**Hearing of the U.S. House Energy and Commerce Committee, Subcommittee on Health**
**"Legislative Hearing on 21st Century Cures"**
**April 30, 2015**

**Questions for the Record – Dr. Kathy Hudson**

The Honorable Joseph R. Pitts

**1. Should there be a link between the unfunded burden of illness relative to typical NIH dollars spent for a similar burden, and program announcements (PAs), requests for applications (RFAs), and requests for proposals (RFPs)?**

NIH currently uses Funding Opportunity Announcements (FOAs) in the form of program announcements (PAs), requests for applications (RFAs), and requests for proposals (RFPs), as a way to call for projects from the extramural community that address promising opportunities and unmet needs, both for health and for science.

NIH takes public health needs into account when setting priorities for resource allocations, while also considering other factors, including scientific opportunity, scientific merit, and portfolio balance. Scientific opportunity is particularly relevant because two diseases that impose similar burdens may not be equally ripe for scientific discovery.

Deciding whether a particular research area is under or overfunded is not straightforward. Much of the NIH portfolio involves basic research, which seeks to understand the basic biological processes involved in both health and disease. The Human Genome Project and BRAIN Initiative are good examples of basic research initiatives. Because knowledge generated by basic research may be applicable to numerous diseases and conditions, this research does not neatly map onto a single disease or condition. NIH believes that a priority-setting process that includes measurements of public health needs but is also informed by these and other factors allows us to fund the best science.

**2. What other mechanisms exist to encourage funding for disorders that are currently underfunded relative to disease burden? How are they currently being applied toward underfunded diseases?**

As noted, NIH weighs indicators of public health need and scientific opportunity when setting priorities. RFAs and RFPs are regularly used during this process to solicit extramural research in targeted disease areas. Moreover, NIH invests significantly in developing research infrastructure, training, intramural activities and partnership with other entities to address targeted disease areas as well.

In recognition of public health challenges either chronic or newly emerging, NIH supports infrastructure often in the form of research centers, networks, and core facilities to enhance research capacity focused on specific diseases or conditions. As just one example, clinical research in stroke is a high priority at the NIH, and new infrastructure through the Stroke Trials Network promises to enhance the capacity of the community to address the most important clinical questions in stroke care.

NIH-supported training grants, alone or linked to research initiatives, provide young investigators the opportunity to gain expertise in under-developed research areas. For example, NIH is supporting research to develop new artificial pancreas technologies, and a recently released RFA will pave the way for pivotal trials to collect data needed for FDA approval of artificial pancreas technologies. In tandem, NIH is also

supporting research training of engineers and behavioral scientists—fields that are critical for propelling progress in this area.

NIH often partners with other entities in the biomedical research enterprise to address areas of high need. For example, the Accelerating Medicines Partnership (AMP) is a public-private partnership between NIH, the Food and Drug Administration, and a group of pharmaceutical and nonprofit organizations. AMP is aimed at identifying new diagnostics, disease biomarkers, and potential therapeutic targets with an integrative structure that allows stakeholder needs and input to inform its governance and shares data among its constituent groups. The initial three disease areas—Alzheimer's, type 2 diabetes, and lupus—are all diseases for which a substantial public health need is present, and for which gaps in our knowledge pose significant risks and barriers for developing potential therapies. The public-private nature of the AMP allows it to address these unmet needs with a targeted approach aimed at reducing barriers to translation and the eventual development of therapies.

NIH considers disease burden not just as the number of people affected at a given time, but also the potential burden of an emergent threat to be contained. The recent Ebola epidemic response in West Africa illustrated how NIH can leverage various flexible funding mechanisms and established infrastructure to address an emergent threat with high mortality rate and a rapidly expanding disease burden. In 2014, for example, more than 30 different therapeutic candidates and more than 20 different vaccine formulations were evaluated using animal models, which were supported by NIH over many years. Researchers in NIH's intramural Vaccine Research Center, in collaboration with GlaxoSmithKline, quickly initiated testing of a new vaccine at the NIH Clinical Center. Furthermore, NIH, with other U.S. government and industry partners, launched a large clinical trial in 2015 to assess the safety and efficacy of two experimental Ebola vaccines in Liberia, one of the areas hardest hit by the disease. The speed by which NIH was able to move against this outbreak illustrates the flexibility by which long-standing research infrastructure can be tapped, along with the initiation of new funding mechanisms, to address public health needs.

**3. What is the best metric for disease impact? The WHO recommends DALYs. Is there a better metric that incorporates both death and disability?**

Because of the challenges inherent in choosing rigorous, comparable data sources and measurements, NIH believes that a careful consideration of appropriate burden measurements on a case-by-case basis for each disease is the best way to approach this question. The majority of rigorous public health research, including the majority of studies conducted by the CDC, uses measurements and data sources selected on an individual basis, based on the best fit for the disease or condition being studied. For example, estimating the number of Americans suffering from headaches (a condition in which medical care is not necessarily sought) will employ much different methodologies than attempts to measure the incidence of severe mental illness, in which the condition may be difficult to diagnose and the patient population often is difficult to reach (e.g., homeless patients). Considering the best approach for each disease and condition ensures that the most appropriate, objective measurements are included. However, this makes comparisons between conditions difficult to make.

NIH is aware of the utility of disability-adjusted life years (DALYs) as a tool for comparison between diseases and conditions. The World Health Organization, along with its academic and nonprofit collaborators, has pioneered the measurement of DALYs across a large range of diseases and countries using its Global Burden of Disease study. Plots of an exploratory analysis of the alignment between NIH funding and several measurements from the Global Burden study, including DALYs, are posted on the NIH web site at http://report.nih.gov/info_disease_burden.aspx. While DALYs are currently the best metric for comparing across diseases that can cause both death and disability, there are significant caveats to using DALYs as the sole means of capturing disease burden. DALYs are a measurement that attempts

to combine death and disability into a single measure in order to compare diseases that impose different types of burden. To calculate this metric, the severity of disability for a given condition is given a subjective weight before being combined with age-adjusted mortality data, and the underlying assumptions behind that weighting are not always clear or consistent between studies. When DALYs are used to compare vastly different diseases that impose a variety of types of burden (financial, disability, mortality, U.S. vs. global), they can provide an incomplete picture of the differences between diseases. Given these concerns, NIH believes that DALYs data should be taken into consideration as one of several measurements in order to form the most comprehensive picture of disease impact.

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The Honorable Leonard Lance

**Dr. Hudson, thank you for testifying before the Committee this morning and lending your expertise as we continue to move forward with this important initiative. One issue which has not been raised today, though it affects five million Americans each year, is what we can be doing to support the furtherance of research in critical care.**

**As you are aware, critical care medicine is the care of patients whose illnesses or injuries present a significant danger to life, limb, or organ function and encompasses a wide array of diseases and health issues. This care is typically provided by highly-trained physicians using complex therapies in the intensive care unit (ICU). Unfortunately, despite the likelihood of a patient requiring care in the ICU throughout their lifetime, and the economic cost of providing this care – last estimated in 2005 to be $81.7 billion per year, representing 13.4% of hospital costs, 4.1% of national health expenditures, and 0.66% of gross domestic product – very few breakthroughs have been made in therapies and treatments for these patients. One reason for this may be that critical care research is complex and involves many departments, specialties, professional societies and research institutes/foundations. Lack of coordination and collaboration among these stakeholders has stymied progress, particularly at the National Institutes of Health (NIH) where critical care-related projects are ongoing throughout the 27 Institutes, leaving the field without a solid foundation from which to advance new treatments and therapies.**

**The NIH recently demonstrated the importance and efficiencies that come from increased coordination among stakeholders by establishing an Office of Emergency Care Research, which serves as hub for basic, clinical and translational emergency care research and training across the NIH.**

**1. Recognizing the distinct difference between emergency care and the unique care occurring in the ICU, Dr. Hudson, what is the rationale for not having a similar office at NIH to coordinate and streamline, as well as identify gaps in, our nation's critical care research?**

A great deal of critical care research is supported at NIH. The Trans-NIH Office of Emergency Care Research (OECR) already advocates for and promotes critical care research where it interfaces with emergency care across the NIH. Creating a new office would result in significant overlap with the existing OECR, which is already focused on many aspects of acute critical care medicine. Below are a few examples of the many clinical studies of ICU patients supported across NIH in just the last two years.

The National Heart, Lung and Blood Institute (NHLBI) supports a large number of ICU-based studies:

- An intervention to reduce ventilator-associated pneumonia in the ICU (5R01HL105903-05).
- An investigation of the relationship between low-level secondhand smoke exposure and susceptibility to acute lung injury in the ICU (5R01HL110969-03).
- A study to improving decision making for patients with prolonged mechanical ventilation (5R01HL109823-03).

- A study of Acute Respiratory Distress Syndrome after isolated traumatic brain injury (1F32HL124911-01).
- A study of skeletal muscle dysfunction in ICU patients (5R01HL113494-02).
- A study of nutrition on patients in the ICU with respiratory distress syndrome (5R01HL093142-05).

Several studies are supported by the National Institute of Nursing Research (NINR):

- Sedation and pain the in the ICU (5K23NS090900-02).
- Early exhaled biomarkers of infection in ICU patients (5R00NR012016-05).
- Oral care in mechanically ventilated ICU patients (2R01NR007652-10A1).
- The effect of endotracheal tube movement on patient discomfort and agitation in the ICU (5F31NR011373-04).
- Pain and hypoxia in premature babies in the neonatal ICU (5R01NR011209-04).

In addition, two studies—one in the control of early sepsis in the ICU (5K23GM094465-05) and another of critically ill patients with sepsis (3P50GM076659)—have been supported by the National Institute of General Medical Sciences (NIGMS).

In the area of neurointensive care, the National Institute of Neurological Disorders and Stroke (NINDS) funds basic and applied research to enable brain protection and resuscitation in persons with critical illness. NINDS-funded investigators are pursuing new methods to monitor brain oxygen, blood flow, intracranial pressure, electrical activity, and neuroimaging to guide care in the critical care unit. Others work to develop neuroprotective drugs, hypothermia, and means to optimize brain metabolism to maintain brain and spinal cord health in persons with critical illness. Advances in neurointensive care have improved the outcomes of persons with a variety of tragic conditions such as subarachnoid hemorrhage, acute stroke, Guillain-Barre syndrome, intracerebral hemorrhage, cardiac arrest, and traumatic brain injury.

In pediatric critical care, The Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) supports critical care research in a number of ways. Investigator-initiated funded projects target such important clinical issues as the role of monitoring of intracranial pressure in traumatic brain injury, improving the quality of in-hospital cardiopulmonary resuscitation, developing bioresorbable splints for airway weakening, and monitoring long-term outcomes from sepsis and other forms of critical illness. The Institute also supports research evaluating the decision-making process and parent-provider communication surrounding critical illness. In addition, the Institute supports a Network of seven, large tertiary care children's hospitals to conduct collaborative, multicenter research on critical illness. Finally, several training programs are funded by the Institute to support young critical care providers wishing to perform research in the field.

**2. Do you believe the creation of a working group within the NIH to assess the particular needs of this field would fall within the scope of this committee's effort to promote policies to accelerate the discovery, development and delivery of therapies and cures?**

NIH currently has an Emergency Care Research Working Group, a trans-NIH body charged with adding value and efficiency to both current and future research on the many conditions relevant to emergency care. As indicated in the answer to the preceding question, many of these conditions involve aspects that are directly relevant to—or overlap with—critical care. Given the scope of this group's charge as well the myriad of activities that are currently being supported by NIH in the area of critical care research, an additional working group does not seem needed at this time. NIH can and does, however, contemplate

what specific scientific questions are not being addressed by its current portfolio of critical care research. This is done through a careful and balanced portfolio and gap analysis. Although these analyses take considerable time and effort to perform, they are nonetheless performed at NIH so that appropriate responses can be determined and subsequently executed. Recent analyses conducted by NICHD on its critical care portfolio, for instance, elucidated the need to heighten attention to areas of research related to multiple organ dysfunction syndrome. Consequently, NICHD sponsored a conference on this topic in the spring of 2015 and received approval to issue a corresponding Program Announcement in Fiscal Year 2017. Analyses such as these have been used to both identify specific areas of need and to focus research efforts in an attempt to fill those needs.