MANUFACTURING

Lab finds NDMA in Zantac can develop during storage

By **Eric Palmer**
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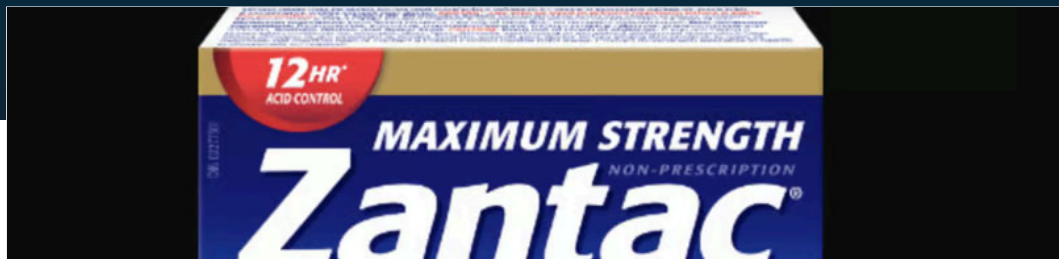
contaminated APIs | ranitidine | Zantac



News findings suggest the level of the impurity NDMA in Zantac and ranitidine generics can grow above FDA recommended levels after testing if the drugs are exposed to high heat during shipping or storage. (Sanofi)

Another testing lab has jumped into the Zantac impurity fray and urged the FDA to recall all ranitidine drugs. Emery Pharma says its testing shows that the level of the suspected carcinogen NDMA can increase if the drug is exposed to high heat, even after it has been packaged.

The Alameda, California independent lab has filed a Citizen Petition (https://www.regulations.gov/document?D=FDA-2020-P-0042-0001) asking the FDA to suspend sales and recall all ranitidine-based products from the U.S. because of the potential contamination, according to a Citizen Petition first reported (https://www.bloombergquint.com/business/carcinogen-in-heartburn-drug-may-build-during-storage-lab-finds) by Bloomberg.

"Our preliminary data indicate that NDMA accumulates in ranitidine-containing drug products on

exposure to elevated temperatures, which would be routinely reached during shipment and during storage. More importantly, these conditions occur post-lot release by the manufacturer. Hence, while NDMA levels in ranitidine may be acceptable at the source, they may not be so when the drug is purchased and subsequently at the time of consumption by the consumer," the petition says.

The suggests the drugs should be stability tested before they are sold and be temperature-controlled during shipping. The lab also suggests the FDA require a warning that the drugs might form potentially cancer-causing NDMA if they are exposed to heat.

RELATED: FDA needs to recall Zantac and other ranitidine antacids, says pharmacy that uncovered impurity (https://www.fiercepharma.com/manufacturing/valisure-fda-needs-to-recall-zantac-and-all-other-ranitidine-antacids-says-pharmacy)

The citizen petition from Emery follows one in October from Valisure which also urged the FDA to recall products. The Valisure petition says that heat from manufacturing can create high levels of N-Nitrosodimethylamine (NDMA). It said it tested batches made by different manufacturers and of different dose forms of the heartburn medicine and that it "detected extremely high levels" of NDMA in every lot of ranitidine that it tested.

RELATED: Glenmark Zantac generic recall comes as Congresswoman assails FDA for inaction (http://fiercepharma.com/manufacturing/glenmark-zantac-generic-recall-comes-as-congresswoman-assails-fda-for-inaction)

The FDA, which is investigating the findings, has asked drugmakers to test all batches of the ranitidine drugs they produce and to not release any that have NDMA above a certain threshold. Many drugmakers decided not to ship or sell generic Zantac after the findings. Some have voluntarily recalled their products and some retailers have decided to quit selling them while the matter plays out.

Still, some have remained on the market. India's Glenmark recalled nearly 2,000 lots of its Zantac generics several weeks ago after testing found NDMA above the FDA-recommended threshold.

The findings from Emery complicates the situation because it suggests the level of the carcinogen could get more toxic after the drugs have been tested. It says that it tested stored ranitidine at different temperatures and for different lengths of time and found that the levels of NDMA can rise during storage.

The petition says that after just five days at 70 degrees Celsius (158 degrees Fahrenheit), the NDMA had risen above the FDA's 96-nanogram limit for NDMA. After 12 days, it was up to 142 nanograms of NDMA. Lower temperatures also caused the NDMA in ranitidine to increase over time.

"I am worried that if it just sits at home at room temperature, it could gradually generate NDMA," Emery CEO Ron Najafi told Bloomberg.

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