November 3, 2021

Division of Dockets Management
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

Re: Valisure Citizen Petition on Benzene in Body Spray Products

Dear Sir or Madam:

The undersigned, on behalf of Valisure LLC ("Valisure" or "Petitioner"), submits this Citizen Petition ("Petition") pursuant to Sections 301(21 U.S.C. § 331), 501 (21 U.S.C. § 351), 502 (21 U.S.C. § 352), 505 (21 U.S.C. § 355), 601 (21 U.S.C. § 361), 602 (21 U.S.C. § 362), 702 (21 U.S.C. § 372), 704 (21 U.S.C. § 374), and 705 (21 U.S.C. § 375) of the Federal Food, Drug and Cosmetic Act (the "FDCA"), in accordance with 21 C.F.R. 10.20 and 10.30, to request the Commissioner of Food and Drugs ("Commissioner") to issue a regulation, request recalls, revise industry guidance, and take such other actions set forth below.

## A. Action Requested

Antiperspirant body sprays are considered over-the-counter drugs and certain deodorant body sprays are considered cosmetics that are regulated by the U.S. Food and Drug Administration ("FDA").[1] Valisure has tested and detected high levels of benzene in specific batches of body spray products, some of which contain active pharmaceutical ingredients aluminum chlorohydrate or aluminum sesquichlorohydrate. The Centers for Disease Control and Prevention ("CDC") states that the Department of Health and Human Services has determined that benzene causes cancer in humans.[2] The World Health Organization ("WHO") and the International Agency for Research on Cancer ("IARC") have classified benzene as a Group 1 compound thereby defining it as "carcinogenic to humans."[3] FDA currently recognizes the high danger of this compound and lists it as a "Class 1 solvent" that "should not be employed in the manufacture of drug substances, excipients, and drug products because of their unacceptable toxicity ... However, if their use is unavoidable in order to produce a drug product with a significant therapeutic advance, then their levels should be restricted" and benzene is restricted under such guidance to 2 parts per million ("ppm").[4] Because many of the body spray products Valisure tested did not contain detectable levels of benzene, it does not appear that benzene use is unavoidable for their manufacture, and considering the long history and widespread use of

[1] Certain body sprays may also be dually regulated as cosmetics under the FDCA, and the designations "drug" and "cosmetic" are not mutually exclusive.

[2] Centers for Disease Control and Prevention, *Facts About Benzene* (2018) (https://emergency.cdc.gov/agent/benzene/basics/facts.asp)

[3] International Agency for Research on Cancer and World Health Organization, *IARC Monographs on the Identification of Carcinogenic Hazards to Humans* (https://monographs.iarc.who.int/list-of-classifications)

[4] Food and Drug Administration, *Q3C – Tables and List Guidance for Industry* (2017) (https://www.fda.gov/media/71737/download)

these products, it also does not appear that they currently constitute a significant therapeutic advance; therefore, any significant detection of benzene should be deemed unacceptable. The National Institute for Occupational Safety and Health ("NIOSH") recommends protective equipment be worn by workers expecting to be exposed to benzene at concentrations of 0.1 ppm and defines "inhalation, skin absorption, ingestion, skin and/or eye contact" as exposure routes.[5, 6] The Environmental Protection Agency ("EPA") has estimated that lifetime exposure to benzene at 0.4 parts per billion ("ppb"), or 0.0004 ppm, will increase the risk of developing cancer in humans at the same 1 in 100,000 exposed persons rate as FDA uses to set regulatory limits on other trace impurities like N-nitrosamines.[7, 8]

Valisure found multiple body spray products that contain levels of benzene that significantly surpass the 2 ppm conditional FDA restriction. The presence of this known human carcinogen in body spray products regularly used by adults and adolescents in large volumes makes this finding especially troubling.

This Petition requests that the Commissioner take the following actions:

1) request a recall of identified batches of body spray products on the basis that, due to contamination with a known human carcinogen, these products are adulterated under Section 501 of the FDCA (21 U.S.C. § 351) and misbranded under Section 502 of the FDCA (21 U.S.C. § 352);

2) conduct examinations and investigation under Section 702 (a) of the FDCA (21 U.S.C. § 372(a)) regarding these products, their manufacturing processes, and the manufacturer submissions made for FDA approval under 704 (a) of the FDCA (21 U.S.C. § 374(a)), and effect labeling revisions as needed;

3) provide information to the public regarding these products under Section 705(b) of the FDCA (21 U.S.C. § 375(b));

4) develop guidance documents for the analysis of benzene in body spray products;

5) review and update the current FDA guidance "Q3C – Tables and List, Guidance for Industry" to include guidance for the acceptable concentration of benzene for drug products, such as body sprays, that do not require benzene for manufacturing and do not

[5] Centers for Disease Control and Prevention. *The National Institute for Occupational Safety and Health (NIOSH), Benzene* (October 30, 2019) (https://www.cdc.gov/niosh/npg/npgd0049.html)
[6] Centers for Disease Control and Prevention. *The National Institute for Occupational Safety and Health, BENZENE: Systemic Agent* (2011) (https://www.cdc.gov/niosh/ershdb/emergencyresponsecard_29750032.html)
[7] Environmental Protection Agency. *Benzene; CASRN 71-43-2*. (https://iris.epa.gov/static/pdfs/0276_summary.pdf)
[8] Food and Drug Administration (February 2021). Control of Nitrosamine Impurities in Human Drugs. (https://www.fda.gov/media/141720/download)

constitute a "significant therapeutic advance," or potentially expand the current statement that benzene "should not be employed in the manufacture of drug substances" to clarify that there is no acceptable level of benzene and define a reasonable limit of detection;

6) review and update the current FDA guidance "Q3C – Tables and List, Guidance for Industry" to include guidance on the permitted daily exposure of benzene for drug products that do not require benzene for manufacturing and do not constitute a "significant therapeutic advance" and separately for drug products that require benzene for manufacturing and constitute a "significant therapeutic advance";

7) develop guidance documents defining the mass of a standard daily total application of body spray, which may include multiple discrete applications, so that a daily exposure of benzene can be calculated for body spray products;

8) request a recall of identified batches of body spray cosmetic products on the basis that, due to contamination with a known human carcinogen, these products are adulterated under Section 601 of the FDCA (21 U.S.C. § 361) and misbranded under Section 602 (21 U.S.C. § 362);

9) review and update regulation and published guidance for cosmetic products to include limitations on various impurities that pose known risks to human health and include benzene in such updates;

10) consider working with the United States Environmental Protection Agency on a joint initiative to address benzene contamination and potentially enter into a formal agreement committing to increase collaboration and coordination in areas of mutual interest relating to benzene contamination;

11) support the increasing number of independent drug quality testing programs in the United States by convening workshops, stakeholder meetings and providing other resources at FDA's disposal to further encourage and connect such programs; and

12) promulgate rules or administrative orders requiring robust independent chemical batch-level testing and verification of the chemical content of batches of drugs and other regulated consumer products and, while these are pending, issue guidance requesting such testing and verification.

**Background on Petitioner**

Valisure operates an analytical laboratory that is accredited to International Organization for Standardization ("ISO/IEC") 17025:2017 standards for chemical testing (PJLA Accreditation Number 94238). Valisure is registered with the Drug Enforcement Administration (License # RV0484814) and FDA (FEI #: 3012063246). Valisure's mission is to help ensure the safety, quality and consistency of medications and supplements in the market. In response to rising concerns about counterfeit medications, generics, and overseas manufacturing, Valisure developed proprietary analytical technologies that it uses in addition to FDA standard methods to test medications and consumer products distributed in the United States.

In an August 7, 2018, inspection of Valisure's facilities by FDA, it was determined that since Valisure's unique testing facility is not a part of the pharmaceutical manufacturing system and does not perform release testing, stability testing or any related services for pharmaceutical manufacturers, Valisure did not require FDA registration. However, Valisure has elected to maintain voluntary registration status with FDA. Valisure also received guidance that since it operates outside of the manufacturing industry using the appropriate ISO guidelines as opposed to GMPs, any product failures or concerns that Valisure identifies should be reported back to the pharmaceutical industry. Valisure has complied with this guidance and routinely provides reports to applicable parties in the pharmaceutical industry.

Given the high potential risk to public safety, Valisure seeks to utilize this Citizen Petition to bring these concerns directly to the attention of the Commissioner and FDA, and to request that they take prompt action.

## B. Statement of Grounds

In addition to the information described above, which is incorporated by reference, Valisure provides the following as its statement of grounds. FDA currently recognizes the danger of benzene and, as a result, has claimed it should not be used in the manufacture of any component of a drug product, and only if its use is "unavoidable" should a strict concentration limit of 2 ppm apply.[4]

There is a recent history of broad drug product recalls due to contamination with probable human carcinogens. Specifically, there have been a multitude of manufacturer recalls of medications,

such as valsartan, irbesartan, losartan,[9] ranitidine, nizatidine,[10] and metformin,[11] due to the detection of the Group 2, "probable human carcinogen" N-Nitrosodimethylamine ("NDMA") in excess of FDA limits. FDA limits for NDMA are defined in both parts per million ("ppm") and permissible daily intake, which is held constant at a specified nanogram level ("ng") per day for all drug products.[12]

Having a constant permissible daily intake or exposure is critical when there is variability in product size and exposures per day; a situation particularly relevant to an individual's application of body spray products. Petitioner is not aware of any FDA guidance on a permissible daily exposure for benzene in any drug or cosmetic product, including body sprays, and requests urgent action on behalf of FDA to issue guidance to fill this gap. Valisure's March 24, 2021 Citizen Petition on benzene contamination in hand sanitizer,[13] Valisure's May 24, 2021 Citizen Petition on benzene contamination in sun care products,[14] and the recent multiple recalls of

[9] Food and Drug Administration. *Search List of Recalled Angiotensin II Receptor Blockers (ARBs) Including Valsartan, Losartan and Irbesartan* (September 23, 2019) (https://www.fda.gov/drugs/drug-safety-and-availability/search-list-recalled-angiotensin-ii-receptor-blockers-arbs-including-valsartan-losartan-and).
[10] Food and Drug Administration. *FDA Updates and Press Announcements on NDMA in Zantac (ranitidine)* (April 16, 2020) (https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-zantac-ranitidine)
[11] Food and Drug Administration. *FDA Updates and Press Announcements on NDMA in Metformin* (October 5, 2020) (https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-ndma-metformin)
[12] Food and Drug Administration. *FDA updates table of interim limits for nitrosamine impurities in ARBs* (February 28, 2019) (https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-and-press-announcements-angiotensin-ii-receptor-blocker-arb-recalls-valsartan-losartan)
[13] Valisure's Citizen Petition on Hand Sanitizer Products Containing Benzene Contamination (filed March 24, 2021) (https://www.regulations.gov/document/FDA-2021-P-0338-0001).
[14] Valisure's Citizen Petition on Benzene in Sunscreen and After-sun Care Products (filed May 24, 2021) (https://www.regulations.gov/document/FDA-2021-P-0497-0001)

certain hand sanitizers, [15, 16] sunscreen[17, 18] and anti-fungal products[19] due to the presence of benzene further underscores the necessity to better regulate benzene and its apparent broad prevalence in the drug and consumer product supply chains.

Although the dangers and carcinogenic potential of nitrosamines, like the aforementioned compound NDMA, have been well documented since the 1960s, a direct link to cancer in humans has not yet been established. In contrast to nitrosamines, benzene has long been directly associated with cancer in humans by epidemiological studies with persistent exposure as low as 0.8 ppm.[20] The hematotoxicity of benzene[21] has been described as early as 1897. A study from 1939 on benzene stated that "exposure over a long period of time to any concentration of benzene greater than zero is not safe," [22] which is a comment reiterated in a 2010 review of benzene research specifically stating, "There is probably no safe level of exposure to benzene, and all exposures constitute some risk in a linear, if not supralinear, and additive fashion." [23] In an October 15, 2021 recall of sunscreen products due to the presence of benzene, Canadian

[15] Food and Drug Administration. Scentsational Soaps & Candles, Inc. Voluntarily Expands Nationwide Recall of Scented Hand Sanitizers Due to the Presence of Methanol (Wood Alcohol), Benzene and Acetaldehyde (May 13, 2021) (https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/scentsational-soaps-candles-inc-voluntarily-expands-nationwide-recall-scented-hand-sanitizers-due#recall-announcement)

[16] Food and Drug Administration. artnaturals® Issues Voluntary Recall of Limited Batches of 8oz Bottles of Scent Free Hand Sanitizer Due to Presence of Impurities (October 26, 2021) (https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/artnaturalsr-issues-voluntary-recall-limited-batches-8oz-bottles-scent-free-hand-sanitizer-due)

[17] Food and Drug Administration. Johnson & Johnson Consumer Inc. Issues Voluntary Recall of Specific NEUTROGENA® and AVEENO® Aerosol Sunscreen Products Due to the Presence of Benzene (July 14, 2021) (https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/johnson-johnson-consumer-inc-issues-voluntary-recall-specific-neutrogenar-and-aveenor-aerosol)

[18] Food and Drug Administration. Coppertone® Issues Voluntary Nationwide Recall of Specific Lots of Pure & Simple SPF 50 Spray (2021 Launch), Sport Mineral SPF 50 Spray (2021 Launch), and Travel-Size Coppertone® Sport Spray SPF 50 (1.6OZ) Aerosols Sunscreen Sprays Due to the Presence of Benzene. (September 30, 2021) (https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/coppertoner-issues-voluntary-nationwide-recall-specific-lots-pure-simple-spf-50-spray-2021-launch)

[19] Food and Drug Administration. Bayer Issues Voluntary Recall of Specific Lotrimin® and Tinactin® Spray Products Due to the Presence of Benzene (October 1, 2021) (https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/bayer-issues-voluntary-recall-specific-lotriminr-and-tinactinr-spray-products-due-presence-benzene)

[20] Glass, Deborah et. al. (2003). Leukemia Risk Associated With Low-Level Benzene Exposure. *Epidemiology* (Cambridge, Mass.). 14. 569-77. 10.1097/01.ede.0000082001.05563.e0. (https://journals.lww.com/epidem/Fulltext/2003/09000/Leukemia_Risk_Associated_With_Low_Level_Benzene.11.aspx)

[21] Santesson GG. 1897. Uber chronische Vergiftungen mit steinkohlen Benzin. Vier todes falle. Arch. Hyg. 31: 336–76

[22] Hunter, F.T. (1939). Chronic Exposure to Benzene (Benzol). II. The Clinical Effects. *Journal of Industrial Hygiene and Toxicology.* 1939 Vol.21 pp.331-54 (https://www.cabdirect.org/cabdirect/abstract/19402700388)

[23] Smith, Martyn T. (2010). Advances in Understanding Benzene Health Effects and Susceptibility. *Annual Review of Public Health.* 2010 Vol. 31:133-148 (https://www.annualreviews.org/doi/full/10.1146/annurev.publhealth.012809.103646)

health regulator Health Canada stated "there is no safe level of benzene."[24] According to the American Cancer Society:[25]

> IARC classifies benzene as "carcinogenic to humans," based on sufficient evidence that benzene causes acute myeloid leukemia (AML). IARC also notes that benzene exposure has been linked with acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), multiple myeloma, and non-Hodgkin lymphoma.

After Valisure's previous detection of benzene in hand sanitizers, FDA essentially confirmed certain findings in requesting that selected hand sanitizers not be used due to the presence of benzene and other contaminants.[26] Furthermore, Valisure's detection of benzene in sun care products has been independently confirmed by industry and appropriate actions taken.[17] In this Petition, Valisure did not utilize the industry standard USP <467> Residual Solvents Procedure using gas chromatography flame ionization detection ("GC-FID") instrumentation due to concern over the possibility that any impurities or other compounds in the products could have overlapping retention times. Instead, Valisure elected to utilize gas chromatography and detection by mass spectrometry ("GC-MS") instrumentation that allows mass spectral separation and utilizing selected ion chromatograms, along with other orthogonal approaches for confirmation of a few select products including high performance liquid chromatography ("HPLC") with UV detection. Gas chromatography conditions followed USP <467> with modifications to reduce run time that closely mirror those recommended by FDA in its August 24, 2020 guidance for impurities detection in hand sanitizer, which includes benzene analysis.[27] Valisure engaged the Chemical and Biophysical Instrumentation Center at Yale University to utilize GC-MS analysis on multiple selected body spray products, the results of which are shown in Tables 2-3.

Evaluating multiple methods had been useful in past drug product contaminations[28] and was performed here as well to help ensure validity of these highly concerning results. HPLC was employed for the identification and quantification of benzene in selected body spray products and confirmed both the identity and levels of contamination beyond 2 ppm.

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[24] Health Canada (October 15, 2021). *Ombrelle Garnier Complete Dry Mist Spray sunscreen recalled due to elevated benzene levels* (https://healthycanadians.gc.ca/recall-alert-rappel-avis/hc-sc/2021/76663a-eng.php)

[25] American Cancer Society. *Benzene and Cancer Risk* (January 5, 2016) (https://www.cancer.org/cancer/cancer-causes/benzene.html)

[26] Food and Drug Administration (October 4, 2021). *FDA updates on hand sanitizers consumers should not use*. (https://www.fda.gov/drugs/drug-safety-and-availability/fda-updates-hand-sanitizers-consumers-should-not-use)

[27] Food and Drug Administration. FDA Guidance Document (August 24, 2020) *Direct Injection Gas Chromatography Mass Spectrometry (GC-MS) Method for the Detection of Listed Impurities in Hand Sanitizers* (https://www.fda.gov/media/141501/download)

[28] Wu, Qian; et. al. (2020): A Broadly Accessible Liquid Chromatography Method for Quantification of Six Nitrosamine Compounds and N,N-Dimethylformamide in Metformin Drug Products Using High Resolution Mass Spectrometry. ChemRxiv. Preprint. (https://doi.org/10.26434/chemrxiv.13202849.v1)

As Valisure has noted in previous FDA Citizen Petitions, some GC-MS methodologies can lead ingredients to break down into a suspected analyte due to elevated GC oven temperatures. Valisure identified such a situation in its September 13, 2019 FDA Citizen Petition regarding the drug ranitidine, and Valisure therefore developed modifications to the existing methodologies to lower temperature and prevent degradation.[29] The GC-MS methodologies described in this petition utilized body temperature (37°C) for oven incubation. 40°C has been previously used for benzene analysis from liquid pharmaceuticals and beverages, and reduced false positive results compared with higher-temperature incubation.[30, 31]

Valisure acquired body spray product samples from many retailers and in many different formulations. Although Valisure has made a good faith effort to obtain samples reasonably representative of the general supply, many brands and formulations are not included in Valisure's analysis presented in this Petition. Even in this limited survey of certain available body spray products within the United States, multiple samples contained significantly detectable benzene and some batches contained up to about 9 times the conditionally restricted limit. There was significant variability from batch to batch, even within a single brand, underscoring the importance of batch-level chemical analysis and the necessity of overall increased quality surveillance of these pharmaceutical and consumer products.

Beyond the significant concern for public health, there is also evidence that benzene poses a serious risk to the environment, marine ecosystems, and United States waterways. Scientific papers published by NOAA have shown that benzene can be rapidly absorbed by fish[32] and short-term exposure (48 hr) to concentrations of benzene at parts per billion levels can significantly reduce survival of certain fish eggs.[33] Strict EPA regulations on benzene are detailed in a report authored by the Agency for Toxic Substances and Disease Registry ("ATSDR"),[34] which stated:

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[29] Valisure FDA Citizen Petition Requesting to Recall Ranitidine (dated September 9, 2019) (https://www.regulations.gov/docket?D=FDA-2019-P-4281)

[30] Kyoung, H. et al. (2008). Evaluation of headspace-gas chromatography/mass spectrometry for the analysis of benzene in vitamin C drinks; pitfalls of headspace in benzene detection. Biomedical Chromatography, Vol. 22, p. 900-905 (https://analyticalscience.wiley.com/do/10.1002/sepspec.19271ezine/full/)

[31] Liu, H. et al. (2011) A general static-headspace gas chromatographic method for determination of residual benzene in oral liquid pharmaceutical products. J Pharm Biomed Anal. Vol. 54(2), p. 417-21. doi: 10.1016/j.jpba.2010.09.006. (https://www.sciencedirect.com/science/article/abs/pii/S0731708510005182?via%3Dihub)

[32] S Korn, N Hirsch, J W Struthsaker (1976). UPTAKE, DISTRIBUTION, AND DEPURATION OF 14C-BENZENE IN NORTHERN ANCHOVY, ENGRAULIS MORDAX, AND STRIPED BASS, MORONE SAXATILIS. *Fishery Bulletin*. 1976 March Vol 74, No. 3: 545-51 (https://spo.nmfs.noaa.gov/sites/default/files/pdf-content/1976/743/korn.pdf)

[33] J W Struthsaker (1977). EFFECTS OF BENZENE (A TOXIC COMPONENT OF PETROLEUM) ON SPAWNING PACIFIC HERRING, CLUPEA HARENGUS PALLASI. Fisher Bulletin. 1977 Vol 75, No. 1: 43-49 (https://spo.nmfs.noaa.gov/sites/default/files/pdf-content/1977/751/struhsaker.pdf)

[34] Agency for Toxic Substances and Disease Registry (August 2007). *Toxicological Profile for Benzene*. (https://www.atsdr.cdc.gov/toxprofiles/tp3.pdf)

> EPA has set 5 ppb [equivalent of 0.005 ppm] as the maximum permissible level of benzene in drinking water. EPA has set a goal of 0 ppb for benzene in drinking water and in water such as rivers and lakes because benzene can cause leukemia.
> …
> EPA recommends 200 ppb [equivalent of 0.2 ppm] as the maximum permissible level of benzene in water for short-term exposures (10 days) for children.

Furthermore, the long-established epidemiological data in humans is utilized by EPA to determine that a lifetime exposure of 0.4 ppb, or 0.0004 ppm, of benzene in air will likely lead to one additional cancer case in 100,000 exposed persons. Although this concentration in air does not directly apply to the level of contamination inside an aerosol product, which is not likely inhaled in its entirety, it does provide rational guidance for calculations of potential exposure for such products as body sprays that may regularly be used indoors and in enclosed spaces. Assuming a 5 gram application of a contaminated aerosol fully evaporates and dissipates into a one cubic meter volume (approximately 35.3 cubic feet), the most contaminated body spray Valisure analyzed could potentially raise the air concentration of benzene to 28 ppb, or approximately 69 times the EPA-estimated threshold for increased cancer risk. In the same scenario, if the contaminated aerosol were used in a bathroom with a total volume measuring 160 $ft^3$ (20 sq ft with 8 ft ceiling), and given more time for the contaminated application to disseminate throughout the space, the entire bathroom air could potentially contain benzene at 6 ppb or approximately 15 times the EPA-estimated threshold for increased cancer risk.

The depth of experience with benzene regulation at EPA and the concern over environmental impact of benzene contamination may offer a rational basis for collaboration between FDA and EPA to expeditiously address the current lack of much needed benzene regulation in drug and consumer products. Such collaboration could efficiently result in regulations applicable for all FDA regulated drug and cosmetic products. Precedence for FDA formally working with EPA through the execution of an agreement committing to increase collaboration and coordination in areas of mutual interest is found in the October 18, 2019 announcement of a Memorandum of Understanding between FDA, EPA and the United States Department of Agriculture ("USDA") regarding food waste.[35, 36]

Although *antiperspirant* body spray products are considered drug products by FDA and many potentially dangerous chemical impurities are specifically limited for drug products (with the notable exception of benzene), there is comparably a significant lack of similar regulation for cosmetic products, such as *deodorant* body sprays, despite significant concern for increased

[35] Food and Drug Administration (October 30, 2019). *MOU 225-19-033*. (https://www.fda.gov/about-fda/domestic-mous/mou-225-19-033)
[36] Environmental Protection Agency (May 27, 2020). *Winning on Reducing Food Waste Federal Interagency Strategy* (https://www.epa.gov/sustainable-management-food/winning-reducing-food-waste-federal-interagency-strategy)

consumer protection and regulatory action.[37, 38, 39, 40] As FDA has acknowledged, the FDCA prohibits the marketing of adulterated or misbranded cosmetics in interstate commerce and specifies a product as adulterated if "it bears or contains any poisonous or deleterious substance which may render it injurious to users under the conditions of use prescribed in the labeling thereof, or under conditions of use as are customary and usual." [41] However, specifically defined limits of "poisonous or deleterious" substances, such as benzene, are not defined and should be reviewed and addressed by FDA.

Petitioner urges the Commissioner and FDA to expeditiously request recalls on the affected batches of products and to take other such actions outlined in this Petition as deemed appropriate.

## Analytical Methods

The method USP <467> Residual Solvents Procedure A was modified from flame ionization detection (FID) to mass spectrometry (MS) detection for benzene in body spray products. The sample preparation and headspace (HS) gas chromatography (GC) methods were also modified to fit body spray product matrices and to allow shorter run time. Identification of benzene is based on the retention time matching to certified reference standards and mass spectral matching to benzene. Quantification of benzene is performed by comparing peak area of benzene in a sample to a validated 11-point calibration curve. Results in parts per million is determined by dividing the micrograms of benzene detected per sample by the grams of material used for each sample.

### Materials and Methods

Agilent 7890B GC equipped with 7697A headspace autosampler coupled with 5977B MS was utilized for sample analysis, and a DB-Select 624 UI, 60m × 0.32mm × 1.8µm GC column (Agilent Technology, Santa Clara, CA) was used to separate benzene from other compounds. Dimethyl sulfoxide (DMSO, GC Grade) was used for sample preparation (Thermo Fisher Scientific, Waltham, MA). Standard of benzene (99.8 % purity) and isotopic labeled benzene standard ($d_3$-, 99.8% purity) was used for retention time verification (Sigma-Aldrich, St. Louis,

[37] A Kaufman, B Rauenzahn, J Chung (May 1, 2021). Does Cosmetics Regulation Need a Makeover? *The Regulatory Review*. (https://www.theregreview.org/2021/05/01/saturday-seminar-does-cosmetic-regulation-need-makeover/)
[38] W F Watt (July 17, 2015). Time for a Makeover: Newly Proposed Cosmetic Safety Legislation. *American Bar Association* (https://www.americanbar.org/groups/litigation/committees/products-liability/practice/2015/time-for-makeover-newly-proposed-cosmetic-safety-legislation/)
[39] A McDougall (March 27, 2012). Cosmetics regulation needs a makeover, industry urges Congress. *Cosmetics Design* (https://www.cosmeticsdesign.com/Article/2012/03/28/Cosmetics-regulation-needs-a-makeover-industry-urges-Congress)
[40] Breast Cancer Prevention Partners (2021). Safer Beauty Bill Package. (https://www.bcpp.org/resource/safer-beauty-bill-package-2021/)
[41] Food and Drug Administration (March 8, 2021). *FDA Authority Over Cosmetics: How Cosmetics Are Not FDA-Approved, but Are FDA-Regulated* (https://www.fda.gov/cosmetics/cosmetics-laws-regulations/fda-authority-over-cosmetics-how-cosmetics-are-not-fda-approved-are-fda-regulated)

MO). USP Class 1 residual solvents mixture was used for calibration confirmation (USP, Rockville, MD). All volumetric glassware used are Class A certified.

Standard and Sample Preparation

Benzene standard was diluted in DMSO. Calibration standards were prepared in 20-mL GC headspace vials to a total of 5 mL volume. Body spray product samples were dispensed into the GC headspace vials at approximately 500 mg and weighed, followed by adding 4.5 mL of DMSO to make up the final volume to approximately 5 mL and gently vortexing to mix. Five (5) mL of DMSO was used as blank samples.

Instrumental Analysis

Table 1 summarizes the major instrumental parameters used for analysis of benzene in the body spray samples.

**Table 1**. Instrumental parameters optimized for benzene detection in body spray samples.

| HS Autosampler | | GC | | MS | |
|---|---|---|---|---|---|
| Oven temperature (Temp) | 37 °C | Carrier gas | Helium | Source Temp | 230 °C |
| Loop Temp | 55 °C | Inlet Temp | 220 °C | Quad Temp | 150 °C |
| Transfer line Temp | 175 °C | Column flow | 2 mL/min | Acquisition type | SIM |
| Vial equilibration | 20 minutes (min) | Split ratio | 5:1 | Gain factor | 1 |
| Injection time | 1 min | Oven Temp Gradient | 60 °C (12 min) > 240 °C at 40 °C/min | Solvent delay | 3 min |
| Vial shaking | 71 shakes/min | GC run time | 18.5 min | | |
| Fill pressure | 15 psi | | | | |

Quality Assurance and Quality Control

Linear non-forcing through zero calibration curve was generated from the peak areas of the 11-point calibration standards. Calibration curve was accepted when the coefficient of determination $R^2$ was equal or greater than 0.995. Lower limit of detection (LLOD) and lower limit of quantification (LLOQ) were determined by spiking known amount of benzene into body spray samples that were pre-screened to be not detected for benzene or lower than the concentration of the lowest calibration standard. LLOD was 0.01 µg (equivalent to 0.02 ppm in body spray products) and LLOQ was 0.025 µg (equivalent to 0.05 ppm in body spray products). The measurement uncertainty was determined to be 25%. USP Class 1 residual solvent mixture was analyzed against the calibration and result of benzene agreed with certified concentration. Values are given for quantification of 2-fold over LLOQ or 0.10 ppm. Therefore, for the data presented in this petition, Valisure is using the nomenclature that any benzene detection of 0.10 ppm or above is "significantly detected," and any detection below this value is described as "< 0.10 ppm" and warrants further investigation but is likely of less concern than products with a defined value of 0.10 ppm or higher.

If sufficient material was available, body spray samples with benzene concentration above the reporting threshold of 0.10 ppm were analyzed in triplicates and reported herein. When the percent standard deviation of triplicates exceeded 20%, replicates were repeated. In many cases variability was high and might be due to inconsistent dispensing from body spray cans and high

sample volatility from inactive ingredients like butane and propane. Notably, lot 21188A was depleted quickly, and replicates were not possible for this sample.

## Analytical Findings

Using the GC-MS method described above for the determination of benzene, Valisure analyzed 108 unique batches from 30 brands of body spray products with the results detailed below. In summary, 59 product batches had detectable levels of benzene, 14 contained benzene in average concentrations between 0.10 ppm and 2.00 ppm and 24 contained over 2.00 ppm. In Tables 2 – 5, an asterisk "*" denotes data generated by the Chemical and Biophysical Instrumentation Center at Yale University from a sample from the same lot and specific product package. For samples where benzene was detected and when sufficient material was available, at least three samples from each batch were tested individually and the amount of benzene detected is reported as an average followed by the percent standard deviation of the results from replicate measurements.

**Table 2.** Product description and results of benzene analysis on various batches of body spray products in which benzene was detected at 2.00 ppm or higher.

| Brand | UPC | Lot | Expiration | Type | Description | API | Percent API | Average ppm | % St Dev |
|---|---|---|---|---|---|---|---|---|---|
| Old Spice | 012044001912 | 11671458SQ | 06/2023 | Antiperspirant | Pure Sport | Aluminum Chlorohydrate (Anhydrous) | 23 | 17.7 | 12% |
| Old Spice | 012044001912 | 11671458SB | 06/2023 | Antiperspirant | Pure Sport | Aluminum Chlorohydrate (Anhydrous) | 23 | 17.4<br>14.1* | 8% |
| Secret | 037000711087 | 11721458SG | 06/2023 | Antiperspirant | Powder Fresh, 24 HR Aerosol | Aluminum Chlorohydrate (Anhydrous) | 24 | 16.2<br>13.1* | 17% |
| Secret | 037000711087 | 11701458SH | 06/2023 | Antiperspirant | Powder Fresh, 24 HR Aerosol | Aluminum Chlorohydrate (Anhydrous) | 24 | 16.1 | 16% |
| Tag | 850007395421 | M 21075 | Unknown | Deodorant | Midnight, Fine Fragrance Body Spray, Long Lasting Scent | N/A (Cosmetic Product) | N/A | 14.1 | 28% |
| Secret | 037000711094 | 12181458SD | 08/2023 | Antiperspirant | Powder Fresh, 24 HR Aerosol | Aluminum Chlorohydrate (Anhydrous) | 24 | 12.5 | 12% |
| Sure | 883484002278 | (L)21175 | 05/2023 | Antiperspirant | Lasts All Day, Unscented, Aerosol | Aluminum Chlorohydrate (Anhydrous) | 10 | 11.1<br>6.41* | 14% |
| Equate | 681131346443 | 1E05 | 05/2023 | Antiperspirant | Dry Spray, Cucumber | Aluminum Chlorohydrate | 20.2 | 6.15<br>3.21* | 5% |
| Old Spice | 037000695707 | 246144504 | Unknown | Deodorant | Below Deck, Powder Spray, Feel Drier & Cleaner, Down Below, Fresh Air | N/A (Cosmetic Product) | N/A | 5.22<br>6.52* | 3% |
| Suave | 079400751508 | 07151AD14 | 07/2023 | Antiperspirant | 24 Hour Protection, Powder, Aerosol | Aluminum Chlorohydrate | 19.1 | 5.21 | 4% |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Right Guard | 017000068060 | Q405410200 | Unknown | Antiperspirant | Sport, Fresh, Up To 48 HR Odor Protection | Aluminum Chlorohydrate | 20 | 5.00<br>5.07* | 10% |
| Secret | 037000798842 | 11091458SN | 04/2023 | Antiperspirant | Cool Light & Airy Smooth Feel, Dry Spray, 48 Hour Freshness, Rose | Aluminum Chlorohydrate (Anhydrous) | 23.5 | 4.85 | 6% |
| Old Spice | 037000730347 | 11001458SC | 04/2023 | Antiperspirant | Sweat Defense, Stronger Swagger, Dry Spray, Sweat & Odor Protection | Aluminum Chlorohydrate | 23.5 | 4.54 | 24% |
| Brut | 827755070108 | (L)21155 | 05/2023 | Antiperspirant | Classic, 24 Hr Protection | Aluminum Chlorohydrate | 20.9 | 4.13 | 7% |
| Sure | 883484002278 | 21172 | 05/2023 | Antiperspirant | Lasts All Day, Unscented, Aerosol | Aluminum Chlorohydrate (Anhydrous) | 10 | 3.59 | 35% |
| Old Spice | 012044001912 | 12631458SB | 09/2023 | Antiperspirant | Pure Sport | Aluminum Chlorohydrate (Anhydrous) | 23 | 3.34 | 16% |
| Right Guard | 017000068060 | Q610900732 | Unknown | Antiperspirant | Sport, Fresh, Up To 48 HR Odor Protection | Aluminum Chlorohydrate | 20 | 2.61 | 16% |
| Secret | 037000798842 | 11991458SR | 07/2023 | Antiperspirant | Cool Light & Airy Smooth Feel, Dry Spray, 48 Hour Freshness, Rose | Aluminum Chlorohydrate (Anhydrous) | 23.5 | 2.58 | 20% |
| Tag | 854152008786 | 0252020203 | Unknown | Deodorant | Sport, Fearless, Fine Fragrance Body Spray, Long Lasting Scent | N/A (Cosmetic Product) | N/A | 2.53 | 46% |
| Sure | 883484002278 | (L)21099 | 03/2023 | Antiperspirant | Lasts All Day, Unscented, Aerosol | Aluminum Chlorohydrate (Anhydrous) | 10 | 2.36 | 9% |
| Brut | 827755070085 | (L)21167 | 05/2023 | Antiperspirant | Classic, 24 Hr Protection | Aluminum Chlorohydrate | 20.9 | 2.34<br>2.47* | 4% |
| Tag | 854152008762 | 0252035602 | Unknown | Deodorant | Sport, Dominate, Fine Fragrance Body Spray, Long Lasting Scent | N/A (Cosmetic Product) | N/A | 2.30 | 36% |
| Suave | 079400785503 | 08091AD00 | 08/2023 | Antiperspirant | 24 Hour Protection, Fresh, Aerosol | Aluminum Chlorohydrate | 19.1 | 2.30<br>2.11* | 9% |
| Suave | 079400785503 | 08091AD02 | 08/2023 | Antiperspirant | 24 Hour Protection, Fresh, Aerosol | Aluminum Chlorohydrate | 19.1 | 2.24 | 6% |

**Table 3.** Product description and results of benzene analysis on various batches of body spray products in which benzene was detected at 0.10 ppm to 2.00 ppm.

| **Brand** | **UPC** | **Lot** | **Expiration** | **Type** | **Description** | **API** | **Percent API** | **Average ppm** | **% St Dev** |
|---|---|---|---|---|---|---|---|---|---|
| Summer's Eve | 041608001310 | 21188A | Unknown | Deodorant | Ultra Freshening Spray, 5in1 | N/A (Cosmetic Product) | N/A | 1.89 | Insufficient Material |
| Secret | 037000729921 | 11101458SN | 04/2023 | Antiperspirant | Cool Light & Airy Smooth Feel, Dry Spray, 48 Hour Freshness, Light Essentials | Aluminum Chlorohydrate (Anhydrous) | 23.5 | 1.64 | 43% |
| Right Guard | 017000068268 | Q601900730 | Unknown | Antiperspirant | Sport, Powder Dry, Up To 48 HR Odor Protection | Aluminum Chlorohydrate | 20 | 1.46 | 7% |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Secret | 037000729914 | 12151458FC | 08/2023 | Antiperspirant | Cool Light & Airy Smooth Feel, Dry Spray, 48 Hour Freshness, Waterlily | Aluminum Chlorohydrate (Anhydrous) | 23.5 | 1.35 | 8% |
| Secret | 037000747727 | 12141458FB | 08/2023 | Antiperspirant | Out Last, Protecting Powder, 48 HR Sweat & Odor, Protection, Dry Spray | Aluminum Chlorohydrate (Anhydrous) | 23.5 | 1.24 | 18% |
| Suave | 079400784902 | 08141AD00 | 08/2023 | Antiperspirant | 24 Hour Protection, Powder, Aerosol | Aluminum Chlorohydrate | 19.1 | 0.97 | 7% |
| Right Guard | 017000068060 | Q631800729 | Unknown | Antiperspirant | Sport, Fresh, Up To 48 HR Odor Protection | Aluminum Chlorohydrate | 20 | 0.91 | 23% |
| Summer's Eve | 041608001310 | 21207A | Unknown | Deodorant | Ultra Freshening Spray, 5in1 | N/A (Cosmetic Product) | N/A | 0.87<br>0.65* | 11% |
| Power Stick | 850241000877 | 4154B861 | Unknown | Deodorant | All-Day Fresh Body Spray, Cool Blast | N/A (Cosmetic Product) | N/A | 0.56<br>0.89* | 36% |
| Old Spice | 037000749479 | 12641458FJ | 09/2023 | Antiperspirant | Sweat Defense, Ulitmate Captain, Dry Spray, 48 Hour, Sweat & Odor Protection | Aluminum Chlorohydrate (Anhydrous) | 23.5 | 0.44 | 19% |
| Soft & Dri | 735303381043 | Q61C313 | Unknown | Antiperspirant | Classic, Signature Soft Scent | Aluminum Chlorohydrate | 20 | 0.36<br>0.46* | 4% |
| Victoria's Secret | 0667552252907 | 1130J5B1 | Unknown | Deodorant | VS Him, Platinum | N/A (Cosmetic Product) | N/A | 0.29 | 16% |
| Power Stick | 850241000877 | 3220B681 | Unknown | Deodorant | Cool Blast | N/A (Cosmetic Product) | N/A | 0.21 | 43% |
| Victoria's Secret | 0667552252860 | 1131J5B1 | Unknown | Deodorant | VS Him, Deepwater | N/A (Cosmetic Product) | N/A | 0.20 | 28% |

**Table 4.** Product description and results of benzene analysis on various batches of body spray products in which benzene was detected at below 0.10 ppm.

| **Brand** | **UPC** | **Lot** | **Expiration** | **Type** | **Description** | **API** | **Percent API** | **Average ppm** |
|---|---|---|---|---|---|---|---|---|
| Arrid | 022600881612 | LL1182 | Unknown | Antiperspirant | Extra Extra Dry, XX, Morning Clean | Aluminum Chlorohydrate | 24.6 | < 0.10 |
| Calvin Klein | 3607342366428 | 924800 | Unknown | Deodorant | Eternity For Men, Aqua, All Over Body Spray | N/A (Cosmetic Product) | N/A | < 0.10 |
| Land of the Free | 3616302027866 | 115506 | Unknown | Deodorant | Great Smoky Mountains, Fresh & Woody, Notes of Birch & Bergamot | N/A (Cosmetic Product) | N/A | < 0.10 |
| Calvin Klein | 3607342366664 | 003500 | Unknown | Deodorant | Euphoria Men, All Over Body Spray | N/A (Cosmetic Product) | N/A | < 0.10 |
| Bath & Body Works | 0667553804006 | 1155P3B2 | Unknown | Deodorant | Marble, Men's Collection | N/A (Cosmetic Product) | N/A | < 0.10 |
| Arrid | 022600886716 | LL1027 | Unknown | Antiperspirant | Extra Extra Dry, XX, Ultra Fresh | Aluminum Chlorohydrate | 24.6 | < 0.10 |
| Calvin Klein | 3607342435179 | 113000 | Unknown | Deodorant | Ck One, All Over Body Spray | N/A (Cosmetic Product) | N/A | < 0.10 |
| Dove | 079400342423 | 03141AX05 | 03/2023 | Antiperspirant | Advanced Care, Moisture With Natural Oil, Dry Spray, Nourished Beauty | Aluminum Chlorohydrate | 20.2 | < 0.10 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Calvin Klein | 3607342366428 | 027600 | Unknown | Deodorant | Eternity For Men, Aqua, All Over Body Spray | N/A (Cosmetic Product) | N/A | < 0.10 |
| Bath & Body Works | 0667553849823 | 1238P3A1 | Unknown | Deodorant | Teakwood, Men's Collection | N/A (Cosmetic Product) | N/A | < 0.10 |
| Dove | 079400528063 | 02121AX04 | 02/2023 | Antiperspirant | Advanced Care, Moisture With Natural Oil, Dry Spray, Original Clean | Aluminum Chlorohydrate | 20.2 | < 0.10 |
| Degree | 079400343642 | 03281AX19 | 03/2023 | Antiperspirant | Motionsense, DrySpray, Sexy Intrigue | Aluminum Chlorohydrate | 23.3 | < 0.10 |
| Nautica | 3614228963121 | 111800 | Unknown | Deodorant | Midnight Voyage | N/A (Cosmetic Product) | N/A | < 0.10 |
| Dove | 079400447890 | 08161AX25 | 08/2023 | Antiperspirant | Men+Care, Dry Spray, Stain Defense, Cool, 48 HR + Comfort | Aluminum Chlorohydrate | 20.2 | < 0.10 |
| Dove | 079400350305 | 02061AX08 | 02/2023 | Antiperspirant | Men+Care, Dry Spray, Clean Comfort, 48 HR + Comfort | Aluminum Chlorohydrate | 20.2 | < 0.10 |
| Dove | 079400447890 | 10080AX38 | 10/2022 | Antiperspirant | Men+Care, Dry Spray, Stain Defense, Cool, 48 HR + Comfort | Aluminum Chlorohydrate | 20.2 | < 0.10 |
| Dove | 079400478764 | 06181AX21 | 06/2023 | Antiperspirant | Men+Care, Refreshing, Eucalyptus + Birch, Plant-Based Moisturizer, Dry Spray | Aluminum Chlorohydrate | 20.2 | < 0.10 |
| Dove | 079400591463 | 07081AX02 | 07/2023 | Antiperspirant | Advanced Care, Moisture With Natural Oil, Dry Spray, Invisible, Clear Finish | Aluminum Chlorohydrate | 20.2 | < 0.10 |
| Axe | 079400471383 | 04180AX15 | 04/2022 | Antiperspirant | Dry Spray, Better Than The Hype, Don't Sweat it - Smell Fresh, 48 H Dry | Aluminum Chlorohydrate | 20.2 | < 0.10 |
| Nautica | 3614223428052 | 107600 | Unknown | Deodorant | Blue | N/A (Cosmetic Product) | N/A | < 0.10 |
| Dove | 079400600592 | 03271AX08 | 03/2023 | Antiperspirant | Men+Care, Invigorating, Lime + Sage, Plant-based Moisturizer, 48 HR | Aluminum Chlorohydrate | 20.2 | < 0.10 |

**Table 5.** Product description of various batches of body spray for which benzene was not detected through initial analysis of at least one sample from each batch.

| **Brand** | **UPC** | **Lot** | **Expiration** | **Type** | **Description** | **API** | **Percent API** |
|---|---|---|---|---|---|---|---|
| Gold Bond | 041167049051 | 21B401 | Unknown | Deodorant | Ultimate, Men's Essentials, Body Powder, Spray, Nightfall, Scent | N/A (Cosmetic Product) | N/A |
| Guy Laroche | 719346140249 | HSU30WV | Unknown | Deodorant | Drakkar Noir | N/A (Cosmetic Product) | N/A |
| Axe | 079400471390 | 12169AX05 | 12/2021 | Antiperspirant | Dry Spray, Non-Stop Hustle, Don't Sweat It - Smell Fresh, 48 H Dry | Aluminum Chlorohydrate | 23.3 |
| Degree | 079400471062 | 07311AX06 | 07/2023 | Antiperspirant | Advanced Protection, 72 H Dry Spray, Powder | Aluminum Sesquichlorohydrate | 17.6 |
| Old Spice | 012044045121 | 11371458GH | Unknown | Deodorant | Fiji, Aluminim Free, Re Fresh, Scent Technology | N/A (Cosmetic Product) | N/A |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Kenneth Cole | 883991093394 | 1025 08:53 | Unknown | Deodorant | Vintage Black, All Over Body Spray | N/A (Cosmetic Product) | N/A |
| Kenneth Cole | 608940557631 | 1D01 13:13 | Unknown | Deodorant | Reaction, All Over Body Spray | N/A (Cosmetic Product) | N/A |
| Suave | 079400446657 | 07311AX17 | 07/2023 | Antiperspirant | Coconut Kiss, Instantly Dry, Dry Spray | Aluminum Chlorohydrate | 23.3 |
| Old Spice | 012044045275 | 11791458GB | Unknown | Deodorant | Sea Spray, Lasting Cologne Scent, Refresh Scent Technology | N/A (Cosmetic Product) | N/A |
| Land of the Free | 3616302027835 | 118005 | Unknown | Deodorant | Acadia, Cool & Aquatic, Notes of Pine & Sea Salt | N/A (Cosmetic Product) | N/A |
| Azzaro | 719346606189 | 91T00Z8 | Unknown | Deodorant | Chrome | N/A (Cosmetic Product) | N/A |
| Davidoff | 3614223708741 | 0253 | Unknown | Deodorant | Cool Water, All Over Body Spray | N/A (Cosmetic Product) | N/A |
| Dove | 079400350695 | 04131AX31 | 04/2023 | Antiperspirant | Men+Care, Dry Spray, Extra Fresh, 48 Hr + Comfort | Aluminum Chlorohydrate | 20.2 |
| Designer Imposters | 026169018434 | 21106E 299295A | Unknown | Deodorant | If You Like Red by Giorgio You'll Love Our, A Little Sexy, Fragrance Body Spray | N/A (Cosmetic Product) | N/A |
| Prince Matchabelli | 045893669309 | 21011E 291067A | Unknown | Deodorant | Wind Song, Extraordinary Fragrance Body Spray | N/A (Cosmetic Product) | N/A |
| Designer Imposters | 026169016348 | 21127E 301357A | Unknown | Deodorant | If You Like Giorgio You'll Love Primo, Fragrance Body Spray | N/A (Cosmetic Product) | N/A |
| Designer Imposters | 026169023681 | 21047E 293497A | Unknown | Deodorant | Like Viva La Juicy, By Juicy Couture? You'll Love Rock It!, Fragrance Body Spray | N/A (Cosmetic Product) | N/A |
| Designer Imposters | 026169022516 | 20357E 289096A | Unknown | Deodorant | Like CK One By Clavin Klein? You'll Love Our You, For a Man Or a Woman, Suberb Fragrance Body Spray | N/A (Cosmetic Product) | N/A |
| Axe | 079400472694 | 01170AX02 | 01/2022 | Antiperspirant | Dry Spray, Non-Stop Hustle, Don't Sweat It - Smell Fresh, 48 H Dry | Aluminum Chlorohydrate | 23.3 |
| Speed Stick | 022200962285 | 4042US25263 | Unknown | Deodorant | Gear, Advanced Performance, Clean Peak, 24/7 Protection, Freshcore | N/A (Cosmetic Product) | N/A |
| Axe | 079400550200 | 07183AX63 | Unknown | Deodorant | Phoenix, Body Spray | N/A (Cosmetic Product) | N/A |
| Axe | 079400260932 | 02283AX42 | Unknown | Deodorant | Apollo | N/A (Cosmetic Product) | N/A |
| Axe | 079400440853 | 2P M6084 | Unknown | Antiperspirant | Signature, Night, 48 Anti Marks Protection | Aluminum Chlorohydrate | 23.3 |
| Axe | 079400471390 | 08020AX28 | 08/2022 | Antiperspirant | Dry Spray, Non-Stop Hustle, Don't Sweat It - Smell Fresh, 48 H Dry | Aluminum Chlorohydrate | 23.3 |
| Right Guard | 017000068114 | Q60A222100 | Unknown | Deodorant | Sport, Original, Up To 48 HR Odor Protection | N/A (Cosmetic Product) | N/A |
| Degree | 079400589569 | 06051AX42 | 06/2023 | Antiperspirant | Motionsense, DrySPray, Ultraclear, Black+White | Aluminum Chlorohydrate | 20.2 |
| Hollister | ASIN:B0080AS2ZM | 111C-D | Unknown | Deodorant | Coastline | N/A (Cosmetic Product) | N/A |
| Degree | 079400590671 | 06111AX17 | 06/2023 | Antiperspirant | Motionsense, DrySPray, Ultraclear, Black+White | Aluminum Chlorohydrate | 20.2 |
| Dove | 079400350305 | 05021AX39 | 05/2023 | Antiperspirant | Men+Care, Dry Spray, Clean Comfort, 48 HR + Comfort | Aluminum Chlorohydrate | 20.2 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Axe | 079400472144 | 10239AX01 | 10/2021 | Antiperspirant | Dry Spray, On Your Grind, Don't Sweat It - Smell Fresh, 48 H Dry | Aluminum Chlorohydrate | 23.3 |
| Degree | 079400589569 | 07011AX55 | 07/2023 | Antiperspirant | Motion Sense, Dry Spray, Ultraclear, Black + White | Aluminum Chlorohydrate | 20.2 |
| Degree | 079400343703 | 06291AX29 | 06/2023 | Antiperspirant | Motion Sense, Dry Spray, Cool Rush, 48 H | Aluminum Chlorohydrate | 23.3 |
| Old Spice | 012044045138 | 12241458GZ | Unknown | Deodorant | Wolfthorn, Aluminum Free, Re Fresh, Scent Technology | N/A (Cosmetic Product) | N/A |
| Old Spice | 012044045152 | 11771458GN | Unknown | Deodorant | Dragonblast, Aluminum Free, Re Fresh, Scent Technology | N/A (Cosmetic Product) | N/A |
| Suave | 079400446640 | 08101AX08 | 08/2023 | Antiperspirant | 24 Hour Protection, Powder, Instantly Dry, Dry Spray | Aluminum Chlorohydrate | 23.3 |
| Suave | 079400446657 | 08101AX20 | 08/2023 | Antiperspirant | Coconut Kiss, Instantly Dry, Dry Spray | Aluminum Chlorohydrate | 23.3 |
| Old Spice | 012044045138 | 11451458GD | Unknown | Deodorant | Wolfthorn, Aluminum Free, Re Fresh, Scent Technology | N/A (Cosmetic Product) | N/A |
| Axe | 079400471383 | 08310AX18 | 08/2022 | Antiperspirant | Dry Spray, Better Than The Hype, Don't Sweat it - Smell Fresh, 48 H Dry | Aluminum Chlorohydrate | 20.2 |
| Old Spice | 012044045114 | 11601458GB | Unknown | Deodorant | Swagger, Aluminim Free, Re Fresh, Scent Technology | N/A (Cosmetic Product) | N/A |
| Duke Cannon | 850020740185 | 21161 | 09/2021 | Deodorant | Dry Ice, Powder, With Menthol to Cool and Activated Charcoal to Deodorize, Trench Warfare | N/A (Cosmetic Product) | N/A |
| Dove | 079400350305 | 07161AX73 | 07/2023 | Antiperspirant | Men+Care, Dry Spray, Clean Comfort, 48 HR + Comfort | Aluminum Chlorohydrate | 20.2 |
| Power Stick | 850241000877 | 2336E5901 | Unknown | Deodorant | Cool Blast | N/A (Cosmetic Product) | N/A |
| Old Spice | 012044045145 | 12011458GB | Unknown | Deodorant | Krakengard, Aluminum Free, Re Fresh, Scent Technology | N/A (Cosmetic Product) | N/A |
| Bath & Body Works | 0667553341259 | 1216J5B1 | Unknown | Deodorant | Bourbon, Men's Collection | N/A (Cosmetic Product) | N/A |
| Axe | 079400454614 | 08100AX01 | Unknown | Antiperspirant | Phoenix, Dry Spray, 48 H Dry | Aluminum Chlorohydrate | 23.3 |
| Degree | 079400471055 | 08191AX07 | 08/2023 | Antiperspirant | Advanced Protection, 72 H Dry Spray, Passion | Aluminum Sesquichlorohydrate | 17.6 |
| Bath & Body Works | 0667554805835 | 1223P3A1 | Unknown | Deodorant | Stone, Men's Collection | N/A (Cosmetic Product) | N/A |
| Hollister | ASIN:B07LBCW6YL | 112C-D | Unknown | Deodorant | So Cal | N/A (Cosmetic Product) | N/A |
| Old Spice | 012044045121 | 03171458GE | Unknown | Deodorant | Fiji, Aluminim Free, Re Fresh, Scent Technology | N/A (Cosmetic Product) | N/A |

Recall Request and Other Actions

This Petition seeks to have the Commissioner and FDA request recalls for the identified batches of body spray products, consistent with FDA's mandate to ensure the safety of the drug supply in America. The 38 batches in Table 2 and Table 3 have significantly detected benzene and should be recalled.

Such recalls are important for public safety. As indicated in Tables 2 - 5, there is significant batch-to-batch variation in benzene content, but many batches of body spray contain no detectable benzene and thus recalls should not overly burden the distribution chain or impact the availability of body spray for use by the public.

Petitioner further requests updates and revisions to the current "Q3C – Tables and List, Guidance for Industry" that consider drug products, such as body sprays, whose manufacture does not require benzene and that do not constitute a significant therapeutic advance, and where the common exposure per individual can vary widely. Regarding the conditional restriction limit on benzene, a substantially lower limit than 2 ppm should be set for such products where, according to current FDA guidance, benzene should not be used at any point in manufacturing, or FDA should potentially expand the current statement that benzene "should not be employed in the manufacture of drug substances" to clarify that there is no acceptable level of benzene and define a reasonable limit of detection. Regarding the highly variable exposure of an individual to body spray products, which can relate to variations in application amount per individual and number of applications per day, FDA should update current guidance with a daily permissible exposure limit, as is the case with nitrosamine impurities. To properly quantify daily exposure, FDA should provide further guidance on the amount of body spray product and number of applications that a daily permissible exposure limit should apply to.

In addition, for the reasons stated above, Valisure requests that FDA conduct examinations and investigation under Section 702 (a) of the FDCA (21 U.S.C. § 372(a)) regarding these products, their manufacturing processes, and the manufacturer submissions made for FDA approval under 704 (a)of the FDCA (21 U.S.C. § 374(a)), and effect labeling revisions as needed. Further, FDA should provide information to the public regarding these drug products under Section 705(b) of the FDCA (21 U.S.C. § 375(b)).

With regard to deodorant body spray products, this Petition urges FDA to request a recall of identified batches of deodorant body spray products on the basis that they contain benzene, a known human carcinogen and, as such, a deleterious substance which may render the affected products injurious to users under the conditions of use in the labeling, or under customary and usual conditions. For this reason, FDA should find that these products are adulterated under Section 601 of the FDCA (21 U.S.C. § 361) and misbranded under Section 602 (21 U.S.C. § 362).

Independent, Batch-level Testing and Certification of Drug Products in the United States

Petitioner is also requesting that FDA promulgate rules or issue administrative orders requiring robust independent chemical batch-level testing and verification of body spray products that are regulated as drugs by FDA. In the interim, while these are pending, FDA should issue formal guidance recommending such testing and verification.

This is necessary in order to serve public health and help protect Americans from adulterated drug products, an issue of growing concern.[42] Grounds for this request are also rooted in strong support from the medical community, as evidenced by a 2019 resolution from the American College of Cardiology ("ACC"), calling for the American Medical Association to advocate for legislation requiring independent testing and verification of the chemical content of batches of pharmaceuticals. The resolution is at Attachment A.

Particularly with quality issues that broadly affect a subset of brands and specific batches of consumer products, independent batch-level testing should be made known to an individual or any purchaser though visible certification on product labels. Independent certification of products can help prevent adulterated products from entering the market and can help ensure consumers, patients, and practitioners continue to feel safe using and recommending or prescribing certified drug and cosmetic brands of products, which are important for public health.

In addition, Petitioner requests that FDA support the expanding number of independent drug quality analysis programs, including that announced at The University of Kentucky,[43] through various means available to it. This may include convening new focused meetings, seminars, symposiums, and similar gatherings to connect programs and healthcare stakeholders that could benefit by learning from and augmenting such programs. It may also include adding such a topic to existing meetings, seminars, symposiums, and similar gatherings when appropriate.

As Valisure's results indicate, relying on industry self-reporting of analytical results is not sufficient protection from potentially dangerous contamination. A proactive drive for broad, independent testing should be combined with decisive action on the part of regulators to quickly request recalls and take other actions as appropriate.

## C. Environmental Impact

Petitioner claims a categorical exclusion under 21 C.F.R. § 25.30, and believes that this Petition qualifies for a categorical exclusion from the requirement to submit an environmental assessment or environmental impact statement. To Petitioner's knowledge, no extraordinary circumstances exist.

## D. Economic Impact

Pursuant to 21 C.F.R. § 10.30(b), economic impact information will be submitted by the Petitioner only upon request of the Commissioner following review of this Petition.

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[42] Stockman, Farah (September 18, 2021). Our Drug Supply Is Sick. How Can We Fix It? *The New York Times* (https://www.nytimes.com/2021/09/18/opinion/drug-market-prescription-generic.html)

[43] Chapin, Elizabeth; Willett, Kristi. (October 1, 2020) UK Drug Quality Testing Leads to Petition to Recall Injectable Drug. *University of Kentucky* (http://uknow.uky.edu/research/uk-drug-quality-testing-leads-petition-recall-injectable-drug)

## E. Certification

The undersigned certifies that, to the best knowledge and belief of the undersigned, this petition includes all the 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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