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Benzene Contamination Concerns: Drugmakers' Next Steps

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Spurred by a March 5 citizen petition to the U.S. Food and Drug Administration, a flurry of class actions have been filed claiming that drugmakers failed to warn consumers about the presence of benzene in popular acne products.

The citizen petition submitted by Valisure LLC alleges that dangerous levels of the chemical benzene — a carcinogenic material at certain concentrations and exposures — are present in acne products containing benzoyl peroxide, or BPO, under certain storage conditions.

Valisure, an independent laboratory that conducted lab tests on the degradation of BPO in over-the-counter and prescription products, called upon the FDA to commence a broad recall of the acne products, restrain their sale, and issue heightened regulations and guidance to protect consumers.

The agency will carefully consider these allegations and study the test results, conduct its own testing, and communicate with industry trade associations and individual companies who may have contradictory data that refutes Valisure's test results.

While awaiting further guidance from the FDA, affected manufacturers should consider a thoughtful, measured approach to this petition and resulting lawsuits that includes assembling internal data and possibly contacting the FDA for product-specific discussions.

Historical Regulation of Benzene by the FDA

Over the last several years, the FDA has focused on the existence of benzene as an inactive ingredient or residual solvent in certain drug products, with a particular focus on propellants.

In 2021, the FDA requested recalls of various drug products due to the presence of benzene contaminants, including product lines such as over-the-counter antifungal sprays, aerosol deodorant and antiperspirant sprays, hand sanitizers, hair and scalp sunscreen sprays, and topical anesthetic sprays. It also published a webpage for consumers on benzene contamination in drugs.

Although the March 5 petition is the first instance in which Valisure has raised concerns regarding benzene as a degradant, rather than benzene as a contaminant or impurity, the organization is no stranger to citizen petitions. According to its website, Valisure is a company that sells its "independent product testing" to fill a "gap in the healthcare supply chain."

In doing so, Valisure has concentrated on benzene contamination through a series of citizen petitions earning FDA attention:

- March 24, 2021: Concerning the levels of benzene in hand sanitizer;
- May 24, 2021: Concerning the levels of benzene in sunscreen and after-sun-care products;
- Nov. 3, 2021: Concerning the levels of benzene in antiperspirant body sprays; and
- Oct. 31, 2022: Concerning the levels of benzene in dry shampoo.

In each instance, the agency issued an interim response letter, primarily concluding that it could not reach a decision on the petitions within the first six months because they raise complex issues requiring extensive review and analysis.

On Dec. 27, 2023, however, the FDA separately issued an alert to manufacturers regarding the risk of benzene contamination from drug components and other potential risk factors.

Next Steps for the FDA

At present, FDA guidance requests that manufacturers avoid use of benzene in any quantity in the manufacture of drug products. If the use of benzene is unavoidable, the agency's standard is that no more than 2 parts per million of benzene be present during the entire shelf life of a drug product.

Although Valisure's March 5 petition alleges that the instability and degradation of certain BPO products at certain temperatures can lead to benzene levels in excess of the limit, Valisure's lab tests did not review the extent of benzene formation at room temperature storage, nor the effects on consumers of prolonged benzene exposure or absorption.

The FDA has cautioned that the Valisure data must be verified as accurate and reproducible before the agency will take action against BPO products. Additionally, the U.S. Pharmacopeia separately raised concerns on the testing methods and procedures used to generate the Valisure findings. These concerns, if substantiated, could lead to disqualification of the Valisure testing data.

In either case, the FDA is likely to face mounting public pressure to investigate and respond to Valisure's allegations, given the size of the market and the number of consumers, including adolescents, that may be affected by an agency action — whether it permits continued marketing of BPO acne products, or requests a market withdrawal.

Currently, there are 31 active new drug applications and abbreviated new drug applications for prescription BPO products listed in the FDA's Orange Book. There are hundreds more BPO products in the over-the-counter market.

If the benzene exposure levels are validated by further investigation, the FDA will carefully weigh the risk-benefit calculus of, and medical need for, the BPO acne treatments, while exploring labeling revisions, usage limitations and storage directions to minimize risks.

Litigation

Leaning heavily on the Valisure citizen petition, several putative class actions involving BPO were filed earlier this month in California and Hawaii federal courts, arguing that BPO products contain unsafe levels of benzene resulting from degradation of BPO.

Arguing the products are "materially different than advertised" because benzene is not listed among the ingredients on product packaging or anywhere else, the plaintiffs contend they were misled to believe that BPO products are safe.

Attempting to state claims for false advertising, breach of warranty, deceptive trade practices and unjust enrichment, the plaintiffs seek recovery for their economic injuries — that is, the cost of the acne products purchased.

Takeaways

Prescription and over-the-counter drug manufacturers are already responsible for monitoring the stability of samples from each lot of their drug products to ensure the quality lasts through the labeled expiration date.

However, all sellers of BPO products may be affected by the class action litigation arising from the Valisure tests, and should take steps to review their batch release and stability data to prepare a defense to a variety of potential claims, if need be.

Manufacturers may wish to review their policies, procedures and internal supervisory roles to ensure compliance with and impact on regulatory obligations related to good manufacturing practices, adverse event reporting, drug shortage notifications and drug application requirements.

They can also confirm or tighten internal product specifications and analytical testing procedures, and scrutinize third-party raw materials and formulations, as well as related contract terms and supply chain partnerships.

To prepare for litigation involving multiple plaintiffs, defendants and jurisdictions, a comprehensive defensive strategy should be employed that includes securing early dismissal on dispositive motions arguing preemption, and alternatively requesting a stay under a theory of primary jurisdiction pending the outcome of the FDA's regulatory process.

The personal care industry is certainly no stranger to litigation stemming from independent studies suggesting an association between particular ingredients and various negative health effects. Although pending litigation involving BPO products does not allege physical injury, such suits are possible in the foreseeable future.

Manufacturers should be prepared to face claims including negligence or gross negligence, negligent misrepresentation, and strict liability for design defects and failure to warn. To mount an effective defense, manufacturers should get a jump on analyzing batch release and stability data, and preparing a scientific defense of their BPO products and related analytical testing programs.

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