and public health. Again, we are excited to see the focus this discussion draft places on antibiotic development and believe these policies will truly make a difference in the patient care and public health.

Sincerely,

[redacted]

Stephen B. Calderwood, MD, FIDSA
IDSA President

February 10, 2015

The Honorable Fred Upton
Chairman
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
Member
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515

Sent via e-mail: Cures@mail.house.gov

Re: Regarding the 21st Century Cures Act discussion draft

Dear Members of the Energy and Commerce Committee:

Thank you very much for the opportunity to comment on the discussion draft of the 21st Century Cures Act. Founded in 2012, Invitae is a genetic information company whose mission is to bring genetic information into routine medical practice to improve the quality of healthcare for billions of people. Specializing in genetic diagnostic testing for hereditary disorders, Invitae is aggregating the world's genetic tests into a single service with better quality, faster turnaround time, and a lower price than most single-gene diagnostic tests today.

Invitae greatly appreciates the many opportunities you have provided for stakeholders to contribute to this ambitious initiative over the past year and, last September, submitted written testimony to the Committee's hearing on "21st Century Cures: Examining the Regulation of Laboratory Developed Tests." For additional background, Invitae also provided public comment at the FDA's public meeting on the draft guidance creating a framework for oversight of laboratory-developed tests as well as written comments to the docket. We note the placeholder in the discussion draft for Subtitle J – Modernizing Regulation of Diagnostics under Title II and encourage the Committee to review our testimony and comments to the FDA. Additionally, once draft legislative language is available, we welcome the opportunity to provide additional feedback on this very important issue that if addressed appropriately can advance precision medicine and accelerate access to innovative molecular diagnostics.

Today, we are writing in support of the intent of Subtitle E—Sensible Oversight for Technology Which Advances Regulatory Efficiency under Title II. A critical component of the delivery of healthcare is software that enables health care providers and patients to access health information for helping to inform treatment decisions with easy yet secure storage, mining, transfer and display of genomic data, clinical decision support tools, workflow and analytics, among many others so long as these are not used as the sole means of diagnosing a disease or used independent of other measures to diagnose a disease or condition. FDA regulation should not hamper access to and the utilization of software for

these uses and Invitae is pleased the Committee is working to reduce this regulatory burden for both medical software and health software. Due to the short timeframe for submitting comments, we wanted to offer our support for your work in this area of health policy. We will continue to review this provision and we look forward to providing additional feedback on the draft language as well as the anticipated section on the regulation of diagnostics.

Thank you again for your ongoing engagement with stakeholders and your efforts to address many of the barriers to accelerate the development of new treatments and diagnostics. Invitae looks forward to being part of this process and please do not hesitate to contact us if we may be of assistance.

Sincerely,
Invitae Corporation

Contact Information:
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The Jett Foundation
Fighting Duchenne Muscular Dystrophy

February 10, 2015

The Honorable Fred Upton
Chairman
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C., 20515

The Honorable Diana DeGette
Committee on Energy and Commerce
U.S. House of Representatives
Washington, D.C., 20515

RE: Jett Foundation Comments on 21st Century Cures Initiative Discussion Draft

Dear Chairman Upton and Representative DeGette:

The Jett Foundation, a not-for-profit organization focused on finding treatments and a cure for Duchenne muscular dystrophy while improving the lives of those affected by DMD, would like to thank you for your leadership in initiating the 21st Century Cures Process which has culminated in the release of this first legislative discussion draft.

We very much appreciate your interest, attention and commitment to addressing the approval process for drugs and devices, specifically those that are focused on rare disease for which there are currently no effective and approved treatments. It is certainly important to ensure the approval process continues to evolve as medicine and technology advance. The once remote possibility for development of genetically targeted treatments that have the potential to save lives and preserve the quality of life for those suffering from rare disease is now a reality.

However, it is our experience that the approval process at the Food and Drug Administration (FDA) has not kept pace with these advances. We support legislative efforts to give FDA additional tools to advance regulatory science and provide rapid access to safe and effective therapies for rare disease. But such legislative efforts, without rigorous congressional oversight, will not be sufficient to ensure the FDA follows-through on the promise offered by the 21st Century Cures initiative.

We have been frustrated, for example, that the FDA has not utilized the tools congress provided the agency in the FDA Safety and Innovation Act (FDASIA) during its ongoing and inexplicable nearly three year review of safe and efficacious treatments for Duchenne.

We also wish to point to a specific concept in the Committee's Discussion Draft that is essential to ensuring the earliest possible access to treatments for rare disease. For many rare diseases, there is a common problem that must be addressed in order to treat the disease. In Duchenne, all boys are missing an exon necessary to produce the protein dystrophin needed to support and sustain muscle. But not all boys are missing the same exon. Drugs currently in clinical trial are designed to address that problem by skipping the missing exon and thereby allowing for the production of dystrophin. Here is the challenge: the largest cohort of boys -- those missing exon 51 -- represents only about 15 percent of the Duchenne population. The population grows smaller with some mutations representing less than one percent of the 1/3500 boys born with

Duchenne. If drug companies are required to essentially begin the FDA approval process anew for each missing exon, it will take decades before all boys will have access to treatments. Further, no drug company could be expected to make such an investment for such a small population likely to benefit from the treatment once it is finally approved.

Section 2051 of the Committee's draft -- "Genetically Targeted Platform Technologies for Rare Disease" -- addresses this problem. It clarifies that FDA can grant accelerated approval to products developed using genetically-targeted therapeutic platform technologies based on extrapolated data, where evidence to support that a product is reasonably likely to have a clinical benefit can be derived from previously conducted clinical studies for products based on a functionally similar platform, thereby serving to accelerate and streamline approval of subsequent applications. Further, Section 2051 requires that a determination for accelerated approval of a product be based on the totality of evidence provided, particularly important for rare diseases where data on any given endpoint may be limited due to the size of the population. Importantly for Duchenne, the provision allows innovators to extrapolate their own data when a platform targets different patient subpopulations within the same disease state or when it targets different conditions or diseases, while providing FDA flexibility to determine the appropriate degree of extrapolation versus new data generation.

We strongly believe that congress granted the FDA the authority and the ability to move forward in the above manner in FDASIA. However, it is apparent that such a clarification -- and through this clarification, an expression of congressional intent -- is both prudent and necessary.

Thank you for the opportunity to provide our perspective on the discussion draft. We look forward to continuing to work with you as the process continues in the hope that it will achieve the consensus goal of bringing innovative and much needed new treatments and therapies to patients, including those affected by Duchenne muscular dystrophy.

Sincerely,

Christine McSherry
Executive Director
The Jett Foundation

Cc: The Honorable Frank Pallone

LEUKEMIA & LYMPHOMA SOCIETY®
fighting blood cancers

www.LLS.org

February 10, 2015

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

RE: 21st Century Cures Discussion Draft

Dear Chairman Upton:

The Leukemia & Lymphoma Society (LLS) appreciates the opportunity to provide our comments on the 21st Century Cures Initiative discussion draft document released on January 27, 2015. We thank and commend you, Congresswoman DeGette, and your colleagues for your thoughtful, bipartisan approach to examining potential policy improvements that will promote the discovery, development, and delivery of better diagnostics, treatments, and cures for the patients you represent.

LLS has been actively engaged throughout this initiative—sharing written comments, testifying at a Cures roundtable in Washington, participating in district roundtables across the country, and presenting legislative proposals to advance our shared goals. We believe the discussion draft marks an important milestone along the path toward a bipartisan law that will quickly begin to make a real impact in the lives of blood cancer patients and their families.

LLS Comments

Title I, Subtitle A – Patient-Focused Drug Development (Section 1001)

LLS strongly supports the patient-centered policies included in this section by Health Subcommittee Chairman Pitts and Congresswoman McMorris Rodgers. Taken as a whole, these policies will magnify the voice of patients throughout the regulatory process—providing the vital insight required to understand what patients need from a new therapy or cure.

As LLS has engaged with members of the Committee on this initiative, we have urged lawmakers to take this opportunity to establish a new framework in which patient engagement is integrated into the dialogue between the FDA and a drug sponsor that occurs throughout the development process. Specifically, LLS and other stakeholders have emphasized the need to streamline the process for determining appropriate patient reported outcomes (PROs) and incorporating the data gathered through these tools into the regulatory process. Data attained through PROs and other patient experience collection methods may dramatically influence the FDA's benefit-risk analysis and could help doctors and their patients to make fully informed decisions when they choose a treatment option.

LLS supports the discussion draft's broad list of issues the FDA would need to address in providing guidance to stakeholders on the parameters of patient experience data, including PROs, registries, and

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other tools to better incorporate the patient perspective in the drug development process. LLS urges that the Committee clarify this language to avoid limiting the FDA's use of patient experience data strictly to the "structured benefit-risk assessment framework". In working with the patient community and other stakeholders, the FDA should have the flexibility to consider new, innovative ways to promote the patient perspective in the regulatory process.

LLS also supports the inclusion of multiple opportunities for public stakeholder input into the section's patient experience data guidance document. The three public workshops required in advance of the release of draft guidance and the public meeting following its release will help ensure the FDA has the information it needs to craft a meaningful final guidance document. LLS also supports the draft's requirement that the Agency publish a report within 5 years of enactment that includes the Agency's ideas on how to (1) improve the then-implemented development and submission process and (2) better use submitted patient experience data to improve risk-benefit assessments.

Given the value of patient engagement throughout the discovery and development process, LLS urges the Committee to incorporate additional policies that promote effective communication among patients, drug developers, and the FDA. To advance this goal, LLS has proposed an independent analysis of the various barriers that limit the involvement of patients in all phases of drug development. From our experience, stakeholders have varying interpretations of existing guidance, regulation, and statute, which only highlights the lack of clarity that unnecessarily inhibits beneficial communication with patients. Once this analysis concludes, Congress, the FDA, and other relevant agencies should begin targeted efforts to provide requisite clarity that ensures patient protections while providing a safe harbor method or methods of engagement for appropriate and productive engagement. LLS would welcome the Committee's inclusion of this proposal and others aimed at promoting appropriate patient engagement throughout the discovery and development process.

Title I, Subtitle B – Surrogate Endpoint Qualification & Utilization (Sections 1021, 1022, 1023, 1024)
The future of cancer care is targeted, precision-based medicine, and our policies should recognize that the existing three-phase clinical trial system may be unrealistic for compounds intended to treat small disease populations. The "standard" approach to drug development is especially difficult for blood cancers, as small populations complicate researchers' efforts to achieve statistical significance or quickly demonstrate an increase in overall survival. That's why LLS has advocated for the FDA to clarify the process for the validation of biomarkers and surrogate endpoints.

LLS appreciates lawmakers' interest in advancing this key reform through the policies outlined in the discussion draft. These policies will help accelerate the qualification and utilization of surrogate endpoints predictive of overall survival and will facilitate faster and less expensive clinical trials that provide patients with timely access to therapies that would otherwise be delayed.

Title I, Subtitle G – Expanded Access (Section 1121, 1122, 1123, 1124, 1125)
In order to improve patient access to investigational drugs through the FDA's expanded access process, LLS has endorsed the "Andrea Sloan Compassionate Use Reform & Enhancement Act" authored by Representative Michael McCaul. This bill would provide greater transparency to patients and physicians

requesting expanded access to an investigational medication and require FDA to provide improved clarity regarding how it uses data from expanded access cases to inform the regulatory process. LLS strongly believes these policies are targeted, thoughtful improvements to a process that represents many patients' last hope, and LLS appreciates that this important package of reforms was included in the discussion draft.

Title II, Subtitle Q – Precision Medicine (Section 2301)
Blood cancer patients are already preparing for the exciting personalized therapies and cures that have been providing promising results in the development stages for years. Drugs and other treatments designed to attack the exact type of cancer within a specific patient have the potential to significantly improve the clinical and medical outcomes for several otherwise-unresponsive blood cancers. These breakthroughs have the potential to speed patient access to interventions that work and avoid wasting precious time and valuable system resources on interventions that would provide no clinical benefit to the patient.

Of course, an integral component to this precision-based approach is a companion diagnostic test, which provides the patient information necessary for the safe and effective use of a corresponding therapeutic agent. Without this accurate diagnostic, patients who could never benefit from a treatment may be prescribed it. Even worse, in a world without an effective diagnostic, patients who would have benefited will miss out on the benefits of the drug, simply because their doctor or their insurer were unaware that the therapy would work for them. Despite the fact that these diagnostic tests are a necessary lynchpin in the success of precision medicine, significant hurdles still prevent companies from developing these essential tools. Low reimbursement rates and a complicated regulatory environment have limited investment in companion diagnostic development.

As the Committee weighs proposals to promote the advancement of precision medicine, LLS recommends that Congress establish a new Essential Companion Diagnostic priority review voucher (PRV) pilot program, building upon the experience of the Agency's existing voucher programs for Rare Pediatric Diseases, which was enacted in 2012. Under this pilot program, the sponsor of a companion diagnostic that is essential for the safe and effective use of a novel therapeutic agent would receive from the FDA a transferable voucher for the future priority review of a pharmaceutical agent. The diagnostic sponsor can sell the voucher to a drug manufacturer, who can use the voucher to file for priority review of a product in development. The diagnostic sponsor's ability to sell such a voucher would establish a significant new incentive for the development of companion diagnostic tests.

Priority review is an FDA designation that directs the overall attention and resources of the Agency to the evaluation of a drug application. Without sacrificing safety, this designation alters the FDA's internal processes such that the timeline for a decision on approval is shortened from ten months or longer to less than six months of the new drug or biologic application. In addition, this voucher does not create new federal spending, as the FDA continues to operate within its appropriated budget. This proposal is a cost-effective way to promote the complementary innovation that is necessary to enable precision medicine therapies and cures to succeed, and LLS urges lawmakers to consider this and other methods of promoting innovation in this area.

Title III, Subtitle A – Clinical Research Modernization (Section 3001, 3021)
Precision medicine will also require unprecedented flexibility in clinical trial design and an enhanced understanding of how best to conduct clinical trials for compounds intended for increasingly limited subpopulations. Similarly, given that any single drug is unlikely to cure multiple cancers, clinical trials examining combination treatments will only expand in their relevance for cancer patients. Quickly determining effective combination treatments is essential, and will have a significant impact on blood cancers. That's why LLS has advocated for policies that make clinical trials more nimble and promote the new designs necessary to ensure that trial accrual is not the reason new innovative drugs do not make it to market.

In light of these recommendations, LLS has advocated for the creation of a single Institutional Review Board (or "Central IRB"), in order to streamline multi-site clinical trials without sacrificing participant protections. As a result, LLS strongly supports the discussion draft's clinical trial reforms offered by Representatives McMorris Rodgers and DeGette, which would promote the changes necessary to facilitate these expansive clinical trials by requiring HHS to reform IRB regulations to ensure cooperative medical research can utilize shared review mechanisms that prevent duplication of effort and unnecessary delays. This reform is an important step to promoting efficient, effective clinical trials.

Another key reform supported by LLS is the promotion of adaptive clinical trial design, which permits sponsors to adapt and make revisions to their clinical trial design as they receive data on the trial's progress in real time. As mentioned above, multi-company, multi-compound combination trials will be key in determining safety and efficacy for treatments of the future. The policies offered by Representative Chris Collins in the discussion draft will help enable this effort by encouraging the use of adaptive trial designs.

Title IV, Subtitle A – National Institutes of Health (Section 4007)
LLS continues to believe that providing adequate funding for the National Institutes of Health (NIH) and its individual research centers should be a top priority for lawmakers advancing this package of reforms. As with many other complex diseases, we still do not understand the cause of blood cancers, and there are no known methods of prevention or screening. Although LLS and other private stakeholders have developed innovative programs that attempt to fill the gaps, the overarching economic incentives create an environment where a shortage of federal funds creates a shortage of scientific discoveries. Adequately funding the discovery process is essential to keeping the United States at the forefront of biomedical innovation.

Recent reductions in funding as a result of inflation, stagnant appropriations, and sequestration have greatly diminished the NIH's ability to fund the new scientific discoveries patients need. LLS hopes that the next version of this legislation will include a substantial funding increase for the NIH, in order to promote this promising research at early stages.

Title IV, Subtitle F – FDA Succession Planning (Section 4121)
The medical technologies of the past decade have brought exciting new types of therapies and cures into focus. At the same time, these new medical breakthroughs are increasingly complex. As a result, a

thoughtful FDA review of their safety and efficacy will continue to require enhanced, specialized expertise within FDA. FDA reviewers need every tool possible to continue to adapt and expand their expertise on the latest technologies, disease information, and patient input. Furthermore, as FDA invests in their expert staff, the Agency needs both the resources and the leadership to ensure they continue to attract and retain this talent.

LLS supports key reforms included in the discussion draft that direct the Agency to focus on professional development, including FDA staff attendance at medical and scientific conferences. These conferences bring together experts from industry, academia, medical practice, and regulatory science, and the insights gained by FDA staff will lead to more informed reviews of FDA-regulated products.

Access Policies

LLS believes many of the policies outlined above will improve the discovery and development processes and lead to new, lifesaving diagnostics, therapies, and cures for blood cancer patients. Yet, if these patients cannot access these breakthroughs, they will be no better off than they are today. Unfortunately, blood cancer patients are particularly susceptible to practices that can place their drugs beyond the patient's financial grasp. The increased use of high coinsurance for many specialty drugs, rather than fixed co-payments, place financial strain on families and sometimes even cause patients to choose between life-saving therapies and other basic necessities. Due to the evolving and complex nature of cancer care, new blood cancer therapeutics are often available only after the patient pays hundreds or thousands of dollars in out of pocket costs.

The Committee can solve this critical patient access problem by working with Representatives David McKinley and Lois Capps, who have been consistent leaders on this issue. In the last Congress, Reps. McKinley and Capps introduced the Patients Access to Treatments Act, aimed at providing more affordable prescriptions in the commercial health insurance market. The Committee should also investigate ways to prevent similar prescription drug plan design abuses within Medicare Part D program.

Similarly, many of the innovative blood cancer therapies being produced today are oral agents, rather than traditional chemotherapies delivered through an IV. Despite this innovation, traditional insurance structures often create significantly higher cost sharing for oral cancer drugs, compared to their traditional infused-drug therapies. This discrepancy is unfair to cancer patients and inhibits innovation in oral cancer therapy. In the last Congress, Representative Brian Higgins introduced the Cancer Drug Coverage Parity Act to solve this issue, and LLS recommends the Committee consider ways to address this outdated benefit design within the 21st Century Cures package.

About LLS

LLS is the world's largest voluntary health agency dedicated to the needs of blood cancer patients. Each year, over 150,000 Americans are newly diagnosed with blood cancers, accounting for nearly 10 percent of all newly diagnosed cancers in the United States. LLS exists to find cures for leukemia, lymphoma, and multiple myeloma and to ensure that blood cancer patients have sustainable access to quality, affordable, coordinated healthcare. LLS funds lifesaving blood cancer research, provides free

information and support services, and advocates for public policies that address the needs of patients with blood cancer. Since our founding 65 years ago, LLS has invested over $1 billon into medical research, and LLS-funded research has been part of the vast majority of FDA-approved therapies for blood cancer.

Conclusion

LLS appreciates the bipartisan work you and Representative DeGette have led in listening to health care stakeholders and thoughtfully considering policies that will make a difference in promoting the development of the next generation of medical breakthroughs. Thank you for your leadership on these important issues and for considering the recommendations we have outlined above. If you have any questions about our comments or our organization, please do not hesitate to contact Brian Connell (by email at brian.connell@lls.org or by phone at 202-989-1805) for further information.

Sincerely,

[redacted]

Lisa Nelson
Vice President, Government Affairs
The Leukemia & Lymphoma Society

cc: Ranking Member Frank Pallone
Health Subcommittee Chairman Joseph Pitts
Health Subcommittee Ranking Member Gene Green
Representative Diana DeGette

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February 10, 2015

BY EMAIL DELIVERY (cures@mail.house.gov)

RE: 21st Century Cures Discussion Document

Eli Lilly and Company (Lilly) appreciates the opportunity to comment on the 21st Century Cures Discussion Document. Lilly is one of the country's leading innovation-driven, research-based pharmaceutical and biotechnology corporations. Our company is devoted to seeking answers for some of the world's most urgent medical needs through discovery and development of breakthrough medicines and technologies and through the health information we offer. Ultimately, our goal is to develop products that save and improve patients' lives.

Lilly applauds the House Energy and Commerce committee's efforts to identify public policy solutions that will accelerate the discovery, development, and delivery of innovative medicines in the United States. We look forward to working with Chairman Upton, Ranking Member Pallone, Congresswoman DeGette, and other Members of the House Energy and Commerce Committee on this initiative.

We support the comments set forth in the letters by the trade associations PhRMA and BIO and specifically highlight Lilly's support and concerns relating to the following provisions contained within the discussion draft document:

- Patient-Focused Drug Development (Sec. 1001)
- Surrogate Endpoint Qualification (Sec. 1021-1024)
- Dormant Therapies (Sec. 1221-1223)
- Access to Data for Research and Quality Improvements (Sec. 2085)
- Clinical Data Sharing (Sec. 2092)
- Utilization of Real World Evidence in Drug Development (Sec. 2101)
- Combination Products (Sec.2141-2142)
- Adaptive Trial Design (Sec. 3021)
- Post-Approval Studies (Sec. 3031)
- Improvements in the Medicare Local Coverage Determination Process (LCD) (Sec. 4161)

In addition to our comments on the provisions in the discussion draft document, we have also highlighted five additional delivery proposals for the committee's consideration. These proposals were also included in the BIO submission to the committee on December 5, 2014.

- Appealability in Medicare Part D
- New Technology Add-On Payments (NTAP) in the Hospital Inpatient Prospective Payment System (IPPS)
- Require CMS, Together with HRSA, to Address Duplicate Discounts
- Incentivizing Innovation in Alternative Payment Models (APMs)
- Modifications to Value-Based Contract Arrangements

Title 1 – Putting Patients First by Incorporating Their Perspectives Into the Regulatory Process and Addressing Unmet Needs

Patient Focused Drug Development (Sec. 1001)

Patient-Focused Drug Development Initiative (PFDD) and Benefit-Risk Assessment (B/R) have emerged as promising and important initiatives to the patient advocacy community, regulators, and the regulated industry. In order to ensure that any data that is collected regarding patient perspectives is actively considered and ultimately shapes relevant decisions throughout the drug development and regulatory review processes, it is important the data are seen as valid from a social sciences perspective and representative of the perspectives of the patient group being studied. To get to this level of quality data, we must advance the science of patient input. Specific recommendations include the following:

- The draft language is a good start but does not go far enough in engaging and relying on experts in the social sciences to establish guidance on appropriate methodologies and approaches to incorporate the patient perspective into development of new medicines and regulatory decision making regarding new medicines.
- It should be made explicit that patient data collected in these scientifically valid methods should be considered as part of the drug development and regulatory decision making process and should transparently be reflected in the reviewers' benefit/risk assessment frameworks.
- The pharmaceutical industry should be acknowledged as a participant in relevant discussions on this topic, particularly given that much of this type of data will, in fact, be collected by the industry during drug development.

Surrogate Endpoint Qualification (Sec. 1021-1024)

Biomarkers (surrogate endpoint biomarkers being a subset of biomarkers) are essential tools to improving the efficiency and the effectiveness of clinical research. Under certain circumstances, they can predict drug efficacy, safety, and dose response more quickly and with greater sensitivity than conventional clinical endpoints and, as such, can substantially accelerate product development and ensure safer medicines. In 2010, FDA issued a draft guidance, which was finalized in 2014, outlining a process sponsors may follow to qualify biomarkers for future use. Unfortunately, publication of this guidance has not spurred increases in the number of qualified biomarkers, at least in part, due to uncertainties with FDA processes for accepting these tools in regulatory decision-making. The discussion draft is a

step in the right direction; however, more should be done. Specific recommendations include the following:

- Any qualification process should stipulate the required levels of evidentiary substantiation and the methods used to evaluate it, including examples. FDA, in partnership with scientific experts in the field, should articulate a framework to describe these standards.
- Given the breadth and depth of expertise required, the qualification efforts for individual biomarkers, including both surrogates and non-surrogates, should leverage external experts as advisors to FDA decision-makers. In a continuously advancing and evolving environment, it is difficult, if not impossible, for any single organization to house expertise in all the relevant areas needed across the multitude of therapeutic areas where works needs to be done. Lilly believes the greatest numbers of patients will be helped by establishing public-private partnerships (PPP) to help operate theses biomarker qualification processes. Use of a PPP to manage any or all of these efforts should only occur with consistent FDA engagement and as part of an FDA supported and sanctioned process in order to ensure buy-in and adoption by the FDA of recommendations made by such partnerships. FDA should remain the final decision-maker regarding the qualification of any biomarker, as informed by expert recommendations from the PPP, and should articulate its decisions, including any specific data gaps, within a reasonable timeframe.
- The draft makes distinctions between surrogate and non-surrogate biomarkers. The proposed timelines are useful and reasonable, but should apply to both surrogate and non-surrogate biomarkers. Reasonable and clearly defined timelines for the qualification process are needed to encourage investment in these efforts.
- The process for qualifying Patient Reported Outcomes (PROs) was notably absent from the draft. It is recommended that consideration be given to its inclusion as they are another type of important drug development tools that provide valuable information that is arguably most relevant to patients. Any approach similar to biomarker qualification could be employed for enhancing the timeliness and predictability of the PRO qualification process.
- The discussion draft would benefit from minor corrections as to confidentiality requirements. Lilly believes FDA should continue to appropriately disclose biomarkers as they are qualified so as to prevent unnecessary human testing or futile qualification efforts by other sponsors. However, the discussion draft language is unclear as to the extent of confidentiality of regulatory qualification decisions. We believe FDA should continue to maintain the discretion to publish regulatory standards and guidance while protecting confidential data or trade secret information.

Dormant Therapies (Sec. 1221-1223)

Lilly supports the inclusion of "The Dormant Therapies Act (DTA)" in the 21st Century Cures draft discussion document. The Dormant Therapies Act builds upon current law to create a new form of intellectual property protection as an incentive for the development of innovative new medicines that address unmet medical needs.

The genesis of the Dormant Therapies Act (DTA) was the product of activities led by the National Health Council, an organization whose primary mission is advocacy for patients afflicted with chronic and debilitating diseases. The DTA has bipartisan and bicameral support. The Senate legislation, S. 3004, was introduced on December 11, 2014 by Senators Hatch (R-UT) and Bennet (D-CO). The House bill, the MODDERN Cures Act, H.R. 3116, has been championed by Rep. Leonard Lance (R-NJ) and attracted the co-sponsorship of 47 Democrats and 48 Republicans in the 113th Congress.

Title II – Building the Foundation for 21st Century Medicine, Including Helping Young Scientists

Access to Data for Research and Quality Improvements (Sec. 2085)

Lilly supports the need to make available Medicare data for evaluation of new care models, quality improvement activities and other patient care activities; however, this will only be impactful if the data and the information generated from the data can be re-disclosed and communicated by all stakeholders in the healthcare ecosystem. There are two issues with Sec. 2085. First, the re-disclosure provisions appear to be more stringent than the present practice using CMS data today. It potentially allows commercial insurers and other qualified researchers to have access to data and analyses that manufacturers are not similarly able to share with insurers, if the research is not able to be disclosed via publication. The inability to publish research from Medicare data analysis in peer-reviewed journals deprives patients and providers of important information needed to make healthcare decisions, slows the learning health system, and adds to the asymmetry in communication and share of voice that exists between industry and commercial insurers, PBMs, and State and Federal agencies. Lilly recommends that allowing CMS's existing solid provision which protect patient and provider privacy, research using Medicare claims data produced by qualified researcher(s) should be allowed to be published in peer reviewed journals and thus shared with the medical and scientific community.

Finally, the prohibition on data use for marketing purposes outlined in Sec. 2085 seemingly precludes the use of analysis or data (and any publication – as described above) from being used in FDAMA 114 even if the analysis met all of the FDAMA 114 requirements.

Clinical Data Sharing (Sec. 2092)

Lilly supports the recommendation for the development and use of registries integrated with practice guidelines, and best practices or standards of care. It will be important to ensure that the process to develop practice guidelines is transparent and is inclusive of all experts and patients.

Utilization of Real World Evidence in Drug Development (Sec. 2101)

Through better use of big data, sponsors can improve pharmaceutical R&D effectiveness and efficiency through advanced modeling and analytic methods. Lilly supports the discussion draft enabling the FDA to consider big data and real world evidence (RWE) when establishing

the safety and efficacy of new medicines – including for both regulatory approval of line extensions and fulfilling post-approval commitments. Specific recommendations include the following:

- It may be necessary to explicitly clarify that RWE may be used, in part, to demonstrate substantial evidence for regulatory decision making purposes.
- This field is evolving quickly, and consortia may be needed to facilitate data interoperability and access, as well as methods development.

Title III – Modernizing Clinical Trials

Combination Products (Sec.2141-2142)

Many of the biopharmaceutical industry's future cures are therapies created by combining a drug and a device. However, inconsistent regulatory guidance, requirements, and/or cross-divisional/office interactions with sponsors create delays that negatively impact timely development of combination therapeutics. Lilly strongly supports the proposed process improvements and clarifications. However, we question the effectiveness of adding a GAO report on the Office of Combination Products (OCP) perspectives, experiences, and training. The inclusion of the GAO report adds another party to the reform effort achieved by Sec. 2141. We are concerned that this may produce counter-productive recommendations.

Adaptive Trial Design (Sec. 3021)

The FDA is also receiving an increasing number of regulatory submissions that use adaptive designs -- as sponsors have seen benefit (in combination with Bayesian methods) in these designs to improve robustness in the interpretation of clinical study outcomes and in the timely, efficient execution of clinical study. Strengthening FDA understanding and acceptance of adaptive trial designs will enable faster and more cost-effective clinical trials while exposing fewer patients to ineffective or unsafe doses or medicines. This can be accomplished while maintaining the same standards of quality. While the discussion draft asks FDA to issue further guidance on these important topics, it does not address other observed issues. Industry experience suggests that existing guidance is not being implemented consistently across the FDA, potentially due to lack of experience with these innovative approaches. Furthermore, industry and FDA lack a clear process for discussing these design proposals and reaching consensus in a timely manner, sometimes leading to the decision to use traditional approaches instead. Strengthening consistency of implementation, either by engagement of outsides experts with relevant experience or through use of management systems that drive toward this consistent implementation, must be a high priority.

Post-Approval Studies (Sec. 3031)

The discussion draft proposes a process for periodically reevaluating post-marketing commitments and requirements to determine if they continue to be scientifically warranted, or if any changes need to be made to the designs or the timelines for such studies. While this is a useful concept, there are ways to accomplish this sort of periodic assessment today. Problems today are largely around the rushed manner in which these studies are discussed and agreed at

the end of the application review period. Opportunities to engage in a more thoughtful discussion of the scientific questions at hand and the most appropriate types of studies to answer each question before solidifying the requirements would be more valuable, potentially utilizing mechanisms for discussion earlier in the review process (such as the mid and/or late cycle meetings that are part of the PDUFA V NME review model).

Title IV – Accelerating the Discovery, Development, and Delivery Cycle and Continuing 21st Century Innovation at NIH, FDA, and CMS

Improvements in the Medicare Local Coverage Determination Process (LCD) (Sec. 4161)

The addition of public comment periods, meetings and disclosure of decisional information are ways in which the NCD/LCD process can work better for both the administration and for manufacturers seeking coverage under the Medicare program. Lilly supports the language including in the discussion document and asks that additional language be included for Congress to direct CMS to ensure that existing NCDs are not applied to new products to limit their coverage.

Additional Delivery Reform Proposals Not Included in the Draft Discussion Document

In addition to the proposals included in the draft discussion document, there are five additional proposals related to the reimbursement of medicines that we would like the Committee to consider including in 21st Century Cures. These specific proposals were included in BIO's delivery-side proposals submitted to the committee on December 5, 2014. Lilly worked closely with BIO to develop the proposals identified below.

Appealability in Medicare Part D

In 2014, a the Senate Special Committee on Aging expressed concern with the inability of Medicare Part D beneficiaries to appeal for a lower-tier cost-sharing amount to be applied to a therapy placed on a plan's specialty tier.[1] Appealability is an especially important tool to improve patient access to needed therapies placed on a plan's specialty tier since cost-sharing for therapies can exceed 33 percent. While currently unavailable to Part D beneficiaries, this appealability of specialty-tier therapies often is available to patients in the commercial market and appealability, in general, is available to Part D beneficiaries for all drugs except those on the specialty tier.[2] As part of its 21st Century Cures legislation, we would like to see changes that would allow Part D beneficiaries to appeal for a lower-tier cost-sharing amount to be applied to a specialty-tier therapy.

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[1] Senate Special Committee on Aging. March 10, 2014. Letter to Marilyn Tavenner (Available at: http://www.aging.senate.gov/imo/media/doc/03.10.14_CMS%20Part%20D%Appeals%20Letter2.pdf).

[2] See Medicare Prescription Drug Benefit Manual. 2010 (Revision 10). 30.2.4 Specialty Tiers (Available at: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/downloads/Chapters6.pdf). This Manual direction is based on 42 C.F.R. 423.578(a)(7).

New Technology Add-On Payments (NTAP) in the Hospital Inpatient Prospective Payment System (IPPS)

Congress should consider changes to the process of obtaining an NTAP under the IPPS. Such changes should take into account how the development of new technologies is incentivized through appropriate reimbursement in other care settings—such as the pass-through payment in the hospital outpatient prospective payment system—but also consider that additional incentives may be required to overcome the barriers to the use of new therapies in the inpatient space due to bundled payment reimbursement in that setting. These changes also should respond to concerns that the current process and criteria by which therapies are assessed is cumbersome, lengthy, and opaque, often leading to a delay in the use of new, innovative therapies in the hospital inpatient space. For example, Congress should consider redefining the newness criteria for an NTAP[3] to refer to the date of approval for each indication rather than the date of the first approved indication. This is especially important for drugs and biologics targeting rare diseases to ensure that patients, for whom other treatments are often nonexistent, are able to access these therapies as soon as they reach the market and to ensure the preservation of incentives to develop therapies in this space. Additionally, Congress should consider the adequacy of current NTAP payment level: NTAP payment amounts[4] may be insufficient for hospitals to cover the costs of the new technology. Raising the payment standard from 50 percent to 80 percent would be consistent with other mechanisms (such as outlier payments) in which there are shared risk for factors or costs extending beyond hospitals' direct control.

Require CMS, Together with HRSA, to Address Duplicate Discounts

Propose that Congress direct the Centers for Medicare and Medicaid Services, together with the Health Resources and Services Administration, to issue detailed guidance describing methodologies and options available to states and covered entities for identifying and billing drugs purchased under the 340B program in a manner that ensures compliance with program prohibitions regarding duplicate discounts pursuant to Section 340B(a)(5)(A) of the Public Health Service Act, to include the application of such prohibitions to drug utilization by Medicaid managed care enrollees.

Incentivizing Innovation in Alternative Payment Models (APMs)

CMS increasingly is working on alternative payment models (APMs) to achieve the "triple aim" of higher quality care for individuals, better health for populations, and lower per capita costs. Alternative payment methodologies and delivery of care models have great potential to achieve these aims and can be structured to adapt to new emerging technologies and cures while still incentivizing the development of cures. However, we also have concerns that improperly designed APMs risk incentivizing the underutilization of care and, if they mainly focus on cost-containment, can limit patient access to innovative therapies. In fact, the

[3] 42 C.F.R. 412.87(b)
[4] The NTAP amount is equal to the lesser of: (1) 50 percent of the amount by which the total covered costs of the case exceed the MS-DRG payment, or (2) 50 percent of the costs of the new technology. 42 C.F.R. 412.88(a)(2).

reimbursement structure of APMs not only has a direct impact on patients' short-term access to innovation, but can establish trends that, in the longer-term, dis-incentivize cutting-edge research and development and stunt the progress of future innovation. To ensure that APMs are fostering an environment that supports the development of modern treatments and cures, while providing quality patient care today, Congress should require all payment demonstration projects—including those conducted by the Center for Medicare and Medicaid Innovation—to specify how they will protect access to innovative therapies.

Specifically, CMS should be required to include mechanisms within APMs that account for the emergence of new technologies and the evolution of medicine and science. This is especially important since these models often are built using retrospective data that inherently may not reflect increasingly personalized medicine, potentially disadvantaging beneficiaries whose providers participate in APMs. One way to account for new technologies is to incorporate a temporary pass-through payment mechanism, similar to what exists for new technologies in the hospital outpatient space. This pass-through payment would reimburse providers separately for the use of these technologies, which may offer significant patient benefit, but would have not been accounted for in a bundled payment system that is built from a retrospective analysis of the costs of providing care to a specific patient population. This pass-through payment also should be exempted from inclusion in the financial measures that affect provider reimbursement, to ensure that providers can utilize the new technologies without being financially penalized until the value of these therapies can be assessed (likely at least 2 years).

An additional protection CMS should consider for providers at financial risk through participation in an APM is an outlier payment that recognizes the inherently higher costs associated with providing quality care to certain patients (e.g., those with complex or chronic conditions, potentially with several comorbidities or other underlying health issues). This type of outlier payment—which exists for Medicare beneficiaries in the hospital inpatient space—would better ensure that providers are not penalized for treating high-cost patients, and, in turn, that these patients would be able to access necessary care.

Finally, to leverage this spectrum of care, CMS should work with stakeholders to consider how best to incentivize coordinated patient care within APMs that does not disadvantage the assessment of care provided by one type of provider in comparison to another. In general, existing APMs tend to focus on the unique needs of the primary care provider and the immediate primary care needs of the patient. However, this limited focus—on one point of care in a patient's interaction with the healthcare system and on near-term care needs—risks missing an opportunity to streamline the coordination and efficiency of care provided to a patient by a spectrum of healthcare professionals.

Modifications to Promote Value-Based Contract Arrangements

Value-based contracting is gaining traction in non-U.S. markets and is a concept that could be adapted domestically to promote patient access to new discoveries and cures. The industry, in general, is open to potentially pursuing innovative, value-based approaches, as long as they do not negatively affect patient access to innovative products more broadly. However, certain

hurdles exist to the widespread utilization of these programs. For example, laws designed to protect against fraud and abuse in "traditional" healthcare delivery and payment systems, such as the Federal Anti-kickback Statute (AKS), may dissuade manufacturers from offering certain innovative contracting arrangements. Another hurdle to value-based contracting is the application of existing laws and regulations for Medicare Average Sales Price (ASP), Medicaid best price, Average Manufacturer Price (including "5i" AMP), prices offered under the Veterans Health Care Act (including Annual Non-Federal Average Manufacturers Price, Federal Supply Schedule/Federal Ceiling Price, and the TRICARE Retail Pharmacy Refund program), and other government pricing calculations, which can result in uncertain and potentially disproportionate negative impacts for certain types of contracting strategies.

In order to facilitate the use of value-based contracting in the U.S., the Committee should create legislative carve-outs for Best Price and all other government pricing calculations and requirements as they relate to products sold or transferred under value-based contracts. To allow for the flexibility needed in the evolving value-based contracting space, Congress should require CMS to work with stakeholders—including industry, providers, patient and caregiver representatives, and payers—to establish parameters through notice-and-comment rulemaking for contracts that meet this statutory exemption (e.g., value-based contracts that financially incentivize measurable quality of care or positive health outcomes). Congress should require CMS to finalize these regulations within one year of the enactment of the statutory carve-outs. Additionally, Congress should expand existing, or create new, statutory exceptions to the AKS to clearly protect innovative value-based contract arrangements that meet certain requirements (e.g., that promote patient access and pose a low risk of patient or program abuse), and direct the Health and Human Services Office of Inspector General to implement such exceptions through the creation of new regulatory safe harbors.

Thank you for the opportunity to provide comments on the draft discussion document. We look forward to continuing to work with Chairman Upton, Ranking Member Pallone, Congresswoman DeGette and the rest of the Committee on this initiative.

Please do not hesitate to contact Sean Donohue at sdonohue@lilly.com or 202-434-7169 with any questions.

Sincerely,

Joseph B. Kelley
Vice President
Global Government Affairs

February 22, 2015

The Honorable Fred Upton
U.S. House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
U.S. House of Representatives
2368 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton and Representative DeGette:

As a lupus patient, longtime advocate and leader of the Lupus and Allied Diseases Association, I would like to applaud you in your efforts to accelerate the discovery, development, and delivery of promising new treatments and cures with the 21st Century Cures Initiative. I especially appreciate your inclusion of policies on patient-focused drug development, biomarker qualification, streamlining the regulatory process, and modernizing clinical trials in addressing unmet medical needs. Based on my experiences as both a lupus patient and advocate, I offer the following comments in response to your request for additional stakeholder input and greatly appreciate the opportunity to assist in ensuring therapies reach those who desperately need them.

I. Systemic Lupus Erythematosus (Lupus) Overview & Impact

Lupus is an extremely complex chronic inflammatory autoimmune disease in which a triggering agent causes the immune system to dysregulate and attack the patient's own tissue affecting virtually any organ system of the body; including the skin, joints, kidney, brain, heart, lungs, blood and blood vessels and there is no known cause or cure. Lupus is a leading cause of kidney disease, stroke and premature cardiovascular disease in young women and is highly individualized, extremely volatile, debilitating, life-diminishing, and potentially fatal. It is estimated that 1.5 to 2 million Americans suffer from lupus,[1] affecting women 9 times more often than men,[2] with 80% of new cases developing between the ages of 15 and 44 during the prime of life.[3] Among rheumatic conditions lupus has a relatively high mortality; 14.5% of all rheumatic disease mortality in 1997.[4]

Presently, no single test exists to identify lupus, resulting in many patients suffering more serious complications before a diagnosis is reached. Lupus is an unpredictable condition in which symptoms come and go (flares) and complications can arise suddenly, frustrating patients and the physicians who treat them. It is also a costly multi-system disease as patients must see several specialists regularly and because it can affect virtually any part of the body it is the prototypical autoimmune disease.[5],[6] It ranges from mild to life-threatening and patients with lupus have an increased incidence of being diagnosed with other autoimmune conditions, including thyroid disease, Sjögren's syndrome, Raynaud's phenomenon, and

[1] Bruskin-Goldring Research Study conducted through telephone survey for the Lupus Foundation of America, 1994
[2] Hahn BH, Wallace, DJ The epidemiology of systemic lupus erythematosus. In *Dubois' Lupus Erythematosus* (5th Edition). Philadelphia: Williams & Wilkins, 1997
[3] Wallace DJ, *The Lupus Book: A Guide for Patients and Families*. New York: Oxford University Press, 1995
[4] Sacks JJ, Helmick CG, Langmaid G, Sniezek JE. Trends in deaths from systemic lupus erythematosus—United States, 1979–1998. *MMWR* 2002;51(17):371–374. Centers for Disease Control and Prevention.
[5] Pisetsky DS, Buyon JP, Manzi S. Chapter 17. Systemic lupus erythematosus. In: Klippel JH, Crofford LJ, Stone JH, Weyand CM. Primer on the Rheumatic Diseases. Edition 12. Arthritis Foundation, Atlanta, GA., 2001.
[6] Rus V, Hajeer A, Hochberg MC. Chapter 7. Systemic lupus erythematosus. In: Silman AJ, Hochberg MC (eds.) Epidemiology of the Rheumatic Disease. 2nd edition. Oxford University Press, New York, 2001.

clotting disorders, as well as a high incidence of co-morbid conditions, such as depression, cardiovascular disease, migraine headaches, fibromyalgia, seizures, atherosclerosis, central nervous system disease, neuropsychiatric manifestations, and gastrointestinal problems.

Many lupus patients experience ongoing inflammation and anemia which contributes to general fatigue, chronic pain and mood disturbances, poor sleep quality, and cognitive impairment. Lupus patients have a significantly lower quality of life than that of patients with other chronic diseases.[7] Fatigue is the most prevalent and incapacitating symptom experienced by about 85 to 92% of lupus patients, resulting in decreased physical and mental function, and 50% of patients rated it as the most disabling symptom.[8] Lupus patients also take a multitude of medications, requiring careful attention to drug-drug interactions and many have unique allergies and sensitivities.

I can tell you from firsthand experience that "Lupus is: extremely complex, difficult to diagnose, potentially fatal, presently incurable, totally capricious, painfully limiting, life altering, dream stealing, career ending, and financially, emotionally, and physically devastating. Living with lupus is like swimming in shark-infested waters. The danger and uncertainty is always present and one is armed with nothing but a will to survive. We try to stay afloat while anticipating the next attack and remain ever hopeful that a rescue ship will soon appear on the horizon."

I once had a life filled with dreams and promise; my future was bright. As a language major I dreamt of going off to Europe, falling in love with a Prince, and living the life of a romance novel character. Instead I was diagnosed with Systemic Lupus Erythematosus, secondary Sjögren's Syndrome and Raynaud's after years of testing, emergency abdominal surgery, and my first brush with death. The numerous aches & pains, digestive impairments, overwhelming fatigue, constant craving for water, itchy, inflamed eyes, intolerance for the sun, cold hands and feet, and recurrent infections I had experienced since childhood finally had a name.

My schedule soon revolved around prescription drugs, doctor appointments and medical procedures, getting enough rest, avoiding the sun, and staying away from people with germs; all while trying to attend college. My athletic days ended abruptly, social occasions were rare, and what remained was a bleak, uncertain future. After experiencing aspirin-induced hepatitis and missing a semester of college, I was finally able to graduate and start a career. For every 2 years I worked, I would end up on disability for a year. I felt like I was constantly chasing my tail and never getting ahead. At my physicians' urging, I finally threw in the towel and filed for disability, winning my case 24 years ago. Lupus stole my dreams of ever being a mother, having a career or being financially secure.

Like many others with lupus, I suffer from several other autoimmune disorders so here are my current numbers: 8 autoimmune conditions, 35 medications per day, monthly treatments costing over $6,000, annual health care costs of about $150,000. I used to weigh 220 lbs. due to drug side effects which made dating as a young woman extremely difficult due to my negative body image and low self-esteem. My entire digestive tract is impaired and it takes 5 different drugs to allow me to digest food each day. I haven't eaten fruits or vegetables in 18 years now and suffer from constant colicky abdominal pain. To date I have had 25 upper GI endoscopies and colonoscopies and so far have refused a colostomy. I am forced to wear compression stockings to maintain a normal blood pressure and avoid blood clots due to hypotension and anti-phospholipid antibody syndrome.

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[7] Pettersson S, Lovgren M, Eriksson L, Moberg C, Svenungsson E, Gunnarsson I, Welin Henriksson E. An exploration of patient-reported symptoms in systemic lupus erythematosus and the relationship to health-related quality of life. Scand J Rheumatol. 2012;14:383–390. doi: 10.3109/03009742.2012.677857.

[8] Zonana-Nacach A, Roseman JM, McGwin G Jr, Friedman AW, Baethge BA, Reveille JD, Alarcon GS. Systemic lupus erythematosus in three ethnic groups. VI: factors associated with fatigue within 5 years of criteria diagnosis. LUMINA Study Group. LUpus in MInority populations: NAture vs Nurture. Lupus. 2000;14:101–109. doi: 10.1191/096120300678828046.

The veins in my arms are pretty much useless due to scarring from decades of lab draws so I am on my second infusaport for monthly labs and all infusions. I have long hair because it is too difficult to hold my arms up to style shorter hair. For the past 3 years, I have been treated with weekly 7-hour infusions for hypokalemia due to my lupus kidney disease. I am also infused bi-monthly for ongoing iron and zinc deficiencies due to disease inflammation and dietary limitations.

Between the stiffness, dizziness and letting the GI therapies run their course, it takes me 3-4 hours each day before I can function well enough to leave my house or a hotel room if traveling. Besides my infusions I have an average of 6-8 medical appointments a week which does not take into consideration the travel time to and from the medical centers since I live in rural upstate NY where the number of specialists are limited. The ubiquitous fatigue I experience is so extreme at times I feel lifeless, like a vampire drained every bit of blood and energy from me. My life is filled with missed opportunities, limitations and loss and I am unable to go to most events I would like to attend. It takes a tremendous amount of self-motivation to manage my medical care, maintain my dignity and attempt to have any quality of life.

Somehow, I have survived thus far due in part to becoming empowered and proactive in my care, the tremendous support of my family and expertise of my health care providers. Being down in the trenches with other lupus warriors from all over the country for 29 years now has also fueled my passion and inspired me as a national advocate. "Like so many others living with lupus every two steps I take forward, I take one backward. It feels like I am constantly climbing a mountain, struggling to reach the peak and place my feet on solid ground, but as soon as I am close to the summit I lose my foothold plummeting backward into the unknown abyss; desperately grasping for anything substantial to grab onto. Not only does this drain one physically but the emotional toll is devastating. Dreams and goals are always being reassessed and some days it is a victory just to get out of bed, shower and put on clean pajamas."

"Imagine helplessly watching someone you love suffer relentlessly from an incurable, ravishing, life-threatening disease. Imagine learning that most lupus patients suffer for years prior to being diagnosed. Many, like your loved one become very ill before a diagnosis can be made. Imagine hoping for a donor as your loved one is repeatedly connected to a kidney dialysis machine. Imagine experiencing the loss of a stillborn child or multiple miscarriages or even a stroke. Imagine having to explain to your loved one that their limbs have been amputated while they were in a coma because of an infection. Imagine watching someone you love lose their job and health benefits only to be forced to then deplete their assets to meet public assistance eligibility standards. This is lupus. Every minute of every day another person loses a little piece of themselves and who knows what potential any of them could have achieved in their lives were it not for this debilitating disease."

II. Lupus and Clinical Trials

Lupus is considered a disease of unmet medical needs due to lack of efficient diagnostic tools, effective therapies, and well-designed clinical trials. Lupus clinical research has been unsuccessful due to the diversity of the patient population, absence of reliable biomarkers, limitations of clinical outcome measures and non-existent uniform control groups. Often, classification criteria are used to define study populations because there are no specific biomarkers. This results in combining patients with various disease manifestations and different pathophysiology and pathogenesis together into one group. The absence of reliable biomarkers is a challenge for clinicians in providing the most optimal patient care and is impeding the development of new lupus therapies.[9] There is a critical need for more sensitive and reliable biomarkers that can predict susceptibility, activity, severity and disease subtype in lupus.

[9] Liu C-C, Ahearn JM. The Search for Lupus Biomarkers. *Best practice & research. Clinical rheumatology* 2009;23(4):507-523. doi:10.1016/j.berh.2009.01.008.

Due to the heterogeneous nature of lupus, unpredictable relapsing and remitting course of the symptoms, lack of validated biomarkers, clinical endpoints and outcome measures, uniform control group, and existence of concomitant medications—usually immunosuppressives, it is very difficult to develop new treatments in lupus. Clinical research trials are not designed to measure what is most important to those who are participating such as improved daily quality of life, reduction in current drug regimen, side effect tolerability, and co-morbid conditions. Patients are concerned with potential cosmetic side effects such as hair loss, rashes, weight gain, gastrointestinal problems; things that may be socially challenging to young women in the prime of their life.

Lupus research should focus on the goals of controlling symptoms, preventing complications, limiting organ damage, increasing survival, improving overall health and day to day functioning for patients. We need innovative, collaborative efforts—private, public partnerships among various stakeholders and multi-center projects.

Understanding the importance of clinical trials in getting new treatments to patients, I participated in clinical research for over 5 years until suffering a serious adverse event and withdrawing from the study. Patients do not all have access to trials in their geographic area and many do not have the resources to travel to participate in trials. Participation is time consuming; anyone who is working, attending school or taking care of their children has limited time. The paper work is complicated and lengthy, and it is difficult to concentrate with fatigue and cognitive problems. Patients do not want to be on steroids or chemotherapy drugs, we just want something that works with few if any side effects.

III. Lupus Therapies

Currently, there are only four FDA-approved treatments for systemic lupus erythematosus: aspirin, antimalarials, corticosteroids, and belimumab. In 2011 the FDA approved the fourth treatment for lupus after many years of limited accepted therapeutic options that included: corticosteroids, antimalarials, and aspirin. These older medications continue to be standard treatment for lupus today.

In addition, the FDA has acknowledged that immunosuppressives are a standard treatment for lupus, even though none are indicated.[10] Belimumab, recently approved in 2011, is a biologic that is only approved in combination with standard treatments. Hydroxychloroquine, the most commonly used antimalarial drug, and corticosteroids, including prednisone were approved in the 1950s. Many of the companies that developed the brand name drugs used for lupus treatment discontinued production, resulting in mostly generic versions remaining on the market.

Due to the heterogeneous nature of autoimmune diseases like lupus, no two cases are alike and treatment is highly individualized; effectively treating patients like me is like balancing on a pinhead. Numerous times therapies have failed me over the years, forcing me and my physicians to take a step backwards and think outside of the box to treat my complicated medical picture. Existing treatments for lupus are absolutely inadequate; many are toxic and cause detrimental side effects with long-term use and since there are only 4 drugs currently approved for lupus many therapies are off-label such as cancer treatments and transplant drugs.

My treatments are tailor made and 14 years ago my physician made the compassionate decision to try an expensive off-label immunosuppressive drug to reduce my steroids. This drug has allowed me the ability

[10] This off-label use is so well accepted that the FDA's news release announcing Benlysta's approval stated, "standard therapy [for Lupus], including corticosteroids, antimalarials, immunosuppressives, and nonsteroidal anti-inflammatory drugs." (FDA News Release. FDA approves Benlysta to treat lupus. Mar. 9, 2011, *available at* http://www.fda.gov/newsevents/newsroom/pressAnnouncements/ucm246489.htm

to function better when I could barely think, walk or raise my arms above my head and had spent months in bone gnawing, soul wrenching pain going from physician to physician begging for help. It is a desperate place to be.

Many treatments have significant side effects, especially with continuing use. For decades the "go to" drug for lupus patients has been prednisone, a corticosteroid. I call it, "the drug you love to hate." It certainly saves your life and fights inflammation quickly, especially in an acute situation, but this comes at a high price with horrific side effects such as glaucoma, cataracts, hypertension, diabetes, acne, atherosclerosis, avascular necrosis, osteoporosis, an increased susceptibility to infections, elevated cholesterol, obesity, edema, fat deposition, manic feelings, and an appetite equal to that of 4 growing teenage boys. Other treatments include immunosuppressives that ablate the entire immune system and antimalarials which can cause retinal toxicity. Off-label therapies such as cancer treatments can cause infertility and miscarriages. Patients get numerous infections and many of us take drugs to treat the side effects of other medications which is ludicrous. Current treatments are just band-aids treating the symptoms and never getting to the root of the problem.

Partially due to allergies to aspirin and nonsteroidal anti-inflammatory drugs, I took prednisone for 30 years straight, and every time my physicians tried to taper me down I would flare. I now have avascular necrosis, osteopenia, glaucoma, and cataracts as a result of steroid use. I am extremely sensitive to inactive ingredients in drugs. For the past year I have been dealing with complications from severe shingles in my eye and on my face. It has permanently damaged my vision and the eye drops have caused complications resulting in more drugs being prescribed. This is a vicious cycle. When the immunosuppressive drugs are reduced, my lupus flares. I have 6-10 infections a year and am allergic to all antibiotics except penicillin so treating any infection that arises is extremely difficult. My physicians are as frustrated as I am with the current status of lupus therapies. I have endured decades of destruction and disfigurements from the treatments I have endured.

Individuals with complex care needs like me require unique strategies and personalized medicine to manage their care. I know that newer, innovative treatments can offer therapeutic advantages over conventional medicines. Older immunosuppressive therapies attacked a patient's entire immune system; causing harmful side effects, while newer targeted therapies target a particular cell or biomarker making the treatment more efficient and safer. Right now we are in dire need of new more efficacious treatments and are unequivocally frustrated with the drug development process regarding lupus and so tired of waiting.

IV. Lupus Subpopulations

Lupus disproportionately affects women of color in the United States; it is 2 to 3 times more common among African-Americans, Hispanics & Latinos, Asians, and Native Americans.[11] Minority women tend to develop lupus at a younger age, experience more serious complications, and have higher mortality rates—up to three times the incidence and mortality of Caucasians.[12] It is estimated that as many as one in every 250 African American women in America has lupus.[13] 90% of those affected are women, but men and children are also diagnosed with lupus.[14]

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[11] National Institute of Arthritis and Muscoloskeletal and Skin Diseases, National Institutes of Health. *Strategic Plan for Reducing Health Disparities.* 2006.
[12] Sacks JJ, Helmick CG, Langmaid G, Sniezek JE, Centers for Disease Control and Prevention, ibid.
[13] Harley JB, Kelly JA. Genetic basis of systemic lupus erythematosus: a review of the unique genetic contributions in African Americans. *Journal of the National Medical Association* 2002;94(8):670-677.
[14] Hahn, BJ & Wallace DJ, ibid,

Mortality rates show the existence of distinct age, sex, and race-specific disparities in lupus; individuals aged 15 to 44 years of age had an occurrence of 36.4%, crude death rates increased with age, were 5 times higher among women than men, were 3 times higher among blacks than whites, and were highest among black women, increasing 69.7% among those aged 45--64 years despite the overall decrease in the mortality rates associated with lupus.[15] Five-year survival in lupus patients has improved from 50% in the 1950s to over 90% currently, but the mortality still remains high compared with the general population.[16]

Eighty percent of newly diagnosed patients are women in their child-bearing years or prime of life.[17] From the time I was diagnosed as a young woman in college, my life took on a new direction. As my classmates looked forward to careers and romances I wondered whether I would ever graduate or even be alive in 5 years. I had been an athlete, physically fit and popular. That all drastically changed with the diagnosis and treatments.

There is no specific test to diagnose lupus, resulting in delayed diagnosis, proper medical intervention, more severe disease manifestations, and worse patient outcomes. Diagnosis is based on numerous medical appointments and lab results, a process of elimination, extreme patience and open to clinical interpretation. One can only hope they see a physician who takes them seriously and was paying attention in medical school when autoimmunity was covered.

I also feel that many of us in our mid 40's to late 60's are an overlooked subpopulation when it comes to research, awareness and interest in lupus. We have beaten the odds and survived and are still dealing with lupus, co-morbid conditions and the devastating effects of the decades of treatments and disease damage. Most of us were diagnosed during the prime of life and have a wealth of information and experience to share about the disease, treatments, lifestyle, coping mechanisms, and survival tips.

V. Conclusion

Since lupus is the prototypical autoimmune disease in that it affects virtually any part of the body including organs, any lupus research initiative has the potential to impact millions of Americans suffering from over a hundred different autoimmune and related conditions. Lupus disease research is under-funded in comparison with other diseases of comparable magnitude and severity. The benefits of lupus research are unquestionably far reaching.

In conclusion, I feel that my perspective as both a longstanding lupus patient and advocate is worthy of your consideration and appreciate the opportunity to provide comments. I applaud you again for the 21st Century Cures Initiative and look forward to collaborating with you to ensure any related legislation moves forward and commend you for including the patient perspective during this process. After all, lupus and other diseases of unmet need do not just affect patients, but also impacts our loved ones and the health care professionals who treat us. As millions in the lupus community eagerly await the development of new therapies, we passionately urge you to accelerate the development and delivery of new, more efficacious treatments and ultimately a cure for diseases of unmet need like lupus and establish public policies to ensure patients have access to these treatments.

Individuals living with conditions of unmet need require individually tailored treatments and unencumbered access to the full array of treatments as prescribed by their treating physicians who are most familiar with the patient's history. Policies such as specialty tier pricing, step therapy, therapeutic

[15] Sacks JJ, Helmick CG, Langmaid G, Sniezek JE, Centers for Disease Control and Prevention, ibid.
[16] Lateef A, Petri M. Unmet medical needs in systemic lupus erythematosus. *Arthritis Research & Therapy* 2012;14(Suppl 4):S4. doi:10.1186/ar3919.
[17] Wallace DJ, ibid.

switching and prior authorizations result in treatment delays. Reducing benefits or limiting treatment choices in the Medicare and Medicaid entitlement programs also result in delay in care. Limiting access to vital life-saving medications disrupts continuity of care, especially in vulnerable populations and increases costs because of unnecessary hospitalizations and emergency room visits. Patients endure physical, emotional, and financial distress due to delays in proper treatment, intolerable side effects from inadequate medicine, and initial cost-sharing for ineffective therapy and medical visits.

The lupus community waited 56 years for a new treatment to be approved and within months of it being approved over 30 states had step therapy protocol applied to the drug. Therefore the new treatment did not make its way to the lupus patient. Just think about this. We fight for disease research funding, we struggle to get patients into clinical trials, we battle for treatments to get FDA-approval, and once approved we fight to get them covered. It took us over 50 years to get a new drug approved for lupus but what good is it if physicians cannot get insurers to cover it and patients can't get it. Think of all of the innovative therapies waiting to be discovered and eventually make their way to patients. Poof they will disappear! There are 50 million Americans with autoimmune disease and the incidence is on the rise. We are at a critical juncture right now in getting new treatments for diseases of unmet need. We all need to step up here and become proactive on this issue.

As Americans, we must recognize that public policy decisions have direct implications on the development of new and safer therapies. Drug research and development needs to be encouraged and supported and not stifled by bureaucracies so that all individuals, regardless of race or socioeconomic status can live longer and healthier lives.

After all, lupus and other diseases of unmet need do not just affect patients, but also impacts our loved ones and the health care professionals who treat us. As millions in the lupus community eagerly await the development of new therapies, we passionately urge you to accelerate the development and delivery of new, more efficacious treatments and ultimately a cure for diseases of unmet need like lupus. Most of us living with lupus cling to the belief that there will be better treatments and a cure during our lifetime. We need innovative research initiatives that include cross-sector collaborations, public-private partnerships and robust basic, clinical and translational projects that will enable scientists to investigate disease pathogenesis and physiology, identify biomarkers, design better clinical trial methodologies, prevent complications, develop precise diagnostic measures and safer, more effective treatments, and ultimately eradicate this devastating disease. It is imperative that the next generation of lupus patients is given the chance at a better quality of life and the opportunity to pursue their dreams.

Sincerely,

Kathleen A. Arntsen
Patient, Advocate and President/CEO
Lupus and Allied Diseases Association, Inc.
P.O. Box 170
Verona, N.Y. 13478
315-264-9101

February 10, 2015

The Honorable Fred Upton
Chairman
Committee on Energy and Commerce
U.S. House of Representatives

The Honorable Dianna DeGette
Chief Deputy Whip
U.S. House of Representatives

RE: Comments on 21st Century Cures Discussion Draft

Dear Chairman Upton and Congresswoman DeGette:

Thank you for your continued leadership on the 21st Century Cures initiative. The Lupus Foundation of America supports your overall vision and efforts to streamline and ensure the discovery, development and delivery paradigm is working effectively and efficiently to bring needed medical treatments to all Americans. The January 27th draft legislation provides a great opportunity to enhance stakeholder dialogue. The Foundation offers the following comments of support and points of clarification on the draft legislation.

The Foundation is the only national force dedicated to improving the quality of life for all people affected by lupus through programs of research, education, awareness, and advocacy. Lupus is an unpredictable and misunderstood autoimmune disease that ravages different parts of the body. It is difficult to diagnose, hard to live with, and a challenge to treat. Lupus is a cruel mystery because it is hidden from view and undefined, has a range of symptoms, hits out of nowhere, and has no known cause and no known cure.

Title I

Subtitle A – Patient Focused Drug Development

The Foundation supports fostering and enhancing the current patient focused drug developments of the Food and Drug Administration (FDA). Specifically, we support: establishing a structure for risk-benefit assessment that includes robust patient experience data; enhancing the use of patient reported outcomes (PROs) in drug development; and, promoting public-private partnerships to help grow and develop PROs.

As the diverse symptoms of lupus wax and wane unpredictably, it is complex to determine what, how, and when to measure. Measuring PROs such as fatigue and steroid sparing are crucial. Other patient reported outcomes to consider include bone density and cardiovascular health.

The Foundation is currently leading the development of the LFA –REAL™ (Rapid Evaluation of Activity in Lupus) system, which is a first-of-its-kind set of tools to monitor lupus disease activity, addressing both the needs and concerns of clinicians and people with lupus. The Foundation is working with the FDA Study Endpoints and Labeling Development (SEALD) division to ensure the PRO portion of the tool is validated for use in the clinical trial setting. The SEALD division needs clarification on its goals and must be properly staffed and resourced to move PRO validation forward for use in clinical trials. Developing a common guidance and/or protocol on PRO development for the various stakeholders would be helpful.

2000 L Street NW, Suite 410 | Washington, DC 20036 | Toll Free: 1.800.558.0121 | Main: 202.349.1155 | Fax: 202.349.1156 | www.lupus.org

Subtitle C – Approval of Breakthrough Therapies
The Foundation supports the clarification that FDA may approve a new drug that has the breakthrough therapy designation on early stage clinical safely and effectiveness data. Approving a drug on early data is vital for people with lupus and other chronic diseases and condition that have waited far too long for therapies that can truly address their disease. Accessing a therapy sooner for people with lupus can make a significant difference in sparing other organs from additional damage.

Subtitle H – Facilitating Responsible Communication of Scientific and Medical Developments
The most commonly prescribed medications for treating lupus are prescribed "off-label," and it is critically important for all stakeholders to have the ability to freely share peer-reviewed information about the safety and efficacy of medications used to treat lupus.

The real-world provides the perfect opportunity to learn more about the richness of medications and their other potential uses beyond their FDA designation. People with lupus must be treated effectively and in a timely manner, with the best resources available-regardless of whether it is indicated for lupus or not. Otherwise the consequences can be costly and life threatening --including lupus flares, organ failure and long-term hospitalizations. It could be considered unethical not to communicate vital off-label information to physicians treating diseases like lupus.

The Foundation would like to work with the Committee to develop and refine legislative language helping promote responsible and effective communication among all stakeholders on the benefits of drugs used off-label to treat diseases such as lupus.

Subtitle L -- Dormant Therapies
The Foundation supports Senators Hatch and Bennet's Dormant Therapies Act. Drug development in lupus is very risky, and many companies may consider research and development for lupus too high-risk to be worthwhile financially. In the last ten years, the lupus community has witnessed many failed attempts to bring new lupus treatments to the market – treatments that are desperately needed.

Lupus is not an orphan disease nor is it a disease impacting tens of millions of Americans. Lupus is an overlooked and chronically underfunded, serious, debilitating, and disabling disease impacting more than 1.5 million Americans. To that end, the Foundation requests Subtitle L include clarification for the definition of unmet medical need.

The Committee has an opportunity to clarify intent behind the phrase unmet medical need. The Foundation is concerned lupus could potentially not qualify as a disease with unmet medical need because there are four treatments that have been FDA approved for use in lupus. Those treatments include: Benlysta®, hydroxychloroquine (an antimalarial), prednisone (a steroid), and aspirin. Benlysta®, approved by the FDA in March 2011, is the first and the *only* drug designed specifically to treat lupus. All other medications used to treat lupus are drugs approved for other indications such as chemotherapies, used to treat cancer, and immunosuppressants, used post organ transplantation. These medications only treat lupus symptoms and often have harsh side-effect profiles.

Lupus not only should meet the definition of unmet medical need, but it defines the very thought of unmet medical need. While there has been one treatment designed for the indication of lupus, it works in a small subset of patients. Lupus is a truly heterogeneous disease and people with lupus deserve an arsenal of treatments. We need to ensure Subtitle L, which at its core is good policy, benefits diseases like lupus.

Title III

Subtitle A – Clinical Research Modernization Act; and,
Subtitle B – Broader Application of Bayesian Statistics and Adaptive Trial Design
The Foundation supports Subtitles A and B that help streamline the clinical trial process and move approved drugs to patients faster. Flexibly in clinical trial design is essential. Adaptive or smaller clinical trials are a must as a large trial and all its requirements are not representative of the real-life clinical setting, especially in lupus. The Foundation is currently working with the FDA and key lupus thought leaders to brainstorm creative ways to move drugs for lupus through the pipeline. Provisions outlined in Subtitle B, such as adaptive clinical trial design, support the Foundation's current efforts.

Subtitle C - Post-approval Studies and Clinical Trials
Enrolling a sufficient number of people with lupus to conduct statistically valid clinical trials is a significant challenge in lupus. The heterogeneity of lupus makes it virtually impossible to assemble uniform patient groups. In addition, the pool of lupus patients available for enrollment in clinical trials is small, which can increase the difficulty of enrollment and delay and lengthen clinical trials.

To that end, the Foundation supports Subtitle C, which provides the ability to revisit and potentially renegotiate post-approval studies and trials. For example, the FDA required a 5,000 patient post-approval study on Benlysta®. This study pulls away patients from other important lupus clinical trials, which are already extremely challenging to recruit for with the disease being so heterogeneous. Having the ability to revisit the need and/or scope of that post-approval study could result in increasing the number of willing patients to enroll in other promising clinical trials.

Title IV

Subtitle A - National Institutes of Health
Balancing science and the uncertainty that exists with scientific discovery and accountability is challenging. There is a clear need for increased accountability for the National Institutes of Health (NIH). However as proposed under Subtitle A, the draft legislation is too prescriptive in its efforts to create that accountability.

For example, requiring the NIH to develop a strategic investment plan is a laudable idea. However, draft language requiring ten strategic focus areas known as Mission Priority Focus Areas sets up the potential for significant scientific loss in areas that are difficult and complex to research such as lupus. In addition, requiring 55 percent of NIH's extramural research budget to be used on basic biomedical research is entirely too prescriptive and does not support letting science and grant applications drive what progressive and interesting research needs to be funded. Congress ought to let science be science, and craft legislative language that supports flexibility and nimbleness of an entity that invests in biomedical research while also creating accountability within the system.

Subtitle S - Continuing Medical Education Sunshine Exemption
The Foundation requests that Subtitle S include not only an exemption for Continuing Medical Education programs but also for donations to Voluntary Health Agency (VHA) activities where a physician may be asked to speak or attend for their expertise on a subject.

On December 3, 2014, the Centers for Medicare and Medicaid (CMS) issued a response to an inquiry from the National Health Council requesting that VHA's be exempt from reporting indirect payments to manufacturers when an applicable manufacturer grants full and independent discretion to the VHA in selecting recipients for funding, including physician travel, honoraria, and/or meals for activities that are vital to a VHA's mission. The response from CMS stated "If an applicable manufacturer provided an unrestricted donation to a VHA to use at its discretion, and the VHA chose to use the donation to make grants to physicians, those grants would not constitute indirect payments because the applicable manufacturer did not require, instruct, or direct the organization to use the donation for grants to physicians…In this situation, the applicable manufacturer is not required to report the donation."

The response from CMS did not provide enough clarification that VHAs are exempt from reporting indirect payment, due to the word "unrestricted" donation. A majority of donations or grants provided by manufacturers are not considered unrestricted due to the fact that grants are for a very specific program that an organization carries out. However, while the grant may be for a specific program, the manufacturer still does not provide the directive that the organization uses the donation for grants to physicians. The Foundation urges you to include legislative language under Subtitle S clarifying that if a manufacturer donation does not specify that the donation is to be used for funding awards or grants to physicians, then the donation to the VHA should be exempt from reporting.

Title V

Subtitle A - Manufacturing Incentives

The Foundation supports Subtitle A encouraging generic manufacturers to prepare, propagate, compound, and process generic medications in the United States.

Recently, the Foundation has heard many concerns throughout the country that people with lupus have been unable to obtain the generic drug, hydroxychloroquine, as well as reports that the price of the medication has increased dramatically. From our research, one factor potentially leading to the shortage is that many U.S. manufacturers have facilities in other countries where drugs are made or where raw ingredients are produced. As you know, in order for medications to be sold in the U.S., they must pass strict FDA regulations to ensure that products are safe for consumption and do not contain false ingredients. If manufacturers do not meet FDA standards, production will stall.

"Hydroxychloroquine is the mainstay of lupus therapy," according to Michelle Petri, MD, MPH. "It prevents half of lupus flares, reduces renal and CNS lupus, reduces blood clots in half, reduces future seizures, diabetes and LDL cholesterol, and improves survival." The Foundation believes that the oversight and regulation of medications would improve if all aspects of the manufacturing process were conducted in the United States, thus reducing the possibilities of drug shortages.

Address the Delivery Process

The Foundation urges you to include additional provisions that address the delivery side of the paradigm. If patients cannot access these new therapies, the discovery and development you seek to foster and accelerate will not deliver the benefits to the very people they are intended to help. To that end, the Foundations ask you to include the Patients' Access to Treatment Act (PATA) in the final bill. The inclusion of PATA will help address access and affordability of medications, and satisfy this important pillar of the paradigm.

Accessing affordable medications is vital for those with such chronic, disabling and often life-threatening conditions such as lupus. Studies show that the higher the out-of-pocket costs, the less likely patients are to take their medications on time, if at all. Foregoing medications often results in disability and other health complications that can lead to poor long-term health outcomes and increase health costs.

Breakthroughs in new medications are helping people with chronic diseases lead productive lives. These medicines, while revolutionary, are complex to manufacture and distribute, and are often very expensive. The cost of specialty medications has pushed health insurers to use enhanced benefit design to balance access and cost. An alarming trend in today's health insurance market is the practice of moving vital medications like biologics into specialty tiers that utilize high patient cost-sharing methods. Specialty tiers commonly require patients to pay a percentage of the cost of the drug or a co-insurance that can range from 25% to 50%, costing the patients hundreds of dollars, even thousands of dollars, per month out of pocket for a single medication.

PATA will soon be re-introduced by Representatives David McKinley (R-WV) and Lois Capps (D-CA). This bi-partisan legislation had more than 140 co-sponsors in the 113th Congress. PATA proposes to 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). This bill would greatly increase access and affordability of specialty medications, thereby reducing disability and constraining health care costs over time.

Appropriations Are Vital

As you move forward with the 21st Century Cures legislation, the Foundation encourages you and your colleagues to find common ground and mechanisms for fully funding a final bill with newly appropriated funds. It is imperative that the provisions set forward in the draft legislation are not funded by cuts to current federal programs. In addition, introducing a bill with a host of unfunded mandates will not help shift the discovery, development, and delivery paradigm, but rather has the potential to slow down or reserve the progress that has been made to date and could cause the proposed new policies to languish.

Your overall vision for the 21st Century Cures legislation is positive, and we look forward to continuing our dialogue with you and your staff to put forward legislation that works for all stakeholders and moves research, drug development, and access to treatments forward for people with lupus. If you have any questions, please contact Kim Cantor, Vice President of Advocacy and Government Relations at (202) 349-1150 or Cantor@lupus.org.

Sincerely,

Sandra C. Raymond
President & CEO

House Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Fred Upton
Chairman

The Honorable Diana DeGette
Committee Member
Co-chair 21st Century Cures Initiative

Via email: cures@mail.house.gov

February 10, 2015

Dear Representative Upton and Representative DeGette:

As one of the nation's leading private lupus research organizations founded and supported by patients and their families to fund novel research, the Lupus Research Institute (LRI) commends you on the comprehensive discussion document to accelerate the discovery, development, and delivery of 21st Century Cures.

On behalf of the LRI, its National Patient Coalition, and lupus patients and their families nationwide, I would like to offer our heartfelt appreciation for the attention you are devoting to the critical importance of engaging the patient perspective in the regulatory process and to modernizing clinical trials.

At this time, we are pleased to provide comments on just a few elements of the 21st Century Cures initiative discussion document as requested in the press release dated January 27, 2015, particularly those that focus on patient engagement. We look forward to participating in this process as it moves forward.

Lupus, the prototypical autoimmune disease, is the perfect example of why we need patient input in the regulatory process and why we need to streamline clinical trials without jeopardizing patient safety. Lupus affects an estimated 200,000 to 1.5 million people, and current epidemiological studies funded by the Centers for Disease Control and Prevention (CDC) are shedding new light on lupus with estimates of 129 cases per 100,000 women and as high as 1 in every 537 black women. Ninety percent of people with lupus are women and this chronic illness is often diagnosed during the child-bearing years, cutting down young women in the prime of their lives. Complex and potentially dangerous with no known cause or cure, lupus is a leading

cause of kidney disease and stroke among young women. Lupus is difficult to diagnose and usually requires extensive treatment, including heavy drug therapies and specialty medical care.

Although mortality rates from lupus have improved over the years, this chronic, debilitating disease is managed by treatments that are of a toxic nature and often cause additional damage. Only four treatments have ever been approved for use in lupus, and in over 50 years, only one new drug has been developed specifically to treat lupus. Lupus has multiple manifestations and can impact any organ. The most feared complication of the disease, lupus nephritis, has no approved treatments.

Lupus clinical trials are highly challenging due to the extreme heterogeneity of the disease and the demographics of the affected population. Belimumab is the only successful new drug approval in 52 years. There have been many late-stage failures but there are reasons to be hopeful. Owing to advances in understanding the biological basis of the disease there are now more lupus therapeutics in preclinical and clinical development than ever before. This year the National Institutes of Health and industry committed $27 million to validate new targets in lupus as part of the landmark Accelerating Medicines Partnership.

To ensure the promise of new treatments is realized, critical obstacles in lupus clinical trials and regulatory assessment must be addressed, and we applaud the efforts of the 21st Century Cures discussion document to do so. Patient perspectives on the impact of the disease and the most meaningful benefits of treatment are essential to guide this process.

As you move forward with the 21st Century Cures initiative toward developing legislation, we encourage you to consider the following:

- We recognize the scourge of cancer and the difficulty of getting treatments for orphan diseases and appreciate special incentives in those areas. For example, in Title 1 Subtitle J qualified indications that would benefit from the proposed streamlined data review include cancer and "other types of indications as the Secretary determines." We need to make sure there is plenty of opportunity for diseases of unmet need like lupus to benefit from this and other proposed legislation and regulations as described in the discussion document. We would like to see diseases that disproportionately impact minority populations be strongly considered when there are a limited number of conditions that can benefit.

- We commend the patient engagement focus laid out in Title I Subtitle A which directs the Food and Drug Administration (FDA) to establish guidance such that patient experience data will be incorporated into the regulatory review process to be built upon the FDA's patient focused drug development initiative. No one knows better than the patient what medication side effects are tolerable and what tradeoffs they are willing to accept in a new treatment. Any risk benefit analysis must include the patient perspective. Providing for a mechanism for all diseases to have input into the regulatory process and not just those selected through the FDA's patient focused drug development initiative would be a major advancement.

- We commend the plan to streamline clinical trials. As you consider changes in this area, please ensure that safety is never jeopardized and that new treatments that ultimately are

approved are accessible to patients.

- We support the idea of an Innovative Cures Consortium as described in Title II Subtitle A which will be a public private partnership and will "award grants and contracts for activities to accelerate the discovery, development and delivery of innovative cures, treatments and preventive measures to eligible small businesses and not for profits."

    - As described in the discussion document, those receiving funds will be required to provide matching funds and/or in-kind contributions. This requirement for private sector matching funds should be designed in a way to allow smaller organizations like the Lupus Research Institute to also benefit from the available grant funds. The LRI's grant program focused on novel research has been highly successful; substantial investment has provided academic-based investigators with the ability to initiate original and creative studies, publish thought-leading breakthroughs and obtain highly competitive NIH funding to continue their innovative research. LRI's investment of over $50 million over 15 years has leveraged another $140 million in NIH research. LRI's strategy has expanded the field and brought in new disciplines, reinvigorating lupus research and resulting in multiple new discoveries and the identification of over 20 new lupus biomarkers for future investigation. We would like to ensure that experience and a proven track record are important considerations in addition to ability to provide matching funds.

    - The Board of Directors will include 22 appointed members of whom 5 will represent Federal agencies, 8 will represent biopharmaceutical and medical device industries and the remaining seats include researchers, patients, providers, insurers, etc. To ensure the patient perspective and participation, we would like to see at least 1 seat designated for a patient. The Expanded Access Task Force as described in Title I Subtitle G does designate 1 patient. We would like to ensure patients are represented in all task forces, boards, etc.

As the prototypical autoimmune disease, accelerating the discovery, development, and delivery of new treatments for lupus can help shed light on the more than 80 autoimmune diseases that impact over 50 million Americans.

We are most grateful for the transparent and collaborative approach you have undertaken to develop the 21st Century Cures discussion document. While our comments here have just scratched the surface, we look forward to continue to work with you as you move toward developing and implementing legislation to enhance the lives of lupus patients.

Sincerely,

[redacted]

Margaret G. Dowd
President and CEO

MCHC
Metropolitan Chicago Healthcare Council
The Trusted Voice and Resource for Healthcare

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February 3, 2015

The Honorable Fred Upton
Committee on Energy and Commerce
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton:

On behalf of the Metropolitan Chicago Healthcare Council (MCHC) which represents more than 180 member hospitals and health care organizations, we appreciate this opportunity to provide comments on the "Advancing Telehealth Opportunities in Medicare" discussion draft.

Telehealth is becoming increasingly vital to our health care delivery system for all types of care, including psychiatric treatment. In Illinois, for example, budgetary cuts at the state and federal levels, among other factors, have caused a 47 percent increase in the number of behavioral health patients in the emergency department (ED), and MCHC data show that, due to limited resources, these patients have an average ED boarding time of more than three times the boarding time of a typical ED patient. According to the Centers for Medicare & Medicaid Services, telepsychiatry is a cost effective alternative to traditional face-to-face medical care; despite this, Medicare is behind the private sector and many state Medicaid programs in promoting telehealth.

MCHC applauds you and the other members of the Energy and Commerce Committee telehealth working group for recognizing the need to modernize Medicare's approach to telehealth and seeking stakeholder comment on the issue. We support the comments developed by the American Hospital Association (AHA) and articulated in its own response to you on this draft. As discussions continue on the "Advancing Telehealth Opportunities in Medicare" draft, we urge you to rely on the AHA's principles and to take into consideration the following comments:

- Medicare utilizes a service-by-service consideration for telehealth that results in a "positive list" of covered services, which has proven to be burdensome, often times resulting in limited coverage. Given how rapidly health care technology evolves, a more efficient approach could be the use of a "negative list" that identifies those things that are not covered.

- In addition, removing geographic and other restrictions only for certain services can create operational challenges. Urban areas, like Chicago, can also suffer physician shortages, and access to certain specialties, including psychiatry, can be limited in all geographic areas, not just rural locales. For example, a schizophrenic patient may not have access to a psychiatrist in the ED in both urban and rural settings due to the shortage of psychiatrists in Illinois.

- Finally, we support the section of the discussion draft that encourages the provision of telehealth services in demonstration projects and models under the Center for Medicare and Medicaid Innovation (CMMI) by waiving the current limitations on what qualifies as an originating site and the geographic location of such sites, as well as the type of provider who may furnish telehealth services. However, it should be made clear that the providers of telehealth services under CMMI demonstration projects and models should be adequately reimbursed for provision of those services.

In conclusion, MCHC strongly agrees with your goal of expanding coverage of telehealth services in Medicare and appreciates the specification of a mechanism for doing so. However, given the growing evidence that telehealth increases access to quality health care, improves patient satisfaction and reduces costs, we believe a more global approach to expanding Medicare coverage of telehealth is warranted. MCHC greatly appreciates the opportunity to provide input and looks forward to continued discussion of this important policy issue.

Please feel free to contact me should you have any questions or require additional information (dosulliv@mchc.com; 312/906-6080).

Sincerely,

Dennis O'Sullivan
Senior Director, External Affairs

MOFFITT CANCER CENTER

To: **House Energy and Commerce Committee**

Fr: **John DeMuro, Federal Government Affairs Director, Moffitt Cancer Center**

Re: **Comments on 21st Century Cures draft legislation**

Date: **February 10, 2015**

Cures Bill section -

Title II –

Subtitle F: Building a 21st Century Data Sharing Framework.

This Subtitle directs NIH to provide data under ClinicalTrials.Gov in a standardized comparative format. It also authorizes a contract for a non-profit or academic institution to compile de-identified data from clinical trials conducted for drugs and devices. The Subtitle also sets up a process for CMS to share greater Medicare data related to improving the quality of patient care. It would also allow clinical data registries to comply with HIPAA instead of the Common Rule. Finally, it would create a commission on data sharing for research and development.

Feedback:

Centralizing the data associated with patients participating in clinical trials is definitely a step in the right direction. Given the fact that only a small percentage of cancer patients participate in clinical trials, it would be even more helpful if the law could somehow encourage the inclusion of all cancer patients, not just those who have been on clinical trials. This could be through an initiative or network that enrolls patients prospectively, at the point of diagnosis, such as is done by Moffitt as part of our total cancer care program and is incorporated into the ORIEN network.

We would also not exclude for-profit entities from eligibility to provide contracted services to compile the data for the data-sharing framework. This work should be awarded based on the demonstrated capacity of a given entity to manage data warehouses with genomic data and health outcomes information.

While a government commission may have some value, we would respectfully note that the ORIEN network is already operationalizing this type of activity; this is why we are recommending steps toward supporting the development of such networks.

Subtitle L: NIH-Federal Data Sharing.

This provision would direct NIH to require that any grant recipient share the data resulting from their research other than individually-identifiable information or information that is a trade secret or privileged/confidential financial/commercial information. The grant need not fund the entirety of the research for this provision to apply.

Feedback:
Having a central repository of data generated through NIH-funded research would create a valuable resource for scientific inquiry. It would be particularly helpful to have published the results of clinical trials that are not effective. For the most part, negative outcomes of clinical trials are not highlighted in scientific journals, and it may be as important to disseminate what is not working as it is to share successes.

Consideration should be given to setting a minimum sample size for the data sets to be shared through such a mechanism, lest conclusions be drawn from samples not large enough to be generalized to wider populations.

Subtitle M: Accessing, Sharing and Using Health Data for Research Purposes.

This subtitle makes some change to HIPAA that would have the effect of facilitating the sharing of Personal Health Information for research purposes. It seeks to alleviate the HIPAA related concerns that inhibit data sharing.

Feedback:
In general we support the removal of any barriers to the use of personal health information for research purposes, provided that the information is obtained with all appropriate patient consents and safeguarding of privacy. It's worth noting,

however, that we cannot point to any specific problems under current law with access to patient information for research.

Title III: Modernizing Clinical Trials:

Sections 3001 and 3002 attempt to reduce the regulatory burden of IRB's by streamlining requirements and eliminating duplication issues that result from multi-site clinical trials.

Feedback:
Streamlining the IRB process in multi-site clinical trials would significantly reduce the expense and cut the timeline for clinical research conducted in multiple sites. Under current regulations, we have conducted multi-site trials which require approval from as many as ten IRBs, each of which is costly and time consuming.

We would also hope that the patient consenting process of clinical trials could be streamlined. Some clinical-trial consent forms are now as long as 25 pages in order to comply with all the regulations. We believe that such lengthy consent forms may discourage patients from focusing on the most important information about the clinical trial in which they are enrolling.

***

Mylan
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Phone 202.507.5313
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Mylan Inc. Comments to 21st Century Cures Initiative
February 10, 2015

Mylan Inc. appreciates the opportunity to provide our preliminary comments to the 21st Century Cures discussion document. We applaud Chairman Upton and Rep. DeGette's passion and leadership, along with their colleagues, to reshape and advance development of new medical treatments and cures. We look forward to an ongoing, productive dialogue to advance successfully this important initiative in a meaningful way and accomplish its objectives. We wish to provide the following initial comments as we work to review the recently released document.

Encouraging faster FDA approvals for rare diseases and unmet needs, along with other positive proposals in the 21st Century discussion document, deserves much consideration and there is much we believe we will support in the document. At the outset, we have focused our initial comments on a few key provisions. The discussion document demonstrates a significant effort. It follows the substantial work that you helped champion with Mylan and the generics industry to ensure a level global playing field in the generics industry, culminating in the passage of the Generic Drug User Fee Amendments of 2012 (GDUFA) and the Food & Drug Administration Safety and Innovation Act (FDASIA). These bills represent the most significant pieces of legislation impacting the U.S. generic drug system since the passage of the Drug Price Competition and Patent Term Restoration Act of 1984, commonly known as "Hatch Waxman". Hatch-Waxman effectively created the U.S. generic drug industry through a public-interest driven, balanced framework that harnessed innovation and maximized competition. It paved the way for patients to receive timely access to more affordable, high quality generic medication. We want to ensure that future legislation continues to strengthen and build on these foundational pillars for mutual success, benefiting patients and leading to an improved healthcare delivery system.

Since our founding in 1961, we at Mylan have been committed to setting new standards in healthcare and to providing the world's 7 billion people access to high quality medicine. We employ a U.S. workforce of more than 6,000 people and we operate numerous manufacturing sites in the U.S., including one of the industry's largest sites, located in Morgantown, WV, which produces over 20 billion doses of medicine annually. Mylan manages a broad portfolio of over 1,300 individual generic products and has nearly 300 ANDAs currently pending with FDA. As one out of every 12 prescriptions in the U.S. is filled with a quality Mylan product (brand or generic), we are proud of our contributions to providing access to high quality prescription drugs for U.S. healthcare consumers. Generic medicines, such as Mylan's, have saved U.S. taxpayers over $1.5 billion dollars over the past 10 years. It is against this backdrop and the foundational pillars described above, that we offer the following comments to strengthen future legislation.

Exclusivity Incentives for Innovation

Mylan appreciates that there are different levels of innovation that can bring new or improved therapies to consumers and supports the goal of providing sufficient incentives to encourage all types of innovation. We are concerned, however, that some of the proposed exclusivity incentives may have unintended consequences. For example, section 1241 as currently drafted appears to eviscerate the careful distinction that has been made for years between the level of innovation and expenditure needed for developing a

new chemical entity, for which 5 years of exclusivity is awarded, and improvements made to existing drugs, for which 3 years of exclusivity is awarded. As drafted, the scope of the provision is quite broad and could effectively allow most, if not all, products receiving 3-year exclusivity to be extended to 5 years. This could result in "evergreening" – where a brand drug developer is capable of maintaining a continual monopoly on a brand by strategically making relatively small incremental changes over time – thereby depriving patients' access to affordable alternatives brought on by generic competition. In addition, we echo the comments that GPhA is providing on other sections that seek to prolong the exclusivity period afforded to brand companies, such as the dormant therapies provisions, which revises existing exclusivity and patent extension provisions to allow a company to extend its monopoly for 15 years.

Proposals to Improve Access and Competition

To help further balance the need for innovative medicines with greater access to therapies and competition and improve opportunities for cost-savings in the healthcare system, we would like to discuss with you some proposals for inclusion in the 21st Century Cures Act. These include proposals to:

- improve affordable access to drugs that are covered by a risk evaluation and minimization plan and for which generic drug development programs are being hampered by limited access to the brand drug;
- create incentives for companies to help prevent or alleviate a drug shortage of a medically necessary product;
- encourage earlier patient access to generic medicine and foster competition, ensuring approval on the earliest legally eligible date;
- expedite and encourage investment in the development of complex generic drugs; and
- increase FDA transparency and help identify areas for administrative improvement through reports to Congress on measures related to ANDAs and inspections, such as number of inspections conducted by country, number of ANDAs FDA was not able to approve by day 181, and delays in ANDA approvals.

We appreciate the opportunity to provide our preliminary comments to the 21st Century Cures discussion document, which we hope to supplement as we continue our review, and look forward to continuing the dialogue in the coming weeks.

Sincerely,

Carmen M. Shepard, Esq.
Senior Vice President, Global Policy and Regulatory Counsel, Mylan

NAMI Responses to the House Energy & Committee 21st Century Cures Legislation

On behalf of the National Alliance on Mental Illness (NAMI), I am pleased to offer our responses to the recent solicitation from the Energy & Commerce Committee on the bipartisan 21st Century Cures initiative.

NAMI is the nation's largest grassroots advocacy organization representing persons living with serious mental illnesses and their families. Through approximately 1,000 affiliates in all 50 states, we support education, outreach, advocacy and research on behalf of persons with serious mental illnesses such as schizophrenia, bipolar disorder, major depression, severe anxiety disorders and major mental illnesses affecting children.

An estimated 11.5 million American adults live with a mental illness that is often seriously disabling, such as schizophrenia, bipolar disorder, and major depression. Based on estimates for 2010, mental illnesses accounted for 21.3% of all years lived with disability in the United States. Among the top 20 causes of years lived with disability, five were mental illnesses: major depressive disorder (8.3% of the total), anxiety disorders (5.1%), schizophrenia (2.2%), bipolar disorder (1.6%) and dysthymia (1.5%).

Suicide is the 10th leading cause of death in the US, accounting for the loss of more than 38,000 American lives each year, more than double the number of lives lost to homicide. The social and economic costs associated with these illnesses are tremendous. A cautious estimate places the direct and indirect financial costs associated with mental illness in the U.S. at well over $300 billion annually, and it ranks as the third most costly medical condition in terms of overall health care expenditure, behind only heart conditions and traumatic injury. In addition, adults living with serious mental illness represent an enormous public health burden resulting from high rates of medical co-morbidities such as asthma, heart disease, COPD and diabetes.

Moreover, these costs are not only financial, but also human in terms of lost productivity, lives lost to suicide and broken families. Investment in mental illness research and services are – in NAMI's view – the highest priority for our nation, Congress and the Energy & Commerce Committee as you consider 21st century cures legislation.

NAMI Supports 21st Century Cures

NAMI continues to share the draft legislation's goals to accelerate "the cycle of discovery, development, and delivery of promising new treatments and cures." This goal clearly addresses the continuum of activity from basic to translational to clinical research through the regulatory processes of approval and ultimately to payment by public and private payers. This draft adjusts key activities of the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the Center for Medicare and Medicaid Services (CMS). From NAMI's perspective as a patient advocacy organization, each of these elements must work in concert to maximize

overall benefits. Innovation and discovery in the laboratory do no good if they are never tested in real world treatment settings. Successful treatments that meet high quality standards are useless if they are not covered by programs such as Medicare and private health plans and accessible to patients.

Title I, Subtitle A – Patient Focused Drug Development

During stakeholder discussions during development PDUFA V, NAMI supported the concept of creating a series of meetings that would bring patient and caregiver voices as early as possible into the drug development process. The patient-focused drug development (PFDD) meetings undertaken by the FDA thus far have been largely driven by the FDA and patient groups and resulted in valuable publicly-available resources written in the voice of patients to help inform new endpoint development, outcome measure selection in clinical trials, and benefit/risk decision making by regulators.

Going forward, NAMI is hopeful that future PFDD meetings can include more scientific rigor through the development of methodologies to guide structured interactions with patients and their families. In our view, this can be done without discounting the experiences learned from interaction reflecting actual disease burden. An analogous process exists with the FDA public comment process, which does not restrict who can offer feedback based on a methodology or level of expertise of the commenter. The agency can gather information through unstructured processes and informal conversations with people and organizations interested in the issues. The current PFDD meetings should allow for both structured and unstructured interactions, and Subtitle A should permit that process to continue even after a methodology is developed.

NAMI would note that Section 1001 under Subtitle A currently only involves patients, caregivers, and patient advocacy groups as agents for collecting "patient experience data." As such as it does not specifically list them as entities that could lead the development of methodologies behind the "patient experience data" collection or suggest research concepts to the Secretary where "patient experience data." NAMI recommend adding the definition of an "entity" under subsection (y) to include patients, family caregivers, and patient advocacy groups, members of the scientific and medical research communities.

Subtitle B-Surrogate Endpoint Qualification and Utilization

FDA has an established a process through which drug development tools like biomarkers, outcome assessments and other endpoints could be qualified for a specific use and then incorporated into clinical trials. Through this process a company or other consortia can opt to work with regulators in a collaborative fashion to reduce the cost of developing these tools individually and produce a tool that once qualified became publicly available. Even with the qualification process in place, sponsors can still interact directly with FDA's product review divisions on the use of unqualified biomarkers and unqualified endpoints in specific clinical trials. FDA has approved the use of unqualified biomarkers and endpoints in trials and unqualified tools served as the basis of many drug approvals.

However, this process of qualification takes time. The process is driven by the slow pace of science and often delayed by a lack of data. The lengthy timeline for qualification has been particularly challenging in neuroscience where there is a striking lack of biomarkers and other

valid endpoints. Sections 1021-1024 of Subtitle B are intended to address the length of time it takes to qualify surrogate endpoints and allow FDA to enter into public-private partnerships (PPPs) to qualify surrogate endpoints.

NAMI has a number of concerns with this proposal. First, the rigid guidance parameters in Section 1021 requiring pre-determined evidentiary standards for what constitutes a surrogate endpoint would negatively impact FDA's flexibility to determine the validity and use of unqualified surrogate endpoints. Second, the short timeframe provided to FDA for issuing this guidance is not reasonable to allow for meaningful consultation with stakeholders. This consultation would be important to ensuring that proposed standards meet the needs of all stakeholders. Third, there are no resources provided to assist FDA in implementing these changes. As written, it would not be possible for FDA to positively improve the qualification process in the aggressive timeframe set forth in the bill. Finally, FDA and other external stakeholders already participate in public-private partnerships (PPPs) on biomarkers and endpoint development, validation and qualification. Caution should be taken in creating additional PPPs with the goal of endpoint development and qualification so as not to supplant successful efforts.

NAMI recommends removing Section 1021-1024. Instead, we suggest that improvements to the qualification process and necessary resources should be addressed as part of PDUFA VI negotiations set to begin later this year.

Subtitle H – Facilitating Responsible Communication of Scientific Medical Developments
NAMI has been concerned for years that while off-label prescribing often occurs in treatment for serious mental illness, it is not always informed by peer reviewed research. This is unfortunate since evidence-based treatment guidelines and articles in peer reviewed journals exist that provide a rigorous scientific basis to treat complex disorders such as bipolar disorder and borderline personality disorder for which there is no on-label indication. It is a simple fact that the FDA label rarely keeps up with the latest and most important scientific studies.

In the past, NAMI has urged the FDA to develop clear rules by which peer reviewed research can be shared with prescribing physicians to ensure that off-label prescribing is informed by the most appropriate and best science. NAMI supports inclusion Section 1141 and urges that it create a safe harbor under which the FDA can provide clarity on communication to physicians.

Subtitle K-Cures Acceleration Network
In 2010, NAMI supported creation of NCATS Cures Acceleration Network at NIH because of its unique ability to aid in the translation of basic scientific discoveries into treatments for a range of diseases including schizophrenia, bipolar disorder and major depression. One approach taken by NCATS has been drug repurposing under its "Discovering New Therapeutic Uses for Existing Molecules" program. Repurposing has had very promising results in treating difficult diseases including HIV/AIDS and certain cancers. NAMI is hopeful that this success in repurposing drugs can soon be realized with respect to treatment for serious mental illness. Section 1202 under Subtitle K would authorize additional funding in fiscal years 2016-2018 for drug repurposing. If authorized and appropriated, NAMI is hopeful that this investment can enable

more opportunities for the use of therapeutic repurposing for neurodevelopmental diseases and conditions.

Subtitle L-Dormant Therapies
As with the drug repurposing program established by NCATS, there is also enormous potential with many drugs and biologics held by industry that were abandoned during earlier development due to their failure to meet clinical endpoints. Advances in science and new data have made some of these drugs and biologics candidates for redevelopment but a lack of time remaining on their patents makes it unlikely that a company will conduct additional clinical studies for them. Most of these medicines will not be re-investigated and it will be at the expense of patients and their families.

As noted in a previous submission to the Committee, NAMI is on record in support of Representative Lance's MODDERN Cures Act. We are pleased that major provisions in this legislation are integrated into this draft as part of Section 1221 of Subtitle L. NAMI continues to support the concept of allowing drugs and biologics designated as "Dormant Therapies" to be tested again for areas where few or no other treatment options exist. Given the current recession that exists with respect to investment in new therapies to treat serious mental illness, Congress needs to put in place mechanisms that will provide additional incentives for the redevelopment of medicines in the private sector.

Subtitle M – New Therapeutic Entities
NAMI support Section 1241 of the draft and the proposed additional two years of exclusivity for significant improvements to existing molecules under Section 505(b)(2) of FFDCA. It will be important for the Committee to clarify that this includes new technologies and delivery systems such as long acting therapies and formulations that improve treatment adherence and fewer adverse events.

Title II, Subtitle A – 21st Century Cures Consortium Act
NAMI supports the creation of the 21st Century Cures Consortium aimed at fostering collaborations and establishing an agenda for accelerating the discovery, development, and delivery of innovative cures and treatments. Representatives from the patient and research communities must have a voice as the Consortium develops recommendations on how to fill gaps and realize opportunities in the discovery, development, and delivery cycle. NAMI is pleased that the Consortium will solicit feedback from stakeholders through their participation as Consortium members, officers, employees, agents, contractors, and Consortium committee members. We recommend that Congress also require that the Consortium gather stakeholder feedback through a public commenting process with appropriate Federal Register notice and opportunity to submit written testimony. To further ensure that any thoughtful idea generated has the best opportunity to be translated into action, Congress should instruct the Consortium to provide legislative recommendations in its reports to relevant Congressional committees.

Title III, Subtitle A – Clinical Research Modernization Act
In recent years, the NIMH has undertaken a number of real world multi-site clinical trials on schizophrenia (CATIE), bipolar disorder (STEP-BD), adolescent depression (TADS), major depression (STAR-D) and first episode schizophrenia (RAISE). The success of these multi-site

trials was based on a streamlined and efficient process for IRB review. NAMI supports Sections 3001 and 3002 of the draft bill. It is important to build on these successes and create further efficiencies in IRB review, subject recruitment and protocol development.

Title IV- Subtitle A -National Institutes of Health

Section 4001 would require the Director of the NIH to develop a "5-year biomedical research strategic investment plan" to make funding allocation decisions, including strategic investment for each institute; have a common format; and identify strategic focus areas. While NAMI is not opposed to the creation of an agency-wide biomedical research investment strategic plan, we are concerned with Congress getting directly involved in the business of dictating the long established peer review process for choosing research awards.

NAMI therefore recommends the removal of "(A) Funding Priority for NIH Overall.—In developing and maintaining a strategic investment plan under this subsection, the Director of NIH shall ensure that at least 55 percent of the funds that are used by the National Institutes of Health to support extramural research for any fiscal year are used to support basic biomedical extramural research."

Extramural grants in particular represent more than 80% of the $31.2 billion NIH budget. Through its approximately 1,200 individuals and $112 million budget, the Office of Extramural Research (OER) provides the infrastructure that makes these grants happen. OER provides the corporate framework for NIH research administration, ensuring scientific integrity, public accountability, and effective stewardship of the NIH research grant portfolio with the ultimate goal of preserving public trust in research. A peer review system that includes scientists, physicians, and other experienced individuals in biomedical fields from around the world evaluate the merit of proposed research and its potential to advance science.

Section 4004 would create a four-year term for each institute and center director at the NIH. NAMI opposes this provision and urges its removal. Currently, the Directorships of NIH Institutes and Centers (i.e., other than that of the NCI, which is appointed by the President under the 1971 National Cancer Act) are filled by the NIH Director and do not require a Presidential Appointment or Congressional Approval and do not have limited terms for their appointment. NAMI fears that the introduction of terms will distract Directors with campaigning and will encourage jockeying among colleagues who should be spending their time on managing research programs.

The NIH Director is already allowed to hire and fire, and IC Directors positions should not be further politicized. Additionally, NAMI opposes the requirement for IC Directors to review R-series Grants to determine "whether the goals of the research program or project are a national priority and have public support." Not only is this requirement completely subjective and impossible to prove either way, but it is also the stuff of political campaigns, not science, and should not be used to award federal funding for research.

Finally, NAMI strongly supports the BRAIN Initiative. This multi-agency collaborative with a number of foundations is already demonstrating tremendous potential to unleash new technologies and undertake basic mapping of circuits and neurons in the most complex organ in

the human body. NAMI supports inclusion of Section 4008 (authored by Representative Tim Murphy) in the current draft. Moving forward it will be important for the BRAIN Initiative to have a strong bipartisan endorsement from Congress.

Subtitle O – Accelerating Innovation in Medicine

In making its coverage decisions, CMS evaluates a new FDA-approved or cleared product based upon clinical evidence and its comparable effectiveness to already-covered products. All too often however, for developers of newer technologies to compile a sufficient level of clinical evidence at the time the product is initially approved or cleared by the FDA. This can lead to a denial of coverage, a decision that is extremely difficult to reverse in the absence of clinical evidence at minimum—and one that means Medicare beneficiaries may never have access to the technology.

NAMI supports inclusion of Section 4301 of the draft bill (authored by Representative Erik Paulsen) to address this challenge by permitting sponsors to "opt-out" of Medicare and its coverage determination process for three years, allowing time for development of necessary clinical evidence. This data will ensure that a future coverage decision is made on the basis of more developed clinical evidence – at no cost to the government. Importantly, the legislation also requires sponsors to provide CMS with published clinical data at the end of each three year period. This provision is critical to establish and maintain an ongoing dialogue between sponsors and CMS, a process that will support future coverage determinations and benefit access to medical devices thereby benefitting overall public health.

Subtitle S – Continuing Medical Education Sunshine Exemption

NAMI supports efforts to provide greater clarity and address the unintended consequences now emerging with respect to the Physician Payment Sunshine Act. NAMI would urge an additional provision to this section clarifying that the law does not cover indirect payments to patient and disease advocacy organizations and voluntary health associations. NAMI recently joined 64 colleague organizations in seeking such a clarification from CMS (see attached letter). Congress should provide CMS with the clarity to address this unintended consequence.

Respectfully Submitted,

Mary Giliberti
Executive Director
National Alliance on Mental Illness
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February 12, 2015

February 9, 2015

The Honorable Fred Upton, Chairman
The Honorable Frank Pallone, Ranking Member
Energy & Commerce Committee
United States House of Representatives
2125 Rayburn House Office Building
Washington, DC 20515

Dear Chairman Upton & Ranking Member Pallone

The National Committee for Quality Assurance (NCQA) thanks you and your Committee members for your leadership in advancing the 21st Century Cures initiative. We are especially pleased to support the provision adding "research" to the definition of "health care operations." This will provide unprecedented access to data on how care in all settings affects the outcomes and care needs of all patient types. This data is now largely squandered by unworkable requirements to obtain individual consent for every single use of clinical records for research purposes.

Efficient researcher access to these records, while maintaining patient privacy, is long overdue. It will unlock a vast and rich trove of information on care delivered in different places to different patients. This will provide important insights not observable in academic institutions where most clinical research is conducted, but which differ significantly from the settings in which most people receive care. It also can reveal much-needed information on people with multiple comorbidities who are increasingly common but commonly excluded from traditional academic clinical trials.

The evidence we glean from better access to this rich data source is particularly important to developers of clinical quality measures like NCQA. That is because measurement can only be applied for care on which there is strong scientific evidence and stakeholder consensus on its appropriateness. With broader and deeper evidence on care in all settings and patient types, we will be able to measure, and thus improve, the quality of substantially more care that people receive.

Thank you again for your important leadership. Please contact Paul Cotton, Director of Federal Affairs, at cotton@ncqa.org or (202) 955-5162 if you would like to follow up on our comments.

Margaret O'Kane,
President

February 10, 2015

The Honorable Fred Upton
2183 Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Upton:

The National Community Pharmacists Association (NCPA) appreciates the opportunity to provide comments on the 21st Century Cures Act discussion draft. NCPA represents the owners and operators of approximately 23,000 small business independent community pharmacies in the United States. Our pharmacies provide about 41 percent of all outpatient prescriptions dispensed in the U.S. and would be directly impacted by several provisions in this discussion draft. NCPA would like to provide comments/recommendations on the following sections of the discussion document.

Section 4281. Establishing PDP Safety Program to Prevent Fraud and Abuse in Medicare Prescription Drug Plans.

This section would establish a pharmacy "lock-in" program under which presumably all beneficiaries that have obtained coverage "for a covered part D drug that is a frequently abused schedule II, III, IV, or V controlled substance, as determined in accordance with utilization guidelines established by the Secretary and the sponsor" to only receive these substances from a single assigned pharmacy. While we share the common goal of cracking down on the endemic prescription drug abuse problem in the United States, we have serious concerns with this approach.

The prescription drug abuse epidemic is complex and wide-ranging in nature. However, at the forefront of prevention efforts must be a focus on reducing the inappropriate prescribing or the overprescribing of controlled substances and the prevention of "doctor shopping." After all, without a physician-issued prescription, a drug abuser cannot obtain these substances through a pharmacy. We would support carefully constructed prescriber lock-in policies; as this is the root cause of many patients being able to obtain multiple prescriptions for the same or similar medications leading to overuse and possible diversion. However, NCPA has serious concerns about the usage of pharmacy lock-in provisions in the Part D program—particularly when it would be the PDP or plan sponsor that selects or chooses the pharmacy.

Currently there are multiple PDP sponsors that have commercial relationships with large retail pharmacy chains (i.e., Humana-Walmart). Our concern is that in this type of program, these PDP sponsors would simply "assign" these types of beneficiaries to pharmacies in which they have a commercial or financial interest in, including mail-order pharmacies they own. Already under the Medicare Part D program, independent community pharmacies are being excluded from participation

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in certain preferred pharmacy networks. CMS has already established multi-pronged criteria to accurately identify "high-risk" patients in the Medicare Part D program, and this opioid overutilization management program is in effect now. NCPA strongly recommends building on the current program in existence before giving plan sponsors the authority to create and operate a lock-in program. That authority should first and foremost reside with CMS.

Section 4282. Part D Suspension of Claims Payment

This section would grant PDP sponsors the ability to suspend payments and clean claim notifications to a pharmacy pending an investigation of fraud unless the Secretary determines there is a good cause not to suspend payments. Part D plan sponsors already have this authority and the Centers for Medicare and Medicaid Services (CMS) have advised plan sponsors of this policy. CMS issued a guideline on December 13, 2011 entitled "Clarification of Medicare Part D Policies with Respect to Overutilization." Although the guidance itself focuses on medications that are frequently the subject of overutilization and "doctor shopping," it clearly provides that the current prompt pay requirements do not prevent plan sponsors from pursuing fraud claims more broadly via the process described at 42 C.F.R. Sec. 423.520. We strongly oppose granting Part D sponsors the unilateral authority to suspend payment to Part D providers—which may limit patient access to needed medications.

Another concern that we have with the draft language is the definition of "credible allegation of fraud" that includes "a complaint made on the Medicare fraud hotline." Certainly, a faceless allegation made on a 1-800 phone number should not automatically be considered "credible" and be sufficient to suspend payment to a Medicare Part D provider-which could result in disruptions in the access to needed medications.

Section 4284. Requiring E-Prescribing for Coverage of Covered Part D Controlled Substances

Although now permitted by the DEA, only a very small percentage of controlled substance prescriptions are now being prescribed electronically. In fact, New York State will likely need to delay implementation of a mandate to e-prescribe controlled substances by March 2015, because systems on both the prescriber and pharmacy sides are not yet ready. Until systems are widely in place to implement this provision, NCPA opposes mandated use, as this will place undue burdens on physicians, pharmacies, and create serious access concerns for patients.

In conclusion, NCPA appreciates the opportunity to provide our thoughts on the 21st Century Cures discussion draft and would welcome the chance to discuss our recommendations in further detail.

Sincerely,

Steve Pfister, Senior Vice President, Government Affairs, NCPA

February 10, 2015

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

Dear Chairman Upton:

We write to offer our comments on the 21st Century Cures Act Discussion Draft, specifically Subtitle N – Medicare Part D Patient Safety and Drug Prevention.

Prescription drug abuse is the Nation's fastest-growing drug problem and represents a patient safety issue and a public health crisis. In fact, unintentional overdose deaths, resulting in approximately one hundred preventable deaths each day, have been classified as epidemic by the Centers for Disease Control and Prevention and such an urgent concern that President Obama proposed increasing funding for programs across various federal agencies to combat the issue... Drug-induced overdose deaths now surpass homicides and car crash deaths in America at a cost of more than $193 billion annually.[1]

While these statistics are troubling, we are concerned that without appropriate, targeted action, restrictions on overall access to prescription medications will be put into place that will harm legitimate access to medications.

For example, the recent action by the Drug Enforcement Administration (DEA) reclassifying certain painkillers as Schedule II drugs, which is the most restrictive category for controlled substances that have medical uses, makes it harder for patients with chronic pain to receive their prescriptions.[2,3] Nursing home patients may also be unintentionally targeted with these onerous burdens as previous reports claim serious delays for legitimate delivery of pain medications.[4]

This widespread policy places a burden on all patients- both legitimate and illegitimate. We agree that this pandemic is seriously harming patient lives and needs to be assessed and prevented, however a more targeted approach than the new DEA action is necessary; Section 4281 of the 21st Century Cures discussion draft accomplishes this goal in the Medicare program by outlining the "Safe Pharmacy Access Program."

<u>Comments on Discussion Draft – 21st Century Cures Act, Section 4281:</u>

This section would identify potential high-risk Medicare beneficiaries and lock them into one prescriber and one pharmacy for filling and refilling "frequently abused Schedule II, III, IV, or V

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[1] ONDCP. http://www.whitehouse.gov/sites/default/files/ondcp/newsletters/ondcp_update_june_2011.pdf
[2] Wall Street Journal. (August 22, 2014). DEA Restricts Narcotic Pain Drug Prescriptions. Found online: http://online.wsj.com/articles/dea-restricts-narcotic-pain-drug-prescriptions-1408647617
[3] LA Times. (August 22, 2014). DEA makes Vicodin harder to obtain legally, but that's half the job. Found online: http://www.latimes.com/opinion/opinion-la/la-ol-vicodin-hydrocodone-dea-restrictions-overdose-deaths-20140821-story.html
[4] New York Times. (March 23, 2010). US Drug Move Said to Deprive Elderly. Found online: http://www.nytimes.com/2010/03/24/health/policy/24pain.html?_r=0

controlled substance[s]".

- *This lock-in program is similar to the Medicaid program, which has been shown to be of benefit with cost savings and accurate identification of prescription drug abusers.*[5] *We believe a similar program instituted within Medicare will result in similar outcomes. We also support the right of the beneficiary to appeal the high-risk classification.*

The discussion draft would also require participants in the "Safe Pharmacy Network" to utilize available technologies such as state prescription drug monitoring programs (PDMPs) or other "drug safety criteria as the Secretary or the PDP sponsor (or MA organization) determines to be appropriate.

- *The proposal relies heavily upon those at the point-of-dispensing to have all the necessary information to determine if the prescription being filled is legitimate in order to prevent abuse by patients but also to ensure that legitimate prescription needs are being met. We believe that requiring the utilization of technology such as PDMPs is a step in the right direction.*

The bill would require the use "an electronic prescribing program" for coverage to be offered for a schedule II-V controlled substance.

- *Using an e-prescribing program is the most efficient way to prevent mistakes in the prescribing process due to human error or misplaced/illegible records in addition to the benefit that both prescribers and dispensers gain when they are able to see a beneficiary's complete record at once. The technology is available and non-prohibitive in both cost and ease of use. We believe more widespread use of e-prescribing will help ensure that legitimate patients have accessibility to their prescription while reducing waste, fraud and abuse.*

Again, we are pleased to express our support for Section 4281 of the Energy and Commerce Discussion Draft on the 21st Century Cures Act. We look forward to working with you and your staff in addressing appropriate medication use and the benefits for curtailing drug abuse to ensure continued access to prescription medications for legitimate patients within the Medicare Part D program.

Sincerely,

Stephen C. Mullenix, R.Ph.
Senior Vice President, Public Policy and Industry Relations
National Council for Prescription Drug Programs (NCPDP)
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[5] http://www.cms.gov/Medicare-Medicaid-Coordination/Fraud-Prevention/FraudAbuseforProfs/downloads/iacompfy08pireviewfinalreport.pdf

NCSBN
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February 17, 2015

Rep. Fred Upton
United States House of Representatives
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Washington, DC 20515

Rep. Diana DeGette
United States House of Representatives
2368 Rayburn House Office Building
Washington, DC 20515

Chairman Upton and Rep. DeGette:

Thank you for the opportunity to provide comments on the 21st Century Cures discussion document. We appreciate the chance to communicate our organization's priorities to you.

The National Council of State Boards of Nursing (NCSBN) is an independent, non-profit association comprising 59 boards of nursing (BONs) from across the U.S., the District of Columbia and four U.S. territories. BONs are responsible for protecting the public through regulation of licensure, nursing practice and discipline of the 5.2 million registered nurses (RNs), licensed practical/vocational (LPN/VNs) and advanced practice registered nurses (APRNs) in the U.S. with active licenses, in addition to the approval of prelicensure nursing education programs in the U.S. NCSBN was created by these boards of nursing to act and counsel with one another and to lessen the burden of government. The mission of NCSBN is to provide education, service and research through collaborative leadership to promote evidence-based regulatory excellence for patient safety and public protection. Through NCSBN, BONs can work together on policy matters that will affect the future of nursing and health care.

NCSBN supports efforts to expand telehealth as a model of care delivery. We recognize technological advances can both reduce the cost of care and increase patient access to care across the country. We strive to offer providers the opportunity to practice safely and competently across state lines without undue licensure burdens.

One way that we have worked to facilitate interstate mobility of nurses is through our Nurse Licensure Compact (NLC), an interstate compact that allows a nurse to have one multistate license (in his or her state of residency) that grants the privilege to practice in other NLC participating states (both physically and electronically), subject to each state's practice laws and regulations. NCSBN launched the NLC in 2000 in an effort to expand the mobility of

nurses as part of our nation's health care delivery system. Currently, 24 U.S. states have adopted the NLC, and that number is expected to grow in the coming years as the NLC is revised to address concerns raised by states that have not yet joined. In addition to the NLC, we have also developed a compact that would facilitate interstate license portability for APRNs, who are increasingly delivering primary care and helping with chronic disease management via telehealth. The APRN Compact maintains most of the same principles as the NLC, including a mutual recognition licensing model that would allow an APRN to practice in any participating state with just one license.

NCSBN is very pleased that the 21st Century Cures initiative is addressing the important reimbursement issues that impact the delivery of patient care through telehealth and would like to offer some constructive comments for consideration in future drafts.

First, we request that the legislation clarify that licensure is based on the location of the patient as recognized by current state and federal laws and regulations. Recent proposals have suggested moving licensure away from the patient's location to the site of the provider. This change would create confusion for nurses, patients, and boards of nursing. In addition to the added confusion, moving licensure to the provider's location would directly conflict with states' constitutional rights. Moreover, providers must be held accountable to the state boards in the states where they are practicing. Patients need to be able to seek recourse in the event that an adverse action occurs with their care. If a provider is not located in their state, that process can often be complicated due to jurisdictional issues. For the reasons listed above, efforts requiring only one state license to practice in all 50 states based on location of the provider, or nationalizing state licensure, would undermine the authority of state BONs and weaken their ability to fulfill their charge to keep the public safe.

Second, we request that the bill clarify that participating providers must comply with all applicable state laws and regulations. Adding this brief language would remove any provider uncertainty regarding their legal obligations, further protects patients from harm, and helps alleviate any potential provider legal confusion.

Third, we believe that any language in the legislation addressing reimbursement should be clearly identified. We suggest adding the phrase, "for the purposes of reimbursement," to the beginning of each section addressing reimbursement issues in order to alleviate potential confusion with licensure laws. For example, the discussion draft cites "any geographic limitation" on page 297 of the discussion document in reference to current geographic restrictions for Medicare telehealth reimbursement. While many in the telehealth community recognize the purpose of this reference, it may cause legal confusion with others unfamiliar with Medicare payment policy. We believe it is important to clarify this ambiguity so that it is not confused with geographic references to state licensure laws.

Fourth, we would like to address the "Sense of Congress Regarding State Medical Board Compacts" section. NCSBN greatly appreciates the inclusion of language acknowledging the important work currently being done in states to facilitate interstate health care practice through health care compacts like our NLC and APRN Compact. In addition to states currently considering the NLC and the Interstate Medical Licensure Compact, other health care compacts are currently being considered or developed for state consideration in multiple practice areas, including physical therapy, psychology, and emergency medical technicians

(EMTs) in efforts to facilitate interstate practice. For this reason, we propose broadening the language to include all professions working on interstate compacts. Our suggested language is as follows:

> *Sense of Congress Regarding State Health Licensing Board Compacts – It is the sense of Congress that States should collaborate, through the use of State health licensing board compacts, to create shared jurisdictional authority, share investigative and disciplinary information, and implement a strategy that enables license portability for the purposes of facilitating telehealth across state lines by health care providers while simultaneously ensuring protection of the public.*

BONs under the NLC facilitate interstate cooperation and coordination through participation in Nursys®, the only national database currently available for verification of nurse licensure and discipline for RNs, LPN/VNs and APRNs. Nursys® allows access to the status of a nurse's license and provides information about any history of discipline. Ultimately, the NLC creates the necessary legal structure that requires BONs to report and share license and discipline information with one another, a key component to ensuring nurse competency and patient safety across the country.

As legislative language of the 21st Century Cures bill continues to develop, NCSBN would like to work with you, your fellow members of Congress, and other stakeholders to resolve issues involving state based licensure.

Once again, NCSBN appreciates the opportunity to provide comments on this important initiative. If you have any questions or need any additional information, please do not hesitate to contact us. Elliot Vice, NCSBN's Director of Government Affairs, can be reached at evice@ncsbn.org and 202-530-4830. We look forward to continuing the dialogue with your group on this very important issue.

Sincerely,

Kathy Apple, MS, RN, FAAN
Chief Executive Officer

National Health Council

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February 13, 2015

Representative Fred Upton
2183 Rayburn House Office Building
Washington, DC 20515

Representative Diana DeGette
2368 Rayburn House Office Building
Washington, DC 20515

RE: 21st Century Cures discussion draft

Dear Chairman Upton and Representative DeGette:

We would like to voice our enthusiasm and support for the 21st Century Cures discussion draft recently released by the House Energy and Commerce Committee. We commend the Committee for advancing this legislation and for bringing many of these critical issues to the forefront of the policy discussion.

The NHC is the only organization that brings together all segments of the health community to provide a united voice for the more than 133 million people with chronic diseases and disabilities as well as their family caregivers. Made up of more than 100 national health-related organizations and businesses, its core membership includes the nation's leading patient advocacy groups, which control its governance. Other members include professional societies and membership associations, nonprofit organizations with an interest in health, and major pharmaceutical, medical device, biotechnology, and insurance companies.

This proposal will impact the way treatments are studied, developed, regulated, and ultimately made available to all Americans, particularly the millions of individuals who suffer from chronic diseases and disabilities. Many provisions in the proposal would enhance aspects of the research and regulatory environments and accelerate pathways for developing promising treatments:

1) *Further Articulating a Process for Patient-Focused Drug Development* (Title I. Subtitle A. Sec. 1001)

   We have been encouraged by the progress made in recent years by FDA and several other stakeholders to help shape and implement Patient-Focused Drug Development (PFDD). We applaud the inclusion of additional provisions in 21st Century Cures to further bolster these efforts by mandating the development of a structured benefit-risk framework for drug evaluation and creation of a clear pathway for the collection, evaluation, and integration of patient

experience data into benefit-risk decisions. These advancements will continue to help ensure that the patient voice is captured when making important regulatory approval decisions.

2) *Facilitating Responsible Communication of Scientific and Medical Developments* (Title I. Subtitle H. Sec. 1141)

We are equally encouraged to see that manufacturers are considering the benefits of engaging with patients throughout the drug development pipeline. However, because manufacturers oftentimes feel their interactions with patients are at risk of being construed as discussions of unapproved medicines or unapproved uses of approved medicines, they are inclined to forgo invaluable input from patients to inform earlier stage research decisions, such as endpoint selection and clinical trial design. We urge the Committee to use this placeholder language as an opportunity to clarify that this type of patient engagement is both legal and encouraged.

3) *Providing FDA the authority to designate new drugs that treat unmet medical needs as "Dormant Therapies"* (Title I. Subtitle L. Sec. 1221-1223)

Bringing promising treatments to all individuals suffering from debilitating and life-threatening diseases remains a critical priority for the patient community. However, existing laws related to patents can discourage investigation of treatments for unmet medical needs. Many promising treatments do not meet the technical requirements of patent eligibility. Additionally, because patent life runs concurrently with research and development, research into products that take longer to develop is less likely to occur. Therefore, we strongly support the creation of Dormant Therapies, which removes technical patent requirements that are unrelated to medical promise and starts the period of protection at FDA approval. This would incentivize researchers to pursue the development of drug compounds on the basis of their promise rather than their patents.

4) *Standardization of data and expansion of data access with appropriate privacy safeguards for the purposes of accelerating research* (Title II. Subtitle F. Sec. 2081, 2082, 2085, 2086, 2087, 2088, 2091, and 2092)

Establishing a data sharing framework to efficiently increase the secure flow of rich data will help unlock the full potential that data holds for robust research and faster cures of debilitating disease. Furthermore, standardizing publicly available registry and research results will help simplify patient access to important information about ongoing clinical trials and therefore facilitate opportunities for patients seeking treatments through these trials.

5) *Allowing patient information to be accessed, used, and shared for research* (Title II. Subtitle M. Sec. 2221)

While privacy is critically important to all people, so too is the need for more research into finding cures and treatments. The use of patient data for research has the potential to unlock information that can be used for research. Therefore, we strongly support these provisions which create flexibility for researchers to share data sets, while strengthening

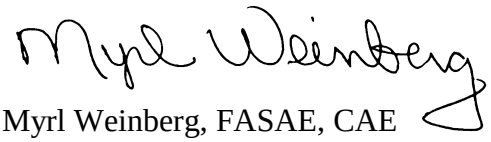
the security of data, provide one-time patient authorization, expand appropriate remote access, allow entities collecting data to use it for research, and treat research like other public health activities.

6) *Reducing Regulatory Duplication and Unnecessary Delays in IRB Review* (Title III. Subtitle A. Sec. 3001-3002)

The Institutional Review Board (IRB) approval process is a necessary safeguard to ensuring appropriate patient protections; however, aspects of the process have proven to be cumbersome and redundant. We commend the Committee for supporting ways to create efficiencies and reduce duplications, which will help expedite reviews and ultimately allow research to progress faster. We support the regulatory changes proposed and encourage Congress to continue to identify other areas where other redundancies may be eliminated.

Please do not hesitate to contact Eric Gascho, our Assistant Vice President, Government Affairs, if you or your staff would like to discuss these issues in greater detail. He is reachable by phone at 202-973-0545 or via e-mail at egascho@nhcouncil.org. You may also reach me on my direct, private line at 202-973-0546 or via e-mail at mweinberg@nhcouncil.org.

Sincerely,



Myrl Weinberg, FASAE, CAE
Chief Executive Officer

National
Multiple Sclerosis
Society

February 10, 2015

The Honorable Fred Upton
House Energy and Commerce
Committee
2125 Rayburn House Office Building
Washington, DC 20515

The Honorable Diana DeGette
House Energy and Commerce
Committee
2125 Rayburn House Office Building
Washington, DC 20515

Sent via e-mail: Cures@house.mail.gov

Re: Feedback on 21st Century Cures Act discussion draft

Dear Chairman Upton and Representative DeGette:

The National Multiple Sclerosis Society (Society) applauds the Energy and Commerce Committee for its continued commitment to the 21st Century Cures Initiative. We congratulate the numerous Representatives who have contributed to this discussion draft of the 21st Century Cures Act and appreciate the opportunity to comment on this proposed legislation on behalf of those living with multiple sclerosis.

Multiple sclerosis (MS)—an unpredictable, often disabling disease of the central nervous system—interrupts the flow of information within the brain, and between the brain and body. Symptoms range from numbness and tingling to blindness and paralysis. The progress, severity and specific symptoms of MS in any one person cannot yet be predicted, but advances in research and treatment are moving us closer to a world free of MS.

The National MS Society sees itself as a partner to the government in many critical areas. While we advocate for governments involvement in accelerating the discovery, development and delivery of new treatments, we do it as an organization that commits over $50 million annually to MS research through funds generated by the Society's fundraising. Since our inception, we have funded $870 million in MS research. Our goal is to see a day when MS has been stopped, lost functions have been restored, and a cure is available.

Due to our unwavering commitment to advance treatments for MS, we adamantly agree with the initiative's overarching goal - to accelerate "the cycle of discovery, development, and delivery of promising new treatments and cures." This goal will help to incentivize, leverage, and harness our nation's abilities to develop new solutions to our most pressing health care needs. Because access to a new treatment or cure is dependent on many interrelated factors—from basic research to coverage by public and private payers—the entire continuum must function in order to be successful. We previously proposed several

policy initiatives that could help to overcome the barriers to developing and delivering innovative treatments and cures to patients with MS. While we are still reviewing the legislative language, below we have outlined our initial reactions to the 21st Century Cures draft.

I. Accelerating Basic Research

Advancing Research Through Data Collection

We thank the Committee for including this data collection system for neurological conditions, including MS, in the 21st Century Cures Act draft and fully endorse its inclusion in the final version. Neuroscientists are making great strides in many areas of brain research but lack basic information about these populations to help advance their studies. Researchers currently lack essential information to assist those who research, treat, and provide care to those suffering from these diseases in our communities. The Advancing Research for Neurological Diseases provision (TITLE IV: SUBTITLE B) would provide accurate data to researchers on incidence and prevalence, as well as risk factors, how diagnosis and treatment varies by gender, ethnicity, and region, and importantly, how these trends change over time. We firmly believe the collection and analysis of this data will help to advance our knowledge of neurological conditions in the future.

Sustainable R&D Funding

The Society endorses the financial support of several vital supplementary programs at the National Institutes of Health (NIH) in the 21st Century Cures Act draft (TITLE I: SUBTITLE K and TITLE IV: SUBTITLE A, Section 4007). Additionally, we strongly support the Committee's inclusion of additional funding for Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative (TITLE IV: SUBTITLE A Section 4008). This program is already providing researchers with innovative tools to identify new ways to treat, prevent and even cure brain disorders but additional funding is needed to ensure this initiative meets the goals that were outlined at its outset.

One glaring aspect that appears to be missing from this draft bill, however, is overall funding for NIH and other federal research streams. While we understand that funding is under the jurisdiction of the Appropriations Committee, we strongly urge that the leaders of this effort reconsider their decision not to include broad-based funding increases to R&D activities in the 21st Century Cures Act. In order to incentivize researchers to go into the field, more predictable funding for the NIH needs to be committed. Researchers need a steady source of funding to conduct continuous research and assure young scientists of a career path. Without such an annual increase, the budget and nation's ability to fund meritorious research effectively and at a level that advances innovation declines with the inevitable increases in the cost of research.

There are numerous bills such as the American Cures Act introduced by Senator Richard Durbin and the Accelerating Biomedical Research Act sponsored by Representatives

Rosa DeLauro, Brian Higgins, and Peter King that could serves a framework to grow our investment in the biomedical research enterprise in a predictable and sustainable way. We encourage the committee to look at these potential policies as possibilities to increasing our leadership in basic research.

R&D Funding Allocation

The Society is very concerned with the inclusion of several provisions, listed below, that fundamentally alter the scientifically-driven peer review system that rigorously evaluates and prioritizes proposals across the basic and clinical research spectrum and awards support to the most meritorious. Specifically, we have apprehension about:

- TITLE II: SUBTITLE O – Helping Young Emerging Scientists
- TITLE IV: SUBTITLE A, Section 4001 – NIH Research Strategic Investment Plan
- TITLE IV: SUBTITLE A, Section 4004 – Increasing Accountability at the National Institutes of Health
- TITLE IV: SUBTITLE A, Section 4005 – GAO Report on Common Fund

While we believe the intention of these provisions is to increase the accountability of NIH funding, we are opposed to vastly changing the current grant framework that would undeniably hinder the advancement of basic science. Specifically, we are concerned with the approach to fund research by looking for the greatest return of investment. The value of investing in basic research and development comes from the accumulation of information gleaned from many studies over time, and it is often difficult or impossible to predict accurately which single project may lead to the next breakthrough. The NIH system for selecting which research proposals are funded is based on the likelihood for a project to exert a sustained, powerful influence on the research fields involved because the research proposal, in part, addresses a contemporary challenge in the field. We strongly urge the Committee to remove the four provisions listed above.

Advancing Science by Encouraging Collaboration

The provision Federal Data Sharing (TITLE II: SUBTITLE L) takes an important step toward encouraging collaboration and data sharing in biomedical research. While clinical trials are mandatory for the development of new therapies, they also require an investment in time and resources by patients, industry and researchers. The Society believes that clinical trial data could also benefit the community by accelerating medical innovation. However, currently most of the data is private and proprietary and is not routinely shared, which prevents researchers from learning about the advances and mistakes gleaned from the trial. We agree with the outlined policy that by mandating the exchange of information, more collective learning will be possible as researchers will have access to their colleagues successes and failures.

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NIH Travel Policy
We note that the Committee has left a placeholder for language relevant to amending NIH travel policy. Continued learning is vital to keeping the NIH on the cutting edge of research. Because the exchange of information is essential, NIH researchers need better access to thought-leaders in their fields and scientific conferences are one of the primary locations to access this information. Often many thousands of scientists in a particular field travel to engage in these scientific exchanges. To ensure that NIH researchers and program managers continue to have full access to the latest scientific information, the Society advocates for rescinding restrictions on travel to scientific conferences.

II. Incentivizing Investment in Drug Development
The Society is pleased that the Dormant Therapies section (TITLE I: SUBTITLE L) would reward investment in treatments and cures for patients where there are unmet medical needs. Currently, many people living with progressive forms of MS have no FDA-approved therapies to treat their disease. Because progression can be slow, it can take a long time for a pharmaceutical company to study whether an agent is working. Additionally, since MS is a disease of the central nervous system, it is more difficult to study. Therefore, due to the increased time and resources needed to study treatments for progressive MS, many companies may not choose to invest in this because of the potential lack of return-on-investment. We agree with the premise of Dormant Therapies that establishing a predictable period through which a company can recoup its investment would incentivize the development of future medical products for unmet needs. Conversely, timely access to generic drugs reduces the significant impact of costs for patients and payers. Therefore, the Society recommends that the Committee consider shortening the protection period in this provision, in order to ensure a better balance.

III. Drug Review and Delivery

Promoting Patient and Caretaker Engagement
The Society is extremely pleased for the inclusion of the Patient Focused Drug Development provision (PFDD; TITLE I: SUBTITLE A) in the 21st Century Cures Act draft, as it will expand and provide additional guidance on how to incorporate the patient perspective in drug review. The risk-benefit paradigm for those living with MS is constantly in flux depending on progression, life stage and previous treatments. Therefore, the Society believes it is critical to keep the patient perspective center to the drug development process by gathering information on the patients' perspective on areas like risks and benefits, targeted endpoints and meaningful outcomes. We encourage the committee to keep this provision in the final bill.

Surrogate Endpoint Qualification and Utilization
The Society supports the development of a framework to consider surrogate endpoints. Research in MS, as well as many other diseases, will benefit from a clearer pathway with

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the FDA on the utilization of surrogate endpoints. Discussion with stakeholders, as noted in the bill, will be important to this process and development of a framework.

Accelerating Approvals For Breakthrough Therapies
While the Society recognizes that accelerated approvals may not be appropriate for every disease area, we appreciate the idea proposed in the Approval of Breakthrough Therapy Provision (TITLE I, SUBTITLE C). For those patients without any current treatments, they are often eager to have access to any available therapy and have a greater risk tolerance for potential adverse effects. Therefore, as long as appropriate studies are in place to determine the risk-benefit threshold for these populations, we believe there could be merit in pursuing an accelerated approval pathway would make potential treatments available sooner.

FDA Funding & Training
The Society endorses TITLE IV: SUBTITLE F—FDA Succession Planning in the 21st Century Cures Act which would provide opportunities for professional development and training for FDA staff in topic areas relevant to their field. Additionally, the Society looks forward to reviewing the language for TITLE IV: SUBTITLE E—FDA Hiring, Travel, and Training. Similar to the NIH, most personnel at the FDA are required to have a deep scientific knowledge, and continued education in their field is a necessity.
Therefore, we recommend that the provision enhances FDA's ability to recruit talent from outside the Agency and that it contain no restrictions on travel to scientific conferences.

Conclusion

On behalf of those living with MS, we thank you for the enormous effort you have invested in drafting this important piece of legislation and for soliciting our input. The Society hopes to be a resource of information, as the bill makes its way through the legislative process. If you have any questions or require any further information, please contact Lauren Chiarello via email at Lauren.chiarello@nmss.org or call 202.408.1500.

Sincerely,

[redacted]

Timothy Coetzee, Ph.D.
Chief Advocacy, Services and Research Officer
National Multiple Sclerosis Society