

THE FDA RESPONSE: OBSTACLES AND DELAYS

THE FDA has decided to move the goal post. It has declared that to approve a new UV filter you must surpass the requirements of a New Drug Application (NDA). The new hurdle set by the FDA is that all such ingredients must pass the stringent requirements of GRASE (Generally Recognized as Safe and Effective). GRASE assumes that new OTC products are unsafe and their safety under all conditions of use must be proven and not the other way around. This is a higher standard than the NDA! For the eight new UV filters going through the supposedly fast-track process of the Time & Extent Application (TEA), this spells delays. The data that was submitted with the TEA applications is now rendered incomplete and inadequate. Thousands, perhaps millions, of dollars, and months, perhaps years, of delays will be the result of this action to get any new UV filter approved in the US.

The FDA sent letters in January to the manufacturers of six of the eight TEA ingredients, basically rejecting their TEA applications and demanding more data



How long will industry have to wait to get FDA's stamp of approval for new sunscreens?

and testing. On Feb. 24, the agency sent the remaining two letters to the suppliers of ecamsule and enzacamene citing that their application was lacking the necessary data to support their safety and effectiveness.¹ The irony is that an extensive NDA was recently approved by the FDA for the use of ecamsule in the US. L'Oréal spent millions of dollars and numerous years to support this NDA. In all fairness, the TEA request to approve a new UVA filter for use across the board in all formulations differs from an NDA that specifies that ingredient in one specific cosmetic formulation. However, this approach is totally impractical for the cosmetic industry, which annually introduces hundreds of variations and line extensions, to remain viable and competitive.

Moreover, the cost and time duration is wholly impractical for UV filters. Unlike a cholesterol- or blood pressure-reducing drug, where the rewards are in the billions of dollars for its manufacturer once the drug is approved, approval of a UV filter does not reap this kind of monetary benefit

for its manufacturer. Paying millions of dollars to support an NDA application, waiting years to complete the process, and applying an Amended NDA for every new SKU and application change, is wholly unworkable for the industry.

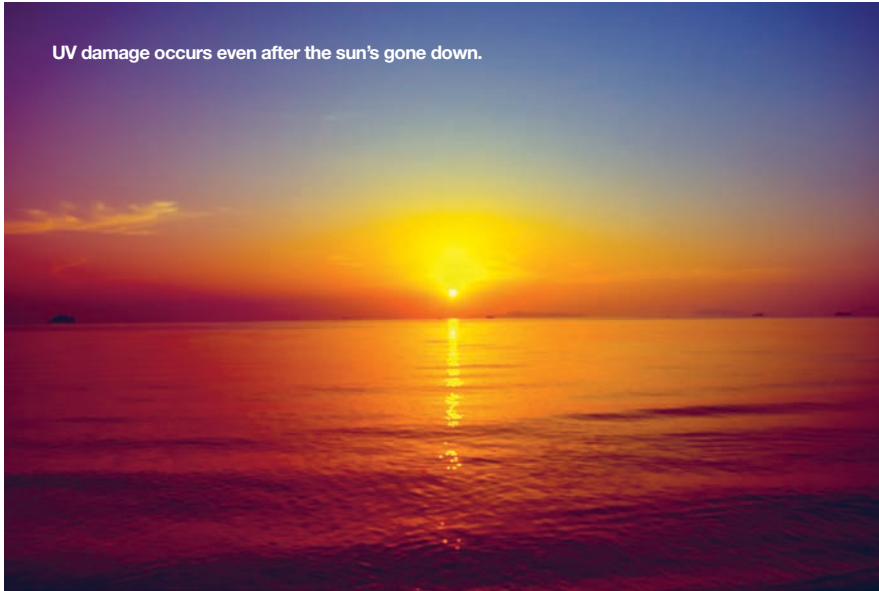
Fundamental Changes

If we do not change a fundamental mindset at the FDA, I am afraid that no new UV filters will ever be introduced in the US—unless through the lengthy, tedious, expensive and severely restrictive NDA. The mindset at the FDA simply requires that any UV filter introduced in the US must go through the process of the NDA—one UV filter at a specific application rate for every single NDA application. An Amended NDA is needed for any modification requiring another dosage and application. Also, the process of the TEA has now been modified to include compliance with all the stringent GRASE requirements. The consequence of this mindset is that the American public will not have access to the most modern and effective UV filters,



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especially those that protect from UVA radiation. That is devastating because it simply translates to thousands if not millions more consumers contracting skin cancer. The price paid, now measured in billions of dollars, that is spent on treatment and diagnosis (not to mention human suffering) to combat this skin cancer is soaring.

There is no escaping the fact that without effective sunscreens that protect from the total rays of the sun, especially UVA, we will not be able to reduce the incidence of skin cancers in the US. The need for protection is obvious. Avoiding the suffering and the disastrous consequences of skin cancer is paramount.

That's not the case in the rest of the world. At least six better UV ingredients have been approved worldwide and, more importantly, dozens more that potentially will be superior in blocking UVB, UVA and IR radiation are in the works. The laboratories in Europe, Japan and elsewhere are buzzing with R&D efforts to create superior sunscreen products and ingredients. The commercial incentive is there—the US is lagging behind. New obstacles put in place by the FDA further disadvantage US companies and deny Americans the protection they deserve.

An Impassioned Plea

If I sound passionate, it's because people like Dr. Curt Cole, Dr. Robert Sayre and

Dr. David Steinberg, along with countless other dermatologists and scientists (including myself), are about to retire without having convinced the FDA of the merits of improving our ingredients and products to combat this epidemic. For more than 25 years we have pleaded with the FDA that our ingredients are woefully inadequate. Our American arsenal of UVA filters is comprised of only three ingredients:

- Avobenzone, which we all know has photostability issues;
- Oxybenzone, which has a cloud of uncertainty relating to its endocrine disrupting activities; and
- Zinc oxide, which has no problems, other than aesthetics and an incompatibility with avobenzone.

The rest of the world has access to at least a half dozen more ingredients, five of which are in the US TEA process, and these ingredients have been used effectively and safely for years, some exceeding 20 years. The five European TEA ingredients have met all the requirements of the TEA process except, presumably, this new hurdle: passing GRASE status and satisfying the FDA.

Night Moves

As we continue to be engrossed with what the Congress introduces in bills supporting the Sunscreen Innovation Act and with the FDA rejecting all the TEA applications,

setting higher and higher standards for approval, research still goes on toward uncovering yet another threat to consumers. This time it's the dark!

In the 1960s, UVB was the only perceived threat. In the 1990s, the threat was expanded to include UVA. Today, UVA protection is considered paramount.

Now, in this century, the infrared (IR) rays are considered important radiation that requires steps for effective protection. In February, Yale University researchers published an article in *Science* suggesting that covering exposed skin, steering clear of the sun during the peak UV hours of 10:00 am to 3:00 pm and always wearing sunscreen may not be enough to shield against skin cancer.

The researchers traced the source of the damage to melanin, the natural tanning pigment that shields the skin of sunbathers from an excess of sunshine. They suggested that melanin is potentially both helpful and harmful because it's a contributory factor in carcinogenesis.

The sun's UV rays create very reactive species of nitrogen and oxygen compounds that stimulate electrons within melanin in a process termed chemiexcitation. This results in bond breakage to the DNA that can happen up to three hours after the skin is exposed to radiation—even after the sun has gone down. This obviously increases the skin's cancer risks. The researchers have advised that an "evening after" sunscreen with antioxidants and other cocktails can offer possible solutions to the threat of after-dark carcinogenic processes.²

As researchers pursue the sources of skin cancer and the ways to protect against it, our government agencies are throwing up roadblocks to getting effective ingredients to the American public. We should encourage research and business by flexibly approving skin protection formulations. ●

References:

1. <https://Federalregister.gov/a/2015-03883> and <https://Federalregister.gov/a/2015-03884>
2. <http://time.com/3715036/sunscreens-afterdark> (Feb. 27, 2015)