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Susan J. Schniepp
is a fellow at Regulatory Compliance Associates, Inc.

Tools of the Trade for Preventing Drug Shortages

A new technical report guides bio/pharma companies in establishing a risk-based approach for prevention and management of drug shortages.

A May 2014 article in *Pharmaceutical Technology*, "Linking Drug Shortages and Quality Metrics," provided information regarding the link between drug shortages including the enactment of the Food and Drug Administration Safety and Innovation Act, FDA's efforts to develop a common set of quality metrics for the pharmaceutical industry, the effort of the industry to establish and maintain quality metrics capable of measuring the suitability of pharmaceutical products for the patient, and the capability of the manufacturer to consistently provide these products without delay. At the time the article was published, there was little practical guidance available to the industry that discussed and recommended potential strategies and tools that could be used by manufacturer's to predict and avoid drug shortages.

In December 2014, the Parenteral Drug Association (PDA) published *Technical Report No. 68* (*TR68*), "Risk-Based Approach for Prevention and Management of Drug Shortages," which provides the bio/pharmaceutical industry with appropriate tools for preventing drug shortages.

PDA technical reports, authored and peer-reviewed by PDA members, are intended to offer practical guidance on pertinent regulatory and scientific topics that affect the global pharmaceutical industry. Members with expertise in manufacture and quality assurance for sterile biopharmaceutical and pharmaceutical products (the majority type of products subject to drug shortages) authored *TR68*. Although PDA technical reports are not officially recognized guidance, they are often referenced by regulators and regulators may be involved in the writing or approving of the report contents.

TR68 addresses the drug shortage issue from a global perspective and offers relevant, proactive advice applicable to the global pharmaceutical industry. In addition, the paper recognizes several contributing factors potentially responsible for drug shortages: manufacturing issues, quality issues, and supply chain or distribution issues. This is important because *TR68* recognizes that the issue of a potential drug shortage goes beyond the quality department within an organization.

The document guides bio/pharmaceutical companies in the assessment of the risk of experiencing a drug shortage.

Global language for global issue

The document provides a common language for the industry to use when discussing drug shortages. It is this author's opinion that it is always important when authoring potential global guidance to establish a common language for the readers. *TR68* accomplishes this objective by placing a glossary at the beginning of the report and references, when possible, existing definitions from recognized, credible sources. The definition for "harm," for example, is taken verbatim from the International Conference on Harmonization's (ICH) Q9 guideline, *Quality Risk Management*. The definition of knowledge management is taken from ICH Q10 *Pharmaceutical Quality Systems*. Using previously established definitions helps the global users of *TR68* understand the context and relationship of this document within the regulatory framework of the industry.

FDA GUIDELINES FOR COMPOUNDNG PHARMACIES

FDA recently issued five draft guidance documents proposing policies for drug compounding and repackaging. The documents provide guidance for organizations considering to register as outsourcing facilities; adverse event reporting for outsourcing facilities; repackaging of certain human drug products; and address mixing, diluting, or repackaging biological products outside the scope of an approved biologics license application. In addition, a draft "memorandum of understanding" between a state and FDA addressing certain distributions of compounded human drug products was issued.

The documents can be found on www.fda.gov.

GLOBE: ZOONAR RF/GETTY IMAGES

Once a common language is established, it is easier for a document user to relate to the narrative portion of the document. The narrative of the technical report describes how the issue of drug shortages is global in nature and delineates current global regulatory and legal reporting requirements applicable to manufacturers when facing issues that may result in drug shortages. These issues are not limited to final product manufacturers but may involve suppliers of raw materials crucial for product formulation.

For example, *TR68* describes how a supply-chain issue, a shortage of acetonitrile in 2008–2009, can prompt a drug shortage. The document discusses how multiple suppliers were unable to provide acetonitrile to the industry because of a series of unforeseen circumstances. This shortage impacted the ability of companies to manufacture APIs that then impacted the manufacture of the final drug product.

The document is designed to guide bio/pharmaceutical companies in the assessment of the risk of experiencing a drug shortage. *TR68* uses a risk triage model to collect and assess existing organizational information to determine drug-shortage risk. The model builds on the concepts of management responsibility, supply chain management, quality risk management, knowledge management, regulatory requirements and a company's compliance history and treats them as integrated interrelated disciplines within an organization.

The examples included in the document provide templates to combine a company's information into a comprehensive set of tools that not only measure the potential for a company to experience a drug shortage, but also identify and delineate gaps in organization structure that may exist in quality systems.

The document takes the aforementioned concepts and provides a framework for capturing the information in one inclusive document. The completed document can be used as a tool to share within an organization or with clients in determining potential process improvements or necessary resources required to address systemic process gaps.

TR68 can be used in part or in total by raw material and API suppliers, contract manufacturing organizations, and pharmaceutical companies to assess and manage organizational, manufacturing, and quality issues that could contribute to a drug shortage. The document provides tools to predict and hopefully prevent drug shortages in the future.

The PDA report authors are Emabelle Ramnarine, Genentech; Maik Jornitz, G-CON Inc.; Michael A. Long, Concordia ValSource; Kevin O'Donnell, Health Products Regulatory Authority; Stephan Rönninger, Amgen; Christopher Smalley, Merck Sharp & Dohme; and Anders Vinther, Sanofi Pasteur. The report is available on www.pda.org. **PT**