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May 20, 2015

Stephen Ostroff, M.D.
Acting Commissioner of Food and Drugs
Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. FDA-2014-D-1524: Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities: Draft Guidance for Industry.

Dear Dr. Ostroff:

On behalf of our nearly 5,000 member hospitals, health systems and other health care organizations, and our 43,000 individual members, the American Hospital Association (AHA) appreciates the opportunity to comment on the Food and Drug Administration's (FDA) draft guidance, "Repackaging of Certain Human Drug Products by Pharmacies and Outsourcing Facilities." We also appreciate the efforts that FDA has undertaken to ensure that stakeholders, including hospitals and health care systems, have the opportunity to provide in-person input into the draft guidance through FDA listening sessions. **The AHA has several concerns about the draft guidance requirements around anticipatory repackaging and beyond-use-dates (BUDs), which are described in further detail below. We urge FDA to address these concerns to ensure the continued safety and availability of repackaged medications, including those that are sold by outsourcing facilities and those prepared in-house by hospital and health care system pharmacies.**

FDA defines repackaging as "the act of taking a finished drug product from the container in which it was distributed by the original manufacturer and placing it into a different container without further manipulation of the drug." The repackaging of medications, both sterile and non-sterile drug products, is a fundamental part of pharmacy practice in hospitals and health care systems. As FDA notes, the most common reasons for using repackaged drugs include: meeting the needs of specific groups of patients (such as pediatric patients or ophthalmic patients who require smaller doses of approved sterile drug products that may not be available commercially); reducing medication errors associated with drawing up a dose from a vial at the point of patient care; reducing the possibility of abuse when controlled substances are left over in a vial after a dose is drawn out; providing a particular sized container to fit into a particular device to administer the drug (e.g. a particular pain medication pump); and providing convenience to the caregiver who administers an injection to a patient.



Hospitals and health care systems often purchase repackaged pharmaceuticals from other organizations, including outsourcing facilities. However, in order to ensure patient safety and the timely availability of appropriate medications for procedures and patient care, they also may repackage medications in-house or centrally within health care systems. For instance, in-house repackaging is necessary if a patient requires a dose for which a manufactured unit-dose or commercially repackaged product is not available or if the repackaged product is needed immediately. Having medications available in a properly labeled unit-of-use (unit-dose) form in hospitals and health care systems increases patient safety, reduces waste, improves the hospital's control of drug distribution, and increases ease of use and efficiency of care. Further, in times of critical need, such as when certain drugs are in short supply, hospital pharmacies can combine and repackage single-dose vials for multiple patients.

In the draft guidance, FDA describes those conditions and requirements that would have to be met in order for a state-licensed pharmacy (such as a hospital or health care system pharmacy) to be able to continue to prepare repackaged drug products without violating the adulteration, misbranding or other requirements of the Food, Drugs and Cosmetics Act. The AHA's comments and recommendations regarding these conditions and requirements are described below.

ANTICIPATORY REPACKAGING

FDA's draft guidance indicates that a state-licensed pharmacy must, in general, repackage drug products after the receipt of a valid prescription for an identified, individual patient or subsequent to a written order in a patient's chart in a health care setting. However, as FDA has recognized, hospital and health care system pharmacies may need to prepare a limited inventory of unit-dose drug products in advance of an individual written order in certain circumstances, for instance, unit-doses of an anesthesia drug prior to a series of scheduled surgical procedures or drugs that are commonly needed for patients with emergency medical conditions. Therefore, the draft guidance states that drugs also may be repackaged (but not distributed) in state-licensed pharmacies in advance of a prescription or a written order in a quantity that reflects the amount of such drug product that the pharmacy has repackaged in the last 14-day period, based on a history of receipt of prescriptions or written orders for such a 14-day period.

The AHA believes that under most circumstances the 14-day anticipatory supply of a repackaged drug would be adequate. However, a larger supply of such products may be needed by a hospital in order to provide care in certain circumstances, such as a disaster or public health emergency that brings a surge in patients requiring repackaged medications, or when the normal supply chain is interrupted for an extended period of time. **Therefore, the AHA recommends that FDA explicitly include in the draft guidance an exception that would allow hospital and health care system pharmacies to repackage more than a 14-day supply in the case of extenuating circumstances, such as those mentioned above.**

BEYOND-USE-DATES

The draft guidance describes FDA's proposed BUD limitations for repackaged drugs. The BUD is the date after which a repackaged preparation is not to be used. Our views on the BUD for sterile drug products repackaged in a state-licensed pharmacy and outsourcing facility follow.

Sterile Drug Products Repackaged in a State-licensed Pharmacy. The draft guidance describes FDA's proposed BUDs for sterile unapproved drug products that are repackaged in a state-licensed pharmacy (such as a hospital or health care system pharmacy). FDA claims that these BUDs are consistent with those established by United States Pharmacopeial Convention (USP) Chapter <797> *Pharmaceutical Compounding—Sterile Preparations* for "medium-risk" compounded sterile preparations. However, the AHA is concerned that the policy described in this draft guidance is unnecessarily stricter than the BUD limits described in USP <797>, particularly for those repackaged drug products that would be considered "low-risk" if they were being compounded, such as fluconazole solution, a commonly used antifungal drug. **To retain greater consistency with USP <797> for activities with comparable risks, the AHA recommends that FDA assign the same BUD limits to repackaged sterile preparations as are applied to compounded sterile preparations in USP<797>, which recognize that low-risk repackaged sterile preparations could be assigned up to a 14-day refrigerated BUD and medium-risk repackaged sterile preparations could be assigned up to a 9-day refrigerated BUD.**

Further, FDA does not address whether stability and sterility testing can extend the standard BUDs for sterile repackaged drug products prepared in a state-licensed pharmacy. **The AHA recommends that FDA clarify that an extended BUD would be permitted if successful stability and sterility testing are conducted by the state-licensed pharmacy, or if the pharmacy uses validated evidence from a well-designed published independent study that shows increased sterility and stability in the same type of environment.** Extending BUDs based on this type of evidence is a common and safe practice currently performed in health care facilities that repackage sterile drug products.

Sterile Drug Products Repackaged in an Outsourcing Facility. FDA's draft guidance also describes BUDs for sterile drug products repackaged in outsourcing facilities, allowing a BUD of 14 days for refrigerated products after the facility completes its required sterility testing. However, the shipment process for these repackaged products means the drug will be available for use by the receiving facility for only 10-12 days or less. **The AHA is concerned that this BUD is too short and would result in increased waste of repackaged drug products and create unnecessary shortages in hospitals and other health care facilities.** Many hospitals are dependent on FDA-registered outsourcing facilities to meet the demand for repackaged drug products, and insufficient resources already exist to meet this demand. **The AHA urges FDA to reconsider the restrictive BUDs in this section of the draft guidance. FDA should allow longer BUDs for outsourcing facilities as long as the outsourcing facility has (1) validated evidential studies to substantiate the stability of the product and (2) conducted sterility testing of each batch that substantiates a reasonable, conservative BUD.**

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Thank you again for the opportunity to comment. If you have any questions, please contact me or Roslyne Schulman, director of policy development, at (202) 626-2273 or rschulman@aha.org.

Sincerely,

/s/

Linda E. Fishman

Senior Vice President

Public Policy Analysis and Development