

2. OVERVIEW OF PRINCIPLES

There are several principles which are used repeatedly in answering the questions raised by the agency. Although these concepts are familiar to many, the following section presents an overview of these principles to aid in the review of this document.

What does the Sun Protection Factor (SPF) Measure:

- The sun protection factor is a number derived from the ratio of the time of exposure to full spectrum UV, 290 - 400 nm, to produce erythema in human skin in the presence of a sunscreen product, applied at 2 mg/cm², or in its absence.
- The wavelengths of UV from 290 - 340 nm are primarily responsible for producing erythema in human skin. The action spectrum for erythema in human skin is well documented.

What do tests of UVA protection factors measure:

- Like the SPF test, a UVA protection factor is a number derived from the ratio of the time of exposure to UV, filtered to allow wavebands from approximately 320 to 400 nm, to produce erythema/pigmentation or tanning in human skin in the presence of a sunscreen product, applied at 2 mg/cm², and in the absence of product.
- The protection factors derived from such tests are strictly defined by the artificial light source.

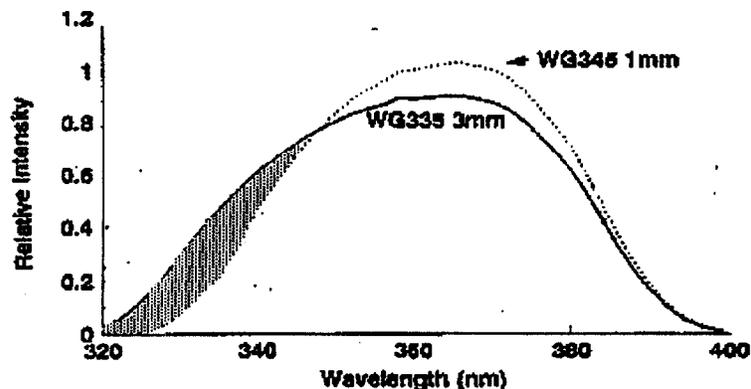
What are some of the concerns related to *in vivo* UVA test methods:

- The fundamental limitation of all proposed human studies of UVA photoprotection is the absence of an endpoint measure that is a true surrogate marker for UVA-induced skin damage, notably carcinogenesis and photoaging.
- The *in vivo* studies require exposure to an artificial UVA source, in some cases at extraordinarily high doses, the human health consequences of which are as yet unknown.
- The existing methods utilize endpoints that are:
 1. redundant with SPF testing, i.e. erythema/pigmentation; and
 2. oxygen and, by definition, UV dose-rate dependent;
- The over emphasis of UVA protection factors on short wavebands of UVA is:

⇒ acknowledged by the test originators. For example, in the publication describing the PFA test, it is stated that: "... the choice of filtration to attenuate the UVB radiation has a profound effect on the protection factors ... [This] results from the rapidly rising sensitivity of skin to UVA radiation for radiation moving from 340 nm towards 320 nm. It is in this same region that UVA absorbers such as oxybenzone and menthyl anthranilate have greatest absorbance. Thus the protection factor depends on the spectral characteristics of the irradiation source in this short-wave UVA II region"³.

This is illustrated in the following figure, taken from Cole and VanFossen (1992) where the highlighted region from 320-340 nm has the "profound effect":

³ Cole C, VanFossen R (1992) Measurement of sunscreen UVA protection: An unsensitized human model. *J Am Acad Dermatol* 26;178-84.



⇒ because *in vivo* methods such as PFA³ and persistent pigment darkening (PPD)⁴ are strictly defined by the light source used where inclusion of short wavelengths of UVA (320-340 nm) significantly impact the protection factors derived from these studies, the resulting protection factors are imperfect and variable due to differences in the artificial light source and the imprecision associated with the filtration of UV.

⇒ the dependence of such tests as PFA and PPD on UVAII explains why protection factors from these studies correlate with the SPF. In fact, by definition, as the SPF increases so too must the PFA/PPD protection factors since blockage of UVAII wavelengths is necessary to achieve high SPF.

- Photochemistry of UV filters can be dramatically different following exposure to a UVA only light source compared to full spectrum UV (290 - 400 nm), which is most relevant to product evaluation and consumers.
- Exposure to a UVA-only source is never encountered in nature, i.e., the division between these UV wavebands is arbitrary and anthropogenic; human skin is exposed primarily to solar UV, which includes *all UV wavebands*.

Concerns related to the determination of protection factors:

- Results expressed as “protection factors” (PFs) are on an exponential scale and give consumers a false impression of magnitude of absorption difference. For example, one product with a UVA-PF = 5 and another with a UVA-PF = 10, attenuate 80% and 90% of UVA, respectively. Therefore, the PFs would suggest a large difference when, in reality, the real difference is small (10%). This same concern has been expressed for SPF by academicians⁵ and the agency¹.
- PFs do not reflect the actual amount of UVA attenuation since such determinations are dependent on the artificial light source x action spectrum (i.e., the action spectrum are wavelength dependent).

⁴ March 3, 2000 Letter/report from L'Oréal Research/Cosmair Cosmetics Corp. to Docket No. 78N-00388: Sunscreen Drug Products for Over-the-Counter Human Use.

⁵ Garmyn MA, Murphy GM, Gibbs NK, Hawk JLM (1986) Are the protection factors assigned to proprietary sunscreen products misleading? *Photodermatol.* 3:104-6. Marks R. (1995) Summer in Australia. Skin cancer and the great SPF debate. *Arch Dermatol* 131:462-4. Damian DL, Halliday GM, Barnetson R.StC. (1999) Sun protection factor measurement of sunscreens is dependent on minimal erythema dose. *Br. J Dermatol.* 141:502-7. Diffey BL (2000) Has the sun protection factor had its day? *BMJ* 320:176-7.

- PFs are product application/dose-dependent. For example, PFs obtained at 2 mg/cm² will be NOT be the same at 1 or 0.5 mg/cm². As well, the ratio of SPF to UVA-PF will also change with product dose/application rate, restricting the usefulness and consumer meaning of any proposed fixed proportionality between UVB and UVA protection factors.
- labeling for PFs would require a complex system that is confusing to the consumer.

Why *in vitro* measures of UVA efficacy are appropriate for the evaluation of sunscreen products

- UV filters are intended to **reduce the dose of UV** without interacting with any biological function. As such, evaluation of their efficacy is uniquely suited for *in vitro* evaluation.
- The biological response to solar simulated light may be affected by product components other than UV filters which may inflate protection factors without reducing the dose of UV to the skin.
- No assumptions regarding the action spectra for UVA-induced acute or chronic skin damage are necessary.
- Obviates the need for human subjects utilizing clinical endpoints with indeterminate value in relation to protection from sunlight.

Why the Procter & Gamble Company supports the Critical Wavelength

- The critical wavelength value is based on the inherent shape of the absorbance curve not its amplitude and, therefore, is independent of application thickness and other undesirable variables characteristic of *in vitro* calculations of absolute protection factors. **It is a fundamental characteristic of a sunscreen product.**
- It can account for photostability of UV filters evaluated using full spectrum UV (290 - 400 nm).
- The critical wavelength determination does not promote the false notion of UVB and UVA as separate entities, but rather as part of a continuous electromagnetic spectrum.
- UV substrate spectrophotometry and calculation of the critical wavelength provides a simple, fast, convenient, reproducible and adaptable procedure for evaluating the UVA./broad-spectrum efficacy of sunscreen products.
- **A combination of *in vivo* SPF and critical wavelength provides a complete description of a product's inherent photoprotective characteristics.** A sunscreen product's critical wavelength value must *always* be considered in conjunction with its corresponding *in vivo* SPF. 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). SPF describes the amplitude of protection (at a given application rate) and critical wavelength provides a measure of the breadth of a product's spectral absorption capability.
- The critical wavelength can quantitatively distinguish between UV filters which differ in their UV absorption spectra, i.e., the critical wavelength for UVB filters < UVB/UVAII < UVAI or broad-spectrum filters.

These principles are the foundation upon which our support for a single threshold UVA labeling scheme using substrate spectrophotometry and calculation of the critical wavelength to determine longwave UVA efficacy is based. As well, these principles are the key elements which serve to support our answers to the questions of the agency.