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Congress of the United States

House of Representatives

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December 18, 2017

The Honorable Scott Gottlieb
Commissioner
U.S. Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Dr. Gottlieb:

Thank you for appearing before the Subcommittee on Health on November 30, 2017, to testify at the hearing entitled "Implementing the 21st Century Cures Act: An Update from FDA and NIH."

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for ten business days to permit Members to submit additional questions for the record, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please respond to these questions with a transmittal letter by the close of business on January 8, 2017. Your responses should be mailed to Zack Dareshori, Legislative Clerk, Committee on Energy and Commerce, 2125 Rayburn House Office Building, Washington, DC 20515 and e-mailed in Word format to zack.dareshori@mail.house.gov.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

Michael C. Burgess, M.D.
Chairman
Subcommittee on Health

cc: The Honorable Gene Green, Ranking Member, Subcommittee on Health

Attachment

Attachment — Additional Questions for the Record

The Honorable Michael Burgess

1. A goal of 21st Century Cures was to help the transition between research generated by NIH and regulated by FDA. Are there areas where this could be improved? One challenge is that NIH funds new clinical trials that may become difficult to complete because a new drug is approved mid-way through the trial for the condition being researched. Could a "memorandum of understanding" allow for pre-approval data to be shared from FDA to NIH earlier in the process to improve coordination of research and regulation?

2. The Least Burdensome Provisions of the FDA Modernization Act of 1997 have been in statute for some time. This concept—that FDA should regulate medical devices in the least burdensome manner, while not sacrificing patient safety—is critical to ensuring that we have reasonable regulation, and avoid the issue of regulation for regulation's sake. 21st Century Cures included a provision to require FDA to conduct an audit on training and use of least burdensome requirements during review of medical devices. Can you tell us what FDA has been doing to implement this section of the law?

3. Supplemental indications, or additional uses for a drug, can be added to the product label when the sponsor provides the necessary data to the FDA to support these new uses. In many cases, the FDA treats each application associated with a drug the same, whether it is the first indication or the eighth indication. Given that aspects of a drug, such as its toxicity profile, becomes better understood over time, a provision was included in 21st Century Cures to improve the efficiency of reviewing potential new uses of a drug by allowing the FDA to review summaries of data rather than internally re-analyzing the complete raw datasets themselves. I understand this is completely up to the FDA to determine when this approach is appropriate, and the review team would have access to the full data at any point. Has this provision been used? How frequently? Do you foresee instances where this can improve efficiency?

4. Patient-focused drug development was an aspect of 21st Century Cures that garnered a significant amount of attention. The law requires the FDA to provide guidance on the use of relevant patient experience and patient input data, including with respect to the structured risk-benefit assessment framework, to inform regulatory decision making. The 21st Century Cures Act provides a timeframe of 5 years for the FDA to issue such guidance. Could you share your thoughts on the impact patient experience perspective data will have on the drug development front, particularly with respect to the risk-benefit framework?

The Honorable Cathy McMorris Rodgers

When asked about the scope of pharmacy practice this summer, you noted that a prescription provides a "line of demarcation" defining the practice of pharmacy and that "the statute clearly defines in my mind the line of demarcation for the legitimate practice of pharmacy." This statement is consistent with the policies expressed in the guidance document entitled "Prescription Requirement Under Section 503A of the Federal Food, Drug, and Cosmetic Act," which states that unless a limited exception applies "to qualify for exemptions under section 503A, the drug product must be compounded after the licensed pharmacist or licensed physician receives a valid prescription order for an individual patient."

Unfortunately, this view differs with FDA policies over the past two years. The agency has redefined the distribution of a sterile compounded preparation to include patient specific dispensing in the draft MOU and repackaging guidance (among other guidances). This, in my opinion, appears to run counter to the DQSA's statutory language, the Food Drug and Cosmetic Act, as well FDA's traditional interpretation of the definitions of "distribute" and "dispense" and will reduce access to compounded sterile preparation prescriptions.

1. Please share with the committee your thoughts on the definitions of "dispense" and "distribute", and how you plan to align the MOU and other guidance with Congress' and your understanding of pharmacy practice.

The Honorable Marsha Blackburn

1. I was glad to speak with you back in July when you called to tell me about your implementation of my SOFTWARE Act with the Pre-Cert for Software Pilot Program and the announcement of the companies selected to participate. Could you please provide this committee with an update on the pilot program, including feedback from the nine participating companies? What lessons has the agency learned so far about how best to regulate innovative, low-risk devices and software?

The Honorable Ben Lujan

Thank you for your response on November 7, 2017, to my letter asking the Food and Drug Administration (FDA) to take concrete steps to enable and communicate the availability of safe and effective, non-opioid drug products. As you know, millions of Americans require clinical treatment for pain relief. I was glad to see that we are in agreement about the importance of combating the opioid epidemic, as you wrote in your November 7 letter.[1]

In light of FDA's belief that all healthcare providers involved in the management of pain should be educated about the safe use of opioids, I would appreciate information related to the following questions:

[1] "FDA believes that all healthcare providers involved in the management of pain should be educated about the safe use of opioids," and "Reducing the scope of the epidemic of opioid addiction is my highest immediate priority as Commissioner." (Dr. Scott Gottlieb, November 7, 2017 letter to Congressman Ben Ray Luján)

1. You wrote, "For the first time, FDA announced its intention to require immediate-release (IR) opioid analgesic products to be subject to the same REMS requirements." You also note that you expect the modified REMS to include revisions related to prescriber education.

    a. What is the agency's timeline to finalize a modified REMS? What considerations is the agency taking into account when considering changes to the education requirements related to the REMS?

2. You wrote, "The new training will be aimed at making sure providers are prescribing opioids only for properly-indicated patients, and only under appropriate clinical circumstances [...as] part of a broader effort to take new steps to make sure providers are properly informed about suitable prescribing and the risks and benefits associated with opioid drugs."

    a. What additional activities does FDA's broader effort include? Who within FDA is responsible for this broader effort to inform providers about suitable prescribing?

2. You wrote, "There have been a small number of non-opioid drug shortages over the past few years, but there continue to be multiple alternative options available to patients."

    a. What are these multiple alternative options to non-opioid drugs that are available to patients? How many alternative options to non-opioid drugs are available to patients?

3. You wrote, "There are few existing classes of analgesics." In Division Director of the Division of Anesthesia, Analgesia, and Addiction Products Dr. Sharon Hertz's March 1, 2016 presentation to the FDA Science Board, she listed existing analgesics as opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), anticonvulsants, antidepressants, local anesthetics, and "other (capsaicin and ziconotide)."[2]

    a. Are these six classes a comprehensive list of existing analgesic drug classes? If not, what additional or alternative classes are there?

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[2] Hertz, Sharon, Division of Anesthesia, Analgesia and Addiction Products, OND, CDER, FDA, "Challenge of developing new pain medicines – developing novel analgesics and abuse-deterrent formulations," March 1, 2016, https://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/ScienceBoardtotheFoodandDrugAdministration/UCM489207.pdf

4. You wrote, "Drug developers may encounter both clinical and nonclinical challenges specific to their drug development program."

    a. What are some examples of clinical and nonclinical challenges that drug developers have faced? Is there a trend of where in the development or regulatory processes the challenges are faced? For example, are the challenges primarily in the review or in the post-market phase? What are some potential incentives to increase the number of non-opioid drugs in the pipeline? Is the main challenge increasing the number of drugs entering the pipeline, or increasing the number of drugs coming out of the pipeline? Do you consider FDA barriers to be clinical or nonclinical?

5. You wrote, "The Agency is open to working with sponsors who are interested in developing new potential treatments."

    a. Have any sponsors already asked FDA to work together to develop new potential treatments? If so, what did FDA respond?

6. You wrote, "Moving forward, we strongly encourage manufacturers and drug developers to contact the Division of Anesthesia, Analgesia, and Addiction Products in the Center for Drug Evaluation and Research so that we can provide targeted advice specific to their drug development program."

    a. Have any manufacturers contacted DAAAP in CDER to request targeted advice specific to their drug development programs? Has FDA provided targeted advice specific to drug development programs?

7. You wrote, "For more information, please see our draft guidance entitled *Analgesic Indications: Developing Drug and Biological Products,* which, when finalized, will provide the Agency's recommendations on such development."

    a. The draft guidance was released in February 2014, "for comment purposes only." It had a 60-day comment period. Since February 2014, approximately 190,000 Americans have died due to opioid overdoses.[3] Is FDA currently in the process of finalizing the guidance? If available, when does FDA anticipate publishing the finalized guidance?

[3] 1,396 days between February 2014 and November 2017; according to CDC estimates, 50,000 Americans died from an opioid overdose in 2016, which is 137 people per day, Time Magazine, "Here's what it would cost to fix the opioid crisis, according to 5 experts," http://time.com/money/5032445/cost-fix-opioid-crisis/

8. You wrote, "We have been involved in discussions with the National Institutes of Health in a series of meetings to facilitate development of non-addictive pain treatment."

    a. What is the structure of this series of meetings? Who is the designated point person at FDA and who is the designated point person at NIH for these meetings? Can I communicate directly with those point people for the meetings? What are the goals of these meetings? Are these meetings open to the public? How many meetings are in the series? How many have already been held? How many are scheduled to occur? When do these meetings occur? Where do these meetings occur?

9. You wrote, "Novel non-opioid medications with the potential to provide effective pain relief, and that satisfy the applicable legal criteria, may be appropriate candidates for such programs," referring to "programs, such as Fast Track and Breakthrough Therapy Designation, which are intended to facilitate the development and expedite the review of products that, for example, are intended to treat a serious condition for which there is an unmet medical need."

    a. How many non-opioid products are currently under review for management/treatment of pain? Of the current products under review, how many/what percentage have applied for and been awarded one of these designations? Are there other tools at your disposal to move these applications through in a timely fashion? If not, what can Congress do to help? In addition to new product approvals, please describe how manufacturers can seek new indications, expanded labels and/or different concentration approvals for non-opioid products already available to patients.

Additionally, please address remaining concerns from my previous letter that you did not address in your November 7 letter:

10. How will FDA address the use of unapproved non-opioid products or unapproved uses of non-opioid products for treatment of acute and chronic pain management? Does the agency intend to incorporate guidance for healthcare practitioners related to the use of unapproved non-opioid products or unapproved uses of non-opioid products for pain management?

11. In my letter on August 31, 2017, I asked: Is FDA aware of any shortage of non-opioid drug products that have been approved to date for the treatment of pain? If so, please provide further information related to the non-opioid drug products that are in shortage, the duration of such shortages, and the steps the agency has taken to address such shortage.

    You wrote in your November 7, 2017 letter, "There have been a small number of non-opioid drug shortages over the past few years," but you did not provide further information related to the non-opioid drug products that are in shortage, the duration of such shortages, and the steps the agency has taken to address such shortage.

    a. As a result, I now ask that you address the following questions:
    b. How many non-opioid drug shortages have occurred between 2007 and 2017?
    c. Which non-opioid drug products have been in shortage?
    d. What was the duration of each shortage?
    e. What was the shortfall in each of those shortages?

12. I asked: Would acute or chronic pain meet FDA's interpretation of "serious condition" for purposes of the agency's expedited programs? If FDA does not interpret current legal authorities to allow such application, why not? What revisions might enable the use of such authorities? Would FDA support such revision? In your November 7, 2017 letter, you did not answer these questions. Please do so now.

I look forward to your responses to, and discussion of, the foregoing questions. Once again, I appreciate your support in moving these vital efforts forward.