>UVA RAYS PROTECTION MEASUREMENT

1.1.1.1.1 Different methods

In 2001, the AAD at the Consensus Conference on UVA protection recommended the use of PPD or APF test methods; coupled with the broadness of protection as characterized by the critical wavelength. Furthermore they insist on the importance of the proportionality of UVA to UVB protection: an increase in the SPF of a sunscreen must be accompanied by a proportional increase in the UVA protection. (American Academy of Dermatology Consensus Conference (2001))

The PPD method is the methodology used to determine ANTHELIOS SX UVA protection level.

Currently there is no international accepted standard method for measuring protection of sunscreens against UVA radiation.
(Lowe NJ. (1995); Chardon AM and Mascotto RE (2004); Cole C. (2001))

1.1.1.1.1.1 In vivo methods

1.1.1.1.1.2 The *in vivo* methods are based on the determination of UVA induced skin responses like pigmentation or erythema. *In vivo* methods are:

- PPF – method (Phototoxic Protection Factor)
- APF – method (Erythemal UVA- Protection Factor)
- IPD – method (Immediate Pigment Darkening)
- PPD – method (Persistent Pigment Darkening)

The UVA protection factor is measured by a similar method to the SPF test procedure, with series of increasing UVA doses for unprotected and sunscreen protected skin.

- **Phototoxic Protection Factor**

The phototoxic protection factor (PPF) was developed to try to decrease the UVA dose necessary to achieve a detectable difference in erythema. This involves

sensitizing the subject's skin with 8-methoxysporalen (8-MOP) either topically or orally. The ratio of the doses (protected/unprotected) required for a minimally perceptible erythema or pigmentation endpoint was determined for the tests compounds as observed at 72hours and 12-18 days post-irradiation.

The use of photosensitizer offers the benefit of requiring a lower dose of UVA to achieve an acute endpoint, but there are a lot of drawbacks: MOP has been determined to be a promoter of UV-induced squamous cell carcinoma and has been implicated in the increased appearance of malignant melanoma in patients undergoing psoralen-UVA. So the risk/benefit is unacceptable for commercial sunscreen facilities.

- **APF-method: erythemal point**

The UVA erythema protection factor (APF) is defined analogously to SPF and assesses the time-induced erythema in UVA-exposed skin. The determination of the minimal erythemal dose of UVA radiation is not practical as UVA irradiation hardly ever leads to erythema in physiological conditions. Skin has to be exposed to a UVA radiation 1000-fold higher than the UVR dose required to produce an erythema.

- **IPD-method (immediate pigment darkening)**

The IPD response occurs during the UVA exposure period and appears as a transient darkening of the skin that fades within the first minute after the exposure is completed.

The IPD method seems attractive since it requires low doses of UVA radiation during a limited exposure time. But it is not often used because the answer is instable with a high variability.

- **PPD-method (persistent pigment darkening) or PFA (Protection Factor UVA)**

The protection is determined as the ratio of the dose required for a minimally perceptible pigment response for the sunscreen treated skin divided by the dose

for the unprotected skin. The PPD test was initially adopted by the Japan Cosmetic Industry Association (JCIA) as the methodology for substantiating UVA protection claims on sunscreen products sold in Japan. The JCIA conducted a validation test demonstrating the reproducibility of this method across laboratories and skin types. This method presents the advantage to also evaluate the photostability of the product. The main drawback is the cost which is relatively high.

1.1.1.1.1.3 In vitro methods

In vitro test methods present the advantages of low cost and speed. The *in vitro* methods used until now are:

• Australian standard (AS);

• The Boots star rating system (UVA/UVB ratio);

• The Broad Spectrum Rating (critical wavelength- Diffey);

• The APP – Method/UV-A Protection Percentage.

These methods are all based on transmission measurements. They differ in detail and the method of calculation.

- **Australian standard:**

This method measures the solar radiation transmitted by a sunscreen product with a spectrophotometer to yield a percentage of UVA radiation absorbed by the product. In Australia and in New Zealand, a product is designated as a long wave protector only if it transmits less than 10% of the UVR between 320 and 360 nm.
So it assures that the product may provide a broadspectrum protection, but this method does not guarantee the level of biological protection provided by the product under use conditions. Furthermore it doesn't take the photounstability into account.

- **Boots star rating system.**

This system is based on a ratio of UVA/UVB transmitted radiation. The areas under the curve in the UVA and UVB are calculated for each sunscreen product. The result is a coefficient between 0 and 1 that provides a rough guide to UVA protection – 0 equating to no UVA protection whereas 1 signifying equivalent protection in UVA and B. The coefficient is assigned a star value.
The problems of this method are that this ratio does not impart correct proportionality, does not take into account photounstability and is not correlated with any biological response.

- **Critical wavelength**

This method was proposed by Dr. Brian Diffey to overcome the problems of the Boots Star Rating System. The critical wavelength of a sunscreen product is the wavelength at which the spectral absorbance of the product reaches 90% of the area under the curve from 290 to 400nm. The wavelength at which the summed absorbance reaches the 90% total absorbance is called the critical wavelength and is considered to be a measure of the breadth of the sunscreen protection. This method relies only on the shape of the UV absorption spectrum and not on its amplitude. The problem of this method is the lack of correlation with *in vivo* results.

- **The APP method (UV-A Protection Percentage)**

This method was proposed by Sayre and Agin to determine the percentage of erythemal UVA radiation blocked by a sunscreen. This technique provided an efficient measure, but did not reach widespread use due to potential operator influence, difficulty in obtaining the substrate, and lack of recognition by the FDA.

In vitro test methods can give meaningful information about UVA protection, but no complete procedure has been yet correlated with *in vivo* test results in a manner that is “fool-proof” for wide scale reliable use and reproducible results.

The main problem of all these *in vitro* methods is that they do not quantitatively measure the magnitude of protection: they only measure the broadness of the UVA absorbance.

The American Academy of Dermatology concluded that measuring broadness alone is not sufficient to accurately describe product performance in the UVA. So, in order to comply with the AAD recommendations for UVA protection of sunscreens and for a broad-spectrum claim, *in vitro* critical wavelength must be combined with an *in vivo* method. (American Academy of Dermatology (2001))

1.1.1.1.2 Status of UVA methods in the USA

Some twenty years ago, the FDA accepted a method to assess UVA protection based on the erythema end-point on skin pre-sensitized by 8-Methoxypsoralen (8-MOP). The use of the 8-MOP on healthy subjects is very controversial because of the possible induction of skin cancer and the long-term marking of the UV-exposed test sites on the skin. Five years ago, the erythema/pigmentation response (PFA method) on unsensitized skin was also recognized as acceptable to the FDA (Food and Drug Administration, (1998)).

In April 1996, the Industry via the CTFA submitted to the FDA a "Consensus Method" for evaluating and labeling the broadness of protection (AAD: American Academy of Dermatology (2001)) in the UVA1 range using *in vitro* spectroradiometric measurements to determine the critical wavelength _c.
In answer to the FDA requesting data based on *in vivo* methods, on August 30, 2000, six sunscreen cosmetic companies (Bath and Body Works, Estée Lauder, Johnson and Johnson, L'Oréal, Mary Kay and Schering Plough) submitted to the FDA (Docket N°78-0038) a proposal for UVA testing and labeling (Schering-

Plough, Bath & Body Works, Estée-Lauder Companies, Johnson&Johnson, L'Oréal USA, Mary Kay: (2000)). In summary, this proposal, in addition to a measurement of broadness of protection as described by the critical wavelength, makes an *in vivo* measurement of the "quantity" of UVA protection provided by a product should be used to fully assess product performance in the UVA range. This could be done using the Protection Factor A (PFA) method and/or the Persistent Pigment Darkening (PPD) method. In addition to the amplitude of the UVA protection, any sunscreen products labeled for UVA protection must demonstrate absorbance to or above 360 nm using standard methods.

Bibliography:

American Academy of Dermatology Consensus Conference on UVA protection of sunscreens: summary and recommendations. J Am Acad Dermatol 44: 505, 2001. J Am Acad Dermatol. 2001; 44(3):505-8

Bernerd F., et al. The sun protection factor (SPF) inadequately defines broad spectrum photoprotection: demonstration using skin reconstructed in vitro exposed to UVA, UVB or UV-solar simulated radiation. Eur J Dermatol. 2003; 13(3) :242-9.

Chardon AM, Mascotto RE: A review of methods for the evaluation and labelling of sunscreen protective efficacy (Esame dei metodi di evaluazione e classificazione dell'efficacia protetti degli schermi solare). Gital Dermatol Vernerol, 139/suppl.: 1-15, 2004.

Cole C. Sunscreen protection in ultraviolet region: how to measure the effectiveness. Photodermatol Photoimmunol and Photomed. 2001; 17: 2-10

CTFA/NDMA taskforce report on Critical Wavelength determination for the evaluation of the UVA efficacy of sunscreen products. Docket 78N-0038, RPT9, April 9, 1996.

Food and Drug Administration (FDA): Sunscreen drug products for over-the counter human use; Final Monograph Fed Register 1999: 64: 27666-27963

Food and Drug Administration (FDA): Sunscreen drug products for over-the-counter human use; amendment to the Tentative Final Monograph; enforcement policy. Fed Register. 63, 56584-56589. October 22, 1998

Levy S.B. Sunscreens for photoprotection. Dermatol therapy 1997; 4: 59-71

Lowe NJ. Prevention of photodamage with sunprotection and sunscreens; Blackwell Science 1995; Photodamage, Barabara A. Gilchrest.

OTC Sunscreen Drug Products. Food and Drug Administration Docket No. 78N-0038

Schering-Plough, Bath & Body Works, Estée-Lauder Companies, Johnson&Johnson, L'Oréal USA, Mary Kay: Submission to FDA Docket 78-0038 - Sunscreen Drug Products for Over-the-Counter Human Use; Final Monograph, re-opening of Administrative Record: Balancing UVB and UVA protection: proportionality, quantitative measurement of efficacy, and clear communication to consumers. August 30, 2000