



A Spotlight on Sunscreen Regulation

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There may be nothing new under the sun, but the U.S. Food and Drug Administration (FDA) is facing calls for something new under the agency's authority over sunscreens. In recent months, the

FDA has declined to permit use of eight new sunscreen ingredients without additional data, although those ingredients have been used in Europe for more than 5 years and despite the recent passage of a U.S. law intended to expedite the marketing-approval process for new products. The controversy says as much about the challenges facing the agency as it does about sunscreen regulation.

Melanoma is a significant public health problem. Each year, 75,000 people in the United States are diagnosed with and 10,000 die from the disease (see graph).¹ The primary cause of melanoma is known: DNA damage resulting from exposure to ultraviolet

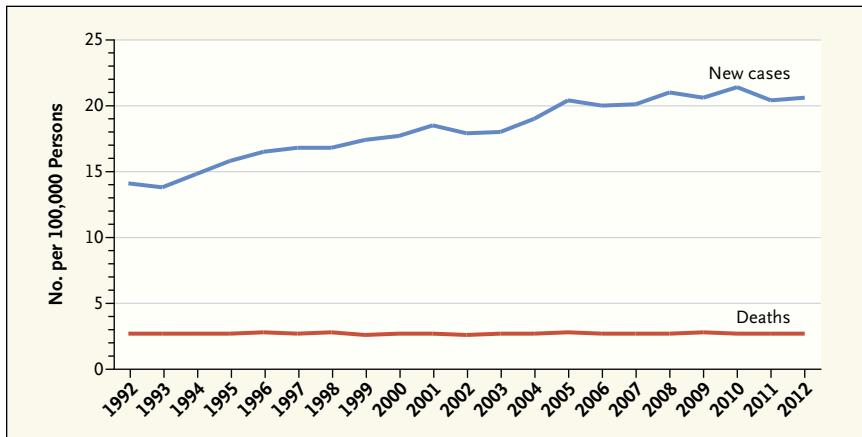
radiation. Nevertheless, melanoma rates have been increasing for decades. Reducing exposure to ultraviolet radiation, from both the sun and artificial sources such as tanning beds, is essential to prevention.

In 2012, the FDA determined that sunscreens blocking a broad spectrum of ultraviolet radiation with a sun protection factor (SPF) of 15 or greater could be marketed as reducing the risk of skin cancer. However, it did not remove from the market other sunscreens, such as those with a lower SPF that may only help prevent sunburns. As a result, some Americans may be purchasing "sunscreens" without knowing

that there's no evidence that they protect against cancer. In addition, many Americans fail to use sunscreen as recommended altogether.

Most broad-spectrum sunscreens marketed in the United States contain oxybenzone or avobenzone to block the type of ultraviolet radiation, known as UVA, that is most closely linked to cancer. Since 1999, the FDA has approved one new ingredient, ecamsule, for use in limited formulations for this purpose. In 2002, the agency established a mechanism for considering data from experience elsewhere, including in European countries, where sunscreens are regulated as cosmetics and other ingredients are widely used. But the agency did not take action on applications submitted through this pathway for more than a decade.

In 2013, advocates for patients



New Cases of Melanoma of the Skin and Deaths per 100,000 Persons, 1992 through 2012.

Data are from the Surveillance, Epidemiology, and End Results Program, National Cancer Institute.

with melanoma, dermatologists, and manufacturers of new ingredients came together in a coalition called Public Access to Sunscreens (PASS). This group argued that the new ingredients would result in products that are more attractive to consumers, such as longer-lasting products that don't require frequent reapplication. Expressing its dismay over the lack of action on the pending sunscreen applications, the coalition pressed Congress to impose tighter deadlines for FDA decision making. This approach, however, did not fully consider the agency's framework for review of sunscreens, resource needs, and public health role.

With respect to new prescription drugs, the FDA generally moves faster than European regulatory agencies, and it approved 41 products in 2014 — the most in 18 years. Key to this pace is the fact that under U.S. regulatory law, the agency tailors its approval decisions to the data at hand, receives extra resources (from user fees) for drug reviews, and if problems emerge after approval, has the ability to move quickly with a range of actions to

protect the public. Although this process is well suited to individual new therapeutics, it is cumbersome for many products intended to be sold over the counter in a wide variety of formulations and concentrations.

Over-the-counter products such as sunscreens are usually regulated through an entirely different process designed for products posing little to no risk, under the standard of "generally recognized as safe and effective." There is no product-specific approval decision; rather, the agency must issue proposed and final rules, with multiple opportunities for public comment, before authorizing each class of products. As with other agency regulations, rules for over-the-counter products generally require economic analyses, with clearance often required from both the Department of Health and Human Services and the White House Office of Management and Budget.

Unlike review of new prescription drugs, the pathway for over-the-counter products is supported by no additional resources. Between procedural requirements and inadequate resources, over-

the-counter product regulation proceeds in slow motion as compared with the rest of the agency. Rulemaking typically consumes many years, or even decades. Existing sunscreen ingredients, for example, are not, even now, the subject of a final regulation by the agency.

Once issued, rules for over-the-counter products allow companies to manufacture a broad array of formulations and dosages and to market them extensively. The agency has little ability to require the collection of data on long-term safety or efficacy. Even if new troubling safety information on over-the-counter products comes to light, the FDA cannot alter its approach quickly. Instead, it must begin the laborious rulemaking process all over again. These limitations understandably lead to a cautious approach to approving products, such as sunscreens, that are designed for long-term use by millions of children and adults in the absence of disease.

Indeed, in early 2014, the FDA released letters finding insufficient evidence to consider several of the new sunscreen ingredients "generally recognized as safe and effective." Then, in September, an FDA advisory committee recommended that the agency collect a broad set of data for evaluating all new sunscreen ingredients, including data on skin irritation, carcinogenicity, and developmental toxicology.²

At the end of the year, with the support of the PASS coalition, Congress passed and President Barack Obama signed bipartisan legislation called the Sunscreen Innovation Act. The new law set deadlines for FDA review and removed several procedural requirements for agency action. However,

the legislation provided no new resources, no new authority for postmarketing safety, and little new flexibility for the agency in the review process.

Soon after the law's passage, the FDA released a proposed decision to reject all eight pending ingredients, citing multiple gaps in data, including key safety studies and reports of adverse events in countries where relevant products are marketed.

The agency's proposal provoked a swift and angry response. In a press release, the PASS coalition stated that the agency "demonstrates clear disregard for increased rates of melanoma and the public's demand for latest sunscreen technology."³ The *Wall*

 An audio interview with Dr. Sharfstein is available at NEJM.org

Street Journal editorial board stated that "the agency's willful culture of control and delay is the real public-health menace. . . . The only solution is to strip the sunscreen police of all powers over the stuff."⁴

These attacks missed their mark. It's no surprise that the FDA would act cautiously given the scientific advice it's received and a legal structure that essentially provides it with just one tool: authorizing extensive marketing of multiple products and formu-

lations. Understanding the FDA means recognizing that the framework for over-the-counter products is not designed to promote innovation, even innovation with potential public health benefits.

In my view, Congress should try again and pass legislation establishing an alternative approval pathway that combines the flexibility of the new drug pathway with the ability to simultaneously approve multiple formulations and concentrations. The FDA should be able to negotiate with sponsors to get the right data without years of rulemaking, establish postmarketing data requirements, consult with other countries' regulators to establish consistent standards where possible, and move quickly in the event that safety concerns emerge. Congress should provide additional resources to facilitate timely analysis and review. That this path is viable is evidenced by the fact that the one approval of a product with a new sunscreen ingredient in the past decade came through the new drug pathway.

More timely and flexible review can expand sunscreen options for consumers and complement other measures to reduce melanoma prevalence. Promising steps include FDA efforts to discourage use of tanning beds and initia-

tives by the Centers for Disease Control and Prevention to promote prevention measures. The federal government should also reconsider whether it makes sense to continue allowing some products to be marketed as sunscreen without evidence of protection against cancer. After all, the ultimate goal is to make meaningful progress against this public health problem.

Disclosure forms provided by the author are available with the full text of this article at NEJM.org.

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DOI: 10.1056/NEJMp1504912

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Synthetic Cannabinoid–Related Illnesses and Deaths

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Synthetic cannabinoids (SCs) were first created in the 1980s as laboratory research tools (ligands) for studying human endocannabinoid receptor systems. SC-containing products supplied

by illicit manufacturers were then marketed throughout Europe as herbal incense, before arriving in the United States in November 2008. The prevalence and variety of SCs on the illicit mar-

ket have steadily increased over the past 6 years, as manufacturers and distributors of SCs and dealers of SC-containing products have attempted to circumvent federal, state, and local laws.