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June 30, 2009

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

Re: Docket No. FDA-2009-N-0143, Risk Evaluation and Mitigation Strategies for Certain Opioid Drugs

Dear Sir/Madam:

The American Society of Health-System Pharmacists (ASHP) is pleased to supplement its oral comments with the following written comments pertaining to the May 27 and 28, 2009 public meeting on Risk Evaluation and Mitigation Strategies (REMS) for Certain Opioid Drugs. For more than 60 years, ASHP has helped pharmacists who practice in hospitals and health systems improve medication use and enhance patient safety. The Society's 35,000 members include pharmacists and pharmacy technicians who practice in inpatient, outpatient, home-care, and long-term-care settings, as well as pharmacy students. Pharmacists in hospitals and health systems are experts in medication use who serve on interdisciplinary patient-care teams. They work with physicians, nurses, and other health-care professionals to ensure that medicines are used safely and effectively.

FDA has indicated that a REMS would be required for long acting and extended release brand name and generic opioid drugs formulated with fentanyl, hydromorphone, methadone, morphine, oxycodone, and oxymorphone. FDA has further indicated that the REMS would be intended to ensure the benefits of these drugs outweigh the risks associated with: (1) use of high doses of long acting opioids and extended release opioid products in non-opioid tolerant and inappropriately selected individuals; (2) abuse; (3) misuse; and (4) overdose, both accidental and intentional. While ASHP understands and supports the need to address misuse and abuse of these medications, and ensure legitimate safe medication use, it is unclear whether FDA is intending to prevent non-medicinal use of opioids, or address the risks associated with legitimate medical prescribing and use of these drugs, or both.

- **The Society strongly recommends that FDA more clearly identify exactly which risks the agency is attempting to mitigate before it implements a REMS for certain opioid drugs.**

- **ASHP further recommends that FDA perform research and gather data to determine which REMS elements will effectively mitigate these risks with minimal impact on patient access and continuity of care, and minimal burden on hospitals and health systems. As part of its research, and prior to applying a broad REMS requirement to certain opioid drugs, the agency should develop pilot REMS programs to gather prospective data to determine a strategy that will mitigate the identified risks with the least impact on patient access.**

Standardization of basic REMS elements

The standardization of basic REMS elements should be FDA's ultimate goal, and a REMS for opioids should cover the entire class of opioid medications. Any attempt to regulate only a portion of the opioid class of medications will drive prescribers, users, and misusers of these medications to the other, less stringently regulated opioids, likely resulting in some patients not getting their needed medications, or less ideal medication regimens which could introduce adverse drug events. Additionally, there will be a greater burden on the health care delivery system since the REMS requirements will not be standarized for all opioids, and pharmacists would likely be required to implement different dispensing or distribution systems within the same class of drugs.

- **If the agency does develop a REMS for opioids, ASHP encourages FDA to consider standardizing basic REMS elements across the entire class of opioid medications, not just the long acting and extended release drugs.**

Exemption for inpatient hospital settings

- **The Society strongly encourages FDA to exempt inpatient hospital settings from a REMS requirement for opioid drugs.**

Under the Food and Drug Administration Amendments Act of 2007, elements to assure safe use within a REMS should, "to the extent practicable, minimize the burden on the health care delivery system." Patients in need of these pain medications when they enter the hospital, or who develop the need after being admitted to the hospital, could receive significant delays in care if these requirements are put in place. Multiple health care providers are involved in the care of the patient in a hospital. Through this interdisciplinary care model, there are built-in checks on each of the health care providers involved in the patient's care, including nurses, pharmacists, and physicians. Patients do not self-administer drugs and there is always a health care professional in the general vicinity of the patient when the medication is administered. Furthermore, many hospitals and health-systems have decision support systems in place to prevent inadvertant overdoses of medications.

Opiates are commonly prescribed in hospitals, and patients respond in varied ways to opiates and need appropriate monitoring and safeguards, even with standard doses. However, since these medications are so commonly prescribed, physicians understand the associated risks and side effects, as do health-system pharmacists. In the hospital setting, education and certification of pharmacists and prescribers will not have a significant impact, since these individuals already have a deep knowledge and understanding of the risks and side effects associated with opioid use.

Administration of certification requirements

ASHP understands that FDA is looking to certify pharmacists, prescribers, and other health care providers or institutions that dispense or directly administer covered opioid products. However, ASHP has some concerns with administering these certification requirements through the Drug Enforcement Administration (DEA). If the FDA does not exempt inpatient hospital settings from a REMS requirement, administering certification requirements through the physician's DEA number could result in many physicians in hospitals who regularly care for patients being unable to prescribe necessary pain medications to their patients (for example, residents or hospital-paid staff at major large health systems), since hospital staff practitioners are not required by the DEA to register with the DEA. Instead, these practitioners may issue medication orders under the hospital DEA registration number. Additionally, in the community pharmacy setting, it is the pharmacy, rather than the pharmacist, that registers with the DEA. Finally, since the Food and Drug Administration Amendments Act of 2007 contains no authority for DEA to be part of an enforcement mechanism for a REMS, it is unclear how such a system would be implemented.

- **ASHP strongly recommends that FDA not administer any certification requirements through the DEA.**

Type of education that should be provided to pharmacists and other health care providers

If FDA does require the certification of pharmacists, prescribers, and other health care providers or institutions under the REMS, FDA could require the basic principles and content areas to be included. Pharmacist education that meets these FDA-required basic principles and content areas could be developed by a joint program of the National Association of Boards of Pharmacy, ASHP, and other pharmacist organizations.

Type of education that should be provided to the patient

ASHP believes that patient education, in conjunction with a prescriber-patient agreement, should be part of a REMS, but there should be no patient registries required under the REMS. Additionally, pharmacists should not be required to "police" the process by verifying the presence of a prescriber-patient agreement, or prescriber certification, in

order to dispense the medication. In the outpatient setting, if a physician writes a prescription but has not followed the REMS requirements, a patient who is unable to get their prescription filled could suffer severe pain and withdrawal symptoms. FDA should ensure that, whatever REMS process is put in place, medications are available to the patient, pharmacists have access to these medications, and there is no delay in care.

The Society questions whether Medication Guides as they are currently written and distributed are valuable tools for counseling patients about drugs with serious risks, since evidence of their usefulness has not been established through adequate, well-designed research. FDA should conduct well-designed research to determine optimal content and format of consumer medication information (CMI), and the research should be patient/consumer-centered. For the comprehensive format of CMI, the goal should be a single, comprehensible document. FDA should examine the use of existing CMI integrated with the relevant MedGuide versus the use of stand-alone documents.

Controls on distributors

ASHP does not believe a REMS should include controls on distributors who distribute products to pharmacies and other health care providers, and it is unnecessary to put controls in place through the distributor. Further, under the Food and Drug Administration Amendments Act of 2007, elements to assure safe use within a REMS should, "to the extent practicable, minimize the burden on the health care delivery system."

The Society appreciates this opportunity to present its written comments. Feel free to contact me if you have any questions regarding our comments. I can be reached by telephone at 301-664-8702, or by e-mail at jcoffey@ashp.org.

Sincerely,

Justine Coffey, JD, LLM
Director, Federal Regulatory Affairs