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TECHNICAL REPORT

UV-A PROTECTION AND SUNSCREENS

CIE 186:2010

UDC: 612.014.481-06
535.31

Descriptor: Optical radiation effects on humans
Ultraviolet rays

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This Technical Report has been prepared by CIE Technical Committee 6-24 of Division 6 "Photobiology and Photochemistry" and has been approved by the Board of Administration of the Commission Internationale de l'Eclairage for study and application. The document reports on current knowledge and experience within the specific field of light and lighting described, and is intended to be used by the CIE membership and other interested parties. It should be noted, however, that the status of this document is advisory and not mandatory. The latest CIE proceedings or CIE NEWS should be consulted regarding possible subsequent amendments.

Ce rapport technique a été élaboré par le Comité Technique CIE 6-24 de la Division 6 "Photobiologie et Photochimie" et a été approuvé par le Bureau de la Commission Internationale de l'Eclairage, pour étude et emploi. Le document expose les connaissances et l'expérience actuelles dans le domaine particulier de la lumière et de l'éclairage décrit ici. Il est destiné à être utilisé par les membres de la CIE et par tous les intéressés. Il faut cependant noter que ce document est indicatif et non obligatoire. Il faut consulter les plus récents comptes rendus de la CIE, ou le CIE NEWS, en ce qui concerne des amendements nouveaux éventuels.

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UV-A PROTECTION AND SUNSCREENS

SUMMARY

Technical Committee TC 6-24 was formed in 1992 due to the importance of the deleterious effects associated with exposure to UV-A radiation and because of a lack of existing guidance/regulations on tests for UV-A protection. The objective was to arrive at an international consensus on such tests. By 1997 the committee had identified one *in vivo* method worth pursuing, i.e. Persistent Pigment Darkening, and several *in vitro* methods that had not yet been validated. It was not possible to reach a consensus at that time, however. In the meantime the development of methods to assess UV-A protection continued and is still on-going, especially on *in vitro* methods. Furthermore, the computer-aided calculation of sunscreen performance - referred to as *in silico* - became more sophisticated and useful. Rather than trying to find a consensus on sunscreen testing the objective of the reactivated TC 6-24 has now been reduced to giving, in the form of a Technical Report, a comprehensive overview as well as an assessment and ranking of the UV-A methods currently under discussion. This report starts with the general principles of UV protection and an overview of UV-A and broad-spectrum UV filters. Then a description and assessment of *in vivo*, *ex vivo*, *in vitro* and *in silico* methods is given.

PROTECTION ANTI-UV-A ET PRODUITS DE PROTECTION SOLAIRE

RESUME

Le comité technique TC 6-24 a été initié en 1992 pour prendre en compte l'importance des effets délétères entraînés par les expositions au rayonnement UV-A et, en raison de l'absence de normalisation, pour tester la protection anti-UV-A. Son objectif était de parvenir à un consensus international pour réaliser de tels tests. En 1997, le comité a sélectionné un test *in vivo* pour une étude approfondie basée sur la réaction cutanée appelée pigmentation immédiate et persistante. Plusieurs méthodes *in vitro* n'étaient pas encore validées. Il fut impossible de parvenir à un consensus. Parallèlement, le développement de méthodes pour évaluer la protection anti-UV-A continuait et se poursuit actuellement, particulièrement vers les méthodes *in vitro*. De plus l'évaluation, aidée par informatique, des performances des écrans solaires - méthode appelée "*in silico*" - devint plus sophistiquée et utilisée. Plutôt que de tenter d'aboutir à un consensus sur les tests d'évaluation des écrans solaires, l'objectif du TC 6-24 se réduit à fournir un rapport technique présentant une vue générale compréhensible ainsi qu'une évaluation et un classement des méthodes UV-A actuellement en discussion. Ce rapport présente les principes généraux de la protection anti-UV ainsi qu'une analyse des filtres absorbant dans l'UV-A et dans un spectre plus large anti-UV. Enfin une description et une évaluation des méthodes *in vivo*, *ex vivo*, *in vitro* et *in silico* sont fournies.

UV-A-SCHUTZ UND SONNENSCHUTZMITTEL

ZUSAMMENFASSUNG

Das Technische Komitee TC 6-24 wurde 1992 angesichts der Wichtigkeit der schädlichen Wirkung von UV-A-Strahlung und dem Mangel an Vorschriften zur Messung des UV-A-Schutzes gegründet. Das damalige Ziel war, einen internationalen Konsensus über UV-A-Messmethoden zu erreichen. Bis 1997 beschäftigte sich die Arbeitsgruppe mit mehreren *in vivo* Methoden, von denen die Persistent Pigment Darkening Methode am weitesten fortgeschritten war. Es war damals jedoch nicht möglich, einen Konsensus zu erzielen. In der Zwischenzeit ging die Entwicklung der UV-A-Schutz-Bestimmungsmethoden, vor allem im In-vitro-Bereich, weiter. Des Weiteren wurden Methoden zur Berechnung der Leistung von Sonnencremes - hier „*in silico*“ genannt - anspruchsvoller und zuverlässiger. Anstatt zu versuchen, einen Konsensus über die UV-A-Testung von Sonnenschutzmitteln zu erreichen, wurde das Ziel des reaktivierten TC 6-24 darauf reduziert, in Form eines Technischen Berichtes eine umfassende Übersicht, sowie eine Beurteilung und Rangordnung der z.Zt. diskutierten UV-A-Meßmethoden zu geben. Dieser Bericht beginnt mit den Prinzipien des UV-

Schutzes und einer Übersicht der UV-A- und Breitband-UV-Filter. Dann werden *in vivo*, *ex vivo*, *in vitro* und *in silico* Methoden beschrieben und beurteilt.

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ABBREVIATIONS

COLIPA	European Association of Cosmetics, Toiletries and Perfumeries
Erythema	reddening of the skin caused by various physical or chemical agents
ESR	Electron Spin Resonance
FDA	Food and Drug Administration
IC	Internal Conversion
INCI	International Nomenclature of Cosmetic Ingredients
<i>in silico</i>	computer simulation
<i>in vitro</i>	testing without living organisms
<i>in vivo</i>	testing on living organisms
IR	infrared
ISC	Inter-System Crossing
iSPF	integrated Sun Protection Factor
JCIA	Japanese Cosmetic Industry Association
MED	Minimal Erythema Dose
MED _p	MED on protected skin, <i>in vivo</i> testing
MED _u	MED on unprotected skin, <i>in vivo</i> testing
MPD	Minimal Pigmenting Dose
MPD _p	MPD on protected skin, <i>in vivo</i> testing
MPD _u	MPD on unprotected skin, <i>in vivo</i> testing
o/w	oil in water
PF	Protection Factor
PMMA	Poly (methyl methacrylate), commonly known as acrylic
PPD	Persistent Pigment Darkening
SPF	Sun Protection Factor
SPF _{in vitro}	Sun Protection Factor, <i>in vitro</i> testing
SPF _{in vitro,adj}	Sun Protection Factor, <i>in vitro</i> testing, with adjusted transmission spectrum
SPF _{in vivo}	Sun Protection Factor, <i>in vivo</i> testing
USAN	United States Adopted Name
UV-A	ultraviolet radiation, $\lambda = 315 \text{ nm} \dots 400 \text{ nm}$ (320 nm ... 400 nm in photobiology)
UVAPF	UV-A Protection Factor
UVAPF _{in vitro}	UVAPF, <i>in vitro</i> testing
UVAPF ₀	UVAPF, without pre-irradiation
UV-B	ultraviolet radiation, $\lambda = 280 \text{ nm} \dots 315 \text{ nm}$ (290 nm ... 320 nm in photobiology)
UVR	ultraviolet radiation, $\lambda = 100 \text{ nm} \dots 400 \text{ nm}$
w/o	water in oil

SYMBOLS

$\varepsilon(\lambda)$	molar decadic extinction coefficient (in $\text{l} \cdot \text{mol}^{-1} \cdot \text{cm}^{-1}$)
$E_{1,1}(\lambda)$	specific extinction (extinction at 1 cm optical thickness and 1 % of the absorber)
$E_{\text{er}}(\lambda)$	erythema spectral irradiance
$E_{\text{PPD}}(\lambda)$	PPD effective spectral irradiance

F_{iSP}	integrated Sun Protection Factor (iSPF)
F_{MED}	Minimal Erythematous Dose (MED)
$F_{\text{MED,p}}$	MED on protected skin, <i>in vivo</i> testing
$F_{\text{MED,u}}$	MED on unprotected skin, <i>in vivo</i> testing
F_{MPD}	Minimal Pigmenting Dose (MPD)
$F_{\text{MPD,p}}$	MPD on protected skin, <i>in vivo</i> testing
$F_{\text{MPD,u}}$	MPD on unprotected skin, <i>in vivo</i> testing
F_{P}	Protection Factor
F_{SP}	Sun Protection Factor (SPF)
$F_{\text{SP,in vitro}}$	<i>in vitro</i> SPF
$F_{\text{SP,in vitro,adj}}$	<i>in vitro</i> SPF, with adjusted transmission spectrum
$F_{\text{SP,in vivo}}$	<i>in vivo</i> SPF
F_{UVAP}	UV-A Protection Factor (UVAPF)
$F_{\text{UVAP,in vitro}}$	UVAPF, <i>in vitro</i> testing
$F_{\text{UVAP,0}}$	UVAPF, without pre-irradiation
$H_{0,t}$	UV-dose necessary to produce a certain amount of radicals for protected skin
H_t	UV-dose necessary to produce the same amount of radicals for unprotected skin
λ	wavelength in nm
M	molar mass
S_0	electronic ground state
S_0^*	vibrationally excited electronic ground state
S_1	first excited electronic singlet state
$s_{\text{er}}(\lambda)$	erythema action spectrum
$s_{\text{PPD}}(\lambda)$	PPD action spectrum
$S_{\text{s}}(\lambda)$	standard sun spectrum
$S_{\text{UV-A}}(\lambda)$	UV-A lamp spectrum for PPD method
T_1	first excited electronic triplet state
$\tau(\lambda)$	spectral transmittance
τ_{eff}	effective transmittance of a sunscreen product

1 INTRODUCTION

Induction of sunburn and skin cancers are mainly attributed to the UV-B part of the solar spectrum (280 nm – 315 nm), but the UV-A portion (315 nm – 400 nm) is also an important factor [1]. CIE has published action spectra for minimal erythema dose and non-melanoma skin cancers [1, 2]. CIE has defined the dividing wavelength at 315 nm, however in medicine and more generally in human health 320 nm is used. Furthermore, the UV-A range has been divided because of different biological effects observed after exposure to UV-A1 (340 nm – 400 nm) or UV-A2 (320 nm – 340 nm) [3, 4]. Given that this report focuses on an industry that uses 320 nm as the boundary for UV-A, we shall take their definition for the purposes of this report, while noting that the CIE definition of UV-A remains as 315 nm – 400 nm. Note also that the continuum of the erythema action spectrum, and changing solar spectrum with solar zenith angle, mean that the contribution of UV-A radiation to the induction of erythema is variable depending on latitude, season and time of the day: about 10 % of the actinic erythema is caused by UV-A radiation from the sun at midday in summer and at temperate latitudes. Sunscreens with a Sun Protection Factor (SPF) $F_{SP} > 10$ used to prevent sunburn must contain chemicals that absorb in the UV-A region [4].

The awareness for the need of UV-A protection emerged about 15 to 20 years ago. In 1991 a UV-A conference was held in San Antonio, Texas. Brian Diffey then said the following:

We do not yet know the importance of UV-A with regard to photoaging ... and ... skin cancer It would seem prudent, therefore, to encourage the development of sunscreens which absorb more or less uniformly throughout the UV spectrum.
Diffey 1991 [5]

So, Diffey was suggesting, despite or rather because of the limited knowledge about skin damage caused by UV-A radiation at that time, that we should protect against UV-A equally well as against UV-B radiation. Now we know a bit more. It was shown recently that UV-A radiation leads to DNA damage and increased levels of the p53 gene product in human skin, which is an indicator for mutations and therefore for the risk of skin cancer. This effect could be suppressed to a significant extent by application of a sunscreen with high UV-A protection in an animal model [6]. Furthermore, it was shown that UV-A plays a role in immunosuppression [7]. UV-A is absorbed in the epidermis and the dermis and thus it plays an important role in premature aging of the skin [8-10].

For these reasons it is without doubt that a certain level of UV-A protection must be ensured in the development of cosmetic sunscreens. While for the measurement of sun protection factors standardized methods are used [11-13], the methods for the assessment of the level of UV-A protection have been a matter of debate for almost 20 years [14]. However, a consensus seems to be in reach for an *in vivo* and an *in vitro* method.

1.1 Terms of Reference (1992)

In view of the importance of UV-A (in matter of skin premature ageing, skin carcinogenesis, immune local or systematic depression), and because of lack of existing regulations to test for UV-A protection, it is proposed to extend the work of TC 6-12 (concerning UV-B protection) on high protection factor (SPF) sunscreens. The goal is to arrive at an international consensus on sunscreen testing for UV-A protection. The report will discuss relative merits of test methods and discuss state of knowledge.

1.2 Scope/State of the Art

Over the last 10 years when the Technical Committee on Sunscreens and UV-A was inactive, findings about damaging effects from UV-A radiation have been confirmed and the development of methods for the assessment of UV-A protection continued. Although UV-A protection method standards are now established in several countries and regions, e.g. Japanese standard in Japan and many Asian countries, Australian standard in Australia and some countries in Europe, Boots Star Rating in Great Britain, there is no harmonization in determination of UV-A protection, as is the case for SPF measurement. Also the US-FDA has recently published a proposed rule on UV-A protection. In this report the various methods are discussed and compared at a scientific level. This should assist trade associations, standardizing bodies and authorities that are involved in the evaluation and setting of UV-A assessment methods.

This report discusses UV-A assessment methods that are currently in use or are emerging. Several *in vivo* methods have already been extensively evaluated and ruled out for different reasons in the preliminary TC 6-24 report (1997 – see Appendix A) and will thus not be considered further. The only *in vivo* method further considered is Persistent Pigment Darkening (PPD) [15]. On the other hand a lot of experience has been gained with instrumental *in vitro* methods. We are now in a position to compare and give recommendations. Furthermore a new class of UV-A assessment methods is emerging, i.e. the computer simulation allowing the determination of the various *in vivo* and *in vitro* performance parameters of a sunscreen [16]. We refer to this new class of method as *in silico*.

1.3 Background - Previous Work (Status of TC 6-24 in 1997, see Appendix A)

The Technical Committee has examined the literature relevant to testing of sunscreens which reduce or block UV-A solar radiation from reaching human skin. The references listed in the appendix formed the basis for all Technical Committee discussions.

The following methods have been reviewed by the committee. These are:

- *in vitro* determination;
- *in vivo* protection against UV-A photo-toxic reactions;
- *in vivo* immediate pigment darkening;
- *in vivo* persistent pigment darkening;
- *in vivo* melanogenesis and erythema;
- human spectroscopic method.

1.4 Comparison of *in vivo* Methods

1.4.1 Phototoxicity

It is the judgment of the Technical Committee that the action spectra of the phototoxic sensitizers have little resemblance to the action spectra of concern to normal individuals and therefore are not relevant to the testing of sunscreens for general purposes.

In addition, the Technical Committee is concerned that there are additional risks to normal individuals who participate in testing which make such testing unjustifiable (carcinogenesis potential of some sensitizers).

1.4.2 UV-A Erythema

In skin able to pigment (type II, type III), the erythema can be obtained for high doses of UV-A radiation ($60 \text{ J}\cdot\text{cm}^{-2}$ – $80 \text{ J}\cdot\text{cm}^{-2}$) but the irradiated skin remains pigmented for weeks or months which is unacceptable from an aesthetic point of view. The duration of exposure with the power of sources commercially available can be longer than one hour, which is considered difficult to deal with for most human volunteers.

1.4.3 Human Spectroscopic Method

Several spectroscopic methods have been proposed for determining the absorption of sunscreen products *in vivo* on human skin. These techniques were developed at the Wellman Laboratory and are presented in work reported by Gillies et al. [17]. They remain today at a preliminary phase of investigation.

1.4.4 Immediate and Persistent Pigment Darkening (IPD and PPD)

At the 1992 meeting of the Technical Committee (see Appendix A), C. Irwin presented a report of a multi-centre study which used immediate pigment darkening as an end-point to evaluate the UV-A efficacy of sunscreen products. Chardon [15] has shown that the pigmentation induced by a UV-A only source (no UV below 320 nm) is stable from 2 hours after irradiation to more than 24 hours and is highly unstable within the first hour after irradiation. He has also shown that the pigmentation response obeys the law of reciprocity and suggested to name Persistent Pigment Dose the minimal UV-A dose necessary to induce a visible pigmentation 2 hours after the end of irradiation. Since then several groups have investigated the immediate pigment darkening reaction and the photoprotection against the

phenomenon by several UV-A sunscreens. In the report that the Technical Committee has reviewed, products containing both chemical UV-A absorbing sunscreen and products containing physical absorbing and scattering agents have been successfully tested. The range of exposures used are below $20 \text{ J}\cdot\text{cm}^{-2}$ and are not dependent on the skin photosensitivity. The delay chosen for the endpoint appeared to be the major difference; reading between 2 hours and 24 hours [15].

1.5 Conclusion from Previous Work

The result of the previous work was that only one *in vivo* method, based on the persistent pigment darkening effect, was worth pursuing. In the meantime this method has been well established and is the basis for UV-A testing in a Japanese standard [18]. Another result was that *in vitro* methods should be considered as well but first should be validated. Also in this respect progress has been achieved, which will be reported in detail.

2 ASSESSMENT OF UV-A PROTECTION BY SUNSCREENS - MECHANISMS OF UV-A ATTENUATION

2.1 General Principles

In sunscreens three mechanisms of UV-attenuation may be distinguished: absorption, scattering, and reflection (backward scattering). But principally, there are two ways in which electromagnetic radiation may interact with matter: absorption and scattering. In the case of scattering, the radiation has no resonance frequencies with energy transitions of the molecule, but the electric dipole of the molecule or of the particle oscillates with the frequency of the radiation. The oscillating dipoles will then emit radiation of the original frequency in diverse directions, leading to attenuation of the radiation in the incident direction. With absorption there is a resonance between the exciting radiation and the energy transition of the molecule, resulting in a transfer of energy to the molecule, which can be described as a quantum effect. When both mechanisms are relevant, the total effect is described as extinction. The strength of the extinction per mol is characterized by the molar decadic extinction coefficient ε [$\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1}$]. A more practical measure is the specific extinction $E_{1,1}$ referring to a 1 % solution of the absorber at 1 cm optical path length. The relationship between both measures is given in the following relationship (M = molar mass [$\text{g}\cdot\text{mol}^{-1}$]):

$$E_{1,1} = \varepsilon \left[\text{l}\cdot\text{mol}^{-1}\cdot\text{cm}^{-1} \right] \cdot \frac{10 \left[\text{g}\cdot\text{l}^{-1} \right]}{M \left[\text{g}\cdot\text{mol}^{-1} \right]} \cdot 1 \left[\text{cm} \right] \quad (1)$$

The principles by which organic UV filters are able to absorb photons and what may happen with the energy afterwards are summarized in the simplified Jablonski diagram in Fig. 1. The excitation of a molecule starts out in most cases from the electronic ground state S_0 . It absorbs an amount of energy $E = h \cdot \nu$, corresponding to one photon, where h is Planck's constant and ν the frequency of the light. Excitation with that energy puts the molecule into an excited electronic state, which is for polyatomic organic molecules in most cases the S_1 state (first electronic excited state). Molecules in the excited state are less stable than in the ground state; thus they quickly give off the energy and, in the ideal case, return to the ground state where they can act as absorbers again.

The absorbed energy can be eliminated via several pathways [19]. From the S_1 state it may be lost directly via fluorescence (a radiative transition) or by undergoing photoreactions. There are also radiationless transitions by which the absorbed energy is redistributed inside the molecule: Intersystem Crossing (ISC) leads to the first triplet state T_1 , and internal conversion (IC) to the S_0^* state, which is the electronic ground state but with the excitation energy now migrated into vibrational modes of the molecule. From the T_1 the energy may be dissipated by emission of a photon (phosphorescence), by energy transfer to other molecules (sensitization) or via photoreactions. The fate of the energy after internal conversion to the vibrationally excited ground state S_0^* can be emission of IR photons or collisional deactivation of the vibrational modes via collisions with surrounding molecules. Since the rate constant for

emission of IR quanta is very small, collisional deactivation will be the main process after internal conversion, rendering the molecule in its electronic ground state S_0 , while having converted the excitation energy into heat. Hence, in terms of photostability, absorbers showing a high rate of internal conversion are most desirable [20].

In case of photoreactions structural changes are involved, which may be reversible as with isomerizations (cis/trans or keto/enol), or irreversible. Irreversible changes leading to decomposition would result in an UV-absorber with a photoinstability problem.

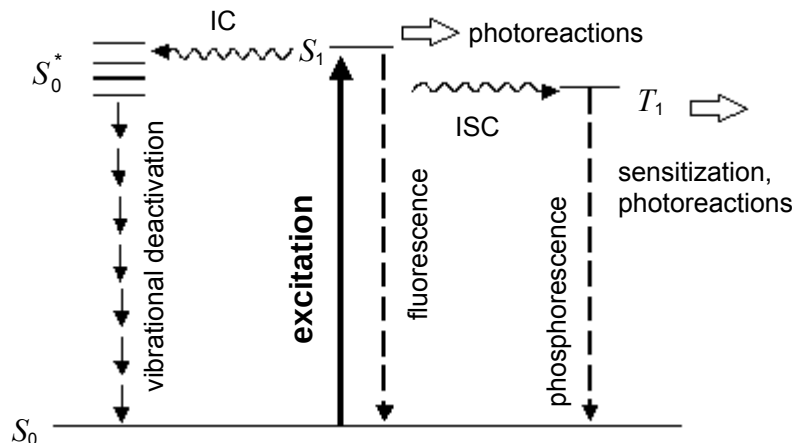


Fig. 1. Jablonski diagram showing excitation of organic molecules by photons and deactivation pathways.

The inorganic oxides TiO_2 and ZnO function mainly by absorption of light, although this main effect is superimposed by some scattering [21]. Being small particulate crystals, these materials are semiconductors with high band gap energy between the valence and conduction band. The band gap of the bulk crystals is in the range of an energy corresponding to wavelengths between 380 nm and 420 nm, but this may alter with the size of the primary particles (the smaller the primary particles, the higher the band gap energy). UV radiation is absorbed by elevating an electron from the valence to the conduction band (Fig. 2). The primary particle sizes of TiO_2 for sunscreen applications are between 10 nm and 30 nm. However, in dispersion, the particles form aggregates with sizes of about typically 100 nm. With ZnO , primary particle sizes from 10 nm to 200 nm are available, but mainly the grades with larger particles are used. The ratio of light attenuation due to scattering and due to absorption depends strongly on the particle size. With the grades used in sunscreen applications, the absorption is by far dominating.

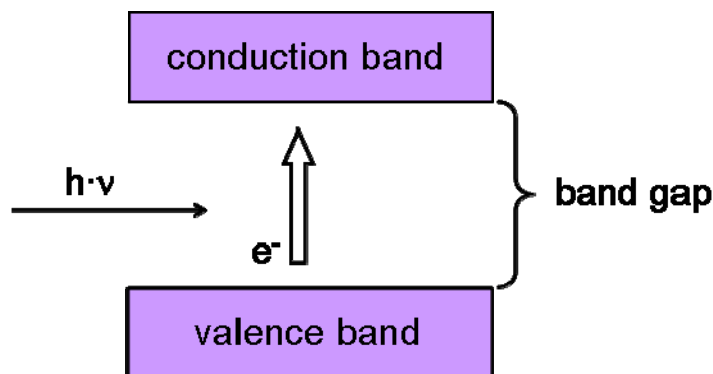


Fig. 2. Mechanisms of absorption with inorganic UV-filters.

2.2 Chemistry

All available organic UV-filters contain at least one benzene ring, and thus, have an excellent ability to absorb energy. The absorption maximum of this moiety can be shifted to longer wavelengths by linking the benzene ring to an extended π -system and substituting it with efficient electron withdrawing groups, carbonyl groups are the most typical. An electron-donating group often appears in the para-position to the carbonyl group, leading to a so-called push/pull substituted conjugated π -system. These substitution patterns bring the ground and excited states closer together, with the result that less energy is required to achieve a photo-induced electronic transition.

The electronic transitions responsible for the absorption of UV radiation by absorber molecules in the spectral range relevant for cosmetic sunscreens are mainly of $\pi \rightarrow \pi^*$ nature; $n \rightarrow \pi^*$ -transitions are also possible, but their intensity is too low for playing a significant role in UV protection efficiency.

2.3 Factors that affect UVR Transmittance of Sunscreens

Besides the chemistry many other factors influence the performance of a sunscreen and its assessment:

- Compliance (amount applied, uniformity);
- Skin of subjects (age, wrinkles, bodysite);
- Properties of the sunscreen;
 - Spectral properties (height and width of extinction);
 - UV filter concentration;
 - Photostability of sunscreen actives;
 - Galenic form of sunscreen;
 - * Emulsion type o/w or w/o, etc.;
 - * Distribution of UV filter in oil and water phase;
- External temperature;
- Delay between application and exposure (recommendation > 15 min).

3 ASSESSMENT OF UV-A PROTECTION BY SUNSCREENS - MATERIALS AND METHODS

3.1 Materials

UV-A/Broad-Spectrum UV Filters:

(See cross-reference list of all approved UV filters in Appendix C.)

Tables 1 and 2 summarize INCI-names, structures, UV-spectroscopic data, registration status, and sources of the current UV-A and broad-spectrum filters.