d) Provide data relative to the determination of the "pre-irradiation" dose concerning the photostability modification to the "critical wavelength" method.

Comment

Based on our studies presented below, we recommend the following formula be used to establish a pre-irradiation dose for the critical wavelength method to assess photostability:

Pre-irradiation dose J/cm^2 = SPF x 2 J/cm^2 (1 MED) ÷ 1.5

Thus, for a SPF 15 product, the dose of full spectrum, 290 - 400 nm, UV from a xenon arc solar simulator with 1 mm WG-320 and 1 mm UG-5 filters would be

$$15 \times 2 \text{ J/cm}^2 \div 1.5 = 20 \text{ J/cm}^2$$

This "dose" of solar simulated UV (290-400 nm) may be considered to be about 1½ hours of noonday or 3 hours of sun exposure in the early morning or late afternoon. Based on our data, this represents a rigorous product challenge which accounts for changes in UV absorbance as a function of UV exposure (i.e., photostability). Most important, pre-irradiation of the samples appropriately addresses photostability issues and provides a consumer-relevant assessment of sunscreen product performance.

Why is pre-irradiation recommended before calculating critical wavelength?

The intent of the pre-irradiation with solar simulated UV in the determination of the critical wavelength is to account for changes in absorbance as a function of UV exposure, i.e., photostability. In this regard, the "dose" of UV should provide a reasonable estimate of what a consumer might experience when using the product.

The pre-irradiation step was added to the original method proposed by Diffey because:

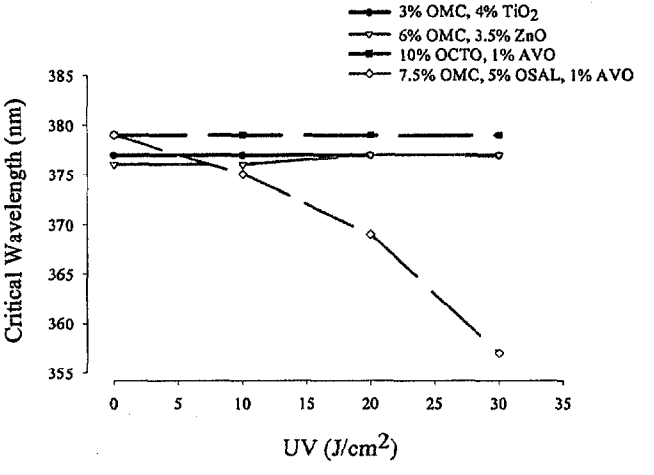
- it is recognized that sunscreen product absorbance spectra can sometimes change upon UV exposure and the change in absorbance particularly at long wave UV (> 340 nm) is not fully accounted for by SPF testing;
- at least one recognized long wave UVA filter may lose its capacity to absorb longwave UVA after exposure to **full spectrum** UV (i.e., both UVB and UVA); and,
- the function of sunscreen products is to absorb UV and this characteristic should be evaluated for the entire UV spectrum to mimic consumer experience

In considering the selection of a "pre-irradiation" dose of solar-simulated UV, the worst case would be exposure to a dose of UV that equaled the SPF of the product (i.e., for an SPF 15, pre-irradiation of 15 MEDs or 30 J/cm^2). However, it was felt that this may not be a typical consumer experience and, as such, would not necessarily be representative of the absorbance spectra that a sunscreen product would have during typical consumer usage.

Because the pre-irradiation dose is a single point estimate of an ever changing phenomenon, we conducted a study to determine what might be considered a reasonable but rigorous pre-irradiation dose. We assessed the photostability of various SPF 15 sunscreen products in the following experiment, which was a part of the Procter & Gamble 1997 report submitted to the Docket 78-0038N[8].

The spectral photostability of 4 model sunscreens was determined using substrate spectrophotometry. Model SPF 15 sunscreens with different combinations of UV filters were prepared. The absorption spectrum and resulting critical wavelength were determined initially and then after irradiation with 10, 20, and 30 J/cm^2 of solar simulated UV.

The effect of increasing doses of UV pre-irradiation (0, 10, 20, 30 J/cm^2) on the critical wavelength value of 4 model sunscreens is presented in the Figure below. The model sunscreen products comprised of octylmethoxycinnamate (OMC) + titanium dioxide (TiO_2), OMC + zinc oxide (ZnO), and octocrylene (OCTO) + avobenzone (AVO), had the same critical wavelength following pre-irradiation up to 30 J/cm^2. In contrast, a prototype product with a combination of active ingredients comprising OMC, octyl salicylate (OSAL) and AVO had significantly lower critical wavelengths concurrent with increasing doses of UV pre-irradiation. The critical wavelength decreased from 379 nm with no pre-irradiation to 357 nm after 30 J/cm^2 of UV pre-irradiation, these spectrally-derived data being indicative of photoinstability on a molecular level.



Photostability of model sunscreen products after increasing doses of solar simulated UV. Each product was exposed to 0, 10, 20 or 30 J/cm^2 solar simulated radiation. Each value is the mean of 5 independent samples. The critical wavelength was calculated from the absorption spectrum obtained using substrate spectrophotometry

We found that the pre-irradiation procedure can readily account for sunscreen product photo-instability. Due to known photochemical processes, this accounting for potential photo-instability can only be appropriately and reliably accomplished through full-spectrum UV (290-400 nm) product irradiation; this is a unique characteristic of this approach versus other procedures that irradiate using sources filtered to give UVA only, which based on our previous work submitted to the agency[15] produce irrelevant and understated photochemistry.

We believe the pre-irradiation is necessary. Arguably the "dose" is arbitrary. However, full spectrum (290 - 400 nm) is required and the dose should be sufficient to detect significant changes in critical wavelength. Based on our data, a pre-irradiation dose of **SPF x 2 J/cm^2 (1 MED) ÷ 1.5** appears to be reasonable and sufficient.

[15] May 2, 2000 letter from Procter & Gamble Company to Docket 78-0038N entitled "Technical concerns and comments regarding the March 3, 2000 submission to Docket No. 78N-0038 Sunscreen Drug Products for Over-the-Counter Human Use by L'Orèal Research/Cosmair Cosmetic Corp.