On May 17, 2018, the Senate Labor HHS Appropriations Subcommittee held a hearing to review the FY19 budget request for the National Institutes of Health. Opening statement and a webcast of the hearing can be found here.

- Dr. Francis S. Collins, M.D., Ph.D., Director, National Institutes of Health
- Dr. Norman Sharpless, M.D., Director, National Cancer Institute
- Dr. Walter Koroshetz, M.D., Director, National Institute of Neurological Disorders and Stroke
- Dr. Anthony Fauci, M.D., Director, National Institute of Allergy and Infectious Diseases
- Dr. Richard Hodes, M.D., Director, National Institute on Aging
- Dr. Nora Volkow, M.D., Director, National Institute on Drug Abuse

In his opening statement, Chairman Blunt (R-MO) noted that during his time as Chairman of the subcommittee, funding for NIH has increased by 23 percent, or $7 billion, in the last three years. He also noted that the investment for Alzheimer's research has nearly tripled, the Precision Medicine Initiative was started, and resources have been targeted to projects such as the BRAIN Initiative, a universal flu vaccine, and efforts to combat antibiotic resistance.

Several members praised the increases the committee has been able to provide to the NIH over the last few years. Blunt said that he has worked closely with Senator Murray and other members of the subcommittee to prioritize their commitment to NIH and noted that he knows they we will continue to do so this year.

Dr. Collins thanked the subcommittee for their sustained commitment to NIH and for the increased funding provided in the FY18 omnibus that provided an "incredible increase" of $3 billion, including funding for opioid- and pain-related research, Alzheimer's disease, antimicrobial resistance, and development of a universal influenza vaccine. He said that NIH has immediately gotten to work to invest those additional resources into groundbreaking research.

Dr. Collins also noted the investment included in the FY19 budget for buildings and facilities, noting also that NIH's Backlog of Maintenance and Repair exceeds $1.8 billion. He said NIH is currently working with the National Academies of Sciences, Engineering and Medicine to identify NIH facilities and infrastructure most in need of repair and he looks forward to providing that report to the Committee as soon as it is final.

He also spoke about the investment in FY18 and FY19 to support a range of activities to advance research on pain and addiction noting that NIH has and will continue to support cutting-edge research on pain, opioid misuse, addiction, and overdose. Specifically, he said NIH will: explore new formulations for overdose reversal medications capable of combatting powerful synthetic opioids; search for new options for treating addiction and maintaining sobriety; continue to research how best to treat babies born in withdrawal through the ACT NOW trial; develop biomarkers to objectively measure pain; build a clinical trial network for pain research; and attempt to find non-addictive and non-pharmacological approaches to chronic pain.

Topics of interest discussed at the hearing include:

Alzheimer's Disease

In his opening statement Chairman Blunt noted the increased funding that has been provided for Alzheimer's disease. Blunt also asked about progress being made in Alzheimer's and dementia noting the big investments that have been made, but asked about progress. Dr. Hodes noted that the increased appropriations have had an enormous effect – in 2015 they funded 152 awards and in 2017 442 awards. He noted that this funding is bringing new people and ideas into the field. Of the new awards, 27 percent were made to early and new stage investigators and 36 percent had never had support in the area of Alzheimer's or dementia. Blunt indicated that something like a blood test to early identify what is happening in the brain would be a big step in the right direction.

Senator Murray asked Dr. Hodes if NIA has looked at its data sharing policies to see if they are working, specifically mentioning data collected about Alzheimer's disease. Dr. Hodes said he thinks that they have had a history in the Alzheimer's community of a strong willingness to share data and he thinks this has increased over past years. He thinks they are at a stage where they are dealing in part with technical feasibilities of making data cross interpretable, sharable and compatible and are working hard at collaborations across Federal agencies and with outside groups to make sharing more effective.

Senator Capito also asked about Alzheimer's and wanted to know if it is true that it is hard to recruit patients for clinical trials. Dr. Hodes said it is a challenge for multiple reasons and there is a need to recruit people not coming through a normal process where they see a clinician after symptoms have started and get referred to a trial. He said there is a need to develop strategies to screen those at high risk and get them to participate in studies where we can intervein early. The All of Us Study presents a good opportunity. He noted that they will make an announcement this summer to look at multiple modalities for recruiting patients into studies.

Senator Moran (R-KS) asked about Alzheimer's and the detection and use of biomarkers to identify those at risk and how the new NIA framework will help drive research forward. Dr. Hodes said the ability to identify the changes that accompany Alzheimer's disease and related dementias early is critical and the ability to track success using biomarkers will be critical. The goal of many is to establish fluid biomarkers allowing the screening of many more people.

Cancer

Senator Reed (D-RI) spoke about the pediatric oncology program and noted the passage of the STAR Act in the Senate. He wanted to know how NCI would use this if it becomes law. Dr. Sharpless didn't want to comment on pending legislation, but said he thinks the intent of the legislation is very laudable to address issues such as survivorship – curing kids but leaving them with lifelong toxicities. This has become a major issue and further research is needed to understand this. Another issue is one of aggregated data and making it usable for the research community.

Senator Reed asked Dr. Collins about the recently announced trans-NIH pediatric research consortium and wanted to know what NIH wants to accomplish with this. Dr. Collins said many institutes are involved in pediatric research and they have convened this consortium to see if they can come up with a more coordinated strategic plan for defining areas of greatest priority and where they can work together on issues such as cancer, Autism, behavioral issues, etc. The effort has just gotten underway and he can report back on how the effort is going at a later date.

Blunt mentioned cancer immunotherapy, the BRAIN initiative, and CRISPR and asked about what Dr. Sharpless hopes can happen at NCI. Dr. Sharpless said it is an exciting time at NCI and there are lots of opportunities. The challenge is that cancer is so much more than just one disease and the modern

approach to cancer has to be different. He thinks NCI should focus on training the workforce so that we have the right kinds of cancer researchers that understand things like basic immunotherapy and big data, and to recommit to basic science – it is not enough to make progress against some cancers, we need to make progress against all cancers. There is also a need to fix the problem of clinical trials – the current structure has led to trials to become smaller, more fragmented and more expensive and there is a need to rethink how we do trials (NCI-MATCH trial is an example). Finally, he said we need to get serious about organizing data and aggregating it so it is available to the research community to get a handle on different kinds of cancers.

Blunt then brought up a recent visit to FDA and immunotherapy. Dr. Collins spoke about PACT where they have a partnership with 12 biopharmaceutical companies to determine if immunotherapy will work or not. In this case there are no concerns about conflict of interest. It is all precompetitive, so in this case companies are contributing both expertise and funding.

Opioids

Senator Blunt asked about the money the committee was asked to include in the FY18 omnibus for partnerships with pharma on opioid research that NIH decided not to move forward on without consulting with the committee.

Dr. Collins responded by saying that they have been in conversation with industry partners for a year about ways to form a partnership to find ways to treat addiction, overdose, and come up with non-addictive treatments for chronic pain. They have been working with 33 companies and have identified areas of opportunity that could be done effectively in a public private partnership in ways that neither can do alone. Things such as sharing data, sharing assets and repurposing compounds that could turn out to be valuable for pain, as well as running clinical trials together in this space. Dr. Collins said that the partnership is very much alive and will move forward. They are close to having the full plan laid out and he expects to be able to say more about how they will conduct this in the next couple of weeks. The controversy was the fact that there are law suits against some of these companies and there is a question as to the role they played in the crisis, so NIH questioned due to reputational risk and ethics whether is was a good idea to receive funds from these companies. Dr. Collins noted that he convened a panel that made a strong recommendation to move forward with the partnership, but not have cash contributions from the companies involved due to the fact that it could appear that recommendations moving forward could have a conflict of interest. The NIH Foundation also convened their board and made a similar recommendation. He apologized for not consulting the subcommittee but reiterated that the partnership will move forward.

Rep. Capito (R-WV) asked Dr. Collins to elaborate on how private partners are contributing dollar wise to the $500 million investment that has been made and how the partnership works. Dr. Collins said NIH has worked intensively across the institutes since investment was made (noted that the money is in the base so it will be there for FY19 and beyond) and are in a place to have a remarkable portfolio that they are ready to launch. He also thanked the committee for making the funding two-year money, so they can carry over some FY18 money into FY19 if necessary, but he also noted that they will spend a significant amount of that money right away. The public private partnership is a modest part of proposal, but an important one. Dr. Collins reiterate the decision not to accept money from the private partners, but other assets that add value like data, compounds, and scientific expertise. He thinks they are in a good place to move the public private partnership and the rest of the portfolio forward rapidly.

Senator Alexander (R-TN) asked about non-addictive pain strategies and treatments for opioid use noting that 95 percent of treatment for opioids is more opioids. He pointed out the new transfer authority included in the omnibus but wanted to know about progress NIH is making towards new strategies and why there are not more non-addictive options like Vivitrol that help people get away from opioids.

Dr. Volkow said it is one of NIDA's priorities to develop non-addictive alternatives for opioid treatment. She noted that part of the problem is that not all patients respond to Vivitrol intervention and it is difficult to induct someone who is addicted directly to Vivitrol. They are trying to expand the alternative medications that can be given to patients and focusing on strategies that are not involved in the opioid system to help individuals recover without opioid medications. Dr. Koroshetz agreed that to stem the opioid problem in the long term it would help to develop non-addictive pain medications to replace opioids. He noted that they have a plan working with industry partners to accelerate the development of new medications and from the basic science point of view have a number of different targets that look promising.

Capito asked Dr. Volkow about neonatal abstinence syndrome and wanted to know where the Act Now trials are being conducted. Dr. Volkow said that the Act Now program is one that will be funded through the new money and will allow NIDA to maximize protocols that will enable them to determine the best interventions for optimal outcomes for neonates, including protocols that do not require the administration of medications to babies. NIDA is working on new medications and new non-medication treatments to get the best outcomes. They are also interested in finding out how the brains of the newborns are affected.

Senator Shaheen (D-NH) asked about new drugs in development and whether when looking at the potential for new drugs if NIDA is looking at separating fentanyl as a particular opioid that requires a different response or lumping it in with everything else. Dr. Volkow said they are not lumping it together because they are hearing from the field that the doses of Narcan are not sufficient to reverse an overdose and that exposure to fentanyl increases the risk of addiction. One of the projects they would like to implement is how to treat someone who is addicted to fentanyl. NIDA is funding researchers that are partnering with pharmaceutical companies to develop a stronger antagonist – longer lasting, more potent, or alternative medications that may not be based on the same mechanism as Naloxone.

Shaheen also wanted to know if NIDA is doing any research to address co-morbidity since so many people abuse substances to treat things like mental illness. Dr. Volkow said that you have to address all issues to be successful. Recognizing that the reality is co-morbidity – addiction with mental health and addiction with pain – and these situations are more challenging than in isolation. Dr. Collins said they are concerned because the deaths are shifting from opioids to heroin and fentanyl.

Big Data

Senator Murray said that one of the questions today is how to use the mass amounts of data being collected, as well as the need to prevent recreating data we already have. She noted that the FY18 omnibus directed NIH to develop a strategic plan to address these issues, which was released last week, and she wanted to know what the plan is for implementing it. Dr. Collins said that plan is very ambitious and lays out what we need to be doing in the areas of infrastructure, data ecosystem, software and tools, the workforce, and sustainability. NIH intends to implement the plan in a number of ways already in place, including moving some of the largest datasets into the cloud and actively recruiting for a Chief Data Strategist. Murray wanted to know about any barriers, such as researchers delaying releasing data

until they publish findings. Dr. Collins said the 21st Century Cures bill gave him some authorities, which has helped. He also feels that the ethic of the scientific community has shifted toward the thought that it is your responsibility to make your data available if someone else might be able to use it.

Other issues of interest

Senator Murray and Senator Blunt asked about the Moderate Drinking Study. Murray wanted to know if NIH is doing anything to ensure that what happened with this study has not compromised studies elsewhere at NIH. Dr. Collins said that enrollment was halted while the agency investigates whether employees improperly solicited funding for the study into the health effects of moderate alcohol consumption while the agency is investigating those actions. He said that he is concerned that this could be the tip of a larger iceberg, so he has convened a panel to look at this and other studies. He wants to ensure that the peer-review process is above reproach and that there are no conflicts of interest. He will report back once he knows more. He said that making sure that one thing that has gone wrong is not part of something larger going on and that the issue can be fixed.

Senator Durbin (D-IL) spoke about e-cigarettes and vaping and marketing these products to children. He asked about the perils or dangers of this type of addiction. Dr. Volkow said this is concerning because 50 percent of teenager say they are starting to vape only with flavors, but also 30 percent are starting to vape with nicotine and are becoming addicted to nicotine. This is a concern because studies have shown that nicotine acts as a primer and people who are addicted to nicotine are more likely to become addicted to other substances because the brain becomes primed to the addictiveness of other substances.

Senator Blunt asked about socialization challenges of the constant exposure to social media and screens and the impact that may have on adolescence and others. Dr. Koroshetz said the pros and cons are yet to be determined. Many are using social media to advance health research, but suggested that while NIMH is looking at teens, NIDA is conducting the ABCD study. Dr. Volkow said that drug taking and experimentation in adolescence is a very social behavior that often follows peer pressure – they are trying to understand how teenagers are interacting with each other and how this effects behavior. They are interested to see how exposure to social communication influences the development of the brain.