Pharmacy Times

Contaminated Compounding Drug Shipments Coming from China, FDA Warns

Author: Meghan Ross, Senior Associate Editor

The FDA is cautioning drug compounders and manufacturers about a potential risk of chemical contamination stemming from Chinese shipments.

After 2 explosions at a chemical warehouse this summer in Tianjin, China, the FDA increased surveillance of drug shipments.

Investigators discovered hydrogen cyanide contamination in 2 shipments from Tianjin Tianyao Pharmaceuticals Co Ltd, about 18 miles from the explosion site. The FDA stopped these contaminated shipments from entering the United States.

Meanwhile, the Tianjin pharmaceutical company had sent 2 other shipments "intended for use in pharmacy compounding" to the United States since the explosion, but the shipments were not found to contain hydrogen cyanide.

The FDA stated that its goal was to prevent drugs contaminated with toxic chemicals associated with explosions from entering the country.

"It is the responsibility of companies that obtain drugs, including finished drug products, active pharmaceutical ingredients, and excipients from the Tianjin City region, to take appropriate precautions to ensure the quality of these products before they are distributed and/or used to further manufacture or compound drugs or drug products," the FDA stated in a press release.

The agency also stressed that compounders should know where their drug ingredients come from, and if they have questions, they should contact the foreign manufacturer for information.

"Companies must remain vigilant to ensure that all shipments are free from contamination associated with the explosion and not contaminated in any way," the FDA stated.

Pharmacy Times

FDA Strengthens Dietary Supplement Regulation

Author: Ryan Marotta, Assistant Editor

As part of an effort to better regulate the growing supplement industry, the FDA today announced today the creation of its Office of Dietary Supplement Programs (ODSP).

The program was initially a division under the agency's Office of Nutrition Labeling and Dietary Supplements, which has been renamed the Office of Nutrition and Food Labeling.

The new office's responsibilities will include: DEFINITION OF "DANGEROUS"?

- Taking action to remove dangerous supplement products from the market.
- Working with the FDA's Center for Drug Evaluation and Research to help remove products falsely labeled as dietary supplements from the market.
- Enforcing the dietary supplement good manufacturing practices (GMP) regulation, with priority given to cases in which GMP violations potentially compromise product safety, fail to ensure product identity, or result in consumer deception.
- Taking action against claims in cases involving serious risk of consumer harm or widespread economic fraud. FDA APPROVED DRUGS?

The elevation of the ODSP will raise the profile of dietary supplements within the FDA and enable a greater number of government resources to be allocated to the effective regulation of these products, according to an FDA press release. In the 20 years since the establishment of the dietary supplement program, the industry has grown from about $6 billion to more than $35 billion in annual sales.

The FDA is also in the process of identifying permanent leadership for ODSP. In the meantime, Bob Durkin will serve as the Acting Office Director of the ODSP until the agency appoints a permanent leader, while Doug Balentine, PhD, has been tasked with leading the Office of Nutrition and Food Labeling.

www.medscape.com

More Kidney Disease With Long-Term Statins Seen in Cohort Study

Marlene Busko | |December 21, 2015

DALLAS, TX — A large, 8-year retrospective study with a median 6.4-year follow-up associated long-term statin use with an increased risk of kidney disease[1]. Statin users, compared with case-matched controls who didn't use statins, showed a 30% to 36% greater prevalence of kidney disease during follow-up averaging 4.5 in the analysis of healthcare insurance plan members published December 1, 2015 in the *American Journal of Cardiology*, with lead author Dr Tushar Acharya (University of California, San Francisco).

However, patients who are taking statins should not stop taking them based on this study, senior author Dr Ishak A Mansi (University of Texas Southwestern, Dallas) stressed in an interview with **heart*wire*** from Medscape. "Our study did not examine whether the benefits outweigh the risk (it was not designed for that)," he noted. Moreover, there is strong evidence for overall benefit of statins for secondary prevention.

Still, this study shows that "despite the use of statins for more than a quarter of a century, there are aspects about its long-term effects in noncardiac diseases that we do not know very well," according to Mansi. "We are missing more extensive, real-world data of the effectiveness of statins on total morbidity and all-cause mortality, and we need further studies specifically focusing on long-term outcomes in primary prevention." Moreover, "the new [ACC] guidelines . . . are projected to increase statin use to many more hundreds of millions of healthy people, and before we do that we better make sure that we are not causing harm," he cautioned.

"Our paper says to scientists, physicians, funding agencies, [and] policy makers: 'Watch out, [it] seems that we still do not know enough about the long-term effects of these drugs on [the] overall well-being of patients.'"

Although the current study "has unique findings . . . it shouldn't be used as a final say in the controversy," he said. "Clinicians should tell their patients that there may be statin side effects we are not aware of, but there are also benefits that we are aware of." Clinicians also need to carefully monitor creatinine levels in patients taking statins.

A Cohort of 43,000 Strong

The researchers analyzed healthcare data from 2003 to 2012 from 30- to 85-year-olds who lived in the San Antonio, TX area and were members of Tricare Prime or Tricare Plus insurance plan for members of the military and their families. All patients were continuously enrolled in the healthcare plan during the study, and there were no missing data.

The overall cohort comprised 43,438 individuals: 13,626 statin users and 29,812 nonusers. The most commonly prescribed statin was simvastatin (73.5%), followed by atorvastatin (17.4%), pravastatin (7%), and rosuvastatin (*Crestor, AstraZeneca*) (1.7%); 38% of the statin users received high-intensity doses. The statin users took the drugs for a mean of 4.65 years.

The researchers matched 6342 statin users in the overall cohort with 6342 nonusers, according to baseline demographics, comorbidities, presence of renal disease, healthcare utilization, and medication use. In this matched cohort, patients had a mean age of 56, and 45% were women.

The researchers also identified a "healthy cohort" of 3982 statin users and 21,988 nonusers, and they matched 3351 statin users with 3351 nonusers. These individuals were all free of diabetes, chronic kidney disease, cardiovascular disease, and conditions that might limit life expectancy or physical activity.

In the overall cohort, statin use was associated with a significantly increased risk of different types of kidney disease.

Risk of Kidney Disease in Overall Cohort, Statin Users vs Nonusers*

Kidney disease	Odds ratio (95% CI)	*P*
Acute and unspecified renal failure	1.30 (1.14–1.48)	<0.001
Chronic kidney disease	1.36 (1.22–1.52)	<0.001
Nephritis, nephrosis, renal sclerosis	1.35 (1.05–1.73)	0.02

*6342 statin users vs 6342 nonusers

In the healthy cohort, patients who received statins had a significantly higher risk of chronic kidney disease (odds ratio 1.53; 95% CI 1.27–1.85, *P*<0.001), but after adjustment for diseases (such as hypertension) that developed during follow-up, this association weakened, suggesting that these factors are implicated in the development of kidney disease.

Long-term Primary-Prevention Statin Trials "Urgently Needed"

"The findings of this study, though cautionary, suggest that short-term [randomized controlled trial] may not fully describe long-term adverse effects of statins," Acharya and colleagues conclude. Statins lower the risk of cardiovascular disease and cardiovascular death, but "on the other hand, statins increase the risk of incident diabetes and possibly kidney diseases, both of which paradoxically increase long-term morbidity and mortality," they continue.

Randomized controlled trials for primary prevention with statins were sometimes prematurely terminated once the efficacy of reducing major acute cardiovascular events was achieved, and these trials rarely had total mortality as a primary outcome, according to the researchers. "Therefore, further studies, specifically primary-prevention studies, are urgently needed in which the long-term effects of statins on total mortality and total comorbidity indices (not only cardiovascular morbidity) are set as the primary outcomes."

Acharya and Mansi have no relevant financial relationships. Disclosures for the coauthors are listed in the article.

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1. Acharya T, Huang J, Tringali S, et al. Statin use and the risk of kidney disease with long term follow-up (8.4-years study). *Am J Cardiol* 2015; DOI: 10.1016/J.AMJCARD.2015.11.031. Abstract

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