ASN LEADING THE FIGHT AGAINST KIDNEY DISEASE

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February 10, 2015

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

The Honorable Diana DeGette
Committee on Energy and Commerce
2368 Rayburn House Office Building
Washington, D.C. 20515

Re: *21st Century Cures* Discussion Draft Legislation

Dear Chairman Upton and Congresswoman DeGette:

On behalf of the American Society of Nephrology (ASN) thank you for the opportunity to provide input to the Energy and Commerce Committee regarding the "21st Century Cures Act" discussion document. ASN commends the Committee for its commitment to accelerating the discovery, development, and delivery of promising new treatments to patients and stands ready to collaborate to achieve this important objective.

ASN, the world's leading organization of kidney health professionals, represents more than 15,000 health professionals and scientists who are dedicated to treating and studying kidney disease and to improving the lives of the millions of patients it affects. ASN particularly supports efforts that bolster the ability of federal agencies and the American research and development enterprise to solve scientific challenges at every level from basic science through care delivery.

Kidney disease affects more than 20 million Americans. There are many unique causes of kidney disease, but when any type of kidney disease progresses to kidney failure, patients require either dialysis or transplantation to stay alive. Currently, 600,000 Americans have complete kidney failure, called end-stage renal disease (ESRD). Kidney disease disproportionately affects racial and ethnic minority populations, is associated with multiple co-morbidities including heart disease and diabetes, and is one of the most costly chronic conditions in the United States.

While America's scientific leadership has yielded important treatments for some patients, others still wait because the state of biomedical research and innovation in certain diseases is not as advanced; kidney disease is among the conditions for which we must accelerate the pace of innovation.

Although people with kidney failure requiring dialysis (ESRD) comprise less than 1 percent of Medicare beneficiaries, they account for nearly 7 percent of Medicare's budget: the Medicare ESRD Program is unique in that it covers every American with kidney failure regardless of age

or income. Yet despite these staggering costs, the fundamental principles of dialysis have not changed and patients with ESRD have seen only incremental improvements in their therapy in decades.

The 21st Century Cures initiative is a significant opportunity to spur research and facilitate development in kidney care and in other diseases where the state of biomedical research and therapies in certain diseases is not as advanced.

TITLE I—PUTTING PATIENTS FIRST BY INCORPORATING THEIR PERSPECTIVES INTO THE REGULATORY PROCESS AND ADDRESSING UNMET NEEDS

SUBTITLE A—PATIENT FOCUSED DRUG DEVELOPMENT

ASN applauds the Committee for prioritizing the inclusion of patient perspectives in the regulatory approval process. The society concurs that the meaningful incorporation of patient experiences into product development and regulatory decision making for medical products is an important objective. While ensuring the safety and effectiveness of medical products remains a paramount responsibility of the Food and Drug Administration (FDA), the FDA also supports the use of patient-reported outcomes (PRO) tools and patient preference metrics. However, the lack of clarity surrounding best practices for their development and application has resulted in slow adoption of these patient-centered tools.

Given that a patient's tolerance for risks will vary based on numerous factors including the severity of the disease or condition, the stage of the chronic disease, and the availability of alternative treatment options, a need truly exists for another set of tools that would allow regulators to better understand how affected patients would assess the overall benefits and risks associated with a product.

As proposed in the discussion draft, the experience of a patient living with a particular disease; the burden of living with or managing the disease; the impact of the disease on daily life and long-term functioning; the effect of current therapeutic options on different aspects of the disease; and patients' willingness to accept various levels of risk based upon potential benefit are all important considerations for a framework that would facilitate the incorporation of patients experience data into regulatory decisions. ASN also supports the concept of convening workshops for patients, representatives from advocacy groups and disease research foundations, FDA staff, and methodological experts to provide input on the development of such a framework.

Reflective of ASN's commitment to facilitating the incorporation of patient preferences into the regulatory process, the society's public-private partnership with the Food and Drug Administration (the Kidney Health Initiative (KHI) mentioned under Title II Subtitle A of this letter) is confronting this topic. KHI's workshop (planned for the second half 2015) will engage kidney disease patients, in conjunction with regulators and industry, to understand their preferences and define future opportunities to develop tools that will assess benefit and risk of medical devices.

SUBTITLE B—SURROGATE ENDPOINT QUALIFICATION AND UTILIZATION

ASN strongly supports the concept of establishing a predictable, transparent process for FDA's consideration, and possible qualification, of surrogate endpoints. In countless areas of medicine—including in the nephrology space—successfully completed large scale controlled

trials have failed to result in new approved products for patients. The reasons for these failures are complex and myriad, but one contributing factor is the lack of validated outcome measures and endpoints to feasibly assess success in many disease states.

For example, trials must reverse kidney failure or reduce deaths to gain approval for new treatments. As a consequence, these endpoints hinder the development of drugs that could potentially intervene earlier in the disease process and slow or halt progression to kidney failure because the trials would be too long and expensive to measure the results against the endpoints. Instead, most trials enroll patients who have already progressed to kidney failure.

The development of validated, robust surrogate endpoints and biomarkers—particularly early in the course of a disease—would accelerate discovery of new treatment and cures in nephrology and in other areas of medicine. The society strongly agrees with the proposal to consult with scientific experts and involve individuals with direct expertise in the relevant therapeutic areas, biostatistics, and pharmacogenetics, in the consideration of any surrogate endpoints or biomarkers to be utilized in regulatory decision-making.

SUBTITLE C—APPROVAL OF BREAKTHROUGH THERAPIES

The current FDA Breakthrough Therapy Designation program is an important effort to date to reduce the time required to bring new drugs to market. ASN is supportive of FDA exploring expanding this effort to approval of drugs that have received breakthrough therapy designation under Section 506(a) of the Federal Food, Drug, and Cosmetic Act (FFDCA) when early stage clinical data provides sufficient evidence under the current safety and efficacy standards, considering the risks and benefits of the drug and the risks associated with the disease or condition for which unmet medical needs exist.

This provision of the draft legislation has the potential to help expedite novel therapies into patients' hands. However, ASN urges greater emphasis in the legislation regarding the consultation with, and role of scientists and other experts, representatives of patient advocacy organizations (including patients themselves) and disease research foundations, and other interested parties through a public process to ensure that regulatory efforts to meet this goal are conducted in the safest, most evidence-based manner.

Subtitle E—PRIORITY REVIEW FOR BREAKTHROUGH DEVICES

Consistent with its support for providing faster access to new drugs, ASN also supports the concept of Medicare and Medicaid coverage of medical devices that have been reviewed and approved under an expedited review process by the FDA—provided, as noted in the discussion draft, that the standards for approval are the same or exceed the same approval standards for devices considered under the standard review process.

Subtitle N—ORPHAN PRODUCT EXTENSIONS NOW

ASN supports federal incentives to encourage industry investment in new therapies for complex diseases, including kidney disease, which is a broad term for dozens and dozens of diseases that affect kidney health and function. Many of these are relatively rare diseases, and consequently, many of the millions of Americans affected by one among this panoply of conditions have no therapeutic option. In lieu of treatment, some will progress to complete kidney failure. The FDA has approved fewer new therapies for kidney disease in the last 10

years than most major diseases. As such, incentives to promote investments in orphan products could be beneficial to patients.

TITLE II—BUILDING THE FOUNDATION FOR 21ST CENTURY MEDICINE, INCLUDING HELPING YOUNG SCIENTISTS

SUBTITLE A—21ST CENTURY CURES CONSORTIUM ACT

ASN believes the proposal described in Section 2001 to establish a public-private partnership to accelerate the discovery, development, and delivery in the United States of innovative cures, treatments, and preventive measures for patients has substantial promise to assist in the development and delivery of new therapies for patients. The society applauds the Committee for including the concept of the 21st Century Cures Consortium in the discussion draft, and offers insights from a similar, successful public-private partnership with the FDA.

To respond to the serious and under-recognized epidemic of kidney disease in the United States, the Food and Drug Administration and the American Society of Nephrology in 2012 founded the Kidney Health Initiative (KHI)—a public–private partnership designed to create a collaborative environment in which the FDA and the greater kidney community can interact to optimize the evaluation of drugs, devices, biologics, and food products. The mission of this public-private partnership between ASN and FDA is to advance scientific understanding of the kidney health and patient safety implications of new and existing medical products and to foster development of therapies for diseases that affect the kidney by creating a collaborative environment in which FDA and the greater nephrology community can interact to optimize evaluation of drugs, devices, biologics, and food products.

Similar to the proposed 21st Century Cures Consortium, the KHI membership and board of directors—which is co-chaired by an ASN member and an FDA staff person—includes the breadth of stakeholders, including patient, health professional, pharmaceutical, device, and dialysis company members, as well as the Centers for Medicare and Medicaid Services (CMS), FDA, and NIH.

Current projects, driven by multi-disciplinary workgroups, focus on the development of clinical trial endpoints, assessment of patient preferences in the approval of medical devices, data standards, value and utilization of pragmatic trials, and much more. With more than 70 members and nearly a dozen active projects tackling the barriers to innovation in kidney disease underway, ASN believes that the collaborative KHI approach to fostering innovation can serve as a model for other areas of medicine where scientific advancements are needed.

SUBTITLE B—MEDICAL PRODUCT INNOVATION ADVISORY COMMISSION

ASN supports the creation of an independent Medical Product Innovation Advisory Commission based on MedPAC. MedPAC has served as a credible, authoritative voice on a variety of health and medical policy issues; its staff and committee members are highly knowledgeable and offer thoughtful insights on complex policy issues. ASN believes a similarly structured entity to advise Congress on issues related to the discovery-development-delivery cycle could help facilitate the innovation process and improve patient access to cures.

SUBTITLE H—COVERAGE WITH EVIDENCE DEVELOPMENT

One of the frequently identified barriers to the development of new medical products is the siloed decision-making between the FDA and CMS. Although the missions of the two agencies are distinct and equally important, from an investment perspective, the possibility that FDA may approve a new medical product only to have CMS—at a much later date—rule unfavorably in terms of necessity or coverage can be a deterrent. This deterrent comes at a cost to patients who might otherwise benefit from a new drug or device on the market. Permitting Medicare beneficiaries to access products that are the subject of ongoing clinical trials would help reduce uncertainty for technology developers and simultaneously benefit patients. Considering the paucity of new therapies in the nephrology space compared to other areas of medicine, patients with kidney disease may stand to benefit significantly from any reduced disincentives to invest in a new product that Coverage with Evidence Development may provide.

ASN supports the concept of subtitle H as articulated in the discussion draft.

Subtitle O—HELPING YOUNG EMERGING SCIENTISTS

Investments in basic and clinical research are the foundation of future therapies and cures. Yet funding increases for the National Institutes of Health (NIH) have not kept pace with rising inflation, compromising our nation's ability to fund promising scientists. This trend is likely a contributing force behind the historic low application success rates and all-time high average age an investigator receives their first research grant.

Not surprisingly, these figures have a chilling effect on the number of young scientists choosing to dedicate their careers to medical research. As the brightest minds turn elsewhere, America's position as the global leader in research and innovation—and in bringing cures to patients—is compromised. ASN supports Congressional efforts to help young, emerging scientists gain a successful start to their research careers. Among these efforts, the society encourages Congress to consider expanding NIH loan repayment programs for MDs and PhDs as a way of promoting science careers, including in the kidney field.

Subtitle P—FOSTERING HIGH-RISK, HIGH-REWARD SCIENCE

The NIH history of funding extramural, investigator-initiated grants has yielded unparalleled dividends in medical discoveries and cures. This successful model of research funding should be robustly and stably funded. However, there may be research funding models that complement this tradition, introducing a component of more high-risk—but high-reward—science to the NIH portfolio.

The private and philanthropic sectors have successfully been using prize competitions for years as a mechanism for spurring scientific and technologic breakthroughs in a number of fields. Unlike traditional research and development models, competitions have the added benefit that the prize is only paid out if a competitor wins, and the competitions also draw competitors from outside those traditionally interested in the space.

The 2007 America Creating Opportunities to Meaningfully Promote Excellence in Technology, Education, and Science Act of 2007 (also known as the America COMPETES Act) authorizing federal agencies to conduct prize competitions. ASN believes Congress should investigate dedicating funding towards prize competitions and other mechanisms that promote consideration of high-risk, high-reward science, especially in fields where innovation has been stagnant, including nephrology. However, the society emphasizes that such high-risk, high-reward science must not come at the expense of traditional research funding models, and that

this approach to promoting innovation should be used only in certain, carefully considered situations.

TITLE III—MODERNIZING CLINICAL TRIALS

SUBTITLE A—CLINICAL RESEACH MODERNIZATION ACT

ASN supports the establishment of a single NIH Institutional Review Board (IRB) for multi-site studies. While IRBs assure that appropriate steps are taken to protect the rights and welfare of clinical trial participants, review of a multi-site study by the IRB of each participating site involves significant administrative burden in terms of IRB staff and members' time to perform duplicative reviews.

When each participating institution's IRB conducts a review, the process can take many months and significantly delay the initiation of research and patient recruitment for clinical trials. Use of single IRBs in multi-site studies, on the other hand, has been shown to decrease approval times for clinical protocols and may be more cost effective than local IRB review.

SUBTITLE B—BROADER APPLICATION OF BAYESIAN STATISTICS AND ADAPTIVE TRIAL DESIGNS

ASN supports the encouragement of the broader application of Bayesian statistics and adaptive trial designs. The topic of Bayesian statistics involves a number of technical issues, and the available methods are rapidly evolving; ASN would be pleased to provide input to Rep. Collins and his office as well as the Committee as this provision takes shape. In general, ASN believes that adaptive designs (Bayesian and non-Bayesian) are a useful new tool for conducting clinical trials efficiently. Hence, the society anticipates that the language in the bill will be helpful for research in many areas of medicine including kidney disease.

TITLE IV—ACCELERATING THE DISCOVERY, DEVELOPMENT, AND DELIVERY CYCLE AND CONTINUING 21ST CENTURY INNOVATION AT NIH, FDA, CDC, AND CMS

SUBTITLE A—NATIONAL INSTITUTES OF HEALTH

Section 4001—NIH research strategic investment plan

ASN supports the provision for NIH development of a Strategic Investment Plan. The society suggests that Congress consider encouraging NIH to examine the federal costs related to the care for each disease area when prioritizing research foci in such a planning effort. The society also believes NIH should seek input and feedback from stakeholders—particularly patients and scientific experts—throughout the planning process; this could easily be achieved by publication of notice in the Federal Register seeking public comments on draft plans.

Section 4003—NIH travel

While ASN recognizes the importance of reforms to prevent the abuse of federal funding for travel, recent travel bans and budget cuts are negatively affecting federal employee participation in scientific meetings and conferences. As noted above, their participation is critical for executing and advancing the mission of NIH, FDA, CMS and other federal public health agencies. Not only is participation in these meeting essential for the exchange of knowledge to

advance science and medical care, it is also in many cases necessary for maintaining professional licenses for practicing medicine.

SUBTITLE F—FDA SUCCESSION PLANNING

Facilitating the professional development and up-to-date scientific knowledge of federal agency staff is crucial to the success of every agency with a mission related to the public health of the United States.

National and international meetings play a critical role in the scientific process and in the implementation of scientific advances by allowing for analytical discussion and interaction between government experts and other physicians and scientists. Such interactions facilitate research and support the collaborative efforts between academia and federal agencies necessary to address serious public health threats and advance the discovery of life saving treatments and diagnostics. As medical and scientific innovation becomes more global, the information sharing, mentoring, and professional collaboration that occurs between U.S. scientists and their colleagues from around the world at these meetings becomes all the more paramount to maintain our nation's role as the leader in research, translational science, and innovation.

Ensuring a robust, well-trained pipeline of agency staff to ascend within agencies—as well as establishing contingency plans should planned staff transitions into key roles not occur—are fundamentally important to the function of federal agencies. Particularly in health care-related agencies, a deep understanding of the history of and nuances related to areas of responsibility is a necessity for developing and implementing or executing policies that affect the public health. As such, ASN commends the Committee's interest in succession planning and encourages the consideration of succession planning at other federal health care-related agencies—particularly CMS.

For example, although nearly 7 percent of Medicare's budget is allocated to the care of patients with kidney failure, CMS does not employ a single nephrologist on its staff of thousands. Although Medicare had nephrologists on staff in the past, the current dearth of nephrologists is problematic and could potentially have been avoided by a succession plan to account for this crucial staff expertise. The lack of internal knowledge regarding the vulnerable, costly kidney patient population creates challenges for the kidney community in communicating with CMS and impedes informed dialogue concerning the best possible policy decisions for patients.

As such, ASN also supports the most efficient possible review and approval processes for federal employees to travel to and participate in scientific conferences and meetings as recommended under Title IV Subtitle A Section 4003 of this letter.

SUBTITLE I—TELEMEDICINE

ASN commends the Committee for seeking input and feedback from stakeholders on telehealth as part of its larger 21st Century Cures initiative. The society concurs that telehealth has significant possibility to facilitate better access to care and holds great promise for improving the health and quality of life for patients nationwide.

While ASN believes that telehealth may increase access to care for some patients and help improve care transitions, the society is concerned that telehealth may (in some instances) be used as an inappropriate substitute for face-to-face visits, or may be used to provide

unnecessary care. The society therefore suggests careful consideration of the scope of the initial program and urges implementation of rigorous testing—ideally in the form of a randomized controlled trial—to ensure that the program or pilots achieve the intended goals.

ASN believes that patients at every stage of kidney disease—from those with early-stage chronic kidney disease (CKD) who may be at risk to progressing, to those who are on dialysis, to those who have received a kidney transplant—may be uniquely poised to benefit from expansion of telehealth opportunities.

According to CMS, more than 51 percent of patients with kidney disease have 5 or more co-morbid conditions. Effective management of these co-morbidities is especially important for patients with earlier stages of kidney disease, during which proper care from a nephrologist can help slow the progression of kidney disease towards kidney failure as well as prevent the advancement of costly co-morbidities that are caused or worsened by kidney disease, such as hypertension. Besides improving patient outcomes, facilitating patient access to subspecialists may contribute to long term cost-savings—particularly to the Medicare ESRD Program by preventing people from requiring dialysis.

ASN supports the proposal to eliminate existing limitations on what qualifies as an originating site, including geographic limitations to rural Health Professional Shortage Areas or counties outside of a Metropolitan Statistical Area. In particular, the society supports permitting patients' homes to qualify as originating sites for the provision of telehealth services. Lifting these limitations would facilitate patient access to care, eliminating the need to travel to interface with their nephrology care team.

Home dialysis is an important treatment option that offers patients significant quality of life advantages, including clinically meaningful improvements in physical and mental health. The society encourages the Committee to the designate the ESRD patient's home and dialysis facility as originating sites in statute. In doing so, the Committee would ensure access to this important treatment option for ESRD patients.

Both kidney transplant recipients and living kidney donors would also be well-served by expanded telehealth options. Kidney donor follow-up consultations, mandated by both Medicare and the United Network for Organ Sharing, typically comprise a simple well-patient visit for which donors must bear the costs of a day off work and travel; were patients' homes to be designed as originating site, many of these consultations could easily be provided via telehealth.

ASN strongly believes that rigorous testing to evaluate whether telehealth services are achieved their intended goals is imperative. The society suggests the use of limited trial runs in the manner of a randomized clinical trial: one group of Medicare patients is allowed to receive care via telehealth while another highly similar group is restricted to presently-available face-to-face interactions. Pre-specified patient outcomes and cost metrics would be analyzed and the cost savings/readmissions-preventing hypothesis verified in close to real-time. Although there is wide consensus that telehealth has the potential to improve patient access, reduce hospitalizations, and reduce costs, these hypotheses remain unproven and therefore must be closely evaluated.

SUBTITLE S—CONTINUING MEDICAL EDUCATION SUNSHINE EXEMPTION

ASN support the provision outlined in Section 4381 that would clarify that peer-reviewed journals, journal reprints, journal supplements, and medical textbooks are excluded from the reporting requirement under the Sunshine Act.

ADDITIONAL RECOMMENDATIONS FOR INCLUSION IN THE 21ST CENTURY BILL

ONLINE RESOURCES FOR PATIENTS TO FIND AND ENROLL IN CLINICAL TRIALS

Patient recruitment for clinical trials is a significant barrier to new drug and device development in many areas of medicine, and is a particular challenge in the nephrology space due to the heterogeneity of kidney diseases and the high rate of co-morbid conditions among kidney patients. Without sufficient patient recruitment, industry cannot bring new therapies to market; many kidney studies languish for lack of volunteers. As such, ASN recommends the Committee consider the development of an online clinical trial enrollment resource to help connect patients with relevant studies. The Lung-MAP (http://www.lung-map.org/), an online tool developed in part by the National Cancer Institute, may serve as a model to help build patient awareness of clinical trials and match them with the most appropriate study.

CONCLUSION

ASN applauds the Committee for its work on this initiative and its commitment to ensuring that the United States continues its preeminence in the discovery, development, and delivery cycle and thus, remains the world leader in innovation. The society is grateful for the opportunity to provide on the discussion draft and hopes this feedback is helpful.

Again, thank you for your time and consideration. To discuss ASN's input please contact ASN Manager of Policy and Government Affairs Rachel Meyer at meyer@asn-online.org or at (202) 640-4659.

Sincerely,

John R. Sedor, MD, FASN
Chair, Public Policy Board
Secretary-Treasurer