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September 16, 2013

Food and Drug Administration  
Center for Drug Evaluation and Research  
10903 New Hampshire Ave  
Building 51, Room 1192  
Silver Spring, MD 20993

VIA ELECTRONIC SUBMISSION:

**Re: FDA-2013-N-0502; Standardizing and Evaluating Risk Evaluation and Mitigation Strategies; Notice of Public Meeting; Request for Comments**

Dear Sir/Madam:

The American Society of Health-System Pharmacists (ASHP) is pleased to submit comments on standardizing the REMS program as published in the May 22, 2013 issue of the Federal Register.<sup>1</sup> ASHP is the national professional organization whose 40,000 members include pharmacists, pharmacy technicians, and pharmacy students who provide patient care services in acute and ambulatory care settings, including hospitals, health systems, and ambulatory clinics. For over 70 years, the Society has been on the forefront of efforts to improve medication use and enhance patient safety.

ASHP is a strong advocate for improving patient safety and medication management. The Society believes that the development of consistent, evidence-based medication use systems is central to achieving safe medication use. Our members serve as important patient advocates and interdisciplinary care providers, helping to ensure the safest use of medications. ASHP appreciates the opportunity to comment and participate on the further improvements of the Risk Evaluation and Mitigation Strategies (REMS) programs. And we appreciate the FDA's efforts to engage stakeholders in the process. ASHP policy on REMS is:

- To advocate for research on the impact of the Food and Drug Administration's Risk Evaluation and Mitigation Strategies (REMS) on patient safety, cost effectiveness, and pharmacy workflow; further,
- To advocate pharmacist involvement in the development and implementation of REMS; further,

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<sup>1</sup> Federal Register Vol. 78, No. 99 pages 30313 – 30317

**TOGETHER WE MAKE A GREAT TEAM**

- To urge computer software vendors to assist pharmacists in the identification of and compliance with REMS; further,
- To advocate that any REMS that include constraint on traditional drug distribution systems be consistent with ASHP policy on restricted drug distribution.<sup>2</sup>

While ASHP is pleased that FDA has the expanded authority to ensure the safety of drugs through REMS, we are concerned about how REMS have been applied in the market place, the lack of standardization of REMS, and the inability to operationalize REMS without undue burden on the medication use system. ASHP believes that the goal of the REMS program should be to develop a systematic approach to evidence-based medication use practices, rather than a separate medication use system for each high risk medication.

**Acknowledgement:**

ASHP would like to recognize the significant number of improvements made to the REMS program and FDA resources since the July 2010 FDA meeting, including the discontinuation of a significant number of REMS, development of the Shared System REMS, and the release of the Guidance document for Medication Guides. The Society applauds the Agency for its continued interest to work with stakeholders.

ASHP members recognize the potential risk of medications that are inappropriately prescribed, dispensed, and monitored, as well as their own responsibility to provide patients with comprehensible information that is useful to both the patient and the provider. However, the Society is concerned that current REMS programs are negatively affecting the already limited time that pharmacists have to care for and ensure the safety of their patients.

We are also concerned about the fragmentation of the drug supply chain since, due to added complexity within the medication use system, any process encouraging a separate distribution system for particular drugs has the potential to increase the risk of error and impact continuity of care.

**Patient Education and Safety:**

As noted in past ASHP comments to the FDA, the Society believe educating patients is of the utmost importance, but there is a lack of research relating to the role, scope, and effects on patient understanding of Medication Guides and resulting patient behavior. Well-designed research is necessary to determine the usefulness and effectiveness of Medication Guides as they are currently written and distributed as patient-counseling tools.

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<sup>2</sup> ASHP Policy 1002: Risk Evaluation and Mitigation Strategies

FDA should look at the elements of REMS (e.g. Medication Guide, communication plan) to ensure they are well-founded and effective at mitigating risk. As a member of the National Quality Forum (NQF), ASHP recommends that FDA look to the process NQF uses for the endorsement of quality measures. The NQF process is rigorous and consensus-building, and can be used by FDA as a model when developing a process to validate that FDA is actually measuring and achieving what they are intending to accomplish with a particular REMS.

ASHP believes that the goal for most REMS is not to achieve zero risk, but rather to provide information to support a risk-benefit discussion and decision. For example, for some drugs, acceptable risk depends on patient-specific factors that range from disease severity and failure of alternative therapies, to an individual's personal risk tolerance.

The goals of REMS must include continued verification and validation that patient knowledge and receipt of information will actually improve outcomes, and should include information on proving that the Medication Guide designed is going to reach safety goals and should require the use of established research methods to sample patient populations on behaviors modified based on receipt of the Medication Guide. This includes development of appropriate incorporation of appropriate health literacy standards.

#### **Registration Process and Verification:**

ASHP would encourage the FDA to continue working with stakeholders to standardize the different elements of REMS and address the concerns raised during the July 24 – 25 2013 meeting, in order to make this monitoring more efficient and generalizable to future REMS. Though the core components REMS are standard, the elements within each component should be analyzed in an effort to standardize to the fullest extent possible.

The lack of standardization results in large amounts of duplication within health care systems. Further, the lack of centralized or standardized methods for accomplishing the elements to assure safe use (ETASU) collectively for all REMS is a burden. Members share with us that they have had to dedicate specific resources to manage and keep up with REMS requirements.

The FDA should take into considerations ASHP's experience with our REMS Resource center when developing a centralized resource. We developed this resource in 2009-2010 to assist pharmacists develop a consistent manner in which to manage patients. Questions for practitioners dispensing drugs with REMS include:

- 1) Why is REMS required?
- 2) Hospital registration required?
- 3) Patient enrollment required?
- 4) Prescriber enrollment required?

- 5) Is pharmacy required to verify patient/prescriber enrollment?
- 6) Medication Guide required?
- 7) Monitoring required?
- 8) Can pharmacy order medication through normal distribution channels?
- 9) What documentation is required?
- 10) Is continuing education required for REMS?
- 11) Are there limits on quantity dispensed?
- 12) Will pharmacy be subject to an audit?

ASHP encourages the FDA to work towards a centralized electronic means for all REMS and the various registration, provider education, and patient documentation requirements, in an effort to eliminate redundancy and the need to maintain separate paper record keeping. This should include mechanisms to routinely and proactively inform practitioners on changes to REMS programs.

**Medication Access, Record Standardization, and Continuity of Care:**

Hospitals and health systems have the unique charge in that we have to provide/obtain all the medications for our patients while under inpatient and outpatient care. Introducing systems that require patients to bring in their own medications or requiring multiple supply chain channels to purchase medications introduces a growing number of variables. Variables that consume time and raise risks to health system's medication use system.

For REMS with restricted distribution, there are operational challenges that are barriers to patient access and burden delivery of care. If the approved REMS includes only delivery to the patient from the distributor, will there be uniform standards for circumstances in which patients are admitted to a hospital and have no ability to obtain the medication?

The Society believes that any qualified dispensing site should be able to purchase and dispense any REMS, provided all of the requirements are met. Compelling examples were shared at the FDA public meeting on July 24 – July 25 2013 that describe the often formidable access problems that occur during transitions of care when a REMS drug is only available through restricted distribution.

REMS should be designed in such a way that they readily accommodate a wide range of dispensers, and ASHP remains hopeful that further standardization will help to reach that goal.

ASHP encourages the FDA to continue open dialogue with providers, including hospital and health system based pharmacists and providers. The Society recommends that the Agency consider convening a stakeholder group with representatives from all health care professions to identify where patients initiate REMS medication therapies. Further consideration should be

given to transitions of care where providers need to obtain access to a REMS drug to manage the patient in the particular setting. A focus of this analysis should be on the IT interfaces between these settings to eliminate as much redundancy as possible and enable or create a vehicle allowing the data and the drug to be accessible to all provider settings. Centralization of REMS information and data needs to become part of e-prescribing systems and integration into electronic health records.

A critical element to ensuring that REMS requirements become incorporated seamlessly into prescribing, authorization, dispensing, and patient monitoring is for the FDA to implement a highly structured electronic submission requirement using the structured product labeling (SPL) model. ASHP has been working closely with National Council for Prescription Drug Programs (NCPDP), the FDA, and a broad base of stakeholders to help define how SPL can best be leveraged to support such REMS standardization efforts. . Achieving such standardization of data content and format is crucial to downstream automation aimed at better integration with, and a resultant reduction in burden to, the existing and evolving healthcare system. Therefore, ASHP recommends that development and implementation of SPL standardization of REMS as a priority project for the Agency

Additionally, the FDA should require provider input in the development and refinement of REMS. This would provide valuable input to ensure the REMS is effective, does not cause undue burden, and address the needs of the various practice settings REMS drugs must be obtained and administered.

The Society appreciates this opportunity to provide comments. Please contact me if you have any questions on ASHP's comments on the Proposed Rule. I can be reached by telephone at 301-664-8806, or by e-mail at [ctopoleski@ashp.org](mailto:ctopoleski@ashp.org).

Sincerely,

A handwritten signature in black ink, appearing to read "Christopher J. Topoleski". The signature is fluid and cursive, with a prominent initial "C".

Christopher J. Topoleski  
Director, Federal Regulatory Affairs