September 11, 2017

Food and Drug Administration
Division of Dockets Management (HFA–305)
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

[Submitted electronically at www.regulations.gov]

Re: Data and Methods for Evaluating the Impact of Opioids Formulations with Properties Designed to Deter Abuse in the Postmarket Setting [Docket No. FDA–2017–N–2903]

Dear Sir/Madam:

The American Pharmacists Association (APhA) values the opportunity to comment on the Food and Drug Administration's (FDA) July 10-11, 2017 public meeting regarding data and methods for evaluating the impact of opioid formulations with properties designed to deter abuse in the postmarket setting (hereinafter, "Public Meeting"). APhA appreciates FDA's issues paper, of "Data Methods for Evaluating the Impact of Opioid Formulations with Properties Designed to Deter Abuse in the Postmarket Setting" (hereinafter "Issues Paper"), which complemented the Public Meeting.[1] APhA, founded in 1852 as the American Pharmaceutical Association, represents 64,000 pharmacists, pharmaceutical scientists, student pharmacists, pharmacy technicians, and others interested in improving medication use and advancing patient care. APhA members provide care in all practice settings, including community pharmacies, hospitals, long-term care facilities, community health centers, physician offices, ambulatory clinics, managed care organizations, hospice settings, and the uniformed services.

APhA would like to commend FDA for taking steps to support the development, safety, and research of abuse-deterrent formulations (ADFs) and their willingness to interface with experts and stakeholders through the Public Meeting. Generally, APhA supports the development, assessment, regulation, prescribing and dispensing of ADFs as an important component of a multipronged approach to addressing abuse of opioid medications. Opioid analgesics offer an effective solution for the treatment of pain and are often the treatment of choice when a patient suffers from pain. APhA recognizes that because these medications are

[1] Food and Drug Administration (2017), Data and Methods for Evaluating the Impact of Opioid Formulation with Properties Designed to Deter Abuse in the Postmarket Setting, available at: https://www.fda.gov/downloads/Drugs/NewsEvents/UCM562743.pdf.

widely prescribed, the risk of misuse, abuse, addiction, overdose and mortality may be greater, and a transition to ADFs could help in preventing some individuals from misusing or abusing these products. As FDA takes steps to incentivize and support the development of opioid medications with progressively better abuse-deterrent properties, we ask the agency to consider the risks of creating barriers to effective pain treatments or limiting patients' treatment options in addition to the potential benefits to public health.

I. Pharmacists Role in Postmarket Evaluation

In response to FDA's Issue Paper and Public Meeting, APhA encourages FDA to consider opportunities to better utilize pharmacists' extensive clinical knowledge, medication expertise and existing relationships with patients. Pharmacists, as the most accessible health care professional, regularly interact with patients and provide patient care services, such as medication management, serving an important role in preventing and reporting medication errors and adverse events. Being on the frontline of care in communities, we encourage FDA to consider different opportunities to gain pharmacists' perspectives as FDA contemplates approaches for postmarket evaluation of opioids with abuse-deterrent properties.

II. Prescription Drug Monitoring Programs (PDMPs)

While PDMPs are noted as a potential source of data in the Issues Paper, APhA believes that coordination and collaboration with key stakeholders is essential to using PDMPs as an effective data source. Data fields in a PDMP vary by state, and states also dictate access to such data. In addition, rates of PDMP reports and checks varies significantly with some states now mandating PDMP reporting. APhA encourages FDA to work with states, technology vendors and standard setting organizations to better harness data in PDMPSs to enhance postmarket evaluation of opioids with properties to deter abuse.

III. Frequency of Reviews

Although opioid formulations with abuse deterrent properties may help curb prescription drug abuse initially, APhA believes that FDA should regularly evaluate these properties. As abuse deterrent products are on the market longer and more widely available, there will be greater opportunities to identify methods to strip the product of its abuse deterrent features. Given the diversion concerns related to opioids, APhA anticipates that some medication's capacity to deter abuse may decline the longer they are on the market. Thus, FDA should consider regularly reviewing and comparing products and certain technologies' capacity for abuse deterrence.

IV. Alternative Use of Postmarket Data

APhA recognizes the difficulty of quantifying the impact that ADFs have on prescription drug abuse, misuse and adverse events, but believes that postmarket data may have additional value in a real world setting. APhA is aware of the push for policies that would require pharmacists to dispense an abuse-deterrent opioid when presented with an opioid prescription. Policies requiring such a substitution are not rooted in current evidence-based research and may

be in opposition to pharmacists' clinical judgment. Given the difficulty in measuring abuse-deterrence and the role of the pharmacist in medication selection, APhA encourages FDA to consider making available postmarket findings to practitioners to help inform substitution policy and clinical decision making.

V. Titrated and Compounded Medication Access

As FDA considers methods to bring more ADFs to market, APhA is concerned that non-ADF medications will be displaced, negatively impacting patient access and medication regimen. If substantially all opioid analgesics are manufactured with abuse-deterrent technology, then pharmacists may face challenges when titrating doses or compounding opioid preparations, which are necessary for some patients. In instances when a standard manufactured strength falls outside of the effective treatment range for patients, pharmacists routinely compound doses to suit the individual patients' needs, such as for special populations (e.g., children, elderly, opioid-tolerant adults). As part of a standard compounding procedure, dosage forms may need to be changed--for example, tablets may need to be crushed in order to obtain the proper amount of drug needed to prepare doses. Tablets that are uncrushable or other challenging formulations such as liquids with mixed dose-dependent reversal agents could create access barriers for patients who need opioid analgesics tailored to their specific needs.

VI. Immediate-Release Opioid Access

While APhA applauds FDA's efforts to increase ADFs approved by FDA, we also want to note the important role immediate-release opioids without abuse deterrent properties play for patients living in pain. The Centers for Disease Control and Prevention (CDC) Guideline for Prescribing Opioids for Chronic Pain – United States, 2016, consistently references immediate-release opioids as a viable treatment option when starting opioid therapy for chronic pain. For example, Recommendation 4 states, "When starting opioid therapy for chronic pain, clinicians should prescribe immediate-release opioids instead of extended-release/long-acting opioids" because the clinical evidence review showed a higher risk for overdose among patients initiating ER/LA opioids than those initiating treatment with IR opioids.[2] In addition, a large number of patients are on treatment regimens that consist of generic immediate-release (IR) opioid analgesics, prescribed an adjunct therapy to suppress breakthrough pain, often by trained pain medicine specialists. Therefore, as FDA aims to increase ADF approvals, it is important that the agency also be aware of the importance of IR opioids to patients and their treating health care providers, including pharmacists. In addition, although pricing is beyond FDA's authority, we also remind FDA that ADFs are generally more costly than non-ADFs and the generic drug approval process for other abuse-deterrent medications is in its infancy. As ADFs' market share increases, it is important that patient access to affordable and effective treatment regimens be maintained.

Thank you for considering our comments as FDA facilitates a market transition to ADFs of opioid analgesics. As FDA moves forward, we ask the agency to balance the perceived benefits to public health with the risks of creating barriers to valuable pain treatment options.

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[2] Centers for Disease Control and Prevention, (March 2016). CDC Guideline for Prescribing Opioids for Chronic Pain – United States, 2016, available at: https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm.

APhA thanks FDA for considering our feedback on this important public health initiative and we look forward to working closely with FDA and other stakeholders throughout the regulatory process. If you have any questions or require additional information, please contact Jenna Ventresca, JD, Director, Health Policy, at jventresca@aphanet.org or (202) 558-2727.

Sincerely,

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Executive Vice President and CEO

cc: Stacie Maass, BSPharm, JD, Senior Vice President, Pharmacy Practice and Government Affairs