Pharmacy Outlook '09

The U.S. Pharmacopeia (USP)

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By Roger Williams

Predicting the future is always risky, but this much is clear: What happened in 2008 will affect the drug and food industries in 2009 and for many years to come.

The past year has been marked by the continued trend of globalization in the food and drug industries, which I wrote about in this publication last year. Unfortunately, in 2008, the difficulties of operating in this environment were driven home by several tragic instances of adulteration in which poor or dangerous products were released into the worldwide marketplace.

Shortcomings of globalization

The most obvious example was the adulteration of the blood thinner heparin, which set off an international scare related to the quality of this widely used drug. In this case, an unscrupulous supplier intentionally adulterated heparin with a lower-cost material (over-sulfated chondroitin sulfate) in response to a shortage, resulting in the deaths of nearly 200 patients in the United States and other countries who suffered complications.

The case of melamine in powdered infant formula last year is another widely publicized instance of dangerous adulteration, which followed that of melamine found in pet food in 2007. In 2008, melamine in infant formula caused the death of at least four infants and sickened 53,000 others in China.

This was another example of deliberate adulteration for commercial reasons, similar to the heparin case. The substitution has since been found in dozens of other food products sold around the world. The full extent of this adulteration and the harm caused by it is probably not yet known. In fact, what we do know about its morbidity and mortality might be the tip of the iceberg.

These tragedies demonstrate the shortcomings of 20th-century safety nets in a 21st-century global manufacturing supply chain. A practice on a remote family farm or a problem in a small manufacturing plant in a single nation can cascade into a global disaster. These shortcomings affect us all — manufacturers, regulatory agencies, retailers, doctors, pharmacists and the many other parties involved in the multilayered production and distribution chain of drugs and food.

But most of all, it affects us as individual consumers of drugs and food. We all have an expectation that the drugs we take to treat our medical conditions are not going to harm us because they have been adulterated with a substandard ingredient or that the food we buy in our local supermarket will not sicken our children. But this expectation and the work of the entire industry are challenged by the existence of those who don't play the game fairly, who are motivated by economic or other even more frightening desires and who put all of us at risk. This makes it critical that all of us become even more vigilant now and over the long term.

Maintaining quality standards

These recent cases of adulteration underscore the importance of quality standards, which brings me to the work of my organization, the U.S. Pharmacopeial Convention (USP), as well as that of the other pharmacopeias of the world. USP's mission is to improve the health of people around the world through public standards that help ensure the quality, safety and benefit of medicines and food.

The existence of good public standards is key to preventing the tragedies of heparin, melamine and the many lesser-known instances of adulteration and contamination of food and drug products that are prevalent around the globe. Quality standards are one component of the existing safety nets that work to protect us all from adulterated drugs and foods. These safety nets also include ethical manufacturers, good regulatory agencies such as a Food and Drug Administration equipped with adequate resources, and ever-vigilant and attentive practitioners, patients/consumers and their families.

But these safety nets are continually challenged, forcing us to change the way we do our work and become better at what we do. The health and welfare of the public literally depend on our becoming more active, creative and vigilant.

In the case of the heparin adulteration, USP — at the request of the FDA — worked quickly to revise its heparin monographs (standards) to include a test for the identified contaminant (over-sulfated chondroitin sulfate) and to secure the supply of the widely used blood thinner.

For those not familiar with USP's work, we rely on volunteer experts to write a monograph, a written standard that describes an article (e.g., drug substance, drug product, excipient or food chemical). A USP monograph provides the name of a substance; its definition; package, storage and labeling requirements; and information on tests needed to ensure that the substance has the appropriate strength, quality and purity.

Together with physical reference materials, monographs give scientists, governments, manufacturers and others a public standard by which to judge an article's quality. Without such a standard, the uniformity, consistency and quality of ingredients and products cannot be assured.

While drug monographs normally designate what should be in a product (rather than what shouldn't be in it), the public health threat facing patients in the case of the heparin adulteration was very real and required immediate action. This resulted in the FDA calling on USP to revise its heparin standards by adding a key test. In fact, it was a drug scare involving glycerin contaminated with diethylene glycol in 1938 that led to USP's standards being written into law via the federal Food, Drug and Cosmetic Act and the public/private partnership that exists today between USP and the FDA. USP standards for drugs are enforceable by FDA.

With the realities of today's complex, global supply chain in 2009, USP will be looking at the monographs of other drugs and food ingredients that might also be likely candidates for adulteration. Unfortunately, bad actors are getting more sophisticated, figuring out ways to trick existing analytical tests, adding some (instead of none) of the intended active ingredient in an attempt to game the system and taking advantage of existing weaknesses in other ways.

We must get ahead of those who mean to do harm. I hope we will not hear of more instances of adulteration in 2009. But USP will continue to work diligently to revise its standards.

Harmonization

While cooperation between USP and manufacturers is vital, the spirit of collaboration must further extend between the U.S. and the rest of the world via harmonization of quality standards for pharmaceuticals. This issue becomes extremely important as we face the challenges of counterfeit and substandard products.

The effort for harmonization has been considered for many years, but the opportunity really took hold about 20 years ago when the Pharmacopoeial Discussion Group was formed. This group consists of the European Pharmacopoeia (EP), Japanese Pharmacopoeia (JP) and

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USP, and it meets at least twice yearly to work on pharmacopeial harmonization topics.

The goal of harmonizing testing requirements used to help assure the safety of pharmaceutical products is all the more crucial as we deal with international crises involving drug quality, such as heparin. USP worked with Europe and Japan in that instance to harmonize our revised standards, but we want to do more on this front in 2009.

Beyond the issue of counterfeit products, nonharmonized standards pose other difficulties. With requirements varying (sometimes greatly) from one country to the next, duplicative testing and wasted resources in the pharmaceutical industry often result. That's bad for the industry and bad for consumers/patients.

And — to take on a larger topic — consumers/patients would benefit not only from harmonized tests for ingredients and products but also harmonization of the ingredients and products in terms of their names, labeling and safety/efficacy outcomes. Both types of harmonization would be good for the health of patients and consumers all over the world.

Reflecting on the tragic episodes of adulteration in 2008 can be depressing, and contemplating the challenges we face can be daunting. However, we are in a time of great innovation, with many scientific advances on the horizon. Industry does good work that saves lives and helps people live better ones. Many other developments are under way that I have not gotten to in this column, including new work involving biologic drugs to address difficult-to-treat medical conditions and the potential of nutraceuticals in benefiting human health, to name a few. As much as I look out for the difficult issues that will no doubt arise, I look forward to the advances 2009 will bring.

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