Benzoyl Peroxide, Benzene, and Lots of Unanswered Questions: Where Are We Now?

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March 2024 proved to be a busy month for benzoyl peroxide in the media! We are now at almost 4 months since Valisure, an independent analytical laboratory located in Connecticut, filed a Citizen Petition on benzene in benzoyl peroxide drug products with the US Food and Drug Administration (FDA) on March 5, 2024.[1] This petition was filed shortly before the annual meeting of the American Academy of Dermatology was held in San Diego, California, creating quite a stir of concern in the dermatology world. Further information on the degradation of benzoyl peroxide with production of benzene was published in the medical literature in March 2024.[2] As benzene is recognized as a human carcinogen, manufacturing regulations exist to assure that it does not appear in topical products either through contamination or degradation over the course of a product's shelf-life.[3]

As anticipated, several opinions and commentaries appeared quickly, both on video and in various articles. The American Acne & Rosacea Society (AARS) released a statement on this issue on March 20, 2024.[4] The safety of the public is the overarching primary concern. This AARS statement does include some general suggestions related to benzoyl peroxide use based on the best assessment to date while awaiting further guidance from the FDA on this issue. Benzoyl peroxide is approved for use by the FDA as an over-the-counter (OTC) topical product for acne and also is in several FDA-approved prescription topical products.[5,6]

The following reflects my personal viewpoint as both a dermatologist and a grandfather who has grandchildren who use acne products. My views are not necessarily those of AARS. Since early March 2024, I have read several documents and spoken to several dermatologists, scientists, and formulators with knowledge in this area, including contacts at Valisure. I was hoping to get to some reasonable definitive answer but have not been able to achieve this to my full satisfaction. There are many opinions and concerns, and each one makes sense based on the vantage point of the presenter. However, several unanswered questions remain related to what testing and data are currently required of companies to gain FDA approval of a benzoyl peroxide product, including:

- assessment of stability and degradation products (including benzene),
- validation of testing methods,
- the issue of benzoyl peroxide stability in commercial products, and
- the relevant magnitude of resultant benzene exposures, especially as we are all exposed to benzene from several sources each day.

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I am certain that companies with benzoyl peroxide products will evaluate their already-approved products and also do further testing. However, in this situation, which impacts millions of people on so many levels, I feel there needs to be an organized approach to evaluate and resolve the issue, otherwise the likelihood of continued confusion and uncertainty is high. As the FDA is the approval body, I am hoping it will provide definitive guidance within a reasonable timeline so that clinicians, patients, and manufacturers of benzoyl peroxide can proceed with full confidence. Right now, we all remain in a state of limbo. It is time for less talk and more definitive action to sort out this issue.

REFERENCES

1. Valisure Citizen Petition on Benzene in Benzoyl Peroxide Products. March 5, 2024. Accessed June 5, 2024. https://assets-global.website-files.com/6215052733f8bb8fea016220/65e8560962ed23f744902a7b_Valisure%20Citizen%20Petition%20on%20Benzene%20in%20Benzoyl%20Peroxide%20Drug%20Products.pdf
2. Kucera K, Zenzola N, Hudspeth A, et al. Benzoyl peroxide drug products form benzene. *Environ Health Perspect*. 2024;132:37702. doi:10.1289/EHP13984
3. US Food and Drug Administration. Reformulating drug products that contain carbomers manufactured with benzene. December 2023. Accessed June 12, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/reformulating-drug-products-contain-carbomers-manufactured-benzene
4. American Acne & Rosacea Society. Response Statement from the AARS to the Valisure Citizen Petition on Benzene in Benzoyl Peroxide Drug Products. March 20, 2024. Accessed June 12, 2024. https://www.einpresswire.com/article/697481595/response-statement-from-the-aars-to-the-valisure-citizen-petition-on-benzene-in-benzoyl-peroxide-drug-products
5. Department of Health and Human Services. Classification of benzoyl peroxide as safe and effective and revision of labeling to drug facts format; topical acne drug products for over-the-counter human use; Final Rule. *Fed Registr*. 2010;75:9767-9777.
6. US Food and Drug Administration. Topical acne drug products for over-the-counter human use—revision of labeling and classification of benzoyl peroxide as safe and effective. June 2011. Accessed June 12, 2024. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/topical-acne-drug-products-over-counter-human-use-revision-labeling-and-classification-benzoyl