

## EDUCATIONAL OBJECTIVES

At the end of this continuing education activity, pharmacists and pharmacy technicians will be able to

- DISCUSS benzene and its associated safety risks
- EXPLAIN the role of independent pharmaceutical testing companies and the FDA's responsibility to recall contaminated products
- DESCRIBE the pharmacy team's role in helping patients navigate product contamination reports



The University of Connecticut School of Pharmacy is accredited by the Accreditation Council for Pharmacy Education as a provider of continuing pharmacy education.

Pharmacists and pharmacy technicians are eligible to participate in this knowledge-based activity and will receive up to 0.1 CEU (1 contact hours) for completing the activity, passing the quiz with a grade of 70% or better, and completing an online evaluation. Statements of credit are available via the CPE Monitor online system and your participation will be recorded with CPE Monitor within 72 hours of submission

ACPE UAN: 0009-0000-21-048-H05-P  
0009-0000-21-048-H05-T

Grant funding: NONE

Cost: \$4 pharmacists  
\$2 technicians

INITIAL RELEASE DATE: August 12, 2021  
EXPIRATION DATE: August 12, 2024

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## Patient Safety Benzene in Sunscreen: The Reasons for the Rhyme

**ABSTRACT:** Sunscreen is essential to sun safety, but people should know when their sunscreen product may do more harm than good. Ideally, people would use sunscreen every day for life, so safety is critical. However, safety data for these products is lacking and recent detection of benzene contamination in certain sunscreen products is concerning. Long-term benzene exposure—including topically—increases the risk of bone marrow damage and blood cancers. An independent pharmaceutical testing company that made this discovery has petitioned the FDA to recall affected products. Some manufacturers have responded by initiating voluntary recalls, but most have not. Pharmacy teams should know where to find up-to-date recall information and be prepared to help patients navigate the sunscreen aisle to find safe products.

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**FACULTY DISCLOSURE:** The author has no actual or potential financial conflicts of interest associated with this article.

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**PAUSE AND PONDER:** How many questions have you fielded about benzene contamination in sunscreen?

## INTRODUCTION

The benefits of sunscreen use are no secret. If used properly, sunscreen can reduce skin cancer risk and prevent or delay skin aging.<sup>1</sup> Sunburns—accidental or as a result of purposeful suntanning—are a major health hazard, and ultraviolet (UV) radiation is the most preventable cause of skin cancer.<sup>1</sup> Experts say that UV exposure causes about 90% of melanomas<sup>1</sup> (the deadliest form of skin cancer) and the risk of developing a potentially fatal melanoma doubles with a lifetime history of five or more sunburns.<sup>2</sup>

Ideally, people would apply sunscreen daily for a lifetime, so the safety of these products is sacrosanct. The lack of data surrounding sunscreen ingredient safety is concerning. The U.S. Food and Drug Administration (FDA). FDA regulates sunscreen as an over-the-counter (OTC) medication.<sup>3</sup> Unfortunately, the FDA has not

updated sunscreen regulations since 2011.<sup>4</sup> In 2019, they released a draft monograph with a goal of updating regulations shortly thereafter, but the proposal was withdrawn in the first coronavirus relief bill due to changes in OTC drug regulation. The FDA is expected to propose new regulations in fall 2021.<sup>4</sup>

Of 16 sunscreen active ingredients that have been marketed, only two—titanium dioxide and zinc oxide—have the United States (U.S.) Food and Drug Administration (FDA) GRASE (generally recognized as safe and effective) rating.<sup>3</sup> The FDA also considers two ingredients—the chemical filters para-aminobenzoic acid (PABA) and trolamine salicylate—unsafe due to safety concerns, so they are no longer used in non-prescription sunscreen products. The remaining 12 active ingredients have insufficient safety data to make a positive GRASE determination: avobenzone, cinoxate, dioxybenzone, ensulizole, homosalate, meradimate, octinoxate, octisalate, octocrylene, oxybenzone, padimate O, and sulisobenzene.<sup>3</sup>

Sunscreen safety doesn't stop with active ingredients. With the recent discovery of carcinogenic contaminants in many sunscreens and after-sun care products, consumers are tasked with selecting a sunscreen product that won't do more harm than good. Pharmacy teams can help concerned consumers select a sunscreen product that does not pose additional health risk.

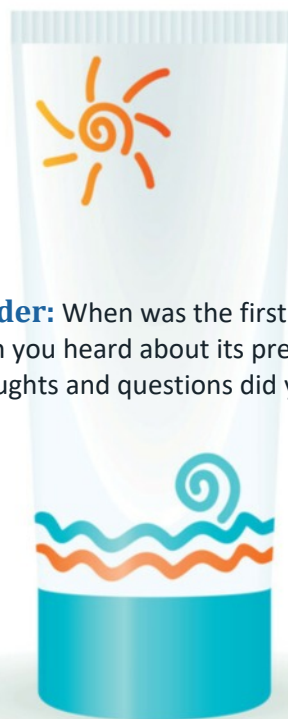
## COMPROMISED SUNSCREEN SAFETY

In May 2021, Valisure—an online pharmacy and a third-party pharmaceutical testing company—issued a statement regarding sunscreen and after-sun care products that they found to contain benzene, a known carcinogen (cancer-causing chemical).<sup>5</sup> They subsequently petitioned the FDA to recall the affected products.

Pharmacy teams may recognize this company, as it's the same one that discovered N-Nitrosodimethylamine (NDMA) contamination in ranitidine, valsartan, and metformin products. Valisure's co-founder suffered complications and relapses caused by batch variability in his own anticonvulsant medication, sparking a passion for drug quality.<sup>6</sup> Now, his company is dedicated to preventing others from suffering adverse effects at the hand of low-quality medications. They introduce a new level of quality control by testing medications at the end of the supply chain to ensure patients receive uncontaminated, superior drug products.

## Benzene and Its Safety Risks

Benzene—a carbon ring—is a common chemical used to make other chemicals. Historians argue about who made the original benzene discovery.<sup>7</sup> Benzene's structure eluded discovery because of its circular structure; chemists tended to think of compounds as linear, not circular. August Kekule, a German chemist, claims to have dreamt of a snake biting its own tail,



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**Pause and Ponder:** When was the first time you heard of benzene? When you heard about its presence in sunscreens, what thoughts and questions did you have?

or possibly six snakes or six monkeys linking hands and tails. He first described this dream at a benzene symposium in 1890, but some historians believe other chemists described benzene before this supposed dream.<sup>7</sup> In any case, manufacturers in various industries today use benzene-derived chemicals to make a variety of things, including<sup>8</sup>

- detergents
- drugs
- dyes
- lubricants
- materials (e.g., plastics, nylon and synthetic fibers, resins, rubbers)
- pesticides

Both natural processes and human activities can expose people to benzene. Benzene occurs naturally in cigarette smoke, crude oil, and gasoline and it is a byproduct of forest fires and volcanoes.<sup>8</sup>

The signs and symptoms of benzene toxicity depend on the route of exposure (see [Table 1](#)). This chemical is toxic to human cells, causing them to malfunction. In the bone marrow, benzene decreases red blood cell production, which can lead to anemia.<sup>8</sup> It can also change the blood levels of antibodies, causing damage to the immune system through loss of white blood cells. The severity of benzene poisoning depends on the exposure amount, route, and length of time and the patient's age and preexisting medical conditions.

The concern with benzene in sunscreen is long-term exposure rather than acute toxicity, given that sunscreen is intended to

**Table 1. Signs and Symptoms of Benzene Exposure<sup>8</sup>**

Inhalation (Immediate*)	Ingestion (Immediate*)	Long-Term (Any Route)
<ul style="list-style-type: none"><li>● Confusion</li><li>● Death (at very high levels)</li><li>● Dizziness</li><li>● Drowsiness</li><li>● Headaches</li><li>● Irregular/rapid heartbeat</li><li>● Lung injury/irritation</li><li>● Tremors</li><li>● Unconsciousness</li></ul>	<ul style="list-style-type: none"><li>● Convulsions</li><li>● Death (at very high levels)</li><li>● Dizziness</li><li>● Irregular/rapid heartbeat</li><li>● Sleepiness</li><li>● Stomach irritation</li><li>● Vomiting (potential for aspiration)</li></ul>	<ul style="list-style-type: none"><li>● Anemia (decreased red blood cells)</li><li>● Excessive bleeding</li><li>● Immune system dysfunction</li><li>● Irregular menstrual periods</li><li>● Leukemia (cancer of blood-forming organs)</li></ul>

\*within minutes to several hours

be used daily for a lifetime. The major effects of long-term benzene exposure (i.e., for a year or more) are bone marrow damage and cancer, specifically leukemia.<sup>8</sup> The primary source of benzene exposure to the general public is inhalation from automobiles or gas stations, but any route that exposes benzene to the bloodstream for an extended period of time increases risk.<sup>8</sup> Effects on the bone marrow cause anemia and immunosuppression, increasing the risk of infection.

Research indicates that there is no “safe” level in benzene in sunscreen products.<sup>9</sup> Risk of long-term health effects are cumulative with additive exposure. Benzene absorption through the skin is especially concerning, given that studies show chemicals in sunscreen products are readily absorbed through skin and into the bloodstream after skin application.<sup>10</sup> Health Canada’s Bureau of Chemical Hazards has also demonstrated that sunscreen application increases the benzene absorption rate through the skin.<sup>11</sup> Benzene contamination in sunscreen products is a serious health concern that manufacturers and consumers should not take lightly.

### The Valisure Petition

Valisure issued a petition to the FDA in May 2021 urging them to recall benzene-contaminated sunscreen and after-sun care products. See **SIDEBAR: A Second-Look at Product Safety** for more information about independent pharmaceutical testing companies. Valisure analyzed 294 batches from 69 brands of sun care products.<sup>5</sup> About 27% of the batches tested (78 samples) contained detectable benzene, with some reporting as much as three times the FDA-accepted concentration limit of 2 ppm.<sup>5</sup> Unfortunately, despite any negative findings, third-party pharmaceutical testing laboratories have no authority to recall medications or consumer products. Valisure petitioned to the FDA, however, to recall 40 batches with significant benzene levels.<sup>5</sup>

Valisure’s petition stresses that while 2 ppm is generally considered safe for many products, sunscreen is not one of them. One



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researcher and clinician from Yale University commented to Valisure, “Considering that human skin has a large total surface area (~1.85 m<sup>2</sup>), and that ~28.5 g of sunscreen is needed per application to properly cover that skin surface, it follows then that there is not a safe level of benzene that can exist in sunscreen products. The total mass of sunscreen required to cover and protect the human body, in single daily application or repeated applications daily, means that even benzene at 0.1 ppm in a sunscreen could expose people to excessively high nanogram amounts of benzene.”<sup>5</sup>

How exactly benzene contamination occurs in sunscreen products is unclear. The FDA classifies benzene as a Class 1 solvent, meaning it should not be employed in the manufacture of drug products or excipients due to unacceptable toxicity.<sup>5</sup> If benzene use is unavoidable to produce a product with significant therapeutic value, levels should be restricted to less than 2 parts per million (ppm). Since Valisure indicated that not all sunscreens they tested contained benzene, it is safe to assume it is not unavoidable for sunscreen manufacturing.<sup>5</sup> Dr. Adam Friedman, a professor and chair of dermatology at George Washington University School of Medicine, says that benzene is not a byproduct of sunscreen filters, mineral nor chemical.<sup>14</sup> Valisure’s CEO says that the most evidence suggests raw material contamination be-

cause the study found contamination in a scattered fashion among brands and even within brands.

## WHAT HAPPENS NEXT?

Typically, the FDA evaluates and assesses the information provided in citizen petitions, like the one Valisure submitted, and initiates its own independent testing and verification process. In this case, the FDA also intends to “continue to monitor sunscreen manufacturing and marketing to help ensure the availability of safe sunscreens.”<sup>14</sup>

## Recall Responsibility

Understanding recalls in general is essential to easing patient concerns. A recall is a means of correcting or removing products that violate FDA laws or present a risk to consumer health from the market.<sup>15</sup> Recalls can be voluntary because manufacturers and distributors fulfill their duties to protect public health and well-being. They can also be initiated pursuant to an FDA request. When the FDA requests that a manufacturer recall a product, that recall is still voluntary, as the FDA is essentially giving the company a chance to recall the product rather than initiating court action.

As of August 5, 2021, the FDA has issued no official recall for benzene-contaminated sunscreen or after-sun products. Pharmacy teams should watch news outlets and look to the FDA website for updates on FDA-mandated recalls on sunscreen and after-sun care products.

## Manufacturers Taking Action

Some companies have issued voluntary recalls in response to the Valisure report, and pharmacy teams should be prepared that others may follow suit. As of August 5, 2021, Johnson & Johnson has voluntarily recalled certain lots of five sunscreen products in response to Valisure’s results:<sup>16</sup>

- Neutrogena Beach Defense aerosol sunscreen
- Neutrogena Cool Dry Sport aerosol sunscreen
- Neutrogena Invisible Daily defense aerosol sunscreen
- Neutrogena Ultra Sheer aerosol sunscreen
- Aveeno Protect + Refresh aerosol sunscreen

Additionally, CVS Health halted sales of two of its after-sun products that were implicated in the Valisure report.<sup>14</sup>

## PHARMACY TEAM’S ROLE

While the FDA has not issued an official recall of all of the sun care products in question, these findings are public. Pharmacy teams should be prepared to field questions from concerned consumers about benzene, the FDA petition, and what responsibilities or obligations the FDA has moving forward.

Patients may be understandably concerned about the safety of their sunscreen products, but pharmacy teams should advise them not to discontinue using sunscreen altogether. Sunscreen is essential to sun safety, and many options that are safe to use

## SIDEBAR: A Second-Look at Product Safety<sup>5,12,13</sup>

Manufacturers generally perform their own safety testing, but third-party independent testing laboratories provide a second level of unbiased testing and quality control. Independent testing companies may also have specialized equipment that manufacturers do not have. These laboratories are often accredited by the International Organization for Standardization (ISO) and/or registered with the FDA or Drug Enforcement Agency (DEA). They can also undergo private, third-party accreditation (e.g., Perry Johnson Laboratory Accreditation) that validates testing competency.



Accredited third-party laboratories also provide a document called a certificate of analysis (CoA) to assist the public in determining product safety and reliability. CoAs attest that an accredited laboratory has performed specified testing on drugs or products and those results were acceptable. Most follow a template that reports active ingredient levels, bacterial levels, and possible contaminants. To obtain a CoA, patients or pharmacy teams should collect the product name, lot number, and expiration date, then do one of the following:

- Contact the manufacturer directly to request the CoA and any other desired information
- Search the Internet, as some companies readily post this information online
- Look for third-party laboratories (e.g., Valisure) that publish their CoAs online

As a general rule, if a product’s manufacturer is unable or unwilling to provide a CoA, it is safe to assume their quality assurance process is poor or nonexistent. If you cannot verify the purity and quality of a product, it is likely not safe to use. Some laboratories will also test products at consumer request for a fee.

are still available. Direct people to Tables 2 and 3 of the testing company’s findings at <https://www.valisure.com/wp-content/uploads/Valisure-Citizen-Petition-on-Benzene-in-Sunscreen-and-After-sun-Care-Products-v9.7.pdf> to determine if their sun care brands contained detectable benzene levels. Many of the products Valisure tested did not contain detectable levels of benzene, so concerned consumers should feel comfortable using those products.<sup>5</sup>

Valisure also acknowledges that they have not tested every sunscreen and after-sun care product available.<sup>5</sup> Of the estimated 11,000 sunscreen products on the market today in the U.S., Valisure only tested 294 of them. The company has initiated a crowdsourcing study to test more sun care products. If patients prefer to have their own preferred sun care brands tested, they are encouraged to submit them to Valisure for free testing. Di-

	 <b>BEST</b>	 <b>AVOID</b>
<b>INGREDIENTS</b>	avobenzone zinc oxide mexoryl SX	oxybenzone vitamin A (retinyl palmitate) added insect repellent
<b>PRODUCTS</b>	cream broad-spectrum water resistant SPF 15-50	sprays powders SPF above 50

**Figure 1. Key Points in the Environmental Working Group Sunscreen Guide**

rect interested individuals to <https://www.valisure.com/valisure-studying-sun-care-product-contamination-2/> for more information on the crowdsourcing study.<sup>17</sup> While they only accept sunscreen and after-sun care samples at this time, concerned consumers can always report a medication concern on the Valisure website. Letting the company know about potentially problematic medications helps them to focus their research and development efforts where consumer concerns exist.

Pharmacy teams should also direct patients to reputable resources to identify sunscreen products that are rigorously tested for harmful ingredients, including the Environmental Working Group (EWG). EWG is a non-profit consumer health advocacy group that publishes a yearly guide to safe sunscreens. Refer people to [https://www.ewg.org/sunscreen/report/executive-](https://www.ewg.org/sunscreen/report/executive-summary/)

[summary/](https://www.ewg.org/sunscreen/report/executive-summary/) to access the EWG’s sunscreen guide.<sup>4</sup> Main points in this guide are summarized in **Figure 1**. Pharmacy teams should familiarize themselves with this guidance and be prepared to guide patients to safe products in the sunscreen aisle.

### CONCLUSION

Pharmacy teams and patients should not take the discovery of benzene in commonly-used sun care products lightly. Long-term exposure to benzene increases the risk of bone marrow damage and cancer. Pharmacy teams should advise patients to continue using sunscreen to protect themselves from UV radiation, but ensure they know where to find reliable safety information. Pharmacy teams should also encourage patients with preferred sun care brands to send their sunscreen products to Valisure for testing while this cost-free option is still available to consumers.

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