March 16, 2018

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


***Sent via Electronic Submission***

Dear Dr. Gottlieb,

ASCO is pleased to provide comments on the “Opioid Policy Steering Committee: Prescribing Intervention—Exploring a Strategy for Implementation; Public Hearing; Request for Comments.”

ASCO is the national organization representing nearly 45,000 physicians and other healthcare professionals specializing in cancer treatment, diagnosis, and prevention. ASCO members are also dedicated to conducting research that leads to improved patient outcomes, and we are committed to ensuring that evidence-based practice for the prevention, diagnosis, and treatment of cancer are available to all Americans.

The opioid epidemic continues to grip the nation; recent data from the Centers for Disease Control and Prevention (CDC) indicates that, on average, emergency department visits for opioid overdoses rose 30 percent across the country from July 2016 through September 2017. A large and growing driver in this epidemic is the use of illicit fentanyl and heroin, which has overtaken prescription opioids as the leading cause of opioid overdose death. The federal government is appropriately approaching this problem on all fronts, including law enforcement, legislation, research, public education, and regulatory and policy changes.

As part of the federal government’s response, the FDA has been examining steps it can take, within its authority, to decrease the amount of prescription opioids that are available for potential misuse or abuse. The FDA has fittingly looked along the entire continuum of a medical opioid prescription, from when a prescriber first considers an opioid prescription for a patient through to the eventuality of unwanted or leftover pills in medicine cabinets across the country. The FDA’s approach has therefore been to look for discrete points along this continuum where the availability of opioids can be lessened.
One of the initial points, of course, is the decision by a healthcare provider to prescribe opioids; here, the FDA is examining the education of healthcare providers and recently released its revised “Blueprint” for healthcare provider opioid education. Patients must also be informed of and understand the risks and benefits of opioid therapy; here, the FDA has approved a Medication Guide and is considering a public health campaign. Patients must also understand the importance of safe storage and disposal; here, the FDA provides information to the public on its website on safe storage of opioids and safe disposal mechanisms such as in-home disposal or drug take-back programs. Finally, the FDA is actively examining its opioid Risk Evaluation and Mitigation Strategy (REMS), under which it may require more safeguards, such as Elements to Assure Safe Use (ETASU). ETASU may include requirements such as physician or patient registration, consent agreements, and other steps the FDA deems necessary to ensure that risks of a drug are mitigated to the extent possible.

We thank the FDA for engaging all stakeholders as the agency considers what next steps to take in its approach to this epidemic. ASCO has taken advantage of this opportunity for public engagement provided by the FDA by submitting earlier letters and comments for consideration, highlighting the special needs of patients with cancer. We have also attended numerous public meetings held by the FDA, including most recently the public hearing entitled, “Opioid Policy Steering Committee: Prescribing Intervention—Exploring a Strategy for Implementation” and the “Public Workshop: Strategies for Promoting the Safe Use and Appropriate Prescribing of Prescription Opioids” sponsored by the Duke Margolis Center for Health Policy, at which the FDA Commissioner, Dr. Scott Gottlieb, provided remarks.

ASCO is very supportive of efforts to mitigate opioid misuse or abuse. As a professional medical society representing professionals who care for patients with cancer, we have advocated for policies that stem the tide of any unneeded opioids, while ensuring access to opioid therapies for patients who need them. We have also encouraged policymakers to examine the impact any changes in laws or regulations have on access, in addition to endpoints such as overdose or number of prescriptions filled. ASCO also participates in the AMA Opioid Task Force, which seeks to involve all healthcare providers in curbing the opioid epidemic, with efforts ranging from provider education to awareness campaigns to offering constructive suggestions to lawmakers.

Below we offer our comments on the questions posed by FDA in its Request for Comments.

**Prescriber Documentation**

1. *If a Risk Evaluation and Mitigation Strategy (REMS) were to specify threshold drug amounts for opioid analgesic prescriptions above which prescribers would be required to provide additional documentation of medical necessity, what should the amounts be and how should they be determined for various clinical indications? What data are there to support such amounts? What additional data would be useful?*

2. *If such measures were required, how should prescribers be made aware of them? Within the Agency’s statutory REMS authority, how should the Agency require sponsors to ensure compliance with them? How should the Agency require sponsors to assess their effect in reducing misuse, abuse, and new addictions?*

ASCO understands that with these approaches the FDA is attempting to decrease prescriptions for “unnecessarily” large amounts of opioids, particularly in the primary/acute pain care settings. The FDA has also previously asked whether specialty societies should be involved in the drafting of guidelines for prescribing opioids for specific conditions. ASCO has stated previously that an approach involving
prescription limits or “unit-of-use” packaging may work for acute, self-limiting conditions such as post-operative settings, but that pain management in the oncology setting is more complex and may require not only higher doses of opioids and chronic administration, but a combination of therapies to achieve desired outcomes.

As emphasized by patient groups and others at the Duke Margolis Center for Health Policy public meeting, we must also look for unintended consequences secondary to threshold drug amounts. Patient groups focused on long-term management of chronic pain continue to raise concerns that patients in legitimate need of these medications are being stigmatized, abandoned, or forced to significantly decrease daily doses that may have served them well for years. These unintended consequences should always be monitored as outcomes secondary to any regulatory or policy changes.

Some individual health plans, drug plans, and states have already begun instituting “hard” limits at the point of sale (i.e. the pharmacy) for dose limits and/or time limits. Most of these limits exempt certain patient populations such as patients in palliative care, patients in hospice care, and patients with cancer. We would urge the FDA to work with sponsors to ensure that any such program as implemented would not adversely impact access for these patients.

Additional REMS Approaches

3. The Steering Committee requests input from the public on whether, in addition to, or in conjunction with the above described prescriber intervention, and to the extent consistent with its statutory authority, the Agency should consider requiring sponsors to create a system that utilizes a nationwide prescription history database to facilitate safe use of opioid analgesics.

4. If this approach were adopted, how should the Agency require sponsors to assess the impact of such requirements?

Prescription drug monitoring databases (PDMPs) have seen a significant increase in use over the past several years. Many states now require prescriber registration with their state PDMP, and mandate regular interval checks of such databases for patients receiving opioids. Forty-nine states, the District of Columbia, and at least one county in Missouri maintain a PDMP, with varying requirements for prescribers and pharmacists.

According to the National Association of State Controlled Substances Authorities¹, 49 states, the District of Columbia, and one county in Missouri use the same standard for data reporting to their PDMPs, and 44 PDMPs currently share data via “PMP Interconnect.” PMP Interconnect was developed by the National Association of Boards of Pharmacy² in 2012, in response to member requests for PDMP interstate data sharing. Additionally, eight states have also received funding to provide “in workflow” PDMPs (i.e. integration of the PDMP into the EMR workflow).

Although some progress has been made in PDMP interoperability, ASCO members continue to report end-user frustration with these systems. Providers who see patients from multiple states—or whose patients see physicians in multiple states—may need to register for multiple PDMPs and experience difficulty in navigating to needed information. As pointed out during the January 30th FDA public

---

¹ Presented at the Opioid Policy Steering Committee Public Hearing, January 30, 2018
² Ibid
hearing, another flaw in the system consists of an inability to do a “broadcast” query on an individual patient. In other words, the provider must determine which states’ PDMPs to check for each individual patient and may therefore be unaware of additional pertinent information held in other states’ PDMPs. ASCO members have also suggested that a more “proactive” PDMP system that pushes alerts to providers could be helpful.

Clearly, a more robust, interoperable system is needed that would allow for checking of the information from numerous states and would also allow for seamless integration of PDMP use into the EMR workflow. While progress is being made, it is having difficulty keeping pace with the needs of—and requirements placed on—providers. The question posed by the FDA regarding a possible nationwide database created by sponsors is a natural one under these circumstances. There is a desire for a simple, streamlined system that would allow for nationwide checking of opioid prescription history, and the existing patchwork of state systems has not so far achieved that aim.

Ultimately, this decision will be driven by patient safety considerations and provider needs for current data without regard for state lines. The FDA and other stakeholders will no doubt have to consider the costs associated with such a decision—e.g. the costs already borne by the states, the “sunk” costs associated with the state PDMPs, the cost of setting up a new nationwide system—as well as other factors such as the feasibility of importation of existing data into a new system, and what role existing state PDMPs would then play (e.g. states have different requirements for the controlled substances they monitor).

The impact of any system that maintains information on patient opioid use, regardless of underlying source (state vs. national/sponsor), should always include an assessment of the unintended consequence of patients being unable to access needed therapies. If a nationwide sponsor-created system is instituted, impact assessment should also include ease of use, timeliness and usefulness of information provided, and how the data is being used to identify “aberrant” prescribers. As ASCO has stated previously, certain providers, including oncologists, can be expected to write more opioid prescriptions than providers in other specialties, therefore any assessment of prescribing patterns should factor in provider specialty, patient population, and any further clinical sub-specialization.

Additional Considerations

5. The proposed Opioid Analgesics REMS includes a Medication Guide and a Patient Counseling Document to educate patients. It also includes a Blueprint for Health Care Providers Involved in the Management or Support of Patients with Pain that contains information on counseling patients and caregivers about the safe use of opioid analgesics. Consistent with its statutory authority, should FDA require sponsors to take additional measures to ensure that health care providers, their patients, and patient caregivers and family members are educated on safe storage and disposal and the risks of misuse, abuse, and addiction associated with opioid analgesics (e.g., a public health campaign targeted at these groups)?

ASCO is strongly supportive of education across all stakeholder populations, and we provide both provider and patient education on pain management and the use of opioid therapies. ASCO has developed a clinical practice guideline on Management of Chronic Pain in Survivors of Adult Cancers. Our guideline development process and conflict of interest policies are rigorous and available online. In addition to the guideline, we have developed multiple resources for clinicians, including Universal Precautions in Chronic Cancer Pain Management and Opioid Risk Stratification and Adherence Monitoring. Additional offerings include guideline pocket cards and mobile apps.
Our patient-centered website, Cancer.net, provides physician-reviewed information on all aspects of the cancer experience, and is a rich resource for patient-centered information on pain. Resources include information on non-pharmacologic and pharmacologic management of pain, the risks and benefits of different approaches to pain management, and a 36-page booklet on Managing Cancer-Related Pain. Cancer.net also provides information regarding the safe storage and disposal of opioids, such as our patient fact sheet, Safe Storage & Disposal of Pain Medications.

Each member and institution in the medical ecosystem has its own role to play in helping to curb the opioid epidemic, and we agree with the FDA that education is a key component. In the aggregate, sponsors may have a wider reach to the general public through mediums such as radio, television, and social media, and a fact-based, thoughtful, carefully-constructed message on opioid safety—especially as it pertains to safe handling, storage, and disposal—could help raise awareness of concrete ways each individual may contribute to opioid safety.

6. Should the Agency consider additional measures intended to improve the safety of patient storage and handling of opioid analgesics?

Various stakeholders are examining mechanisms to improve the safe storage of opioids, including basic approaches such as lock-boxes and more complex approaches involving radiofrequency ID (RFID), bottles that dispense only the needed number of units at pre-defined intervals, and other processes taking advantage of health information technology. While we encourage the exploration of such practical approaches to safe storage, until these solutions are more widely available we believe that patient and caregiver/family education is critical. Providers who prescribe opioids, state public health agencies, and the federal government can all play a role in impressing upon patients and the public the importance of safe handling and storage, and this message should be emphasized at every turn.

7. How might use of unit-of-use packaging play a role in encouraging appropriate prescribing of opioid analgesics?

As stated earlier in these comments, ASCO believes such an approach may be feasible in acute, self-limiting conditions such as post-operative pain, but does not believe that unit-of-use packaging is appropriate in cancer care.

8. Should the Agency require sponsors to create a mechanism by which patients could return unused pills, and if so, to whom?

Unused pills in the home can certainly present an unnecessary hazard, and statistics point to a disturbing number people who admit to obtaining prescription opioids from friends or family. ASCO supports “take-back” programs and has made information on these programs available on its patient website. Existing take-back sites include some pharmacy chain locations; in addition, sponsored events throughout the year provide additional opportunities for households to rid themselves of unwanted prescription medications. However, not all patients can easily find information on how to dispose of unwanted medications, and the sporadic nature of “take-back” events may make it difficult for patients to identify opportunities in their communities. Due to the possibility of theft and potential associated injury and liability, it is crucial that these take-back sites are secure, and/or pills are promptly destroyed or removed to secure locations. Given that pharmacies that dispense opioids have mechanisms in place for safe storage, we would encourage these pharmacies to also act as take-back locations. In addition, secure public spaces such as police stations might be considered. Finally, at least one state legislature
has suggested that physician offices could provide such services; some practices may be willing and able to function as take-back sites, but the same cautions regarding safety and security would apply, and participation should be voluntary based on the practice’s assessment of its capabilities.

We thank the FDA for the opportunity to provide these comments and look forward to working with the agency on this issue.

Sincerely,

Bruce E. Johnson, MD, FASCO
President, American Society of Clinical Oncology