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ONE HUNDRED FOURTEENTH CONGRESS

Congress of the United States
House of Representatives

COMMITTEE ON ENERGY AND COMMERCE
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MEMORANDUM

April 29, 2015

To: Subcommittee on Health Democratic Members and Staff

Fr: Committee on Energy and Commerce Democratic Staff

Re: Hearing entitled "Legislative Hearing on 21st Century Cures"

On Thursday, April 30, at 10:00 a.m. in room 2123 of the Rayburn House Office Building, the Subcommittee on Health will hold a hearing titled "Legislative Hearing on 21st Century Cures." The hearing will provide an opportunity to hear testimony from FDA and NIH on proposed legislation aimed at improving the discovery, development and delivery of new pharmaceuticals and medical devices. The discussion draft is a significant revision of the discussion document released by the Majority on January 26, 2015.

I. BACKGROUND

The discussion draft is the result of a bipartisan effort by the Committee, working with the Administration and a diverse group of stakeholders, to improve the original version that was released by Chairman Upton in January of this year. It is still very much a work in progress, as is evidenced by the fact that there are still sections with titles but no text, and sections with text that is in brackets because the language has not been agreed to.

The document has been reorganized into three titles: Title I – Discovery; Title II – Development; and Title III- Delivery. Title I covers NIH provisions, Title II covers FDA provisions along with a few CDC provisions, and Title III covers CMS provisions. Thus, the section numbers of the original and new documents bear little relationship to each other. The document contains 26 subtitles and 48 sections. Rather than address each of the sections, this memo discusses those that appear to be the most important or the most controversial. We refer you to the section by section, attached with this memo, for a short description of each section.

The document contains several new sections requested by Democratic Committee staff. Sections 1001 and 1002 provide significant new funding for NIH, including $10 billion over five years in new mandatory money. Section 1123 establishes a public private partnership to foster better utilization of patient registries to gather information on the natural history of diseases, particularly rare diseases. Section 2242 enables improved efficiency of trials of medical devices

by removing the requirement that they be conducted under local rather than centralized institutional review boards. Section 2243 facilitates drug and device research by allowing waivers of informed consent for certain low risk testing while maintaining appropriate human subject protections. Section 2261 facilitates the hiring and retention of scientific experts at FDA by removing the limit of the number of members in the Senior Biomedical Research Service (SBRS), by expanding eligibility for the SBRS to include expert drug and device reviewers, and by raising its salary cap. Section 2264 facilitates FDA's ability to collect certain voluntary information that may aid in medical product development by exempting the collection of this information from the Paperwork Reduction Act.

II. TITLE I—DISCOVERY

A. Subtitle A—National Institutes of Health Funding

i. Section 1002. NIH Innovation Fund

This section would increase funding for NIH by establishing a NIH Innovation Fund that would receive $2 billion in mandatory funding each year for five years. That mandatory funding stream would supplement and not supplant the discretionary funding NIH receives. Specifically, the mandatory funding stream would only be accessible if NIH is appropriated at least the same amount of discretionary funding NIH received in the previous fiscal year. The NIH Innovation Fund would specifically direct funding to support precision medicine research, research by young scientists, and for other purposes to be determined.

Federal funding for scientific research, particularly funding for the type of early-stage, basic research that NIH is known for, is one of the most promising ways that we can facilitate the discovery of new treatments and cures. For example, between 1998 and 2005, federally funded biomedical research contributed to the development of 48 % of all drugs approved by the FDA and 65% of drugs that received priority review in that period.[1]

Despite the importance of NIH research to the development of new treatment and cures, we have seen a decline in funding for NIH in recent years. Between FY 2003 and FY 2015, NIH lost a total of more than $8.2 billion in funding when adjusted for inflation.[2] That cut represents a 22% decrease in NIH funding over that period.[3] One result of having less spending power today than in 2003 is that the application success rate for research project grants has significantly declined. The total application success rate for research project grants in FY 2003 was 32 % compared to 18 % in FY 2014.[4]

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[1] Bhaven Sampat and Frank Lichtenburg, *What are the Respective Roles of the Public and Private Sectors in Pharmaceutical Innovations?*, Health Affairs (Feb. 2011) (online at http://content.healthaffairs.org/content/30/2/332.full.pdf+html).

[2] Congressional Research Service, *NIH Funding: FY 1994-FY 2016* (Mar. 6, 2015) (R43341) (online at http://www.crs.gov/pages/Reports.aspx?PRODCODE=R43341&Source=search).

[3] *Id.*

[4] National Institutes of Health, *NIH Data Book, Fiscal Year 2014* (2014) (online at http://report.nih.gov/nihdatabook/).

This legislation aims to reverse that trajectory by creating the NIH Innovation Fund. The NIH Innovation Fund would make critical investments in research that could lead to improvements in health and reductions in disease and disability. Specifically, the mandatory funding would support such critical research priorities as precision medicine and research projects conducted by emerging scientists. The funding for precision medicine could be used to support the Precision Medicine Initiative included in the President's FY 2016 Budget as well as other efforts to advance precision medicine. The President's FY 2016 Budget included $200 million to expand current cancer genomics research and to launch a national research cohort of at least one million individuals. Providing targeted funding for research by young emerging scientists would help ensure that more young emerging scientists are able to obtain the NIH funding necessary to establish their biomedical research careers.

B. Subtitle B—National Institutes of Health Planning and Administration

i. Section 1024. Exemption for the National Institutes of Health from the Paperwork Reduction Act Requirements

This section would exempt certain NIH research activities from Paperwork Reduction Act (PRA) requirements that unnecessarily delayed research efforts by NIH scientists. The PRA requires that agencies obtain Office of Management and Budget (OMB) approval before requesting most types of information from the public. For example, information includes forms, interviews, and recordkeeping requirements.[5]

ii. Section 1025. NIH Travel

This section would make clear that hosting scientific conferences and travel by NIH scientists to scientific conferences is essential to advancing NIH's mission.

iii. Section 1027. NCATS Phase IIB Restriction

This section would help the National Center for Advancing Translational Research (NCATS) speed all phases of translational research. Like all other NIH institutes and centers, NCATS should be able to support all phases of clinical trials without any restrictions.

C. Subtitle C—Supporting Young Emerging Scientists

i. Section 1042. Improvement of Loan Repayment Programs of National Institutes of Health

This section would build upon NIH's efforts to encourage the next generation of scientists to pursue biomedical research careers. It would increase the cap for NIH's loan repayment programs for clinician researchers. It would also require NIH to issue a report on its efforts to attract, retain, and develop young scientists. This section also includes a provision to provide additional funding for emerging scientists. The funding mechanisms used are still under discussion.

[5] HHS, *Information Collection / Paperwork Reduction Act* (online at http://www.hhs.gov/ocio/policy/collection/).

In order to remain the world leader in biomedical innovation, a robust pipeline of scientists entering the biomedical research workforce is critical. That means that there should be an environment where early career scientists see careers in biomedical research as viable. Because scientists have a less than one in six chance of winning funding from a research project grant application, there is great concern that early career scientists may not pursue biomedical research careers or abandon those careers out of fear that they will not be able to support themselves or their career.

The NIH has several initiatives underway that support young scientists. The NIH Director's Early Independence Award provides funding for early career scientists to move from terminal degree or medical residency program directly into independent research positions. The NIH Pathway to Independence Award provides funding to support the timely transition of early career scientists from a mentored postdoctoral research position into an independent research position. The NIH Director's New Innovator Award provides funding for new investigators who propose highly innovative projects.

As discussed above, the new NIH Innovation Fund would provide funding research projects conducted by young emerging scientists. Additionally, this section would improve the loan repayment programs at NIH. Currently loan repayment programs for clinician scientists are capped at $35,000 per year and are limited to certain types of research projects or researchers. This legislation would increase that cap to $50,000 per year and expand the types of research projects that clinician scientists in the NIH loan repayment programs can pursue.

D. <u>Subtitle D—Capstone Grant Program</u>

i. Section 1061. Capstone Award

This section would provide NIH funding to outstanding scientists who are at the end of their careers to support the conclusion or transition of their research projects. Section 1061, the Capstone award, would be particularly helpful for transitioning their research programs to other scientists or making it possible for research organizations to sponsor new research programs.

E. <u>Subtitle E—Promoting Pediatric Research through the NIH.</u>

i. Section 1081. National Pediatric Research Network

ii. Section 1082. Global Pediatric Clinical Trial Network Sense of Congress

This section would build upon current pediatric research efforts underway at NIH. It would also express support for the creation a global pediatric clinical trial network.

F. <u>Subtitle F – Advancement of NIH Research and Data Access</u>

i. Section 1102. Standardization of Data in Clinical Trial Registry Data Bank of Eligibility for Clinical Trials

This section would require NIH to accept submissions of clinical trial certain inclusion and exclusion criteria in a standardized format. The current proposal is still under discussion.

NIH currently requires that recruitment information including age, sex/gender, and whether the clinical trial accepts healthy volunteers be provided in a standardized format in clinicaltrials.gov. Additionally, current law requires that the database be searchable by primary disease or condition studied. While there remains support for increasing the amount of data that is submitted in standardized format when feasible, there are questions about how far this provision goes. Although this section has been slightly narrowed from the version that appeared in the initial discussion document, the current requirement would still create data integrity concerns and could present challenges for those who submit data into and use the database.

G. Subtitle G—Facilitating Collaborative Research

i. Section 1122. Clinical Trial in Data System

This section would create a research sharing system for trials solely funded by the federal government in order to allow the use data beyond an individual research project. This section is still under discussion. There is general support for the sharing of data from clinical trials solely funded by the federal government. However, this provision would require the sharing of individual-level data from all clinical trials funded by NIH. There is still outstanding questions as to whether the benefit of sharing all of this data is worth the increased burden it could place on scientists and the NIH. The value of requiring the disclosure of individual-level data on all clinical trials is not clear. NIH currently has studies underway to determine when requiring individual data sharing is valuable to advancing future scientific inquiry and discovery. Until those studies are complete, it could be premature to establish a statutory requirement for the submission of individual-level data from all clinical trials solely funded by the NIH.

H. Subtitle H—Council for 21st Century Cures

i. Section 1141. Council for 21st Century Cures

This section would create a Council to provide advice on accelerating discovery, development, and delivery of innovative cures, treatments, and preventive measure for patients.

III. TITLE II—DEVELOPMENT

A. Subtitle A—Patient-Focused Drug Development

i. Section 2001. Development and use of patient experience data to enhance structured risk-benefit assessment framework

Engaging patients in the drug development process has long been supported by FDA through the inclusion of patients in advisory committee meetings, and in meetings with FDA and product sponsors during the review. This engagement helps to inform FDA's understanding of a condition's impact on patients' daily life and available treatment options.

Congress has also supported engaging patients in the drug development process, and to this end, the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA) required FDA to develop and implement strategies to include patients' perspectives during the medical product development process and regulatory discussions. FDASIA also included the

development of the "Patient-Focused Drug Development initiative" as a part of the reauthorization of the Prescription Drug User Fee Act V (PDUFA). The goal of this initiative is to more systematically gather patients' perspectives on their condition and available therapies to treat their condition. As a part of this initiative, FDA is holding at least 20 public meetings over the course of PDUFA V each focused on a specific disease area. FDA has held nine such meetings thus far.[6]

Section 2001 of the discussion draft would build on these efforts and direct FDA to implement a structured risk-benefit assessment framework in the drug approval process that incorporates patient experience data, including information about the impact of a disease or a therapy on patients' lives. FDA is required to publish guidance regarding implementation of such framework no later than three years after enactment, to convene a public meeting to solicit stakeholder input on the guidance, and to convene a series of workshops meant to inform the methodologies for collecting patient experience data.

B. Subtitle B—Qualification and Use of Drug Development Tools

i. Section 2021. Biomarkers, surrogate endpoints, and other drug development tools

ii. Section 2022. Accelerated approval development plans

Biomarkers, which are measurable indicators of biological and pathological processes, hold the potential to improve and accelerate the drug development process. Such use of appropriate biomarkers can help predict what populations will respond best to a new therapy earlier in the development process, leading to lower development costs and accelerated approval. Biomarkers can also help aid in the understanding of the progression of certain diseases.

FDA has established a "Biomarker Qualification Program," a collaborative effort within the Center for Drug Evaluation and Research (CDER) to support efforts by external scientists and clinicians in the development of these critical tools. The goals of the program are to "provide a framework for scientific development and acceptance of biomarkers for use in drug development; facilitate integration of qualified biomarkers in the regulatory review process; encourage the identification of new and emerging biomarkers for evaluation and utilization in regulator decision-making; and support outreach to relevant external stakeholders to foster biomarker development."[7] Through this program, FDA has qualified four biomarkers thus far.

Sections 2021 and 2022 are meant to codify this effort and further facilitate the development of biomarkers and surrogate endpoints. The discussion draft requires the agency to issue guidance establishing a framework by which FDA would qualify biomarkers, surrogate endpoints, and other drug development tools. The discussion draft also directs the agency to issue guidance to assist with the qualification of drug development tools of biomarkers by

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[6] Food and Drug Administration, *The Voice of the Patient: A Series of Reports from FDA's Patient-Focused Drug Development Initiative* (online at http://www.fda.gov/ForIndustry/UserFees/PrescriptionDrugUserFee/ucm368342.htm).

[7] Food and Drug Administration, *Biomarker Qualification Program* (online at http://www.fda.gov/drugs/developmentapprovalprocess/drugdevelopmenttoolsqualificationprogram/ucm284076.htm).

clarifying the review process of a qualification submission. The discussion draft also provides for greater transparency into the qualification process through making publicly available qualification submissions and determinations to foster the use qualified drug development tools by multiple product sponsors, and supports the consultation with medical research consortia with expertise in this area during the qualification process. Finally, the discussion draft directs the Secretary to establish a process for the submission of an accelerated approval development plan that would allow for the use of surrogate endpoints as the basis of accelerated approval.

As noted, FDA is currently working with stakeholders on the development and use of biomarkers in drug development. However, as Dr. Woodcock has stated in testimony before the Energy and Commerce Committee, "Scientific understanding of diseases varies widely and is likely to remain the most important limiting factor for developing targeted therapies and personalized medicine. When we do not understand the disease pathways, biomarkers appearing to be linked to disease progression often fail because they are not, in fact, in the causal pathway for the disease."[8] The development of biomarkers would best be helped through policies that build on FDA's efforts, and help facilitate the understanding of the natural history and progression of diseases. This section is still under discussion.

C. SUBTITLE C – FDA Advancement of Precision Medicine

i. Subtitle 2041. Precision medicine guidance and other programs of Food and Drug Administration

Precision medicine is an emerging approach to medical treatment that would tailor prevention and treatment to the individual patient based on genes, environment, and lifestyle.[9] To help achieve the goal of personalized medicine, more must be done to better understanding the underlying disease or condition of the patient in order to better predict what treatments will be most effective for that individual. President Obama's FY 2016 budget proposal includes $215 million for the Precision Medicine Initiative[10]. Of this funding, $200 million would be directed to NIH to expand cancer genomics research to initiate new studies of how a tumor's DNA can be used to predict and treat tumor cells, and to launch a national research cohort of one million or more individuals to share their genetic information over time. In addition, $10 million would be directed to FDA to recruit scientists and clinicians with expertise to advance regulatory science and accelerated evaluation of new technologies, as well as funding to modernize the regulatory framework for next generation sequencing technologies. It is also proposed that the Office of the National Coordinator for Health Information (ONC) receive $5 million under the initiative to develop technology and define standards and certification criteria to enable the exchange of genomic data.

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[8] Testimony of Janet Woodcock, M.D., Director of the Center for Drug Evaluation and Research, FDA, Committee on Energy and Commerce (July 11, 2014) (online at http://democrats.energycommerce.house.gov/sites/default/files/documents/Testimony-Woodcock-HE-21st-Century-Cures-Incorporating-Patient-Perspective-2014-7-11.pdf).

[9] National Institutes of Health, *Precision Medicine Initiative* (online at http://www.nih.gov/precisionmedicine/).

[10] FACT SHEET: President Obama's Precision Medicine Initiative (online at https://www.whitehouse.gov/the-press-office/2015/01/30/fact-sheet-president-obama-s-precision-medicine-initiative).

Section 2041 of the discussion draft seeks to build on the announcement of the President's Precision Medicine initiative by defining the term 'precision medicine' and requiring FDA to issue and periodically update guidance related to the requirements to meet the definition of a precision drug, and to assist in the development of such drugs, how expedited or priority review will be applied to such drugs, and identifying population subsets for purposes of developing precision drugs for serious diseases.

FDA has long supported the advancement of precision medicine[11] and has made development of targeted drug therapies a priority, approving 30 such therapies since 2012. The agency also continues to work on personalized drug dosing and the appropriate use of biomarkers to ensure patients are receiving the right dose of the right treatment. Given that the agency is already utilizing its authority to advance precision medicine, the requirement to publish draft guidances in this area is unnecessary and may serve only to divert agency resources from advancing this truly important goal.

ii. *Sec 2022. Accelerated Approval Development Plans*

This section creates a process by which drug sponsors and FDA can agree to a plan for the steps needed to get approval of a drug that qualifies for accelerated approval. This section was added very late in the process and does not reflect any technical comments from FDA. Therefore, the section is still under discussion.

D. <u>SUBTITLE D – Modern Trial Design and Evidence Development</u>

i. *Section 2061. Broader Application of Bayesian Statistics and Adaptive Trial Designs*

ii. *Section 2061. Utilizing Evidence from Clinical Experience*

iii. *Section 2063. Streamlined Data Review Program*

Clinical trials are studies done in patients to answer questions about whether a product is safe and effective when used. Data from these studies are used to help inform the development of drugs and devices. One goal of 21st Century Cures is to ensure that clinical trials are being conducted in the most efficient way possible. FDA has issued guidance meant to help facilitate this goal by outlining various enrichment strategies meant to help sponsors select appropriate study populations. [12] FDA has also undertaken a number of efforts to help speed clinical trials,

[11] Food and Drug Administration, *Pacing the Way for Personalized Medicine: FDA's Role in a New Era of Medical Product Development* (Oct. 2013) (online at http://www.fda.gov/downloads/ScienceResearch/SpecialTopics/PersonalizedMedicine/UCM372421.pdf).

[12] Food and Drug Administration, *Draft Guidance for Industry, Enrichment Strategies for Clinical Trials to Support Approval of Human Drugs and Biological Products* (Dec. 2012) (online at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM332181.pdf).

including accepting flexible clinical development designs, the use of surrogate endpoints, creating clinical trial networks and master protocols, and working closely with industry sponsors throughout the development process to help plan efficient clinical trial programs.[13]

The discussion draft includes a number provisions to help build on the work of FDA including: Section 2061, which would require FDA to issue guidance to assist sponsors in incorporating adaptive designs and Bayesian statistical modeling into their clinical protocols and new drug applications; Section 2062, which would require FDA to establish a program to evaluate the potential use of evidence from clinical experience to help support the approval of a new indication for a drug and to help support or satisfy post-approval study requirements; and Section 2063, which would require FDA to establish a streamlined data review program that allow for the submission of clinical data summaries to support the approval or licensure of specified new indications of drugs and biologics if certain qualifying criteria are met.

E. SUBTITLE E – Expanding Patient Access

i. Section 2082. Expanded access policy; and, Section 2083, Finalizing draft guidance on expanded access

FDA allows sponsors to expand access to investigational products while they are still undergoing clinical trials through compassionate use programs. These programs allow patients with serious or life-threatening diseases for which there are no comparable alternative treatments access to investigational drugs. In recent years, patients and providers have expressed concern that access to investigational drugs was too difficult. This criticism has led to introduced legislation in more than 20 states that would help to make it easier for patients to access investigational therapies. To help address questions from industry, providers, and patients regarding FDA's implementation of regulations on expanded access, the agency released a draft guidance answering a number of common questions regarding this topic, including: the types of submissions that can be used, the information that must be included in an access submission, the appropriate role for a physician and FDA in determining if access for a patient is appropriate, among other questions. Further, in February 2015, FDA released a new draft document, "Individual Patient Expanded Access Applications: Form FDA 3926[14], which simplifies the application process for requesting access to investigational products allowing physicians to complete the form in 45 minutes versus the 100 hours needed to complete the previous form.[15]

Section 2082 of the discussion draft would require certain sponsors to make publicly available their policy regarding expanded access, including the contact information, process, and

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[13] Testimony of Janet Woodcock before Committee on Energy and Commerce (July 11, 2014).

[14] Food and Drug Admiration, *Draft Guidance for Industry, Individual Patient Expanded Access Applications: Form FDA 3926* (online at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM432717.pdf).

[15] Dr. Peter Lurie, Associate FDA Commissioner for Public Health Strategy and Analysis, FDA Voice Blog, *A big step to help the patients most in need* (Feb. 4, 2015) (online at http://blogs.fda.gov/fdavoice/index.php/2015/02/a-big-step-to-help-the-patients-most-in-need/?source=govdelivery&utm_medium=email&utm_source=govdelivery).

criteria for such requests, as well as the length of time the sponsor anticipates will be needed to acknowledge the request. Further, Section 2083 of the discussion draft directs FDA to finalize the draft guidance entitled "Expanded Access to Investigational Drugs for Treatment Use – Qs & As"[16] no later than 12 months after the date of enactment.

F. SUBTITLE F – Facilitating Dissemination of Health Care Economics Information

i. Section 2101. Facilitating dissemination of health care economic information

Drugs or devices approved by FDA must be accompanied by labeling also approved by the agency that includes information needed for safe and effective use of that product. This information is used by a health care provider to prescribe and use the product for indications described in the labeling. Any use of such product that is not communicated in the product labeling is considered off-label use and has not been reviewed by FDA for safety and efficacy of the product for those uses. FDA does not regulate the practice of medicine, and does not prohibit doctors from prescribing medical products for off-label use. Many products that are used to treat cancer are used off-label, with the intent to prolong life or improve the quality of life. Off-label use is also common for pediatric populations as many products on the market are approved based on studies conducted on adults.

Manufacturers have argued that FDA's regulations regarding communication about off-label use of their products are outdated and have expressed the desire to share information regarding the economic value of their products with payors. Section 2101 would facilitate the dissemination of healthcare economic information to payors, formulary committees, or other similar entities. This proposal would limit the information a manufacturer could share with payors, formulary committees, and other similar entities to "analysis (including the data, inputs, clinical, or other assumptions, methods, results, and other components comprising the analysis) that identifies, measures, or describes the consequences, including the separate or aggregated clinical consequences and costs of the represented health outcomes, of the use of a drug." This clarification will provide manufacturers with the ability to provide information about the economic value of their product to payors, but ensure safeguards continue to remain to prevent the promotion of the product for uses that have not been approved by FDA as being safe and effective. It is important to note that payors and formulary committees are a sophisticated and skeptical audience who are likely to evaluate critically all such information they receive from manufacturers.

G. Subtitle G – Antibiotic Drug Development

i. Section 2121. Approval of Certain Drugs for Use in a Limited Population of Patients

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[16] Food and Drug Admiration, *Draft Guidance for Industry, Expanded Access to Investigational Drugs for Treatment Use – Qs & As* (May 2013) (online at http://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm351261.pdf).

This section reflects a bill sponsored by Reps. Green and Shimkus that would enable antibiotics and antifungal drugs intended to treat serious and life threatening infections to be approved for limited populations based on more limited data than would be needed for approval for broader use. According to the CDC, each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibiotics and at least 23,000 people die each year as a direct result of these infections.[17] However, relatively few companies are investing in developing such drugs because the return on investment is much lower than for other classes of drugs. From an economic perspective, one of the problems of antibiotics is that they work too well. They cure a patient, and do so in a relatively short period of time, and so are not as economically valuable as drugs that have to be taken for a lifetime to treat chronic diseases. Additionally, the need to reserve new antibiotics for use only when necessary depresses their economic return.

FDA strongly supports legislation that would facilitate the approval of important new antibiotics. However, it has significant concerns that the language as drafted would not achieve that goal.

FDA has three principal concerns with the current draft. First, it would force FDA into an unworkable and burdensome meetings process.

Second, it could be read to intend to lower the approval standards. The fact that it provides a list of the kinds of studies and data that FDA may use as a basis for approval for these drugs implies that FDA might otherwise not consider them to be an acceptable basis for approval. The list also could be taken to imply that FDA could use such studies and data as the basis for approval only for this class of drugs, because they are not specified for use in other situations. FDA sees no need for listing the criteria for approval in the legislation.

Third, the bill does not mandate that a logo or statement accompany the name of the drug in all places in which that name is used. The logo or statement is needed to alert doctors, pharmacies and formularies that these drugs were approved based on limited studies, and therefore should only be used in a limited population for which their risk benefit ratio warrants their use. Without the ability to "brand" the drugs in this way, FDA will not have the confidence that the drugs will be appropriately limited in their use. Without such confidence, FDA will not be able to approve them without the level of data and information necessary to show they are safe and effective in a larger population.

Committee staff continue to work with FDA and stakeholders on improving the section.

ii. Section 2122. Susceptibility Test Interpretive Criteria for Microorganisms

This section streamlines the process by which FDA can clear or approve updates to antimicrobial susceptibility testing devices. These test kits help providers and companies determine how well particular antibiotics are working as bacteria develop resistance to them. It directs FDA to establish a dedicated website containing a list of new and updated susceptibility test criteria standards. These standards may be established by recognized standard development

[17] Center for Disease Control and Protection, *Antibiotic/Antimicrobial Resistance* (online at http://www.cdc.gov/drugresistance/).

organizations that meet certain transparency and conflict of interest requirements, if the standards are agreed to by FDA. This section is not in brackets because it reflects input from FDA and has been accepted by the Committee.

iii. Section 2123. Encouraging the Development and Responsible Use of New Antimicrobial Drugs

This section is based closely on the "Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms Act" (DISARM). It provides an additional Medicare reimbursement bump for new "superbug" antibiotics that are developed as a last line of defense against highly-resistant infections. Antibiotic resistance has been named the top public health threat by the World Health Organization (WHO), and accordingly, there has been a worldwide effect to stem the tide of antibiotics use to preserve the antibiotics we have today, and develop new antibiotics that are capable of treating so-called "superbugs" that are virtually impossible to treat. Stewardship of antibiotics and development of new antibiotics is a priority of the Administration, and most recently, Congress incentivized the development of new Antibiotics in the last FDA user fee reauthorization with an additional five years of exclusivity and other FDA regulatory benefits for certain new antibiotics. This provision is a highly complex and technical policy with broad impact, and accordingly, the Committee continues to work in a bipartisan manner on this issue.

H. <u>Subtitle H—Vaccine Access, Certainty, and Innovation</u>

i. Section 2141. Timely Review of Vaccines by the Advisory Committee on Immunization Practices

ii. Section 2142. Review of Processes and Consistency of ACIP Recommendations

iii. Section 2143. Meetings Between CDC and Vaccine Developers

The three sections in this subtitle create and formalize processes for the making of vaccination scheduling recommendations by the advisory committee on immunization practices (ACIP); for CDC review of the ACIP recommendations; and for meetings between CDC and vaccine developers. While the goal of the legislation is to improve all these processes so as to speed up both the development of new vaccines and the scheduling of their use, CDC is concerned that it might, in fact, have the opposite effect.

ACIP currently works very well, it holds meetings regularly, it operates in an open and transparent manner, and it moves as quickly as the data and information allows. There are also questions as to whether CDC is not already being responsive to meeting requests by vaccine manufacturers. Therefore, this section remains under discussion.

I. <u>Subtitle I—Repurposing Drugs for Serious and Life-Threatening Diseases and Conditions</u>

This section is now only a placeholder. Dr. Francis Collins, Director of NIH, has often spoken about his interest in incentivizing the development of drugs that have failed clinical trials because of lack of effectiveness, but were found to be safe. Often there is considerable knowledge about how they work, and they might prove useful for a different indication than the

one that failed the clinical trial, or for the same indication but with a different population subgroup. However, because they are often at the end of their patent life by the time new uses are considered, those new indications are not pursued. There is agreement to discuss with the Majority potential approaches to incentivizing development of such drugs for unmet medical needs for serious and life-threatening illnesses.

J. Subtitle L —Medical Device Regulatory Process Improvements

i. Sections 2181 – 2208. Medical Device

These sections all are intended to improve the efficiency of FDA oversight of medical devices. They address problems and concerns that had been identified by medical device companies. FDA worked closely with the medical device industry to understand their issues and to come up with solutions that addressed them without in any way undermining or weakening FDA's standards and procedures for reviewing and clearing medical devices. We reached agreement with the Majority on these provisions, and thus they are in the draft without brackets.

K. Subtitle M – Sensible Oversight for Technology Which Advances Regulatory Efficiency (SOFTWARE Act)

i. Section 2221. Health software

ii. Section 2222. Applicability and Inapplicability of Regulation

iii. Section 2223. Exclusion From Definition of Device

Mobile medical applications provide individuals with the opportunity to manage their own health and wellness, as well as access health information when needed. The widespread use and development of these types of applications, along with their growing sophistication, has led to questions among manufacturers and application developers about how such medical mobile applications should best be regulated. FDA has maintained that it would only regulate certain applications that pose potential risks to public health, stating in the agency's February 2015 guidance that the agency mobile medical apps are a mobile app that meets the definition of a device, and "either is intended to be used as an accessory to a regulated medical device; or transform a mobile platform into a regulated medical device."[18] FDA also outlined that the agency intends to exercise enforcement discretion over mobile apps that do not meet the definition of a device under FFDCA and pose a lower risk to the public.

Sections 2221, 2222, and 2223 of the discussion draft includes a new version of H.R. 3303, the SOFTWARE Act, which was introduced by Health Subcommittee Ranking Member Gene Green (D-TX), and Reps. Marsha Blackburn (R-TN), Greg Walden (R-OR), Diana DeGette (D-CO), and G.K. Butterfield (D-NC). The language included in the discussion draft defines the term "health software" and "accessory" and clarifies the types of software that will be

[18] FDA, Guidance for Industry and Food and Drug Administration Staff, "Mobile Medical Applications," (February 9, 2015), accessed at: http://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf

regulated by FDA as medical devices. It also directs FDA to promulgate final regulations regarding the regulation of software no later than two years after enactment and to consult with patients, industry, and health care providers, among others, to inform the issuance of these regulations. This proposal is intended to provide creating clarity for developers and reviewers around what constitutes software for purposes of FDA regulation.

FDA had significant concerns with the prior version of these sections. This version is much improved, but discussions continue as there is not yet consensus on language.

L. Subtitle N–Streamlining Clinical Trials

i. Section 2241. Protection of Human Subjects in Research; Applicability of Rules

This section represents a longstanding interest of Rep. DeGette and Rep. McMorris Rogers to improve the efficiency of clinical trials while maintaining protection of the patients in those trials.

A principal effect of the section would be that research covered by both FDA and HHS human subject regulation would be subject only to the relevant FDA regulations. Therefore, it would eliminate HHS authority over research that is also subject to the Food Drug & Cosmetic Act. The Administration believes this could weaken protections over research using human subjects. This section is bracketed as we continue to work on it.

ii. Section 2242. Use of Non-Local Institutional Review Boards for Review of Investigational Device Exemptions and Human Device Exemptions

This section would eliminate a statutory requirement that all medical device research be overseen by local institutional review boards, even when centralized review boards are otherwise acceptable to all parties and would enable a more efficient investigational process.

iii. Section 2243. Alteration or Waivers of Informed Consent for Clinical Investigations

This section would facilitate drug and device research by allowing waivers of informed consent for certain low risk testing while maintaining appropriate human subject protections.

iv. *Section 2261. Silvio O. Conte Senior Biomedical Research Service*

This section would facilitate the hiring and retention of scientific experts at FDA by removing the cap on membership in the Senior Biomedical Research Service, by expanding eligibility to include expert drug and device reviewers, and by raising its salary cap.

v. Section 2262. Enabling FDA Scientific Engagement

This section is aimed at encouraging the Administration to remove barriers to attendance by FDA employees of scientific conferences and meetings.

vi. Section 2264. Collection of Certain Voluntary Information Exempted from Paperwork Reduction Act

This section would ease FDA's collection of certain voluntary information from patients and other stakeholders that may facilitate drug development by exempting it from the PRA.

IV. Title III—DELIVERY

The Centers for Medicare & Medicaid Services (CMS) and HHS Office of the National Coordinator (ONC) will not be testifying at this hearing. The CMS and ONC provisions in this draft are fairly different from the last draft, and most are still under development. DISARM (Sec. 2123, see III., G., iii.), Sunshine Act Exemptions (Sec. 3041), Disposable Medical Technologies (Sec. 3061), and Medicare Part D Patient Safety and Drug Abuse Prevention (Sec. 3151) are bracketed because the language is not final and may change substantially before the next draft. In addition, the sections on Interoperability (Sec. 3001) and Telemedicine (Sec. 3021) are not included in this draft. These policies have broad impact, and the Majority and Minority staffs have agreed to continue working on them in a bipartisan manner.

i. Section 3001. Interoperability

Since 2009, the federal government has invested more than $28 billion through the HITECH Act and subsequent legislation to accelerate the development and adoption of health information technology (health IT). The HHS Office of the National Coordinator (ONC) is responsible for the administration's Health Information Technology efforts. ONC has helped guide our health system into wide use of electronic health records (EHR), but the next, necessary step is EHR interoperability. Though 94 % of hospitals and 78 % of doctors' offices now use certified EHRs, it is imperative that these EHRs are interoperable—that is, that they can exchange information with each other in a meaningful way. Barriers persist in getting widespread and effective *sharing* of this electronic health information. In other words, most of the health care system has adopted health IT, but these health IT systems are not interoperable. ONC is exploring ways to achieve nationwide interoperability of health technology, but ONC recently put out a report identifying barriers. The Committee has agreed to continue working in a bipartisan manner with the Administration on solutions to remove these barriers and achieve nationwide interoperability.

ii. Section 3021. Telemedicine

The Energy and Commerce Committee has long been interested in finding bipartisan solutions to incorporate telemedicine into our health care system. Broadly defined, telemedicine is a method by which health care services can be delivered remotely by relying on information and communication technologies. Such technologies include videoconferencing, Internet links, and mobile devices. The Energy and Commerce Committee Bipartisan Telemedicine Member Working Group continues to work toward a telemedicine policy, and the Committee supports these efforts.

iii. Section 3151. Establishing PDP Safety Program to Prevent Fraud and Abuse in Medicare Prescription Drug Plans

This section is based closely on the Medicare Part D Patient Safety and Drug Abuse Prevention Act. As noted by MedPAC, GAO, OIG and others, there is growing concern about potential overuse and inappropriate prescribing of opioids among Medicare Part D beneficiaries. An evaluation performed by a Centers for Disease Control and Prevention expert panel found that patient review and restriction programs used in state Medicaid programs have generated savings and reduced narcotic prescriptions, abuse, and visits to multiple doctors and emergency rooms. However, current law does not permit the use of such programs in Medicare Part D plans. Essentially, these provisions would require prescription drug plans in Part D to develop a safe prescribing and dispensing program for beneficiaries that are prescribed a high volume of controlled substances. These provisions are also similar to the Medicare Prescription Drug Integrity Act of 2013, and provisions in an earlier draft of the Protecting the Integrity of Medicare Act of 2015 (PIMA). The Committee continues to work towards final language on this provision that appropriately addresses inappropriate prescribing and dispensing of these types of drugs but also ensures that beneficiaries that need these medications do not experience any unintended barriers.

V. WITNESSES

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