April 2, 2019

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

Re: Risk Evaluation and Mitigation Strategies Assessment: Planning and Reporting; Draft Guidance (FDA-2018-D-4628)

Dear Sir/Madam:

The American Pharmacists Association ("APhA") welcomes the opportunity to respond to the Food and Drug Administration's (FDA's) draft guidance, "REMS Assessment: Planning and Reporting" (hereinafter, "Draft Guidance"). APhA, founded in 1852 as the American Pharmaceutical Association, has a membership of nearly 60,000 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, physicians' offices, hospitals, long-term care facilities, community health centers, managed care organizations, hospice settings and the uniformed services.

APhA appreciates FDA's efforts to improve the Risk Evaluation and Mitigation Strategy (REMS) program by providing instructions to applicants on developing and submitting REMS Assessment Plans to FDA. APhA applauds FDA for seeking to standardize assessments and for suggesting those assessments contemplate whether the REMS is meeting its goals and objectives. In addition, APhA supports clarifying that REMS with elements to assure safe use (ETASU) should assess whether the burden on the healthcare delivery system is having the least impact to the greatest extent possible. While we generally welcome the intent of the Draft Guidance, APhA offers the below comments for further improvement and consideration by FDA.

I. REMS Assessment – Overview

The Draft Guidance indicates four factors applicants should contemplate when designing a REMS program which includes an Assessment Plan. One of the factors applicants' REMS program design should consider is the type and extent of additional supports and resources stakeholders within the healthcare delivery process may require to effectively mitigate a

medication's risks.[1] While significant efforts have been made in recent years to streamline and standardize REMS programs and make them less burdensome, APhA's members continue to express concerns about REMS programs' burdens. Therefore, APhA appreciates FDA's efforts to better account for the needs of healthcare stakeholders and practice impact during design processes.

However, APhA believes more clarity can be added to the Draft Guidance to better account for healthcare stakeholders' practical needs, such as methods to improve efficiency and communication. For example, consideration of healthcare practitioners' variable workflows and available resources, including different methods of communication between practitioners, should be considered during design processes. There are multiple ways pharmacists and other health care practitioners can satisfy different REMS requirements which can be considered in design, assessments and potentially, through modifications.

APhA also suggests FDA work with then Centers for Medicare & Medicaid Services, other payers and applicants to develop strategies to identify mechanisms to provide adequate payment for practitioner services, including pharmacist-provided patient care services, that are not covered by payers but required under REMS. Currently, the is a lack of evidence detailing the amount of time and resources practitioners and health care facilities spend to satisfy various REMS components which can make determining appropriate coverage and reimbursement difficult, and impact patient access.[2,3,4] Evaluation of this area could be addressed in REMS program design and subsequent assessments.

II. Developing the REMS Assessment Plan

In the Draft Guidance, FDA outlines five assessment categories, *Program Outreach and Communication, Program Implementation and Operations, Knowledge, Safe Use Behaviors* and "*Health Outcomes and/or Surrogates of Health Outcomes"*. The Draft Guidance also provides applicants with flexibility in selection metrics and sources of assessment data. While APhA supports FDA's efforts to better plan and incorporate assessments into REMS programs, we encourage the agency to consider further standardizing program assessment. For example, using process and outcome metrics to evaluate effectiveness of REMS elements may be more meaningful if results can be compared to other programs. However, such comparisons will be more difficult if different metrics or sources of data are used among REMS programs. Comparing assessments that use standardized metrics could permit replication of effective REMS programs, elimination of ineffective ones and refinement of others, among other benefits.

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[1] *See* Food and Drug Administration (January 2019). REMS Assessment: Planning and Reporting *Draft Guidance*, Docket No. FDA-2018-D-4628, stating "which stakeholders within the existing healthcare delivery system may require additional support to effectively mitigate the risk, as well as the type and extent of the support that may be required (e.g., training about how to manage the risk, verification that laboratory monitoring was conducted)."

[2] *See* Kim, D.D., Pope, E. Wilkinson, C.L., Graff, J.S., Neumann, P.J. & Chambers, J.D. (2018). Factors Predicting Restrictions on U.S. Commercial Payer Coverage of Specialty Drugs, *Value in Health,* 21(1), S95.

[3] *See*, Moride Y. (2018) Risk Management and Minimization. In: Bate A. (eds) Evidence-Based Pharmacovigilance. Methods in Pharmacology and Toxicology. Humana Press, New York, NY

[4] *See* Boudes, P.F. (2017). Risk Evaluation and Mitigation Strategies (REMSs): Are They Improving Drug Safety? A Critical Review of REMSs Requiring Elements to Assure Safe Use (ETASU), *Drug in R&D,* 17(2), 245-254.

Therefore, to improve REMS assessments and programs more broadly, APhA recommends FDA work with stakeholders to develop standardized metrics to assess effectiveness.[5]

In addition, APhA notes standardized metrics may help better capture the impact of REMS requirements on practitioners' workflow, including additional time and resources spent by health care practitioners. Data gathered from assessments using metrics focused on workflow and resources utilized could be used in cost-benefit analyses to help practitioners build a case for compensation and program support. APhA suggests FDA modify the Draft Guidance so applicants' assessment plans consider how data from REMS programs can be made available more broadly.

III. Considerations for Measuring Barriers to Patient Access and Burden on the Health Care Delivery System

APhA appreciates FDA's recommendation for applicants to assess how the REMS may burden the health care delivery system and ultimately result in barriers to patient access. We believe stakeholders obtaining health care practitioners' feedback and more carefully considering workflows and required resource utilization in different settings will better elucidate the impact of REMS.

As FDA considers access to REMS medication, APhA recommends FDA include factors beyond REMS requirements that may also impact patient access. For example, APhA members have indicated REMS programs can be complicated to identify and implement but that these issues are compounded when manufacturers impose additional requirements in excess of REMS program requirements. In assessing barriers, APhA encourages applicants to also provide company-specific policies, such as those associated with limited distribution, that could also burden the health care delivery system and impede patient access.

IV. REMS Assessment Submissions

The Draft Guidance indicates REMS Assessment Submissions should include a discussion of whether the REMS goals and objectives are being met and proposed modifications to the REMS or revisions to the REMS Assessment Plan. As noted above, patient access issues and practitioner burdens associated with REMS programs may require solutions beyond the scope of the content included in the REMS and subsequent submissions to FDA. For example, a manufacturer could work with payers to identify payment mechanisms to help overcome potential patient access issues, yet it is not clear whether this information would be viewed as helping mitigate risks. Therefore, APhA encourages FDA to provide additional examples of steps applicants may take to mitigate risks that are not typically associated with REMS requirements.

APhA supports FDA's efforts to improve the REMS program and continues to encourage a systematic, standardized process for REMS programs to minimize the impact on patient access

[5] *See* Reiss, S.M. (2011). APhA 2011 REMS white paper: Summary of REMS stakeholder meeting on improving program design and implementation, *Journal of the American Pharmacists Association,* 51(3), 340-358.

and the health care system. Should you have any questions please contact, Jenna Ventresca, Director, Health Policy, by email jventresca@aphanet.org or phone (202) 558-2727.

Sincerely,

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Executive Vice President and CEO

cc: Mitchel Rothholz, RPh, MBA, Chief Strategy Officer, American Pharmacists Association