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August 20, 2024

Submitted electronically

Robert Califf
Commissioner, Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Citizen Petition

Dear Commissioner:

A. Action Requested

The undersigned submits this petition under section 21 CFR 10.30 of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of Food and Drugs to recall and suspend sales of benzoyl peroxide (BPO) from the US Market due to the presence of benzene at levels the FDA has determined present a "life threatening" health hazard and illegal to sell under current FDA guidance.

B. Statement of Grounds

The Food and Drug Administration's ("FDA") is responsible for protecting the public by ensuring the safety, efficacy, and security of US consumers who use drug products.

In 2010, the FDA issued a "final rule to include benzoyl peroxide as a generally recognized as safe and effective (GRASE) active ingredient in over-the-counter (OTC) topical drug products." 75 FR 9776, OTC Monograph M006 (Part 333, subpart D, Topical Acne Drug Products for OTC Human Use). These benzoyl peroxide ("BPO") products are intended to be used one to three times a day as needed. 21 CFR 333.303(d)(1).

Pursuant to 21 CFR 330.10(a)(12), "[t]he Commissioner [of Food and Drugs] may propose on the Commissioner's own initiative to amend or repeal any monograph established pursuant to this section."

Pursuant to 21 CFR 330.10(b), "[a]ny product which fails to conform to an applicable monograph after its effective date is liable to regulatory action."

The BPO acne treatment products ("products") currently being sold to US consumers fail to conform to the applicable monograph because the products contain high levels of benzene and/or degrade to form benzene during the shelf-life of the products, which render the products adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act.

The FDA recognizes that "[b]enzene is a carcinogen that causes leukemia and other blood disorders"[1] and classifies benzene as a "Class 1" solvent that should be "avoided" in drug manufacturing.[2] FDA guidance provides: "Solvents in Class 1 [e.g. benzene] should not be employed in the manufacture of drug substances, excipients, and drug products because of [its] unacceptable toxicity."[3]

Within the past several months, petitioner has acquired numerous different BPO acne treatment products previously sold to US consumers and has individually purchased several other BPO products "off the shelf" from different manufacturers. These BPO products were subsequently tested *at room temperature* by an independent certified laboratory.[4] As illustrated below, the results make clear that the products contain dangerous levels of benzene and that this is an industry-wide problem:

1. **CeraVe Foaming Cream Wash 10 % BPO – 597.05 ppm benzene**
2. **CeraVe Foaming Cream Cleanser 4% BPO – 191.48 ppm benzene**
3. **Clearasil 5IN1 Spot Treatment – 374.57 ppm benzene**
4. **Clearasil 5IN1 Spot Treatment – 445.07 ppm benzene**
5. **Equate Acne Treatment Gel – 592.46 ppm benzene**
6. **Equate Acne Treatment Gel – 625.66 ppm benzene**
7. **Equate Acne Treatment Gel – 561.17 ppm benzene**

[1] FDA alerts drug manufacturers to the risk of benzene contamination in certain drugs, 12/27/2023, at https://www.fda.gov/drugs/pharmaceutical-quality-resources/fda-alerts-drug-manufacturers-risk-benzene-contamination-certain-drugs.
[2] Q3C – Tables and List: Guidance for Industry (Center for Drug Evaluation and Research, Food and Drug Administration, 2017), at https://www.fda.gov/media/71737/download.
[3] *Id.*
[4] The testing referenced herein was not conducted by Valisure and are wholly independent of the testing and results disclosed by Valisure in its March 5, 2024 citizen petition regarding BPO products. Unlike Valisure's testing—which heated its BPO products to 34°C, 50°C and 80°C respectively—the BPO products identified herein were not subjected to elevated temperatures during testing.

8. **MDacne Customized Treatment Cream – 359.94 ppm benzene**
9. **Neutrogena On-The-Spot -- 209.54 ppm benzene**
10. **Neutrogena On-The-Spot – 187.56 ppm benzene**
11. **La Roche-Posay Effaclar Duo 5.5% BPO – 261.21 ppm benzene**
12. **La Roche-Posay Effaclar Duo – 311.97 ppm benzene**
13. **Neutrogena On-The-Spot -- 187.56 ppm benzene**
14. **Obagi Medical – Clenziderm MD – 319.79 ppm benzene**
15. **Obagi Medical – Clenziderm MD Therapeutic Lotion 5% BPO – 59.94 ppm benzene**
16. **Obagi Medical – Clenziderm MD Therapeutic Lotion 5% BPO – 80.47 ppm benzene**
17. **Padagis – 270.03 ppm benzene**
18. **PanOxyl Acne Foaming Wash 10% BPO – 349.45 ppm benzene**
19. **PanOxyl Acne Foaming Wash 10% BPO – 378.51 ppm benzene**
20. **PanOxyl -- 563.68 ppm benzene**
21. **PanOxyl – 606.90 ppm benzene**
22. **Perrigo Acne Medication Wash 10% BPO – 655.68 ppm benzene**
23. **Perrigo Acne Medication Wash 10% BPO – 350.71 ppm benzene**
24. **Perrigo Acne Treatment Gel – 434.39 ppm benzene**
25. **Perrigo BPO 2.5% BPO – 168.97 ppm benzene**
26. **Proactive+Skin Smoothing Exfoliator – 209.29 ppm benzene**
27. **Rugby BPO Topical Wash USP 10% – 434.64 ppm benzene**[5]

According to the FDA's Center for Drug Evaluation and Research ("CDER"), the levels of benzene detected in the products above present a "life threatening" health hazard and exceed the ICH[6] and USP[7] guideline value of 2 parts per million ("ppm"), meaning the products are

[5] Petitioner is willing to provide copies to the FDA of each benzene test identified herein upon request.
[6] The term "ICH" refers to The International Conference on Harmonization (ICH) Q3C Impurities: Residual Solvents guidance (December 1997), at https://www.fda.gov/media/71736/download?attachment.
[7] The term "USP" refers to United States Pharmacopeia (USP) Residual Solvents, at https://www.uspnf.com/sites/default/files/usp_pdf/EN/USPNF/generalChapter467Current.pdf.

illegal to market and distribute in the US.[8] *See* Exhibit A (CDER Health Hazard Evaluation, July 8, 2021).

More specifically, in July 2021, the CDER conducted a "Health Hazard Evaluation" on "Multiple Aerosol Sunscreen Products" manufactured by Johnson & Johnson. *See* Exhibit A. The evaluation was requested following testing which showed benzene levels ranging "from 11.2 to 23.6 ppm" in Johnson & Johnson's aerosol sunscreen products. Specifically, the agency requested "an evaluation of the likelihood and risks associated with using aerosol sunscreens that contain benzene 11.2 to 23.6 ppm," which "levels exceed the guideline value provided by ICH [Q3C] and USP" limits, states the report. The evaluation concluded that serious adverse effects, including potential for "life-threatening" issues or "permanent impairment of a body function" were "likely to occur" at exposure levels within that range. In addition, the evaluation stated that "individuals with altered skin absorption (i.e., infants, elderly, broken skin) and individuals who are exposed to benzene from other sources . . . may be at greater risk."

Further, on December 27, 2023, in response to reports of benzene contamination in various drug products, the FDA issued an "Alert," stating: "Drug manufacturers with a risk for benzene contamination should test their drugs accordingly and should not release any drug product batch that contains benzene above 2 ppm[.] … *If any drug product batches with benzene above 2 ppm are already in distribution, the manufacturer should contact FDA to discuss the voluntary initiation of a recall*[.]"[9]

When, by the FDA's own assessment, the level of benzene in drug products already in distribution present "life threatening" health hazards that warrant a voluntary recall, *immediate action is required*. Regrettably, manufacturers have done nothing to warn consumers of the dangers associated with using their BPO products. And worse, they continue to profit from the sales of these adulterated products every single day.

US consumers deserve accountability from the agency responsible for protecting them. Amost six months after being notified by Valisure of the dangerous levels of benzene in numerous manufacturers' BPO products, the FDA has done nothing to warn consumers about this clear and present danger. This petition is thus intended to arm the FDA with additional evidence so it may take immediate action. There is no reason to debate why one BPO product contains 59 ppm benzene (Obagi Therapeutic Lotion) on the low end and another contains 625 ppm (Equate Acne Treatment Gel) on the high end. This is because *all such products contain*

[8] "The United States Pharmacopeia (USP) Residual Solvents limits the concentration of benzene to not more than 2 parts per million (ppm)." Exhibit A. Similarly, "the ICH assessment says: 'From the data of human leukemia and exposure concentrations of benzene, it was calculated that a daily intake of 0.02 mg was associated with a lifetime cancer risk of 10^{-5} and provides a guideline value for benzene of 0.02 mg per day (2 ppm).'" *Id*.

[9] FDA alerts drug manufacturers to the risk of benzene contamination in certain drugs, 12/27/2023, at https://www.fda.gov/drugs/pharmaceutical-quality-resources/fda-alerts-drug-manufacturers-risk-benzene-contamination-certain-drugs.

vastly more than 2 ppm benzene—the level at which the FDA has said a recall is necessary—and present an ongoing health hazard to US consumers.

At minimum, the Commissioner should demand that manufacturers immediately cease marketing the products to US consumers, then work with manufacturers to discuss the voluntarily initiation of a recall. The Commissioner's failure to take immediate action in light of the evidence presented by petitioner and others will lay bare the agency's inability to protect consumers from dangerous drug products. Please do something! And soon.

C. Economic Impact

Will be provided at the request of the Commissioner.

D. Environmental Impact

Petitioner is categorically excluded from this requirement.

E. Certification

The undersigned certifies, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner which are unfavorable to the petition.

Respectfully submitted,

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[10] Disclosure: Petitioner represents consumers who purchased BPO products contaminated with dangerous levels of benzene.