December 19, 2017

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

Re: FDA-2017-N-5608

Dear Commissioner Gottlieb:

The American Cancer Society Cancer Action Network (ACS CAN) appreciates the opportunity to submit comments regarding questions relevant to the Food and Drug Administration's (FDA's) newly established Opioid Policy Steering Committee. ACS CAN, the nonprofit, nonpartisan advocacy affiliate of the American Cancer Society, supports evidence-based policy and legislative solutions designed to eliminate cancer as a major health problem. As the nation's leading advocate for public policies that are helping to defeat cancer, ACS CAN ensures that cancer patients, survivors, and their families have a voice in public policy matters at all levels of government.

We share the FDA's concern about the public health emergency that exists today as a result of inappropriate use of prescription opioids and the harms associated with such use. As a nation, we must take steps to address the issue and ACS CAN welcomes the opportunity to represent the voices of cancer patients and survivors in such efforts. Many cancer patients and survivors legitimately need access to opioids to treat their pain. However we also recognize that our patient population is not immune to the risks of opioid addiction, particularly as more and more cancer patients survive their treatment and go on to live longer lives. ACS CAN supports policies that take a reasonable, balanced approach to addressing the opioid addiction epidemic and its associated risks, without harming patients who are using the medications appropriately to treat their pain.

Pain is one of the most feared symptoms for cancer patients and survivors - nearly 60 percent of patients in active treatment and 30 percent of patients who have completed treatment experience pain.[1] Pain can be caused by the cancer itself, for instance when tumors interfere with normal body function. Pain can also be caused by cancer treatments. For example, research has concluded that about one-quarter of women who have had breast cancer surgery

[1] Institute of Medicine. (2011). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education and Research. National Academy of Sciences.

have significant and persistent breast pain six months after the procedure.[2] Integrative pain care that includes non-drug therapies along with medications is encouraged to keep patient pain under control. While not the only tool, opioid medications are recognized as a mainstay of treatment for moderate to severe cancer pain and can be a beneficial treatment for managing serious, persistent pain for patients being actively treated for cancer and for cancer survivors.

ACS CAN believes in a balanced approach that recognizes the need to maintain access to pain medication for individuals with cancer and other diseases whose pain otherwise prevents them from working, living independently and enjoying a quality of life. We are concerned that the emphasis on reducing inappropriate use of opioids often ignores how these efforts may impede medically necessary access to these products, and we continue to have these concerns after reviewing the policies FDA discusses in this docket.

I. Assessing Benefit and Risk in the Opioids Setting

FDA asks for comments on its approach to assessing benefits and risks when making regulatory decisions regarding opioids, specifically:

1. *How should FDA tailor, or otherwise amend, its assessment of benefit and risk in the context of opioid drugs to ensure that the Agency is giving adequate consideration to the risks associated with the labeled indication of these drugs and the risks associated with the potential abuse and misuse of these products?*
2. *Are there specific public health considerations other than misuse and abuse that FDA should incorporate into its current framework for benefit and risk assessment as a way to reduce the opioid addiction epidemic? That framework includes, but is not limited to, how FDA makes regulatory decisions to approve new opioids, evaluates their use in the postmarket setting, or limits or influences their prescribing through product labeling or other risk management measures.*

ACS CAN comments: We are concerned that both of these questions focus almost exclusively on the risks of opioids without acknowledging or asking for comments on the benefits. When making the types of decisions referenced here and in the rest of FDA's questions, we urge FDA to not forget the many cancer patients and survivors with serious pain who benefit from treatment with opioids. In fact, the foundational article referenced in FDA's prelude to these questions acknowledges in its first paragraph that opioids "have significant benefits when used as prescribed."[3]

As FDA alludes to in its question, there are public health considerations to be made when examining the risks of opioids. But there are also public health benefits to consider. Appropriately treating patients with cancer and other serious illnesses and alleviating their pain

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[2] Miaskowski C, Cooper B, Paul SM, et al. (2012). Identification of Patient Subgroups and Risk Factors for Persistent Breast Pain Following Breast Cancer Surgery. J Pain; 13(12) pp 1172-1187.

[3] Gottlieb, Scott and J. Woodcock. "Marshaling FDA Benefit-Risk Expertise to Address the Current Opioid Abuse Epidemic." Journal of the American Medical Association. *2017;318(5):421-422. Doi:10.1001/jama.2017.9205.* Available at http://jamanetwork.com/journals/jama/fullarticle/2643333.

have public health and wider societal benefits. Physical activity is beneficial after a cancer diagnosis, reducing the risk of recurrence or death and improving quality of life.[4] A patient whose pain is appropriately treated is more likely to be able to engage in physical activity, and therefore reduce their risk for cancer or a recurrence. Additionally, patients whose pain is appropriately managed may be able to return more easily to their normal functions of daily living, and to work. Pain is a consistent predictor of poor work outcomes in the general population[5,6] and while not well documented for cancer patients specifically, there is some evidence of similar findings.[7] For example, among breast cancer patients, women with arm pain and range of motion limitations are more likely to experience losses in productivity compared to women without pain.[8]

Regarding using a benefit/risk framework to make decisions on approving new opioids, while we agree the risks of misuse and abuse must be considered, cancer patients should not be denied access to an innovative new treatment based solely on the risk of people using the drug illegally or misusing their prescribed drug. FDA already has a process to consider and address such risks through the Approved Risk Evaluation and Mitigation Strategies (REMS) program. We encourage FDA to use this tool, which is already at its disposal, to consider potential new drug approvals.

Regarding FDA evaluations in postmarket settings, we again urge FDA to consider the benefits as well as risks. Additionally, we support FDA and other agencies collecting more data after an opioid has already been introduced into the market and performing evidence-based analysis to answer such questions as:

- What particular populations are at risk for misusing or abusing opioids, particularly in the context of patients who are being treated for pain?
- To what extent are risk factors evident in patients who are legitimately being treated with opioids, as opposed to individuals who are misusing an opioid prescription or obtaining the drug through some other means?
- What are evidence-based risk mitigation strategies?
- How are current guidelines, like the Centers for Disease Control and Prevention (CDC) Guideline, impacting patient access to opioids? Such an analysis must go beyond simply examining whether use of opioids or number of prescriptions has decreased, because those simple data points do not differentiate between appropriate and inappropriate, or legal and illegal use.

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[4] Rock CL, Doyle C, Demark-Wahnefried W, et al. Nutrition and Physical Activity Guidelines for Cancer Survivors. CA Cancer J Clin 2012; doi: 10.3322/caac.21142

[5] Breivik H, Cherny N, Collett B, et al: Cancer-related pain: a pan-European survey of prevalence, treatment, and patient attitudes. Ann Oncol 20:1420-33, 2009

[6] Cancelliere C, Donovan J, Stochkendahl MJ, et al: Factors affecting return to work after injury or illness: best evidence synthesis of systematic reviews. Chiropr Man Therap 24:32, 2016

[7] Guy GP, Jr., Ekwueme DU, Yabroff KR, et al: Economic burden of cancer survivorship among adults in the United States. J Clin Oncol 31:3749-57, 2013

[8] Quinlan E, Thomas-MacLean R, Hack T, et al: The impact of breast cancer among Canadian women: disability and productivity. Work 34:285-96, 2009

- How are prescribing limits impacting patient access to opioids? Such an analysis must go beyond simply examining whether use of opioids or number of prescriptions has decreased, because those simple data points do not differentiate between appropriate and inappropriate, or legal and illegal use.

Postmarket analyses must include the impacts on patients who do or could benefit from proper treatment with opioids.

II. Steps to Promote Proper Prescribing and Dispensing

FDA references the 2016 Centers for Disease Control and Prevention (CDC) *Guideline for Prescribing Opioids for Chronic Pain*[9](CDC Guideline) while asking for comments regarding steps it could take to promote proper prescribing and dispensing, specifically:

1. *Should FDA consider adding a recommended duration of treatment for specific types of patient needs (e.g., for specific types of surgical procedures) to opioid analgesic product labeling? Or, should FDA work with prescriber groups that could, in turn, develop expert guidelines on proper prescribing by indication?*

ACS CAN comments: ACS CAN urges FDA to clarify what it considers to be "proper prescribing and dispensing" – and to use a standard supported by adequate, high-quality evidence. ACS CAN does not believe that the CDC Guideline meets this evidentiary standard. ACS CAN expressed strong objections to the CDC Guideline when it was drafted,[10] including the lack of evidence on which the guideline is based and the methodology used to develop the document.

Our concerns regarding the evidence used to justify the recommendations in the CDC Guideline are particularly relevant to this question. CDC purported to follow a widely used framework for producing evidence-based recommendations; however, the 12 recommendations were based on "very low quality of evidence" or on "low quality of evidence," yet six of the seven recommendations with evidence rated "very low" and all of the recommendations with "low" evidence ratings were designated as "strong" recommendations. The discordance between strength of evidence and strength of recommendations seems to indicate that the rationale statements relied heavily on expert opinion, but this was not explicitly acknowledged.

Expert opinion has a role in the practice of medicine, but not in FDA labeling, therefore we strongly suggest that any provision of information regarding prescribing be done outside of the product label unless it meets the high evidentiary bar expected for other information found in the label. Furthermore, if FDA were to move forward with such changes, we strongly urge the agency to use a process that is open, transparent, and involves the opportunity for public comment.

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[9] Dowell, D., T. M. Haegerich, and R. Chou. "CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016." Item 6 in "Determining When to Initiate or Continue Opioids for Chronic Pain." Morbidity and Mortality Weekly Report Recommendations and Reports 2016;65(No. RR-1):1-49. DOI: http://dx.doi.org/10.15585/mmwr.rr6501e1.

[10] See ACS CAN comments on the Centers for Disease Control and Prevention's (CDC's) Draft Guideline for Prescribing Opioids for Chronic Pain, 2016. Submitted October 1, 2015. Available at: https://www.acscan.org/sites/default/files/ACSCAN_Comments_CDC_Opioid_Guidelines_Final.pdf

Of the two options posed in FDA's question, ACS CAN would recommend FDA implement the second, "work with prescriber groups that could, in turn, develop expert guidelines on proper prescribing by indication."

2. *If opioid product labeling contained recommended duration of treatment for certain common types of patient needs, how should this information be used by FDA, other state and Federal health agencies, providers, and other intermediaries, such as health plans and pharmacy benefit managers, as the basis for making sure that opioid drug dispensing more appropriately and consistently aligns with the type of patient need for which a prescription is being written?*

ACS CAN comments: FDA must seriously consider the impact of requiring recommended treatment duration information on opioid package labeling. It is likely, as the question implies, that this information would have serious influence on all the stakeholders referenced. Again, we recommend that FDA not use product labels as a tool to influence prescribing or dispensing. But if FDA does move forward with such changes to labels, we urge the agency to conduct extensive consumer testing and outreach to stakeholders before such requirements are launched to determine the likely impacts and refine its requirements. Additionally, FDA must monitor the impact of such requirements post-launch for unintended consequences and potential course correction.

III. Requirements for Prescriber Education

In light of recent discussions and new rules being implemented or discussed in certain states, FDA asks for comments on mandating education or training for healthcare professionals who prescribe opioids, including specifically:

1. *Are there circumstances under which FDA should require some form of mandatory education for health care professionals to ensure that prescribing professionals are informed about appropriate prescribing and pain management recommendations, understand how to identify the risk of abuse in individual patients, know how to get patients with a substance use disorder into treatment, and know how to prescribe treatment for—and properly manage—patients with substance use disorders, among other educational goals? Are there other steps FDA could take to educate health care professionals to ensure that prescribing professionals are informed about appropriate prescribing and pain management recommendations?*
2. *How might FDA operationalize such a requirement if it were to pursue this policy goal? For example, should mandatory education apply to all prescribing health care professionals, or only a subset of prescribing health care professionals? If only a subset, how would FDA construct a framework that focuses mandatory education on only that subset—for example, by requiring mandatory education only for those writing prescriptions for longer durations as opposed to those for very short-term use?*
3. *What steps should FDA take to make implementing such mandatory education efficient and more feasible? For example, should FDA work collaboratively with state public health agencies, state licensing boards, provider organizations, such as medical specialty*

societies and health plans, or with other stakeholders, such as pharmacy benefit managers, to integrate or avoid duplicating their educational programs or requirements? What other steps might FDA consider to make implementation less burdensome and more effective?

ACS CAN comments: ACS CAN agrees with FDA that provider education is an important way to address the opioid epidemic. We also view this as an opportunity to educate more providers on palliative care and pain management more generally. ACS CAN has identified expanding provider education on palliative care – along with building public awareness and increasing research – as a top organizational priority.[11]

While ACS CAN is open to reasonable education requirements being developed for prescribers of opioids, we stress that any requirements should be harmonized to the greatest degree possible across agencies and entities with a stake in such education, including, but not limited to DEA, CMS, and state and professional licensing and accreditation bodies.

If FDA is to create such requirements or engage with other agencies or partners in instituting education requirements, it is crucial that such requirements do not negatively impact appropriate patient access to opioids, pain management treatment more generally, or palliative care for patients who have a legitimate medical need. Excessive or uncoordinated requirements could prompt providers to simply forgo certification and therefore treatment of patients in pain. FDA must closely monitor the effects of any new requirements to determine how they are impacting treatment access.

It is also important to recognize that medical recommendations for multi-modal pain management frequently are not matched by corresponding coverage by insurers, setting up the possibility that education would be moot if providers cannot provide the recommended care because of payment restrictions.

IV. Additional Matters for Consideration

FDA invites interested parties to submit additional policy considerations or recommendations for actions that FDA could or should undertake to help the Agency better address the opioid addiction crisis.

ACS CAN comments: ACS CAN believes there are other policy changes the Opioid Policy Steering Committee should seriously consider to reduce misuse and abuse of opioids without denying access to cancer patients and survivors who need pain treatment. ACS CAN encourages the committee to consider the following actions:

- Expanding drug take-back programs that allow patients to safely dispose of unused or expired medications. FDA could explore changes to package labeling that provide patients with information about how to safely dispose of medications, and the particular importance of doing so with certain types of medications, including opioids;

[11] See http://patientqualityoflife.org/wp-content/uploads/2017/04/PQLC-PCHETA-Bill-Summary-115th-Congress-03.28.2017.pdf

- Requiring childproof packaging;
- Requiring manufacturers to provide opioids in blister packs for short duration treatments; and
- Encouraging or requiring states that have not already done so to provide interoperability in the state's prescription drug monitoring program with neighboring states.

Additionally, ACS CAN urges FDA and other federal and state agencies to engage in careful implementation monitoring. We are concerned that many surveillance efforts regarding the opioid epidemic seem to focus solely on the efforts' impact on overall prescribing or opioid utilization – not making any distinctions between reductions in access to opioids for patients who truly need them versus patients or users who are not appropriate recipients. FDA and other stakeholders must develop and use more sophisticated evaluative instruments to truly see the impact of education requirements and any other policies that could impact patient access.

Lastly, ACS CAN encourages FDA to work with other relevant agencies to focus more research and evidence development on pain management, particularly non-opioid or less addictive options. While we recognize that such research is not always within FDA's scope, FDA is an important stakeholder in this area. ACS CAN is supportive of the National Pain Strategy[12] and the Federal Pain Research Strategy,[13] and we urge FDA to continue to participate in these and other important multi-stakeholder efforts to increase research and give clinicians and cancer patients more tools to effectively manage pain.

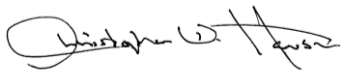
Conclusion

On behalf of the American Cancer Society Cancer Action Network we thank you for the opportunity to submit comments to the FDA Opioid Policy Steering Committee. We stand ready to work with you and other stakeholders to address the opioid crisis while also ensuring that cancer patients and survivors maintain access to the treatments they need. If you have any

[12] National Pain Strategy: A Comprehensive Population Health-Level Strategy for Pain. https://iprcc.nih.gov/sites/default/files/HHSNational_Pain_Strategy_508C.pdf
[13] Interagency Pain Research Coordinating Committee. Federal Pain Research Strategy. https://iprcc.nih.gov/sites/default/files/iprcc/FPRS_Research_Recommendations_Final_508C.pdf

questions, please feel free to contact me or have your staff contact Keysha Brooks-Coley, Senior Director of Strategic Alliances, at Keysha.Brooks-Coley@cancer.org or 202-661-5720.

Sincerely,



Christopher W. Hansen
President,
American Cancer Society Cancer Action Network