4g

g) <u>Provide information concerning the appropriate proportionality between UVB (relative to SPF) and UVA absorption in sunscreen products</u>.

Comment

It is altogether agreed that as the SPF of a sunscreen product increases, so to should the UVA protection. However, assigning a fixed proportionality based on protection factors has no biological basis and, more important, is misleading to consumers.

In contrast, by virtue of the method, critical wavelength ensures commensurate UVB/UVA protection without the need of a fixed ratio of protection factors. To be explicit, if two products (A and B) share the same critical wavelength but exhibit differing *in vivo* SPF values (15 and 30, respectively), then according to the critical wavelength calculation, Product B *must* have been formulated with significantly more long wavelength UVA protection than Product A (i.e. commensurate with SPF).

To more completely respond to this question, we have broken it down into 2 parts: (1) Concerns with Fixed Proportionality based on protection factors, and (2) Experimental data supporting commensurate UVA protection guaranteed by the Critical Wavelength.

(1) Concerns with Fixed Proportionality based on protection factors

- **The ratio of protection factors, i.e., SPF (UVB-PF) to UVA-PF, for the same product will change with dose/application rate.**

Establishing a fixed proportionality based on protection factors will only be applicable provided consumers apply the same dose used in the controlled, clinical test. Because there is ample data to suggest that consumers do not used a dose of 2 mg/cm^2 of sunscreen product[19], the establishment of a fixed proportionality based on protection factors obtained in product testing would be misleading.

This very important consideration is most readily understood by considering the following examples. The figure and table present hypothetical absorbance curves for the same product applied at two doses. As noted previously in this document, absorbance is the most fundamental property of all sunscreens. The "absorbance curve" is a fingerprint for a sunscreen product. That is the shape of the absorbance curve remains the same regardless of the amount of product applied. This is clearly illustrated below in Fig A

Fig. A

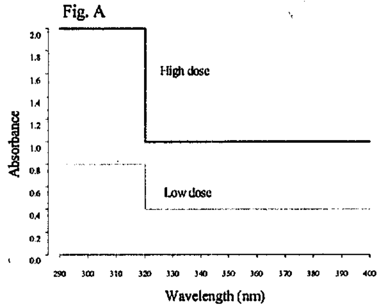
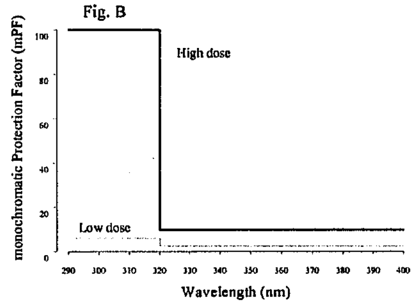


Fig. B



[19] Bech-Thomsen N, Wulf HC (1993) Sunbathers' application of sunscreen is probably inadequate to obtain the sun protection factor assigned to the preparation. *Photodermatol. Photoimmunol. Photomed.* 9:242-4. Wulf HC, Stender IM, Lock-Andersen J (1997) Sunscreens used at the beach do not protect against erythema: a new definition of SPF is proposed. *Photodermatol Photoimmunol Photomed* 13:129-132. Diffey BL, Grice J (1997) The influence of sunscreen type on photoprotection. *Br J Dermatol* **137**:103-5.

	UVB-PF	UVA-PF	UVB-PF/UVA-PF Ratio[1]	Critical Wavelength (nm)
Low Dose	6.3	2.5	2.5:1	386
High Dose	100	10	10:1	386

[1]UVB-PF/UVA-PF Ratio was calculated from the mPF curves.

What is clear from this hypothetical example is the dependence of monochromatic protection factor (mPF) as well as the ratio of UVB-PF/UVA-PF on the dose or application density for UV filters. As such, the determination of a protection factor and mathematical variations such as the ratio of UVB-PF/UVA-PF only applies to the conditions under which it was tested and has very limited meaning for consumers.

In contrast, the Critical Wavelength, which is based on the inherent shape of the absorbance curves, is the same regardless of the dose or amount of product applied. As such, the generated value is not dependent on the study conditions. Products with an appropriate Critical Wavelength such as greater than or equal to 370 nm would provide proportional broad protection against solar UV independent of consumer application.

The second example is taken from an article written by Dr. S. Forestier[20] (L'Orèal Recherché), entitled "Pitfalls in the *in vitro* determination of Critical Wavelength using absorbance curves". In this example, Product B was prepared and *in vitro* transmittance was measured. Using the absorbance curve for Product B, two additional hypothetical absorbance curves were calculated using the following equations:

Product A: $A_A(\lambda) = A_B(\lambda)/1.39$
Product C: $A_C(\lambda) = A_B(\lambda)/0.66$

Again, using the relationship between mPF and absorbance, i.e., Log mPF = A, the mPF for Products A, B and C was calculated. The absorbance and mPF curves for Products A, B and C are illustrated in Fig 1 and Fig. 2 (these figures were recreated from the Forestier paper). The Predicted SPF, Critical Wavelength, UVA-PF/UVB-PF ratio and UVB-PF/UVA-PF ratio from the mPF curves are recreated from the paper and presented in the Table that follows.

Forestier states that "Figure 2 shows graphically the dramatic difference of the UVA protection for the 3 products". Further, he notes that "Whereas the critical wavelength is the same for these curves it is obvious that absorption is different". These data lead Dr. Forestier to the conclusion that ". . .critical wavelength is a robust method which unfortunately is unable to assess photoprotection".

As well, however, these data represent absorbance curves for **the same product applied at different doses**. As such, they demonstrate the effect of applying different doses of the same product on the critical wavelength but more importantly on the ratio of UVA/UVB protection factors. Again, from the data presented in Table 1 below, it is obvious that depending on the dose or amount applied, the "protection factor" or ratio of "protection factors" for any sunscreen product will change.

[20] Forestier S. (1999) Pitfalls in the *in vitro* determination of Critical Wavelength using absorbance curves. *SÖFW-Journal*, **125**, 8-9.

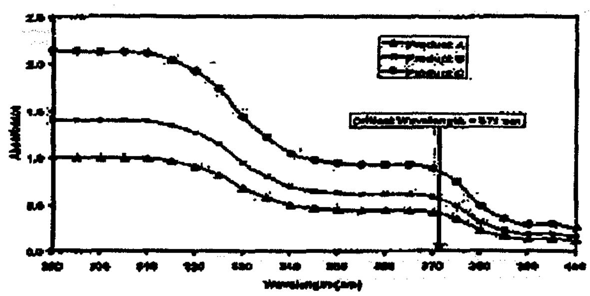


Fig. 1 Absorbance of the products A, B and C

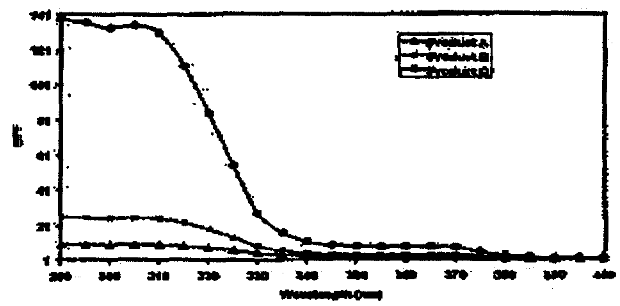


Fig. 2 Monochromatic protection factors of the products A, B and C

Spectroradiometric characteristics of Products[1]

	Predicted SPF	Critical Wavelength (nm)	UVA-PF/UVB-PF ratio from mPF curves
Product A or "low dose"	7.7	371	0.81
Product B or "mid-dose"	15.5	371	0.54
Product C or "high dose"	44.9	371	0.29

[1] Recreated from Forestier, S (1999) SÖFW-Journal, **125**, pg. 8-9.

Importantly, **these data demonstrate three very important points**

1. that in order to maintain the same critical wavelength for increasing SPF products, more UVA protection is needed.
2. critical wavelength is not dependent on the "dose"
3. the proportionality between UVA/UVB based on protection factors changes as the dose or application density changes.

- **There is no biological basis for establishing a strict UVB/UVA proportionality.**

The establishment of a fixed proportionality such as 3:1 or 4:1 for UVB/UVA protection is arbitrary. There is not one piece of biological data supportive of such a fixed ratio. This proportionality could only serve as a benchmark which manufacturers could meet to make a claim or otherwise support the marketing of their product. Of course, arguments in support of a fixed ratio abound, although such rationalization is generally based on assumptions and the ability of existing or planned sunscreen products to pass. Regardless, in the absence of any biological reasons, the establishment of any ratio is arbitrary.

(2) *Experimental data supporting commensurate UVA protection guaranteed by the Critical Wavelength*

In addition to being independent of application density, **the Critical Wavelength ensures UVA protection commensurate with SPF.** To better understand the relationship between SPF and critical wavelength, we refer to the Procter & Gamble 1997 submission[8] from which the following study was originally presented.

Two model sunscreens, oil in water emulsions containing 6% octyl methoxycinnamate (OMC) and either 3.5% ZnO or 4% TiO_2 were prepared with an estimated SPF equal to 15. Similar products with an estimated SPF equal to 30 were prepared by the addition of 10% octocrylene (OCTO), a UVB/UVA II absorber. The estimated SPF was determined by comparing the *in vitro* absorbance curves for the model sunscreens to those from marketed products in which SPF had been determined *in vivo*. The absorption spectrum was measured and critical wavelength value determined for all 4 model sunscreen products.

The effect of doubling the product SPF on critical wavelength is presented in Table below. For the two examples evaluated, the products estimated to provide an SPF 15 combining OMC with either TiO_2 or ZnO had critical wavelengths of 372 nm and 376 nm, respectively. When 10% OCTO was added to the formulations to increase the UVB/UVA II absorbance and provide an estimated SPF of 30, the critical wavelength values were markedly reduced to below 370 nm.

In this example, the only way for the SPF 30 products to maintain their critical wavelengths above 370 nm would be to increase the concentration of the existing UVA filters, namely TiO_2 or ZnO, or avobenzone.

Effect of doubling the SPF on the Critical Wavelength

Sunscreen Actives[1]		**Estimated SPF[2]**	**Critical Wavelength (nm)**
UVB/UVA II	**UVA I**		
6% OMC	4% TiO_2	15	372
6% OMC, 10% OCTO	4% TiO_2	30	364
6% OMC	3.5% ZnO	15	376
6% OMC, 10% OCTO	3.5% ZnO	30	368

[1]OMC: octylmethoxycinnamate; OCTO: octocrylene; TiO_2: titanium dioxide; ZnO; zinc oxide
[2]Estimated SPF was determined by comparing the *in vitro* absorption curves for the model sunscreens to those of marketed products in which SPF had been determined *in vivo*.

This commensurate relationship between SPF and UVA protection is another reason why the critical wavelength method is the only one needed to determine UVA efficacy of sunscreen products.