THE BILL WILL FINALLY PASS, BUT WILL THE FDA?

President Obama had the Sunscreen Innovation Act (SIA) on his desk before Thanksgiving week.[1] Time to give thanks and celebrate. His signature has the potential to protect a needlessly at- risk population from sun damage. The Senate passed the SIA on Sept. 17, 2014 and soon after, on Nov. 14, the House passed the Senate version of the SIA. The FDA will have six months or so to reach a conclusion on the safety of the eight TEA (Time and Extent Applications) and if all goes well, we may finally have some desperately needed UV filters. These eight ingredients have been in use safely in Europe and the rest of the world for many years, exceeding a dozen years for some UVA ingredients. Now, it is time to give the US more advanced protection.

But, hold on. Although it sounds like all is fine and dandy, the FDA has signaled recently that it will not go down without a fight! At meetings held Sept. 4 and 5, 2014, the Non-prescription Drugs Advisory Committee (NDAC) not only agreed with FDA's currently stringent proposed standards for evaluating the safety of sunscreen monograph ingredients, it suggested that the agency should require additional tests to evaluate the impact of long-term use, actual use and bio-availability in specific populations![2]

These added tests would cost millions and take a substantial amount of time to complete. Under other considerations, once again, the FDA is creating impossible barriers for approving urgently needed new and improved UV filters for the sun care industry.

The problem, in my humble opinion, is multifold. Without better new ingredients, protection from the ravaging rays of the sun is lacking in the US. Everyone acknowledges that European and Japanese sun protection products are superior to ours. Why not approve them? Why the delays?

Part of the problem is the mindset of the FDA and its medical advisory board. Each time we meet with them we hear the same mantra: "If you really want us to approve a new UV ingredient, apply for an NDA (New Drug Application)!" Their request demonstrates a lack of understanding of the cosmetic industry. It is not practical nor is it necessary. When the pharmaceutical industry applies for an NDA for a new blood-pressure reducing pill and requests a few dosage forms, it justifies spending millions of dollars and waiting for a few years to get the NDA approved. The financial gains, once approved, can often be measured in billions of dollars!

In contrast, the cosmetic industry, including the sun care industry, creates hundreds of dosage products in the form of new carriers (such as gel, mousse, lotion and cream) with dozens of SPF ratings, broad-spectrum ratings, new and improved innovations that highlight unique ingredients, essential oils, natural extracts and fragrances. In a given year, a new UV filter that has been approved via the NDA route, may be used in thousands of SKUs. According to the FDA, each change requires an Amended NDA. A requirement that is impractical, unworkable and outright illogical.

Out of Date

The roster of available UV filters in the US is out of date. The 1978 ANPR (Advanced Notice of Proposed Rulemaking) allowed the unrestricted use of 21 UV filters. Since then, 37 years ago, only three ingredients have been added, namely, avobenzone, zinc oxide and L'Oréal's Ecamsule. At the same time, many of the originally approved UV filters have been discontinued. Today, we have a situation where the main UV filters, outside of the three recently approved ingredients, represent 1960 technology at best. The cinnamates, salicylates and benzophenones are small molecules that penetrate the skin and do not adequately protect against UVA. In fact, a new National Institute of Health (NIH) study has found that the presence of benzophenone–type UV filters could lead to delays in fertility in men.[3] Newer broad-spectrum UV filters are desperately needed.

This goal can only be achieved via two routes. American ingenuity in research and development is one. Industry has absolutely no incentive to create ingredients that have a snowball's chance in hell of returning an investment. The second route is to either grandfather in the new ingredients or to adopt, through the TEA process, the proven and reliable European UV filters that have years of safe use worldwide. I know that we have reached this same conclusion before, and it is terribly frustrating to witness the efforts of the PASS (Public Access to Safe Sunscreens) Coalition, numerous individuals and organizations, all of whom are ignored by the FDA and its advisory committee. So we have to wait and see what kind of clout

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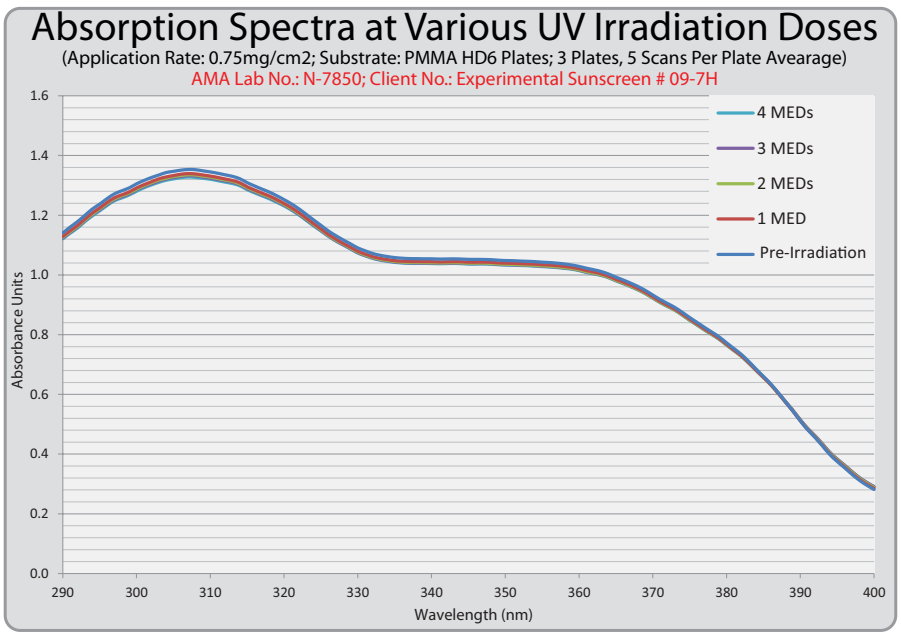
Table 1: Sunscreen Photostability Analysis of Experimental Sunscreen

SUNSCREEN PHOTOSTABILITY ANALYSIS				
AMA Lab No.:	N-7850			
Client No.:	Experimental Sunscreen # 09-7H			
Area Under the Absorption Curve (AUC) Analysis				
Pre-Irradiation (AUC)	1 MED (AUC)	2 MEDs (AUC)	3 MEDs (AUC)	4 MEDs (AUC)
110.88	109.96	109.67	109.55	109.34
% Difference from Baseline (Pre-Irradiation):	-0.83%	-1.09%	-1.19%	-1.39%
UVA:UVB Ratios Analysis (Per BOOTS STAR RATING SYSTEM)				
Pre-Irradiation (UVA:UVB Ratio)	1 MED (UVA:UVB Ratio)	2 MEDs (UVA:UVB Ratio)	3 MEDs (UVA:UVB Ratio)	4 MEDs (UVA:UVB Ratio)
0.4646	0.4661	0.4663	0.4672	0.4678
ABS % Difference from Baseline (Pre-Irradiation):	0.32%	0.36%	0.55%	0.68%
Critical Wavelength				
Pre-Irradiation	1 MED	2 MEDs	3 MEDs	4 MEDs
379.00 nm	379.00 nm	379.00 nm	379.00 nm	379.00 nm

Fig 1: Absorbtion spectra at various UV radiation doses



and muscle The Sunscreen Innovation Act will have convincing the FDA to introduce desperately needed UV filters.

Let's Escalate the Debate

This issue of Happi will be distributed during the Annual Scientific Meeting of the Society of Cosmetic Chemists (SCC). Members of the SCC are urged to debate this issue of the non-availability of new, effective sunscreen ingredients, especially filters that protect skin from damaging UVA. The debate should escalate to request that organizations in concert with the PASS Coalition should become actively involved to insure that the recently enacted Sunscreen Innovation Act in Congress will be implemented promptly and not delayed or diluted. I am aware that the Personal Care Product Council is debating this issue and would hope that its response is timely and effective. No one is suggesting that the FDA abandon its role as the vanguard for protecting the American consumer from fraudulent or ineffective products. Rather, we are urging the FDA to consider the safety record of those proposed UV filters in the TEA, including some that have been in use for over a dozen years with no reported adverse effects. Skin cancer is not only on the rise in the US, but it is also reaching epidemic proportions, and every day we experience delays in implementing new, safe and effective measures and protocols, we only add to the rising statistics of skin cancer in the US. Further delays will also contribute to the misery of those who will needlessly be inflicted with this deadly disease. According to the US Surgeon General, melanoma cases are up 200% in US and cost $8 billion annually.[4]

In my October column, I described new protocols and cosmetic formulations for superior UVA protection utilizing two of the proposed TEA ingredients, namely bisoctrizole and bemotrizinol.[5] I reported on several formulations that tested in-vivo (2 subjects) at an SPF of >50, their critical wavelengths >380 nm and imparting an outstanding broad spectrum protection. These formulations were made with and without avobenzone, as well as with inorganic particulates (ZnO and TiO2) containing the TEA ingredients only. These formulations were also analyzed for photostability. Our preliminary results indicate that all formulations were extremely photostable. A modification of FDA broad spectrum testing method (21 CFR 201.327(i)) was used at AMA laboratories to evaluate the photo-stability of submitted test material.[6]

Test products were applied to the roughened PMMA plate (roughened side upper most) by weight, at an application rate of 0.75mg/cm^2. The spectrometric measurements were conducted using Labsphere's UV-2000S Benchtop Sunscreen Analyzer. The Solar Light Xenon Arc Fade Test UV Simulator – LS1000-6S-UV was used as

a UV source of pre-irradiation. The spectrometric measurements were collected at baseline (pre-irradiation) and again after the samples were exposed to UV radiation levels of 1, 2, 3 and 4 MEDs. The transmittance values were measured at 1 nanometer intervals on three different plates with 5 measurements per plate. Measurements of spectral irradiance transmitted for each wavelength λ through control PMMA plates coated with 15 microliters of glycerin (no sunscreen product) were obtained from five different locations on the PMMA plate.

Using the obtained data, the following parameters have been calculated:

- Area under the Absorption Curve Star Rating System. The index of UVA protection is defined as the area (per unit wavelength) under the UVA portion of the absorbance curve, divided by the area (per unit wavelength) under the UVB portion of the same curve: *UVA: UVB Ratio=UVA Absorbance per unit wavelength /UVB Absorbance per unit wavelength*

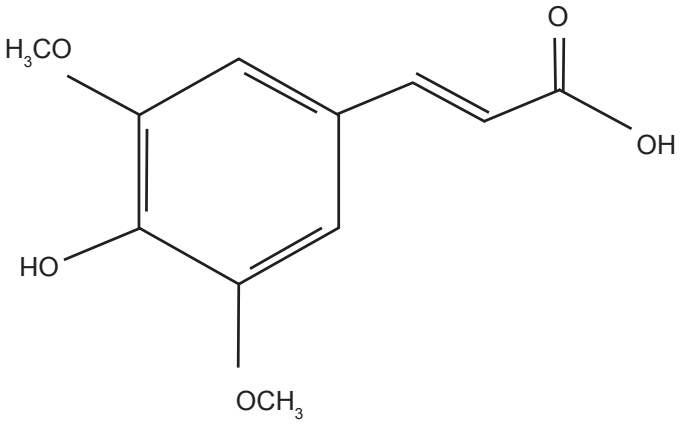
"The chosen definition of photostability, for the purpose of this method, is the retention of at least 95% of the minimum UVA:UVB ratio required to remain in the same star rating category. If degradation to less than 5% below the minimum ratio for the given category occurs, the product is deemed sufficiently photostable…".[6]

- Critical Wavelength—the wavelength at which the area under the absorbance curve represents 90% of the total area under the curve in the UV region.

The raw data for one of the samples analyzed earlier containing no avobenzone with the TEA ingredients, tested extremely photostable as shown in Table 1 and Fig. 1.

This whole exercise of formulating sunscreens with TEA ingredients as reported earlier, utilizing the TEA ingredients without avobenzone, shows that it is easy to achieve superior, broad spectrum, high to moderate SPF ingredients that are extremely photostable. The rest of the world discovered this many moons ago and, presumably, the actual safety record of utilizing those TEA ingredients is stellar. It is time that we join the rest of the world in producing better solar protection for our populace!

Fig 2: Sinapinic acid and its esters block UVA radiation.



Finally, two additional new R&D developments worthy of mention include the recent paper published in the Journal of the American Chemical Society, Timothy Zwier and colleagues at Purdue University noted that the harsh UV radiation that plants are exposed to daily can cause serious damage to plant DNA. Tests have shown that plants produce sinapate esters and send them to the outer layer of their leaves to protect themselves.[7] What potential lies in learning from plants?

The second recent development has been Shiseido's claims to have developed a sunscreen that actually enhances UV protection once in contact with water or perspiration. The Ionic Mineral Sensor, a technology that causes the minerals in water or perspiration to bond, improving the water repellence of the sunscreen, and making the sunscreen film on the skin more uniform with a higher protection effect. The Wetforce technology will be incorporated in sunscreen products to be launched next spring.[8]

Innovation Is Still Needed

In conclusion, despite the new SIA, innovation is still needed. The FDA is totally missing the mark by not approving efficient protection from the ravaging rays of the sun; our population is over-exposed and under-protected. Skin cancer is on the rise. At the same time, innovation and research in the field of sun care is rapidly diminishing due to the roadblocks set by over-regulation. In contrast to my over 30 years of reviewing research and developments in sunscreens, during the past few years, I have witnessed very few scientific advancements in the field of UV filters in the US. Innovation is down and skin cancer rates are up. If this situation does not change, it will be a sad day for American ingenuity and our pride in creating superior technical innovations for the market.●

I would like to thank the staff of AMA Laboratories, New City, NY; for conducting the photostability studies in their laboratories.

The views expressed in this column are Nadim Shaath's and are not shared by other members of The PASS Coalition.

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