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Impact of Sunscreen Regulations in the United States on Suncare Development

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It is estimated that five million skin cancer incidences are diagnosed in about three million patients in the United States annually (1% of the population). These incidences of skin cancer are more than breast, prostate, lung, and colon cancers combined. There are about a 100,000 new cases of malignant melanomas (MM), the deadliest form of skin cancer, and almost 10,000 die each year from MM (1).

It is well known that skin cancer is due mostly from ultraviolet radiation, although credible evidence has surfaced that other wavelengths of the solar spectrum, most notably the high-energy frequency visible rays, and the infrared rays may also cause damage to the skin (2,3).

Concerns that I—and others—have expressed for many years about burgeoning skin cancer rates also pertain to the development of ultraviolet filters incorporated into sunscreens in the United States. Presently, in the United States, with the exception of zinc and titanium oxides, the filters are poorly designed and rely on technology developed in the last century, and thus they are all smaller molecules of molecular weights (MW) (Daltons) of less than 400. This makes them less efficient in ultraviolet (UV) absorbance, protecting predominantly in the UVB region, with the molecules small enough to permeate the bloodstream when applied to the skin. As the new U. S. Food and Drug Administration (FDA) data revealed (which will be discussed in more detail later in this article), all the small molecule filters tend to penetrate the skin. The Centers for Disease Control reported that oxybenzone was found in the breast milk of mothers as well as in the blood of 96% of Americans who were tested (4).

As new data surface about skin cancer incidences and the lack of adequate ultraviolet filters to protect us from UV radiation, in particular the UVA region, it is obvious that scientists and regulators need to triple their efforts in protecting the consumer. Of the 16 filters currently approved by the FDA, only four UV filters offer some protection from the UVA region. They are avobenzone (which, unfortunately, is photo unstable), oxybenzone (which is currently under severe attack from environmentalists and the medical community), menthyl anthranilate (which practically no one uses), and finally zinc oxide (which has its own challenges in formulations). On February 26, 2019, the FDA proposed new rules governing the regulation of sunscreens in the United States (5). If approved (see discussions in the following text), then it will basically render zinc oxide and titanium

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dioxide as the only two approved and Generally Recognized as Safe and Effective (GRASE) category I filters in the United States. Finally, the European time and extent application (TEA) filters, all eight of them, were categorically rejected by the FDA under the TEA process.

Let us now review the current FDA regulations in the United States. Sunscreens are regulated as drugs and not cosmetics in the United States. They are regulated as cosmetics in most of the world, including all of Europe, ASEAN countries, Japan, China, India, Hong Kong, Korea, Taiwan, Russia, the Middle East, and Mercosur countries. Australia has both "therapeutic" and "cosmetic," whereas Canada classifies sunscreens as both "drugs" and "natural health products" depending on the product. Classifying sunscreens as drugs exposes both their use and approval to the extensive scrutiny that drug approvals undergo in the United States. For approval, they will need a New Drug Application (NDA), a TEA approval, or are grandfathered in by the FDA as they did in 1978 when they published the Advanced Notice of Proposed Rulemaking (ANPR). Recently, however, the FDA has suggested that all filters and sunscreens be subjected to in vitro permeation testing (IVPT), the Maximum Usage Trial (MUsT) tests, and the developmental and reproductive toxicology (DART) test. Those new hurdles will undoubtedly eliminate most of our currently approved ultraviolet absorber filters in the United States.

The ANPR classified 21 UV filters as category I. It specified the level they could be used in sunscreens. They were allowed in sunscreen products in any combination so long as they had their appropriate Sun Protection Factor (SPF) and UVA testing completed as required by the FDA. The ANPR was followed by a "Tentative Final Monograph" (TFM) on sunscreens issued in 1993, then the "Final Rule" was implemented in 2012, and finally the "Proposed Final Rule" in 2019. No final monograph has yet been issued. The deadline imposed by the Congressional Sunscreen Innovation Act of November 26, 2019 has come and gone, and all indications are that it will be another 12–18 months before the finalization of the sunscreen monograph.

In all honesty, the FDA has serious issues to consider. Way back in 1978 when the ANPR was released, solar radiation protection by sunscreens was minimal, skin cancer rates were not well documented, available technology for designing ultraviolet filters was primitive, and achieving a tan was not the rage at the time. Affluency, people seeking the sun, and vacationing in popular resort destinations in the middle of winter were not fashionable or affordable. As the incidence of skin cancer spiraled out of control, new measures for protection—including the use of sunscreen—became paramount. Today, sunscreens are used by the vast majority of consumers in the United States. Many products are targeted for year-round daily use. Sunscreens sold today are recommended for both day and night use, rain or shine, and UV filters have been incorporated into a wide variety of sunscreens, skincare lotions, night creams, lip balms, haircare and anti-aging products. Many sunscreens were poorly formulated and rely predominantly on UVB protection with little or no UVA broad-spectrum protection. The sunscreen products today may contain up to six UV filters with a total percentage of UV filters well exceeding 25% of the formulation. Maximum SPF values were regulated by the ANPR in 1978 at 15, then 30 by the TFM in 1993, and then 50 by the Final Rule in 2012, with companies today insisting that the consumer needs higher SPF's reaching 70 and even higher than 100!! Collectively, these developments have startled the FDA, suncare manufacturers, and researchers alike. When sunscreens were approved in 1978, most of the current usage was never envisioned but ultimately led to the FDA's current stance to regulate or overregulate sunscreens in the United States.

Nevertheless, the FDA released the conditions for compliance of sunscreens with the Final Rule of December 2012 as follows:

(i) It must have an SPF of at least 15.
(ii) It must be a broad spectrum with a critical wavelength of at least 370 nm.
(iii) It must comply with a modified Principal Display Panel-Drug Facts.

It allowed companies to claim that "sunscreens reduce the risk of skin cancer and early skin aging when used as directed." In my opinion, the claim should not be addressing skin cancer and skin aging but instead that "sunscreen reduces or eliminates (or protects from) the harmful solar radiation." Period!

In their "Proposed Final" that was issued on February 26, 2019 (5), only two filters (zinc oxide and titanium dioxide) were classified as GRASE category I filters. Two other filters (PABA and trolamine salicylate) became category II ingredients (i.e., cannot be used anymore), and the remaining 12 ingredients (avobenzone, oxybenzone, octinoxate, octocrylene, octisalate, homosalate, meradimate, ensulizole, cinoxate, padimate O, dioxybenzone, and sulisobenzone) were classified as category III ingredients (i.e., require further extensive testing). The FDA specified that at a minimum two tests were required, namely, the MUsT test and the DART test, before any of those category III ingredients can be reclassified as GRASE category I filters.

In the FDA's "Proposed Final" of February 26, 2019, other changes were also proposed:

(i) Powders, wipes, towelettes, body washes, and shampoos were disallowed if they can contain UV filters with sunscreen claims.
(ii) Spray sunscreens will require further safety testing.
(iii) The maximum SPF allowed will now be SPF 60+. The marketing of SPF values up to 80 may be allowed but would require an NDA.
(iv) The UVA and Broad Spectrum labeling now needs to satisfy not only the critical wavelength test but also a new standard according to the formula below:

$$\mathrm{UVAI/UV} \geq 0.7$$

(v) Insect repellent/sunscreen combination products would now be classified as category II (i.e., not allowed). Many petitions were sent to the FDA requesting reversal of this proposal.

In May 2019, the FDA released the first of two MUsT tests on sunscreens in the *Journal of the American Medical Association* (JAMA) revealing that four UV filters (avobenzone, oxybenzone, octocrylene, and ecamsule) failed the test because of skin penetration far exceeding the proposed safety levels of 0.5 mg/mL (6). In January 2020, the FDA released its second MUsT study also in JAMA (7), which revealed that six UV filters failed the test, bringing the total UV filters that failed the test to seven (avobenzone, oxybenzone, octocrylene, octinoxate, octisalate, homosalate, and ecamsule) when both the May 2019 and the January 2020 reports were completed.

The Personal Care Product Council set up a work group to lobby the FDA to consider new data on eight of the remaining 12 category II filters (avobenzone, oxybenzone, octinoxate, octisalate, homosalate, ecamsule, octocrylene, and meradimate). No decision by the FDA on this proposal was reached to date.

The backdrop of all those developments date back to Hawaii's 2018 bill in their state legislature (sponsored by State Senator Mike Gabbard) that banned both oxybenzone and

octinoxate by January 2021 because of their perceived impact on coral reefs (8). This was followed by many countries banning both UV filters including the island of Palau and the U.S. Virgin Islands, as well as similar proposals for Key West, Florida, and the State of California. This debate has caught the attention of Congress which is currently legislating the new Over-The-Counter Reform Act. The legislation is expected to pass in early 2020* (See Footnote). The fiscal year 2019 Appropriations Bill currently has language directing the Environmental Protection Agency to coordinate a study with the National academy of Science to investigate the safety of all sunscreen ingredients and their impact on coral reefs and the environment. They were also tasked to evaluate the impact of banning those sunscreen ingredients on public health. The debate goes on!

Let me summarize the impact of all the regulations passed, proposed, and in development on the approval of safe and effective sunscreens in the United States. With Hawaii currently proposing a ban on all sunscreens that contain any UV filter, other than zinc oxide and titanium dioxide (9), chemists may have no choice but to develop all new sunscreen products using only these two inorganic filters, zinc and titanium oxides. This, of course, is an impractical and intolerable proposition. For one thing, the supply industry of those two raw materials is certainly not ready for such a huge demand. Major shortages or delays in product release will understandably occur. Will the consumer, who is used to low-priced mass marketed products, be willing to pay much more for products with similar protection? Will the consumer who is used to elegantly designed products tolerate aesthetically unappealing sunscreen products with zinc and titanium oxides? Will the consumer—who is used to SPF 60, 70, and even 100—accept SPF ratings of 35 or a maximum of 50? Will the consumer accept not having access to the convenient spray sunscreens that will now be difficult to formulate with these two inorganic filters? Are we providing the consumer with the most effective broad-spectrum sunscreen products to combat the epidemic rise of skin cancers lately with only those two ingredients? The questions are numerous, and the obvious answer is that it would be impractical, if not impossible, to create an innovative and effective industry with just those two mineral sunscreens.

So, what is the solution?

Obviously, part of the answer lies in the need for better-designed UV filters. We could start out with approving a few of the pending TEA European ingredients. Many of them have been used safely for years worldwide and are designed according to the Dalton 500 principle to reduce skin permeation. Molecules that have MW greater than 500 are generally much less permeable to the skin. This could be tested, and, perhaps, the IVPT, the MUsT test, and the DART test would be a requirement before their approval by the FDA. An evaluation of what constitutes an unsafe level of permeation causing diseases should be conducted. A more realistic safety level of a value different from 0.5 ng/ml may be more appropriate.

Do I agree with the FDA's reluctance to issue a final monograph especially because the usage of sunscreens today is massive? To a certain extent they are currently on the right track in critically evaluating all sunscreen ingredients, but, in my opinion, they are a tad too late. Better late than sorry? True, but their reluctance to approve safe and effective European TEA ingredients, and to instead relegate all the 12 category I ingredients that have been used since 1978, as non-usable, non-GRASE, without alternatives, casts a major shadow on their use for current skin cancer prevention and protection. How can a nonscientific average consumer use those products while the FDA is reporting that they

are being absorbed into our blood and are unsafe to use? Publishing their studies in JAMA without an alternative is a travesty that casted doubts on the current protocols in combating the rising incidence of skin cancer.

We need options and real solutions now for adequate protection from the harmful radiation of the sun. We need new safer ingredients and protocols for sun protection. Let us start out with approving the tried and true European filters. Also, allow American ingenuity the opportunity and the path to introduce new effective and safe ingredients to combat the rising incidents of skin cancer.

* Footnote: Since I wrote this article in January 2020, Congress released its Over-The-Counter Reform Act on March 25, 2020 as part of the 2 Trillion dollar stimulus package. For a review, please read my May and June "The Sunscreen Filter" column in HAPPI Magazine for all the recommendations pertaining to Sunscreens in the Reform Act.

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