EUROPEAN COMMISSION
ENTERPRISE AND INDUSTRY DIRECTORATE-GENERAL

Consumer goods
Cosmetics and Medical Devices

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STANDARDISATION MANDATE ASSIGNED TO CEN CONCERNING

METHODS FOR TESTING EFFICACY OF SUNSCREEN PRODUCTS

1. MOTIVATION

This standardisation mandate relates to Council Directive 76/768/EEC of 27 July 1976 on the approximation of the laws of the Member States relating to cosmetic products (hereinafter the Cosmetics Directive). The Cosmetics Directive is based on article 95 EC-Treaty and aims to ensure free circulation of cosmetic products into the Community market. It determines that the person responsible for placing the cosmetic product on the market has to have "proof of the effect claimed for the cosmetic product, where justified by the nature of the effect or product" readily accessible to the competent authority concerned.

Sunscreen products are cosmetic products and fall within the scope of application of Cosmetics Directive. The proof of effect is particularly relevant for these products, as the efficacy of sunscreen product is important for the protection of public health.

Moreover, standardised testing methods for the efficacy of sunscreen products facilitate the free movement of goods in this important sector of cosmetic products.

Therefore, creation of a standard for the testing of efficacy of sunscreen products is deemed necessary.

2. DESCRIPTION OF THE MANDATED WORK

The Commission invites CEN to establish a European standard for testing methods for the efficacy of sunscreen products.

For the purpose of this mandate, "sunscreen product" shall mean "any preparation (as, for example, cream, oil, gel, spray) intended to be placed in contact with the human skin with a view exclusively or mainly to protecting it from UV radiation through absorbing, scattering or reflecting radiation".[1] The European standard for testing methods for the efficacy of sunscreen products shall address:

[1] Cf. Art. 1 of the draft "Recommendation on efficacy and claims relating to sunscreen products"

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- Protection from sunburn (i.e. mainly UVB radiation);
- Protection from UVA radiation;
- Determination of the critical wavelength, i.e. the wavelength for which the section under the integrated optical density curve starting at 290 nm is equal to 90% of the integrated section between 290 to 400 nm.

Two of the testing methods submitted with this mandate are *in-vivo* tests on human volunteers. Apart from these *in-vivo* methods, CEN is invited to consider also *in-vitro* testing methods which:

- lead to results comparable to those obtained with the *in-vivo* methods;
- are reproducible; and
- take photo-degradation into account.

In order to facilitate a wide acceptance of the standard, CEN will take into account the testing standards as currently considered in the draft "Commission recommendation on efficacy and claims relating to sunscreen products"[2] and, in particular, the standard(s) or other standardisation deliverables under preparation or published as a result of ISO/TC 217 "Cosmetics". CEN will avoid any unnecessary duplication of work with the international standards organisations, particularly by using the provisions for parallel approval procedures provided for in the existing co-operation agreements ("Vienna Agreement").

3. BODIES TO BE ASSOCIATED

As appropriate, CEN will ensure that the representative organisations of consumers interests (ANEC), environmental protection (ECOS), workers (ETUI-REHS), small and medium-size enterprises (NORMAPME) and every relevant industrial organisation, in particular COLIPA[3], take part in the elaboration of the standard.

4. EXECUTION OF THE MANDATED WORK

CEN will deliver a draft European standard and submit it to a public enquiry by 30 April 2008.

CEN will publish a final European standard by 30 September 2009. By that date the standard will be available in English, French and German, and the correct title of the standard will be available in the other Community languages

At the latest six months after the publication of the European standard by CEN, it will be implemented as a national standard by all national standards institutes in all Member States and every conflicting national standard will be withdrawn.

The acceptance of this mandate by one of CEN will trigger the standstill period referred to in Article 7 of Directive 98/34/EC of 22 June 1998.

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[2] Description of the testing standards annexed.

[3] The European Cosmetic Toiletry and Perfumery Association.

Annex 1: Determination of the sun protection factor

INTERNATIONAL

SUN PROTECTION FACTOR (SPF)

TEST METHOD

May 2006

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1.1.9. CTFA South Africa

1.1.10. Jill Gardiner, Technical Director

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1.1.17. Pamela Bailey, President and CEO

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1.1.23. JCIA

1.1.24. Toshitaka Makino, Senior Managing Director

Colipa

Bertil Heerink, Director General

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HISTORY OF SPF METHOD

The Sun Protection Factor (SPF) determined in vivo is now a universal indicator of the efficacy of sunscreen products against sunburn.

Historically, the first known studies establishing the basis for the SPF or Index of Protection (IP) started in the 1930's and were published in the 1940's by H. Blum et al. and in the 1950's by R. Schulze. These studies and other works by standardisation and scientific groups lead to the historic definition of the concept of minimal erythema dose (MED) and SPF and to the first standard method for SPF determination and labelling which was issued by the FDA in the USA ('Proposed Monograph') in 1978. This was followed in 1984 by the DIN67501 norm in Germany, which was applied mainly in Europe. These two standards differed mainly in respect of the type of UV source used (respectively xenon arc lamp or natural sunlight and mercury lamp) and the rate of product application on skin (2.0 and 1.5 $mg.cm^{-2}$), which lead to some discrepancies in protection factors measured.

All standards issued subsequently retained the artificial xenon source and the application rate of 2.0 $mg.cm^{-2}$. Standards similar to the FDA were then issued by the Standards Association of Australia (SAA) in 1986, which included both SPF and water resistance testing, and by the Japan Cosmetic Industry Association (JCIA) in 1991. These methods were revised in 1986, 1993, 1997, and 1998 (Australian Standard) and in 1999 (Japanese Standard). The South African Bureau of Standards (SABS) presented a similar method in 1992, which was revised in 2002. A new version of the FDA standard ('Tentative Final Monograph') was issued in 1993. The implementation of the 1999 version ('Final Monograph') has been postponed indefinitely. This suspension is to provide time for introducing specific methods for UVA testing and labelling. The New Zealand Standards joined the Australian Standards for their joint new version (AS/NZS 2604:1993) in 1993 and their revised version of 1998.

The European Cosmetic, Toiletry and Perfumery Association (COLIPA), in its 1994 SPF test method, introduced new techniques to characterise and specify the emission spectrum of the UV source and to colorimetrically select skin types. At the same time, two high SPF standard products were proposed to take into account the increase in SPF values. The Austrian Önorm in 1998 and the new DIN standard of 1999 were aligned to the COLIPA 1994 Method.

More recently, Korea, Columbia and Mercosur (2002) have adopted methods referring to FDA or COLIPA standards. China is also considering adopting an SPF standard.

COLIPA, JCIA and CTFA-SA began discussion on the harmonisation of the SPF measurement method in 2000. A joint agreement of the international SPF Test method was reached in October 2002.

In 2005, CTFA expressed its interest in having a common international SPF methodology with Colipa, JCIA and CTFA-SA. This updated version is the achievement of discussions which started in June 2005. Minor amendments have been introduced to the guidelines which reflect and translate the experience of technicians and experts.

INTRODUCTION

The level of sun protection has traditionally been estimated using the sun protection factor or SPF test, which utilises the erythemal response of the skin to ultraviolet (UV) radiation. The SPF is a ratio calculated from the energies required to induce a minimum erythemal response with and without sun product applied to the skin of human volunteers, using ultraviolet radiation usually from an artificial source.

The method described in the following sections is a guide to help the experienced technician to perform the test. Certain procedures are critical to obtaining the correct result and these are described in the appendices and the accompanying CD-ROM, which shows the correct procedure for weighing and application of products.

All procedures in the guideline may be subject to revision and so technicians performing the test should ensure that they are working to the most recent revision of the method.

Local national regulation relating to the use of volunteers (hereafter referred to as subjects) in clinical studies must be complied with.

1.1.25.1. ETHICAL CONSIDERATIONS

The basic principles for testing on human subjects are described by the following reference documents:

- World Medical Association Declaration of Helsinki incorporating its various revisions (1964 – 1975 – 1983 – 1989 – 1996 –2000 2002 2004).
- National Regulations regarding human studies.

In accordance with these basic principles, the following points are emphasised since they apply directly to SPF measurement studies:

- Sun protection measurements are performed to assess the level of protection that properly applied cosmetic products provide to consumers exposed to sunlight. Such studies should not impart harmful, long-lasting effects on human volunteers.

- Tests have to be performed by trained and qualified personnel in order to avoid any damage to the skin of the volunteers involved in the test.
- Prior to starting any test the study supervisor of the testing facility must hold adequate information on the product to be tested, its pre-clinical safety assessment and any possible warnings.
- Children shall not participate in SPF measurement tests.

1.1.26. DEFINITIONS OF TERMS

A. UV RADIATION

The spectral limits conventionally accepted by photobiologists and dermatologists for SPF determinations are:

UVB: 290nm - 320nm

UVA: 320nm - 400nm

UVA II: 320-340nm

UVA I: 340-400nm

B. MINIMAL ERYTHEMA DOSE (MED)

The Minimal Erythema Dose in human skin is defined as the lowest ultraviolet UV dose that produces the first perceptible unambiguous erythema with defined borders appearing over most of the field of UV exposure, 16 to 24 hours after UV exposure.

The MED on unprotected skin is referred to as 'MEDu' and the MED on sunscreen-protected skin is referred to as 'MEDp'.

C. SUN PROTECTION FACTOR (SPF)

An individual Sun Protection Factor (SPFi) value for a product is defined as the ratio of the Minimal Erythema Dose on product protected skin (MEDp) to the Minimal Erythema Dose on unprotected skin (MEDu) of the same subject:

$$SPFi = \frac{MEDi\ (protected\ skin)}{MEDi\ (unprotected\ skin)} = \frac{MEDpi}{MEDui}$$

The SPF for the product is the arithmetic mean of all valid individual SPFi values obtained from all subjects in the test, expressed to one decimal place.

1.1.27. THE METHOD

1. OUTLINE OF THE METHOD

Some of the technical terms used in this method are defined in 'Definitions and Terms' above.

The International SPF Test Method is a laboratory method that utilises a xenon arc lamp solar simulator (or equivalent) of defined and known output. To determine the Sun Protection Factor, incremental series of delayed erythemal responses are induced on a number of small sub-sites on the skin of selected human subjects. The test is restricted to the area of the back between waist and shoulder-line.

An area of each subject’s skin is exposed to ultraviolet light without any protection and another (different) area is exposed after application of a test sun protection product. Furthermore at least one further area is exposed after application of an SPF reference sunscreen formulation.

By incrementally increasing the UV dose, varying degrees of skin erythema (redness due to superficial vasodilatation) are generated. These delayed erythemal responses are visually assessed for redness intensity 16 to 24 hours after UV radiation, by the judgement of a trained evaluator.

The minimum erythemal dose (MED) for unprotected skin (MEDu) and the MED obtained after application of a sun protection product (i.e. the MED for product protected skin, MEDp) must be determined on the same subject on the same day. More than one product may be tested on the same subject in any single test.

An individual sun protection factor (SPFi) for each subject tested is calculated as the ratio of MEDpi/MEDui.

The sun protection factor for the product (SPF) is the arithmetic mean of all valid SPFi results from each and every subject in the test and should be expressed to one decimal place. A minimum of 10 valid results and a maximum of 20 shall be used for the calculation of SPF.

Confidence limits (95% Confidence Interval) for the mean SPF should fall within the range of ± 17% of the mean SPF.

Every test shall include an appropriate high or low SPF reference sunscreen formulation depending on the expected SPF of the test formulations (refer to appendix V). The obtained SPF for a SPF reference sunscreen formulation should fall within the expected range.

2. TEST SUBJECTS

2. 1. Selection of test subjects

2.1.1 Skin phototype of subjects

The skin phototype of subjects included in the SPF test panel shall be phototypes I, II, or III according to Fitzpatrick or shall have an ITA° value >28° by colorimetric methods (see COLIPA Guidelines “Guidelines for the colorimetric determination of skin colour typing and prediction of the minimal erythemal dose (MED) without UV exposure”) and be untanned on the test area.

A trained scientist or technician should examine each subject to ensure that there is no condition which might put the subject at risk and that the results of the test could not be compromised by adverse skin conditions such as sun damage, staining and previous history of abnormal response to the sun. (Appendix I)

2.1.2 Frequency of participation in tests

Since a sufficient interval after a previous test is needed in order to allow for reversal of skin tanning resulting from that previous test, a test site that has been exposed to UV should not be used in a subsequent test until two months have elapsed and the site is clear.

Informed, written (signature) consent must be obtained from all subjects.

2.2. Number of subjects

A minimum of 10 valid results and a maximum of 20 valid results shall be recorded for each test. A maximum of five individual results may be excluded from the calculation of the mean SPF but each exclusion has to be justified. All individual results must be included in the report, even if not included in the calculation of mean SPF. A minimum of 10 valid results is only sufficient if the 95% confidence interval (95%CI) of the mean SPF is within ± 17% of the mean SPF (e.g. if the mean SPF is 10.0, the CI shall lie between 8.3 and 11.7). Otherwise, the number of subjects is increased stepwise from 10 until the statistical criterion is met (up to a maximum of 20 valid results from a maximum of 25 subjects tested). If the statistical criterion has not been met after 20 valid results from the maximum 25 subjects, then the test shall be rejected. For details on statistical definitions, sequential procedure and calculations refer to Appendix IV

3. TEST AREA

The back is the chosen anatomical region for the test area. The individual test sites should be delineated within the region between the scapula line and the waist. Skeletal protrusions and extreme areas of curvature should be avoided.

4. SOURCE OF ULTRAVIOLET RADIATION

The artificial light source used must comply with the source spectral specifications as described in section 4.1 below and Appendix II. A xenon arc solar simulator with appropriate filters is recommended.

4.1 Quality of ultraviolet radiation

The UV solar simulator shall emit a continuous spectrum with no gaps or extreme peaks of emission in the UV region. The output from the UV solar simulator shall be stable, uniform across the whole output beam (particularly important for a single large-beam) and suitably filtered to create a spectral quality that complies with the required acceptance limits (Table 1 below and Appendix II)

To ensure that appropriate amounts of UVA radiation are included in the spectrum of the solar simulator throughout the entire UVA range, the total radiometric proportion of the UVA II (320-340nm) irradiance of the simulator must equal or exceed 20% of the total UV (290-400nm) irradiance. Additionally, the UVA I region (340-400nm) irradiance must equal or exceed 60% of the total UV irradiance.

The source spectral specification is described in terms of cumulative erythemal effectiveness by successive wavelength bands from 290 nm up to 400 nm. The erythemal effectiveness of each wavelength band is expressed as a percentage of the total erythemal effectiveness from <290 to 400 nm, or as the *Relative Cumulative Erythemal Effectiveness* (%RCEE). The RCEE% values of the acceptance limits are given in Table 1 and Appendix II.

Table1: %RCEE acceptance limits for the UV solar simulator output

Spectral Range (nm)	Measured %RCEE

	Lower limit	Upper limit
<290		<0.1%
290-300	1.0	8.0
290-310	49.0	65.0
290-320	85.0	90.0
290-330	91.5	95.5
290-340	94.0	97.0
290-400	99.9	100.0

4.2 Total irradiance (UV, visible and near infrared rays)

When total irradiance is strong, an excessive feeling of heat or pain may occasionally be induced in the irradiated skin of subjects. Therefore, it must be confirmed that the maximum irradiance that will be used (UV, visible and near-infrared rays) will not to induce an excessive feeling of heat in the skin, prior to conducting a SPF test. In some cases, it has been found that irradiation of total irradiance 160 mW/cm2 induced this feeling in the majority of sub-sites, whilst irradiance of 120 mW/cm2 did not induce it.

4.3 Uniformity of Beam

When a large-beam UV source is used to simultaneously expose several sub-sites within an irradiation series by varying the exposure time; the intensity of the beam should be as uniform as possible. The minimum beam irradiance, at any point, shall be no more than 10% lower than the maximum beam irradiance at any point. If the variation exceeds 10%, then appropriate compensation for different irradiance should be made in the exposure time on each sub-site

4.4 Maintenance and Monitoring the UV solar simulator output

Before UV exposure of each test site, the UV irradiance should be checked with a radiometer calibrated against a spectroradiometric measurement of the solar simulator output. It is recommended that a complete spectroradiometic check (UVA & UVB) of output spectrum and intensity be made by the laboratory at least once a year and each time a significant physical (optical) component is changed. It is strongly recommended that an independent expert conduct this annual inspection

The simple use of specified filters is not in itself adequate assurance that the UV output is of the correct quality. Detailed instructions for ensuring correct lamp output are given in Appendix II and in the COLIPA Guidance document: "Guidelines for Monitoring UV-Light Sources".

5. SPF REFERENCE SUNSCREEN FORMULATIONS

A reference formulation is to be used as a methodological control to verify the test procedure. Therefore one reference formulation must be measured on the same day as products are tested. Expected SPF ranges for the reference sunscreens are shown in Table 2 and in Appendix V.. If the mean SPF obtained in any test does not fall within the indicative range of the reference values or the 95% confidence interval (CI) of the mean for the reference formulation used does not fall within a range of ±17% of the measured mean SPF, then the entire test has to be rejected.

At least one reference sunscreen formulation must be used per test. Whether a low or high SPF reference formulation is to be used depends on the expected SPF of the test products.

- **Expected SPF below SPF 20**

Any of the following reference sunscreen formulations shall be used: P2 or P3 or P7

- **Expected SPF equal to or greater than SPF 20**

Either of the following reference sunscreen formulations shall be used: P2 or P3

If a high SPF reference formulation is used there is no necessity to also include the low SPF reference formulation in the test even though there may be low SPF test products. The Table reporting the results of the low SPF test products may therefore list two different reference formulations; the range for each must fall within the indicative range. The recommended reference sunscreens are as follows.

Table 2: SPF and acceptance limits for reference sunscreen formulations

Reference Sunscreen Formulation	Mean SPF	Indicative Range (± 2SE)	
		Lower limit	Upper limit
P2	16.6	14.2	19.0
P3	16.2	13.8	18.7
P7	5.1	4.4	5.9

The formula details and manufacturing information for these reference formulations are given in Appendix III.

6. PRODUCT QUANTITY AND APPLICATION

The amount of product applied and the uniformity of spreading on the test sites affects the magnitude and variability of the test results. It is therefore very important to follow the recommendations set out below. A CD-ROM is provided to help training in product weighing and application.

6.1 Ambient conditions

Product application, UV exposures and MED assessment should be carried out in stable conditions, with the room temperature maintained between 18 and 26 °C.

6.2 Product application site

The minimum area for a product application site shall be 30 cm^2 and the maximum shall be 60 cm^2**.**

The unprotected test site used to determine MEDu must be in close proximity to the MEDp test sites.

The positions of the test products and reference sunscreen test sites must be randomly distributed on the back over the whole test group of subjects in order to reduce systematic error arising from anatomical differences in skin.

There must be a minimum distance of 1 cm between the borders of adjacent product application sites.

Before product application, the test area may be cleaned, but only by using a dry cotton pad or equivalent.

The product application site(s) should be delineated with a skin marker and/or a template made from non-absorbent material.

6.3 Amount of product applied

The amount of test product and reference sunscreen formulation applied to the skin before spreading shall be 2.00 $mg.cm^{-2}$ ± 2.5%. The sensitivity of the balance should be at least 0.0001g, i.e. with at least 4 decimal places.

Care must be taken to prevent evaporative loss of volatile components when the product is being weighed and before application to the skin. It is important that the total quantity of weighed product is transferred to the product application site. A method of weighing by loss is strongly recommended. Liquid type products consisting of two layers must be shaken strongly before weighing in order to ensure a homogeneous dispersion.

6.4 Mode of delivery

6.4.1 Lotions, liquids, milks, creams and sprays

To aid uniform coverage, droplets (approximately 15 per $30cm^2$, 30 per $60cm^2$) of the product should be deposited with a syringe/pipette, then spread over the whole test site with light pressure, using a finger cot (if appropriate). If employed, a new finger cot must be used for each product. Spreading time should be in the range of 20 to 50 seconds depending on the surface and ease of spreading of the product.

6.4.2 Powders

In the case of powder products, aliquots of powder should be transferred to the skin in a grid-like manner, using a spatula or finger as shown in the CD-ROM. The accumulated powder is tapped and then spread over the whole test site using a finger with or without a finger cot. Alternatively, the tip of a pre-loaded cosmetic applicator puff may be used instead of a finger. In this case, it is important to verify that 2 mg/cm^2 of test powder product remains on the skin after spreading, by weighing the powder remaining on the tip of the applicator puff. Purified water or another suitable solvent that has no UV protection properties may be applied before the powder application to help the sample adhere to the application site. Subjects should be in the prone position to prevent the samples from falling off the surface.

6.5 Waiting time between application and UV exposure (drying time)

Exposure of the test site to the sequence of UV doses shall start 15 to 30 minutes after the application of the product(s). Any extraneous exposure of the test sites to UV light (artificial or natural) should be avoided during this period and for a period of 24 hours before the exposures as well as 24 hours after exposure.

7. UV EXPOSURES

A warm up time, typically 10 minutes, should be allowed for the UV solar simulator to stabilise before starting the subjects' exposure.

7.1 Position of subjects

When subjects are being exposed they may be seated or be in the prone position (except for the testing of powder products which should be tested in the prone position). The subject should be positioned in a way to ensure that the complete amount of test product is evenly applied and remains on the skin. The position shall be the same for product application, for UV exposure and for MED assessment.

7.2 Exposure sub-sites

The test sub-sites intended for UV exposure should be free from blemishes and have an even colour tone.

A non-absorbent template may be used to demarcate the sub-sites of UV exposure (large-beam UV solar simulator). The minimum acceptable area of each exposure sub-site is 0.5 cm^2. The recommended area is at least 1 cm^2.

The minimum distance between borders of each exposure sub-site (spots) should be at least 0.8 cm and each sub-site must be of the same area.

7.3 Provisional individual MEDu

Before starting the main test, it may be necessary to determine a provisional individual MEDu in order to centre the UV dose ranges for the exposures of MEDu and MEDp. This can be performed either by applying a preliminary series of UV exposures up to 1 week before the test or by estimating the provisional MEDu by colorimetric technique (ITA) without UV exposure (Appendix I, Colipa Guidance document "Guidelines for the colorimetric determination of skin colour typing and prediction of the minimal erythemal dose (MED) without UV exposure".

7.4 Incremental progression of UV dose

For the unprotected site, the centre of the total UV dose range should be established using the subject's provisional MEDu or the estimated MEDu (see point 7.3). A minimum of 5

sub-sites centred on the provisional/estimated MEDu shall be exposed with incremental UV doses using a recommended geometric progression of either 1.12 or 1.25.

For the product-protected site, the centre of the UV dose range is that of the unprotected MED multiplied by the expected SPF of the product. A minimum of 5 sub-sites centred on the expected MEDp shall be exposed with incremental UV doses using a recommended geometric progression of either 1.12 or 1.25. A maximum geometric progression of 1.12 must be used for expected SPF greater than 25 (> 25). Smaller geometric progressions may be used but must also be consistent throughout the exposure sequence.

7.5 Product removal

After UV exposures, reference and test products may be removed gently, using a cotton pad with a mild lotion such as make-up remover, for example.

8. MED ASSESSMENT PROCEDURE

The minimal erythema dose for unprotected skin (MEDu), that for protected skin (MEDp) and that for the reference sunscreen formulation shall be determined on the same day.

8.1 Time of assessment of MED

The MED shall be assessed when the erythemal response is optimal, i.e. 20 ± 4 hours after UV exposure (between 16 and 24 hours). During the time interval between UV exposure and MED assessment the subject must avoid any extra UV exposure (artificial UV light or sunlight) to the exposed area.

8.2 MED assessment

The MED is assessed visually. Visual assessment should be performed in sufficient and uniform illumination. At least 450 lux are recommended. The observer's eyesight should have been checked for normal colour vision. A yearly check of acuity of vision is recommended.

It is recommended that erythemal responses should be observed in a 'blind' manner: The observers of erythemal responses on any subjects should not be the same persons as

performed product application and exposure, nor should they be aware of the test design (randomisation of sites and UV-doses) on that subject.

8.3 Data rejection criteria

Test data shall be rejected under the following circumstances:

- The exposure series on a subject fails to elicit an erythemal response on any sub-site, 20 ± 4 hours after exposure.
- Erythemal responses within an exposure series are randomly absent 20 ± 4 hours after exposure.
- All sub-sites in the exposure series show an erythemal response 20 ± 4 hours after exposure.

When one or more of the above criteria applies to the exposure series on unprotected skin or to the reference sunscreen formulation exposure sites, then all data for all products on that subject must be rejected.

When one or more of the above criteria applies to a product treated exposure series, then all data for that product on that subject must be rejected.

If data has to be rejected on more than 5 subjects, then the whole test must be rejected.

8.4 Expression of MEDs

MEDs shall be expressed in terms of energy ($J.m^{-2}$, $mJ.cm^{-2}$), or MED units or time (seconds). Units of time may only be used where the flux rate of the solar simulator is constant throughout the test. All irradiance measurements made for a specific study must be made using the same radiometer.

9. CALCULATION OF THE SUN PROTECTION FACTOR AND STATISTICS

The SPF result for the test product is calculated as the arithmetical mean of all valid individual SPFi values

The minimum number of valid SPFi values shall be 10 and the maximum number of valid SPFi values must be 20. The actual number of subjects tested is defined as the number required to produce a mean SPF with a 95% confidence interval (CI) which falls within a

range of ± 17% of the measured mean SPF The full statistical procedure for this calculation is described in Appendix IV..

10. REPORTING OF DATA

It is recommended that the following information be included in the test report:

- Subject information (number, name or identification code, skin phototype or ITA° value
- Individual MED for unprotected skin, test product protected skin and reference sunscreen protected skin
- Individual SPF for each test product and for the reference sunscreen
- Identification of the technician who conducted the test, by subject.
- Mean SPF values and individual SPFi values expressed to one decimal place, including all valid data and rejected data.
- Standard deviation on the mean and 95% CI
- Identification of the UV source
- Product name, code and expected SPF

An example of a typical result table is shown in Appendix IV (Table 7).

In addition to the above information, evidence of conformity with the required %RCEE acceptance limits shall be provided for the last internal measurement and for the most recent external inspection (date of measurement should be provided).

APPENDIX I

1.1.28. SELECTION CRITERIA FOR THE TEST SUBJECTS

1. RATIONALE

In the pre-selection of subjects for the determination of the Sun Protection Factor (SPF) of sunscreens, the criterion of skin phototype is traditionally used because the individual MED may vary widely among subjects depending on their ability to sunburn and to suntan. This variation of the unprotected MEDu generally leads to a corresponding and dependent variation in the protected MEDp. Because the SPF is expressed as the ratio of MEDp to MEDu, these variations should be partially compensated for and generally should not affect the calculated SPF.

However, it has been noticed that, as the skin melanisation increases (from skin phototype I to IV), exposure times increase and the SPF tends to decrease. In addition, comparing subjects of the same phototypes (I to IV) untanned and then after suntanning, led to the same conclusion. These observations suggest that only skin phototype I-III should be utilized in the SPF test and that the inclusion of tanned subjects with these phototypes should be avoided.

The correlation studies between the individual SPF of sun protective products and the colorimetric skin characteristics of the subjects' skin at the time of the SPF determination showed that SPF begins to significantly decrease when the Individual Typology Angle (ITA°) of the subjects falls under the value of about 28° (i.e. from "intermediate" skin colour category to "tanned" category). These findings justify the exclusion of skin phototype IV or "tan/mat" skin colour category.

Measuring the skin colour in the L*a*b* system as defined by the "Commission Internationale de l'Eclairage" and characterising this colour by the ITA° value at the time of the SPF test may allow the selection of subjects, tanned or not according to their actual response to UV light at that moment.

2. SELECTION CRITERIA FOR THE SUBJECTS

2.1 Skin phototypes

Subjects should be selected using Fitzpatrick skin phototype or colorimetric ITA° value. The skin phototype of subjects shall be I, II, III (untanned) or the colorimetric ITA° value of subjects shall be greater than 28°

- The Fitzpatrick skin phototype definitions, are based on the first 30 - 45 minutes of sun exposure after a winter season of no sun exposure, i.e.:

Type I:	Always burns easily: never tans
Type II:	Always burns easily: tans minimally
Type III:	Burns moderately: tans gradually
Type IV:	Burns minimally: always tans well
Type V:	Rarely burns: tans profusely
Type VI:	Never burns; deeply pigmented

- Colorimetric ITA values and skin Colour Categories are defined by the colorimetric descriptors of Chardon et al. (1990) using the CIE (1976) L*a*b* colour space (See Colipa Guidelines: Guidelines for the Colorimetric Determination of Skin Color Typing and Prediction of the Minimal Erythemal Dose (MED) without UV Exposure):

Very Light	-	ITA° values		> 55°
Light	-	ITA° values	from	> 41 to 55°
Intermediate	-	ITA° values	from	> 28 to 41°
Tan (or Matt)	-	ITA° values	from	> 10 to 28°
Brown	-	ITA° values	from	> -30 to 10°
Black	-	ITA° values		≤ -30°

where: **ITA° = [Arc Tangent ((L* - 50) / b*)] 180 / 3.1416**

2.2 Medical and Ethical considerations

- It is recommended that new subjects should first be interviewed by a health professional to establish their medical status and suitability prior to inclusion into the subject panel.

- Subjects should be checked visually by a trained scientist or technician before participating in a study: Their skin colour must be uniform over the whole test area without pigmentation, nevi, or the like and no sunburn (erythema) must be present on the test area. Subjects should have had no sun exposure on the back area for at least 4 weeks prior to SPF testing.

- Human subjects should be adequately informed of the aims and potential risk (direct or secondary effects) of the study and any discomfort they may experience. Each subject must give a written agreement to participate in SPF tests (free informal written consent is mandatory prior to entering the study, according to the general declaration of Helsinki).

- When there is some doubt on the provisional SPF value of the test product, a screening should first be performed on a restricted number of subjects (at most 5). The range of UV doses on product protected skin is progressively increased on consecutive subjects until a MED response is achieved.

2.3. Exclusion criteria

The following conditions shall automatically exclude a subject from the test group:

- Children (SCCNFP/0557/02) and persons below the age of consent
- Pregnant or lactating women
- Subjects taking medication with photosensitising potential
- Subjects taking anti-inflammatory dosage of medication
- Subjects with dermatological problems
- Subjects with a history of abnormal response to the sun
- Subjects accustomed to using tanning beds
- Subjects having marks, blemishes or nevi or presenting with existing sun damage in the test area

2.4 Frequency of subject participation (interval between two tests)

There shall be a sufficient interval between two successive UV exposures to the same test site for resolution of discoloration resulting from previous tests, i.e. not less than two months.

APPENDIX II

DEFINITION

1.1.29. OF THE

UV SOLAR SIMULATOR OUTPUT

1. INTRODUCTION

The aim of these specifications is to define practical criteria for testing the spectral compliance of UV solar simulators used for SPF determination, *e.g.* xenon arc.

2. RATIONALE FOR SPECIFICATIONS

2.1 UV range.

Because UV rays are responsible of most of the sun's damaging effect on skin, the erythemal protective efficiency of sunscreen products is tested within this range of wavelengths. Therefore, the definition of the spectrum of the UV solar simulator is limited to the terrestrial UV-wavelengths, i.e. from 290 to 400 nm.

Wavelengths below this range (< 290 nm) do not occur in terrestrial sunlight and should be excluded, whilst those above this range (> 400 nm) may cause undesirable side effects (particularly thermal effects) and should be removed using appropriate devices.

2.2 Sun UV spectra

Measured solar spectra have been published taking into account different geographical latitudes and altitudes, and variations due to year, season, time of day and ozone content.

For the purpose of this method, a set of selected representative spectra were compiled, from which the tropical Australia sun spectrum was chosen as a reference of maximal sun (RCEE%, 87% at 290 – 320nm).

2.3 Erythemal balance between wavelengths

The erythema induced by sunlight UV in unprotected human skin is mainly generated by wavelengths between 295 and 320 nm, with a maximum effectiveness around 308 nm. For this reason, some previous attempts to standardise UV solar simulator output concentrated on UVB wavelengths alone. However, when a high SPF product is tested, the erythemal contribution from UVA wavelengths can become important, especially if the sun product protects predominantly in the UVB wavelengths. Therefore, it is necessary to include all UVA and UVB wavelengths when standardising the UV solar simulator output.

2.4 Test criteria.

The accuracy of the SPF measured is dependent on the absorbance characteristics of the sunscreen filtering system to be tested in conjunction with the source spectrum. Therefore, it is important to define the source by the spectral distribution of its erythemal efficacy as well as its overall spectral irradiance characteristics.

Thus, the source spectral specification is described in terms of cumulative erythemal effectiveness by successive wavelength bands from 290 nm up to 400 nm. The erythemal effectiveness of each wavelength band is expressed as a percentage of the total erythemal effectiveness from less than 290 nm to 400 nm, or as the *Relative Cumulative Erythemal Effectiveness* (%RCEE). Wavelengths below 290 nm should be excluded from any source by appropriate filters. Wavelengths above 400 nm should be limited as much as possible and are not included in the calculation of %RCEE. Since RCEE values and the distribution of the UVA proportions of the UV spectrum are calculated as relative percentages, the spectral irradiance need not be measured in absolute energy units, however absolute irradiance measurements are needed to determine the total irradiance of the source.

2.5 UV solar simulator and filtration

A lamp that produces a continuous spectrum that can readily be adapted to fulfil the %RCEE acceptance limits for the output between 290 nm and 400 nm by using specific optical filters. To ensure uniformity in spectral shape in SPF testing, it is recommended that UV solar simulators utilising a xenon arc lamp, filtered with a dichroic UV filter to minimize IR radiation, and UV shaping filters such as Schott WG320 and UG11/1mm or equivalent filters be used.

The simple use of the recommended filters is not, in itself, an adequate assurance that the UV output is of the correct quality and so the spectral output must be confirmed by spectroradiometric measurement.

2.6 UV solar simulator acceptance limits.

The limits prescribed in terms of % RCEE values are shown in Table 1. They have been determined from the measured spectral outputs of actual UV solar simulators.

3. MODE OF OPERATION

3.1 UV solar simulator acceptance limits.

The %RCEE limit values referred to in §2.3, are given in Table 1. The upper and lower limits of the acceptance range are shown in columns 2 and 3. The actual %RCEE values, for an individual solar simulator, calculated from spectroradiometric measurements, shall fall within the limits listed in columns 2 and 3 of Table 1 and those also reported in Table 2, columns 9 and 10.

These practical limits, take into account the uncertainty in spectroradiometric measurements and in optical components of the solar simulators. They have been defined and restricted as tightly as possible.

Table 1: %RCEE acceptance limits for the UV solar simulator output

Spectral Range (nm)	Measured %RCEE	
	Lower limit	Upper limit
<290		<0.1
290-300	1.0	8.0
290-310	49.0	65.0
290-320	85.0	90.0
290-330	91.5	95.5
290-340	94.0	97.0
290-400	99.9	100.0

To ensure that appropriate amounts of UVA radiation are included in the spectrum of the solar simulator throughout the entire UVA range, the total radiometric proportion of the

UVA II (320-340 nm) irradiance of the simulator must equal or exceed 20% of the total

UV (290-400 nm) irradiance. Additionally, the UVA I region (340-400 nm) irradiance must equal or exceed 60% of the total UV irradiance.

3.2 Quality of the UV solar simulator output

3.2.1 Spectroradiometric measurements

The output spectrum of the UV solar simulator, including all filters and optical components, shall be measured with a spectroradiometer. The spectroradiometer should be fitted with a double monochromator and its resolution bandwidth should be less than or equal to 2 nm (1 nm is recommended) in order, to ensure that all energies are represented in an amplitude range of at least 5 decades. Measurements must be made in steps not exceeding the bandwidth.

The instrument should have been calibrated against standard light-sources for wavelength accuracy (mercury lamp) and for linearity of signal response at all wavelengths over an irradiance range covering the actual source measurement range.

The units of source irradiance should be in actual spectral energy ($W/m^2.nm$, $mW/cm^2.nm$).

Further instructions for the UV solar simulator identification and measurement can be found in COLIPA Guideline: “Guideline for Monitoring UV-light Sources".

3.2.2 Radiometric measurements

The UV irradiance of the solar simulator is controlled with a radiometer that has been previously calibrated for this source spectrum against the spectroradiometric measurement (§ 3.2.1).

An UV dose is the result of multiplying the UV source irradiance by the exposure duration. When a large-beam UV solar simulator is used, allowing simultaneous exposure of several sub-sites by varying the exposure time, the uniformity in beam irradiance should be as high as possible. This uniformity can be measured with the radiometer. The range of irradiance variation over the entire exposure site should be less than 10%. If the variation exceeds 10%, then appropriate compensation for different irradiance levels should be made in the exposure time on each sub-site. This criterion is not applicable to simulators with light-guides or multiple small beams, exposing all sub-sites for the same duration but with varied irradiance values.

A suitable warm-up time (typically 10 minutes) should be allowed for the UV solar simulator to stabilise before starting exposures. This is to ensure a consistent irradiance over the whole exposure period.

3.3 Calculation of Relative Cumulative Erythemal Effectiveness (%RCEE)

An example of calculations for a xenon-arc UV solar simulator that complies with the output specifications is given in Table 2.

The spectral irradiance of the UV solar simulator (Table 2: column 2) is multiplied by the CIE (1987) standard skin erythemal action spectrum (col. 4) to obtain the spectral erythemal effectiveness of the UV solar simulator (col. 5).

The CIE (1987) erythema effectiveness E at each wavelength is calculated in relative units from the following formulae:

$E = 1.0$	for wavelengths $250 \text{ nm} < \lambda \leq 298 \text{ nm}$
$E = 10^{0.094 (298-\lambda)}$	for wavelengths $298 \text{ nm} < \lambda \leq 328 \text{ nm}$
$E = 10^{0.015 (139-\lambda)}$	for wavelengths $328 \text{ nm} < \lambda \leq 400 \text{ nm}$

The spectral erythemal effectiveness values (col. 5) of the UV solar simulator spectrum are then integrated from 280 nm to the various successive reference wavelengths (290, 300, 310, 320, 330, 340 and 350nm) in order to produce the cumulative erythemal effectiveness for each wavelength band (col. 7) and the total erythemal effectiveness calculated up to 400nm (T value, last row, col. 6 or 7). Integration can be performed by approximation techniques such as the trapezium or rectangle methods using a spreadsheet, applying wavelength intervals of 1 nm. The example shown uses the trapezium method to calculate the areas of each 1 nm interval from 280 to 400 nm (col. 6), which are then summed to each reference wavelength to give the cumulative erythemal effectiveness value (col. 7). Finally, the percentage relative cumulative erythemal effectiveness (%RCEE, col. 8) is calculated at the reference wavelengths as the percentage ratio of the cumulative erythemal effectiveness (col. 7) at each of these wavelengths to the total integrated value at 400 nm (T value, col. 7).

3.4 Evaluating compliance.

For each reference waveband, the %RCEE values of the source (Table 2, col. 8) shall comply with those specified in Table 1 (or in Table 2, col. 9 and 10). All values must lie within the acceptance limits. If the UV solar simulator spectrum is outside the limits in any of the wavebands, then the filtration needs to be adjusted to comply with the spectral output specifications.

In addition, the solar simulator spectrum shall include less than 0.1% of UVB-RCEE below 290 nm and, to ensure that the solar simulator contains the correct balance of UVA:UVB, the system should contain • 60% UVA I (340-400 nm) and • 20% UVA II (320-340 nm).

The total irradiance of the source can be calculated using various techniques as described in the COLIPA guidance document: "Monitoring UV-light Sources".

3.5 Adjusting UV solar simulator output.

If the output spectrum of the UV solar simulator needs to be adjusted to fit the acceptance specifications, this will be achieved either by checking the xenon lamp's elapsed life and replacing it if necessary, or by adapting the spectral shaping filters within the UV solar simulator, particularly the thickness of the short cut-off filter. .

If the total irradiance of the UV solar simulator exceeds 1600W/m^2, the irradiance can usually be reduced by lowering the electrical current supplying the xenon lamp, provided that the current remains in the normal operational stability range. If total irradiance is adjusted in this way, then the quality of the emission spectrum should be checked again to ensure that the acceptance specifications are met.

Table 2: Example of calculation: Xenon-Arc UV source and RCEE Values

1	2	3	4	5	6	7	8	9	10
	UV Source		Eryth. A.S.	Spectral	Interval	Cumulative	**Sol. Sim.**	**RCEE range**	**accept.**
W.L.	Irradiance	Normalised	(CIE-1987)	Eryth. Effic.	Eryth. Effic.	Eryth. Effic.	**%RCEE**	**Lower**	**Upper**
nm	{S, W.m^{-2}.nm^{-1}}	to 320nm	{E}	{E*S}	1/2.{E*S}.dl	Sum{E*S}	Sum{E*S}/T	**limit**	**limit**
280	1,523E-05	1,75E-06	1,00E+00	1,52E-05					
281	1,848E-05	2,12E-06	1,00E+00	1,85E-05	1,69E-05				
282	2,904E-05	3,34E-06	1,00E+00	2,90E-05	2,38E-05				
283	1,878E-05	2,16E-06	1,00E+00	1,88E-05	2,39E-05				
284	2,139E-05	2,46E-06	1,00E+00	2,14E-05	2,01E-05				
285	2,837E-05	3,26E-06	1,00E+00	2,84E-05	2,49E-05				
286	2,935E-05	3,37E-06	1,00E+00	2,94E-05	2,89E-05				
287	2,627E-05	3,02E-06	1,00E+00	2,63E-05	2,78E-05				
288	2,927E-05	3,36E-06	1,00E+00	2,93E-05	2,78E-05				
289	4,308E-05	4,95E-06	1,00E+00	4,31E-05	3,62E-05				
290	4,405E-05	5,06E-06	1,00E+00	4,40E-05	4,36E-05	2,74E-04	0,00%	**-**	**< 0.1%**
291	5,500E-05	6,32E-06	1,00E+00	5,50E-05	4,95E-05				
292	8,279E-05	9,52E-06	1,00E+00	8,28E-05	6,89E-05				
293	2,379E-04	2,73E-05	1,00E+00	2,38E-04	1,60E-04				
294	8,219E-04	9,45E-05	1,00E+00	8,22E-04	5,30E-04				
295	2,685E-03	3,09E-04	1,00E+00	2,68E-03	1,75E-03				
296	8,029E-03	9,23E-04	1,00E+00	8,03E-03	5,36E-03				
297	2,102E-02	2,42E-03	1,00E+00	2,10E-02	1,45E-02				
298	5,030E-02	5,78E-03	1,00E+00	5,03E-02	3,57E-02				
299	1,041E-01	1,20E-02	8,05E-01	8,39E-02	6,71E-02				
300	1,886E-01	2,17E-02	6,49E-01	1,22E-01	1,03E-01	**2,29E-01**	**4,0%**	**1**	**8.0**
301	3,352E-01	3,85E-02	5,22E-01	1,75E-01	1,49E-01				
302	5,358E-01	6,16E-02	4,21E-01	2,25E-01	2,00E-01				
303	8,051E-01	9,25E-02	3,39E-01	2,73E-01	2,49E-01				
304	1,126E+00	1,29E-01	2,73E-01	3,07E-01	2,90E-01				
305	1,563E+00	1,80E-01	2,20E-01	3,43E-01	3,25E-01				
306	2,009E+00	2,31E-01	1,77E-01	3,56E-01	3,50E-01				
307	2,576E+00	2,96E-01	1,43E-01	3,67E-01	3,61E-01				

308	3,081E+00	3,54E-01	1,15E-01	3,54E-01	3,60E-01				
309	3,700E+00	4,25E-01	9,25E-02	3,42E-01	3,48E-01				
310	4,248E+00	4,88E-01	7,45E-02	3,16E-01	3,29E-01	3,19E+00	**55,7%**	**49,0%**	**65,0%**
311	4,769E+00	5,48E-01	6,00E-02	2,86E-01	3,01E-01				
312	5,384E+00	6,19E-01	4,83E-02	2,60E-01	2,73E-01				
313	5,978E+00	6,87E-01	3,89E-02	2,33E-01	2,46E-01				
314	6,399E+00	7,36E-01	3,13E-02	2,01E-01	2,17E-01				
315	6,896E+00	7,93E-01	2,52E-02	1,74E-01	1,87E-01				
316	7,250E+00	8,33E-01	2,03E-02	1,47E-01	1,61E-01				
317	7,731E+00	8,89E-01	1,64E-02	1,27E-01	1,37E-01				
318	8,060E+00	9,26E-01	1,32E-02	1,06E-01	1,16E-01				
319	8,338E+00	9,58E-01	1,06E-02	8,85E-02	9,74E-02				
320	**8,700E+00**	**1,00E+00**	**8,55E-03**	**7,44E-02**	**8,15E-02**	**5,01E+00**	**87,4%**	**85,0%**	**90,0%**
321	8,988E+00	1,03E+00	6,89E-03	6,19E-02	6,81E-02				
322	9,320E+00	1,07E+00	5,55E-03	5,17E-02	5,68E-02				
323	9,547E+00	1,10E+00	4,47E-03	4,26E-02	4,72E-02				
324	9,755E+00	1,12E+00	3,60E-03	3,51E-02	3,89E-02				
325	9,913E+00	1,14E+00	2,90E-03	2,87E-02	3,19E-02				
326	1,015E+01	1,17E+00	2,33E-03	2,37E-02	2,62E-02				
327	1,029E+01	1,18E+00	1,88E-03	1,93E-02	2,15E-02				
328	1,042E+01	1,20E+00	1,46E-03	1,52E-02	1,73E-02				
329	1,060E+01	1,22E+00	1,41E-03	1,50E-02	1,51E-02				
330	1,071E+01	1,23E+00	1,36E-03	1,46E-02	1,48E-02	**5,35E+00**	**93,3%**	**91.5%**	**95.5%**
331	1,085E+01	1,25E+00	1,32E-03	1,43E-02	1,45E-02				
332	1,099E+01	1,26E+00	1,27E-03	1,40E-02	1,42E-02				
333	1,108E+01	1,27E+00	1,23E-03	1,36E-02	1,38E-02				
334	1,120E+01	1,29E+00	1,19E-03	1,33E-02	1,35E-02				
335	1,127E+01	1,29E+00	1,15E-03	1,29E-02	1,31E-02				
336	1,135E+01	1,30E+00	1,11E-03	1,26E-02	1,28E-02				
337	1,143E+01	1,31E+00	1,07E-03	1,22E-02	1,24E-02				
338	1,149E+01	1,32E+00	1,04E-03	1,19E-02	1,21E-02				
339	1,160E+01	1,33E+00	1,00E-03	1,16E-02	1,18E-02				
340	1,166E+01	1,34E+00	9,66E-04	1,13E-02	1,14E-02	**5,48E+00**	**95,5%**	**94%**	**97.0%**
341	1,176E+01	1,35E+00	9,33E-04	1,10E-02	1,11E-02				
342	1,185E+01	1,36E+00	9,02E-04	1,07E-02	1,08E-02				
343	1,189E+01	1,37E+00	8,71E-04	1,04E-02	1,05E-02				

344	1,194E+01	1,37E+00	8,41E-04	1,00E-02	1,02E-02				
345	1,196E+01	1,37E+00	8,13E-04	9,72E-03	9,88E-03				
346	1,200E+01	1,38E+00	7,85E-04	9,42E-03	9,57E-03				
347	1,204E+01	1,38E+00	7,59E-04	9,14E-03	9,28E-03				
348	1,212E+01	1,39E+00	7,33E-04	8,88E-03	9,01E-03				
349	1,215E+01	1,40E+00	7,08E-04	8,60E-03	8,74E-03				
350	1,220E+01	1,40E+00	6,84E-04	8,34E-03	8,47E-03	**5,57E+00**	**97,2%**		
351	1,224E+01	1,41E+00	6,61E-04	8,09E-03	8,22E-03				
352	1,230E+01	1,41E+00	6,38E-04	7,85E-03	7,97E-03				
353	1,231E+01	1,42E+00	6,17E-04	7,59E-03	7,72E-03				
354	1,229E+01	1,41E+00	5,96E-04	7,32E-03	7,46E-03				
355	1,234E+01	1,42E+00	5,75E-04	7,10E-03	7,21E-03				
356	1,233E+01	1,42E+00	5,56E-04	6,85E-03	6,98E-03				
357	1,232E+01	1,42E+00	5,37E-04	6,62E-03	6,73E-03				
358	1,234E+01	1,42E+00	5,19E-04	6,40E-03	6,51E-03				
359	1,234E+01	1,42E+00	5,01E-04	6,19E-03	6,29E-03				
360	1,233E+01	1,42E+00	4,84E-04	5,97E-03	6,08E-03	5,64E+00	98,5%		
361	1,230E+01	1,41E+00	4,68E-04	5,75E-03	5,86E-03				
362	1,225E+01	1,41E+00	4,52E-04	5,54E-03	5,64E-03				
363	1,217E+01	1,40E+00	4,37E-04	5,31E-03	5,42E-03				
364	1,212E+01	1,39E+00	4,22E-04	5,11E-03	5,21E-03				
365	1,200E+01	1,38E+00	4,07E-04	4,89E-03	5,00E-03				
366	1,183E+01	1,36E+00	3,94E-04	4,66E-03	4,77E-03				
367	1,171E+01	1,35E+00	3,80E-04	4,45E-03	4,55E-03				
368	1,153E+01	1,33E+00	3,67E-04	4,24E-03	4,34E-03				
369	1,130E+01	1,30E+00	3,55E-04	4,01E-03	4,12E-03				
370	1,102E+01	1,27E+00	3,43E-04	3,78E-03	3,89E-03	5,69E+00	99,3%		
371	1,073E+01	1,23E+00	3,31E-04	3,55E-03	3,66E-03				
372	1,042E+01	1,20E+00	3,20E-04	3,33E-03	3,44E-03				
373	1,005E+01	1,16E+00	3,09E-04	3,11E-03	3,22E-03				
374	9,649E+00	1,11E+00	2,99E-04	2,88E-03	2,99E-03				
375	9,370E+00	1,08E+00	2,88E-04	2,70E-03	2,79E-03				
376	8,977E+00	1,03E+00	2,79E-04	2,50E-03	2,60E-03				
377	8,597E+00	9,88E-01	2,69E-04	2,31E-03	2,41E-03				
378	8,195E+00	9,42E-01	2,60E-04	2,13E-03	2,22E-03				
379	7,707E+00	8,86E-01	2,51E-04	1,94E-03	2,03E-03				

380	7,176E+00	8,25E-01	2,43E-04	1,74E-03	1,84E-03	5,72E+00	99,8%		
381	6,703E+00	7,70E-01	2,34E-04	1,57E-03	1,66E-03				
382	6,147E+00	7,07E-01	2,26E-04	1,39E-03	1,48E-03				
383	5,577E+00	6,41E-01	2,19E-04	1,22E-03	1,31E-03				
384	4,994E+00	5,74E-01	2,11E-04	1,06E-03	1,14E-03				
385	4,423E+00	5,08E-01	2,04E-04	9,03E-04	9,79E-04				
386	3,860E+00	4,44E-01	1,97E-04	7,61E-04	8,32E-04				
387	3,348E+00	3,85E-01	1,91E-04	6,38E-04	7,00E-04				
388	2,846E+00	3,27E-01	1,84E-04	5,24E-04	5,81E-04				
389	2,389E+00	2,75E-01	1,78E-04	4,25E-04	4,74E-04				
390	1,996E+00	2,29E-01	1,72E-04	3,43E-04	3,84E-04	5,73E+00	100,0%		
391	1,626E+00	1,87E-01	1,66E-04	2,70E-04	3,06E-04				
392	1,297E+00	1,49E-01	1,60E-04	2,08E-04	2,39E-04				
393	1,016E+00	1,17E-01	1,55E-04	1,57E-04	1,83E-04				
394	7,810E-01	8,98E-02	1,50E-04	1,17E-04	1,37E-04				
395	5,916E-01	6,80E-02	1,45E-04	8,55E-05	1,01E-04				
396	4,438E-01	5,10E-02	1,40E-04	6,20E-05	7,37E-05				
397	3,247E-01	3,73E-02	1,35E-04	4,38E-05	5,29E-05				
398	2,312E-01	2,66E-02	1,30E-04	3,01E-05	3,70E-05				
399	1,593E-01	1,83E-02	1,26E-04	2,01E-05	2,51E-05				
400	1,073E-01	1,23E-02	1,22E-04	1,31E-05	1,66E-05	5,73E+00	100,0%	99.9	100.0%
	UV irrad ($W.m^{-2}$):	8,03E+02	UVe irrad. ($W.m^{-2}$.ery), T :		**5,73E+00**	**Conclusion:**	Complies		

APPENDIX III

1.1.30. SPF REFERENCE SUNSCREEN FORMULATIONS

1.1.31. *FORMULAE and PROCESS INFORMATION*

P2: High SPF REFERENCE FORMULA

	Ingredients		**% w/w**
Phase 1:	Lanolin		4.5
	Cocoa Butter		2.0
	Glyceryl Stearate	(‘Glyceryl Monostearate SE’) 3.0	
	Stearic Acid		2.0
	Octyl Dimethyl PABA	7.0	
	Benzophenone-3	(‘Oxybenzone’)	3.0
Phase 2:	Water		71.6
	Sorbitol		5.0
	Triethanolamine		1.0
	Methylparaben	0.3	
	Propylparaben		0.1
Phase 3:	Benzyl Alcohol		0.5

Manufacturing process

Melt the ingredients of the fatty Phase 1 and heat to 80-85°C.

Heat Phase 2 to 80-85 °C, until completely solubilised.

Add Phase 1 into Phase 2, while stirring Phase 2 with a homogeniser (Moritz type).

Cool to 50°C while stirring, then add Benzyl Alcohol and complete cooling. Compensate for water loss and homogenise.

Physicochemical Data

Appearance:	White yellowish fluid emulsion.
pH:	8.6 ± 0.5
Viscosity:	250mPa·s (at 10mn, Contraves TVB rheometer, rotary body N°3)
Density:	0.95 $g.cm^{-3}$

Analytical Data

HPLC:	Octyl Dimethyl PABA:	6.9 to 7.1 % w/w
	Benzophenone-3:	2.8 to 3.2 % w/w

1.2. Photometric Data

Typical data for a 100 mg/l solution in Isopropanol:

Max.:	309.4 nm	Abs. Max.:	0.909
	290 nm	Abs.:	0.540
	320 nm	Abs.:	0.671
	340 nm	Abs.:	0.120
	400 nm	Abs.:	0.000

Formulation Stability

At least 2 months at 45 °C and 12 months at 20°C.

P3: High SPF REFERENCE FORMULA

	Ingredients	**% w/w**
Phase 1:	Cetearyl Alcohol (and)	
	PEG-40 Castor oil (and)	
	Sodium Cetearyl Sulphate	3.15
	Decyl Oleate	15.0
	Ethyl Hexyl Methoxycinnamate	3.0
	Butyl Methoxy Dibenzoylmethane	0.5
	Propylparaben	0.1
Phase 2:	Water	53.57
	2-Phenyl-Benzimidazole-5-Sulphonic Acid	2.78
	Sodium Hydroxide (45% solution)	0.9
	Methylparaben	0.3
	Disodium EDTA	0.1
Phase 3:	Water	20.0
	Carbomer (‘Carbomer 934P’)	0.3
	Sodium Hydroxyde (45% solution)	0.3

Manufacturing process

Heat Phase 1 to 75-80 °C.

Heat Phase 2 to 80 °C (if necessary boil until solution is clear and cool to 75-80 °C).

Disperse Phase 3 carbomer in water by stirring with an Ultraturrax (rotor / stator disperser), then add Sodium Hydroxide for neutralisation.

Add Phase 1 into Phase 2 while stirring Phase 2.

Add Phase 3 to Phases 1 & 2 while stirring and homogenise for about 3 minutes.

Adjust pH with Sodium Hydroxide or Lactic Acid and stir until completely cool.

Compensate for water loss and homogenise.

Physicochemical Data

Appearance: White to slightly yellowish emulsion.

pH: 7.8 – 8.0

Density: 0.950 – 0.970 g/cm^3

Viscosity: 1800 to 3000 mPas (Haake VT 181 Rheometer, Rotary body MV II ST, Process U = 4, Reading time: 20 seconds)

Analytical data

HPLC:	Phenyl-Benzimidazole Sulfonic Acid:	2.43 to 2.97 %
	Ethyl Hexyl Methoxycinnamate:	2.70 to 3.30 %
TLC:	Butyl Methoxydibenzoylmethane:	0.40 to 0.60 %

Formulation stability:

At least 12 months at 20 °C.

P7: Low SPF REFERENCE FORUMULA

	Ingredients	% w/w
Phase 1:	Lanolin	5.00
	Homosalate	8.00
	Petrolatum	2.50
	Stearic Acid	4.00
	Propyl Parahydroxybenzoate	0.05
Phase 2:	Methyl Parahydroxybenzoate	0.10
	Disodium Edetate	0.05
	Propylene Glycol	5.00
	Triethanolamine	1.00
	Purified water	74.30
	Total	100.00

Manufacturing process and analytical controls

Heat phase A and phase B separately to 77 to 82°C, with constant stirring, until the contents of each part are solubilized. Add phase A slowly to phase B while stirring. Continue stirring until the emulsion formed is cooled to room temperature (15 to 30°C). Add sufficient purified water to obtain 100 grams of standard sunscreen preparation.

Assay the standard homosalate sunscreen preparation by the following method to ensure proper concentration:

(1) Preparation of the assay solvent. The solvent consists of 1 percent glacial acetic acid (V/V) in denatured ethanol. The denatured ethanol should not contain a UV radiation absorbing denaturant.

(2) Preparation of a 1-percent solution standard homosalate sunscreen preparation. Accurately weigh 1 gram of the standard homosalate sunscreen preparation into a 100 millilitre volumetric flask. Add 50 millilitres of the assay solvent. Heat on a steam bath and mix well. Cool the solution to room temperature (15 to 30°C). Then dilute the solution to volume with assay solvent and mix well to make a 1-percent solution.

(3) Preparation of the test solution (1:50 dilution of the 1-percent solution). Filter a portion of the 1-percent solution through number 1 filter paper. Discard the first 10 to 15 millilitres of the filtrate. Collect the next 20 millilitres of the filtrate (second collection). Add 1 millilitre of the second collection of the filtrate to a 50-milliliter volumetric flask. Dilute this solution to volume with assay solvent and mix well. This is the test solution (1:50 dilution of the 1-percent solution).

(4) Spectrophotometric determination. The absorbance of the test solution is measured in a suitable double beam spectrophotometer with the assay solvent and reference beam at a wavelength near 306 nanometers.

(5) The concentration of homosalate is determined by the following formula which takes into consideration the absorbance of the sample of the test solution, the dilution of the 1-percent solution (1:50), the weight of the sample of the standard homosalate sunscreen preparation (1 gram), and the standard absorbance value (172) of homosalate as determined by averaging the absorbance of a large number of batches of raw homosalate: Concentration of homosalate = absorbance x 50 x 100 / 172 = percent concentration by weight.

Formulation stability:

At least 12 months at 20 °C.

Table 5: Origin and Country of use for each sunscreen product

Reference sunscreen	Original Name	Country (Aug.2002)
P2	CTFA Proposed Reference Formula	Europe (COLIPA)
P3	COLIPA Reference Formula C202/101	Europe (COLIPA), Japan (JCIA), Australia/NZ
P7	8% Homosalate lotion (FDA Reference)	USA, Europe (COLIPA), Japan , South Africa, Australia/NZ

APPENDIX IV

1.2.1. CALCULATIONS and STATISTICS

1. GENERAL EQUATIONS

1.1 Individual Sun Protection Factor (SPFi)

The individual SPFi of each product on each subject is calculated from the individual MED on unprotected skin (MEDui) and the individual MED on product protected skin (MEDpi) according to the equation:

$$SPFi = MEDpi / MEDui \quad (1)$$

1.2 Product Sun Protection Factor

The SPF of the product is the arithmetical mean of the individual SPFi values obtained from the total number (n) of subjects used, expressed to one decimal point:

$$SPF = (\sum SPFi) / n \quad (2)$$

Its standard deviation (s) is:

$$s = \sqrt{[(\sum(SPFi^2) - ((\sum SPFi)^2 / n)) / (n - 1)]} \quad (3)$$

1.3 95% confidence interval

The 95% confidence interval (95%CI) for the mean SPF is expressed as:

$$95\%CI = SPF - c \text{ to } SPF + c \quad (4)$$

c is calculated as: $c = (t\ value) \,.\, SEM = (t\ value) \,.\, s / \sqrt{n}$

$$c = t \,.\, s / \sqrt{n} \quad (5)$$

$$CI[\%] = 100 \,.\, c / SPF \quad (6)$$

where:

SEM = the standard error of the mean,

n = total number of subjects used,

t = t value from the 'two-sided' Student-t distribution table (7) at a probability level $p = 0.05$ and with degrees of freedom $\nu = (n - 1)$

N	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**	**18**	**19**	**20**
t value	**2.262**	**2.228**	**2.201**	**2.179**	**2.160**	**2.145**	**2.131**	**2.120**	**2.110**	**2.101**	**2.093**

(7)

For spreadsheet calculation t value can be modelled by: $t = 2.03 + 12.7 / n^{1.75}$ (for $n \geq 4$)

2. EXPERIMENTAL CALCULATION PROCEDURE

2.1 Sequential procedure

An SPF test is begun by testing the product on an initial panel of n' subjects (n' must be at least 10). The individual sun protection factors (SPFi) for the product on each subject are then calculated according to equation (1), i.e.:

$$SPFi = MEDpi / MEDui \quad (1)$$

From these individual SPFi values a provisional mean sun protection factor for the initial n' subjects ($SPF_{n'}$) is calculated according to equation (2), together with a provisional 95% confidence interval ($95\%CI_{n'}$) using equations (4), (5) and (6) and t-table (7), i.e.:

$$SPF_{n'} = \sum SPFi / n' \quad (9)$$

$$95\%CI_{n'} = SPF_{n'} - c_{n'} \text{ to } SPF_{n'} + c_{n'} \quad (10)$$

$c_{n'}$ is calculated as $c_{n'} = t_{n'} . s_{n'} / \sqrt{n'}$ (11)

where $s_{n'}$ = standard deviation from the first n' subjects calculated according to equation (3):

$$s_{n'} = \sqrt{[(\sum(SPFi^2) - ((\sum SPFi)^2 / n')) / (n' - 1)]} \quad (12)$$

$$CI_{n'}[\%] = 100 . c_{n'} / SPF_{n'} \quad (13)$$

If the calculated provisional $CI_{n'}[\%]$ is greater than 17 % of the provisional mean $SPF_{n'}$ value, then testing of the product shall continue on additional subjects until the provisional $CI_{n'}[\%]$ is ≤ 17 % of the mean provisional SPF.

If this criterion is not fulfilled after 20 subjects, then the entire test shall be repeated.

2.2 Predicted number of subjects (n*)

If the $CI_{n'}$[%] on the provisional $SPF_{n'}$ is greater than 0.17 $SPF_{n'}$, then the predicted, likely total number of subjects (n*) necessary to meet the statistical criterion can be estimated according to the following formula and rounded-up to the nearest integer:

$$n^* = (t_{n'} \cdot s_{n'} / C_{n'})^2 \qquad (14)$$

where:

$t_{n'}$ = t statistic from t-table or equation (7), with n' results,

$s_{n'}$ = best estimate of population standard deviation (ie from the n' results),

$C_{n'}$ = 17% of mean $SPF_{n'}$, representing the required confidence interval.

EXAMPLE : When n* is calculated after the first 10 data, then:

$$n^* = (2.262\ s_{n'} / 0.17\ SPF_{n'})^2$$

i.e.

$$n^* = (13.30\ s_{n'} / SPF_{n'})^2 \qquad (15)$$

3. EXAMPLES

3.1. Example 1

TABLE 6 is an example of a table gathering data, calculations and results. When data are entered in spreadsheet software, all calculations can be performed automatically.

TABLE 6 shows the results for product EX1 with expected SPF 10. After 10 subjects had been exposed, the results were:

$$SPF_{n'} = 11.4 \qquad (9)$$

$$s_{n'} = 2.4 \qquad (12)$$

$$c_{n'} = 1.7 \qquad (11)$$

$95\%CI_{n'}$ = 9.7 to 13.1 (10)

$CI_{n'}[\%]$ = 14.9 % (13)

Since the $CI_{n'}[\%]$ was smaller than 17 % of the mean SPF no further testing was necessary and the final SPF of the product EX1 was:

SPF = 11.4 with **CI[%] = 14.9 %** **(2,6)**

3.2. Example 2

TABLE 7 shows the results for product EX2 with expected SPF 20. After 10 subjects had been exposed, the results were:

$SPF_{n'}$ = 21.3 (9)

$s_{n'}$ = 6.0 (12)

$c_{n'}$ = 4.3 (11)

$95\%CI_{n'}$ = 17.0 to 25.6 (10)

$CI_{n'}[\%]$ = 20.3 % (13)

The relative variation of the results was higher than in Example 1 and the statistical criterion was not met ($CI_{n'}[\%]$ was greater than 17 % of the mean SPF). The test had to be continued and the likely total number n of subjects necessary was calculated as:

$$n = (t_{n'} \cdot s_{n'} / C_{n'})^2 = (2.262 \times 6.0 / 3.61)^2 = 14.1 \quad (12)$$

Therefore, five subjects were added and the newly calculated provisional results were:

SPF_{15} = 21.2 (9)

s_{15} = 6.2 (12)

c_{15} = 3.4 with $n = 15$ and $t_{15} = 2.145$ (11)

$95\%CI_{15}$ = 17.8 to 24.6 (10)

$$CI\,[\%]_{15} = 16.2\ \% \qquad (13)$$

The criterion was met after the fifteenth subject ($CI_{n'}$ [%] smaller than 17 % of the mean SPF) and the final SPF of product EX2 was:

SPF = 21.2 with CI[%] = 16.2 % (2,6)

TABLE 6 : Example of calculation with 10 subjects (expected SPF 10)

Harmonised SPF TEST Result Table									Laboratory:							
Product Code: .....EX1.....				Expected SPF:...10.....					Date: ..... Data sheet N°: .2. of ..3..						UV source:....Xe..MP.....	
	TEST		SUBJECTS						RESULTS					CONCLUSION:		
Subj. N°	Exposure date	Technician name	Subject code	Skin ITA°	Photo type	MEDu (mJ.cm-²)	MEDp (mJ.cm-²)	SPFi	$SPF_{n'}$	$s_{n'}$	$c_{n'}$	$CI_{n'}$[%] ($100.c_{n'}/SPF_{n'}$)	n	CIn'[%] =< 17% ?		COMMENTS
1				56,4	I	19	290	15,3	-	-	-	-		-		
2				48,6	II	29	370	12,8	-	-	-	-		-		
3				58,1	I	23	230	10,0	-	-	-	-		-		
4				43,5	II	37	420	11,4	-	-	-	-		-		
5				44,0	II	29	230	7,9	-	-	-	-		-		
6				42,7	II	23	290	12,6	-	-	-	-		-		
7				34,9	III	46	370	8,0	-	-	-	-		-		
8				57,0	I	19	260	13,7	-	-	-	-		-		
9				54,8	II	29	370	12,8	-	-	-	-		-		
10				45,3	II	23	230	10,0	**11,4**	2,4	**1,73**	15,1%	8	**Complies**		
11																
12																
13																
14																
15																
16																
17																
18																
19																
20																
FINAL RESULT:			**Mean SPF = 11.**		**11,4**		**s = 2.4**		**c = 1.7**		**CI[%] = 15.1 %**			**95%CI: 9.7 - 13.1 (n = 10)**		

TABLE 7 : Example of calculation with 15 subjects (expected SPF 20)

Harmonised SPF TEST Result Table									Laboratory:							
Product Code: .....EX2.....				Expected SPF:..20....					Date: ..... Data sheet N°: .3. of ..3.					UV source:..XE..MP.....		
	TEST		**SUBJECTS**						**RESULTS**					**CONCLUSION:**	**COMMENTS**
Subj. N°	Exposure date	Technician name	Subject code	Skin ITA°	Photo type	MEDu (sec.)	MEDp (sec.)	SPFi	$SPF_{n'}$	$s_{n'}$	$c_{n'}$	$CI_{n'}$[%] ($100.c_{n'}/SPFn'$)	n	$CI_{n'}$[%] =< 17% ?	
1				56,2	I	35	700	20,0	-	-	-	-		-	
2				42,5	II	44	1094	24,9	-	-	-	-		-	
3				50,6	II	35	875	25,0	-	-	-	-		-	
4				32,8	III	68	875	12,9	-	-	-	-		-	
5				45,1	II	44	1094	24,9	-	-	-	-		-	
6				47,9	II	35	875	25,0	-	-	-	-		-	
7				29,4	III	85	1367	16,1	-	-	-	-		-	
8				54,3	II	44	560	12,7	-	-	-	-		-	
9				43,3	II	35	1094	31,3	-	-	-	-		-	
10				59,9	I	44	875	19,9	**21,3**	6,0	**4,31**	20,3%	14	Does not comply	
11				35,0	III	68	875	12,9	**20,5**	6,3	**4,20**	20,5%	17	Does not comply	
12				48,8	II	44	1367	31,1	**21,4**	6,7	**4,26**	19,9%	18	Does not comply	
13				36,5	I	35	875	25,0	**21,7**	6,5	**3,92**	18,1%	16	Does not comply	
14				47,1	II	44	700	15,9	**21,2**	6,4	**3,71**	17,5%	16	Does not comply	
15				38,1	III	55	1094	19,9	**21,2**	6,2	**3,43**	16,2%	15	Complies	
16															
17															
18															
19															
20															
FINAL RESULT:			**Mean SPF = 21,2**				**s = 19.9**		**c = 21.2**		**CI[%] = 16.2 %**			**95%CI: 17.8 - 24.6 (n = 15)**	

APPENDIX V

1.2.2.

1.2.3. SPF OF REFERENCE SUNSCREEN FORMULATIONS

A ring test was performed in 2004 by the COLIPA Task Force 'Sun Protection Measurement' at six laboratories.

Taking all the data into account, the following values could be attributed to the reference sunscreen formulations:

REFERENCE	SPF		SE	Range (+/- 2.0 SE)
P2	SPF 15	16.6	1.20	14.2-19.0
P3	SPF 15	16.2	1.22	13.8-18.7
P7	SPF 4	5.1	0.38	4.4-5.9

APPENDIX VI

Thanks to the Members of COLIPA, CTFA / SA, JCIA and CTFA, who contributed to the writing of the updated version of the International SPF Test Guidelines

APPENDIX VII

1.2.4. ADDITIONAL READINGS

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Annex 2:

Determination of the UVA protection factor based on the principles recommended by the Japanese cosmetic industry association (method published 15.11.1995)

1. AIM

To determine the UVA Protection Factor (UVA-PF) of a sunscreen product using the persistent pigment darkening method according to the principles recommended by the Japan Cosmetic Industry Association (version dated 15.11.1995).

2. SUBJECTS SELECTION

The UVA-PF value is determined on a minimum of 10 subjects, as long as the variation of results lies within the specific range: the standard error (SEM) must lie within 10% of the measured PFA value (mean value).

If this statistical criterion is not reached then testing of the product shall continue on additional subjects until the criterion is fulfilled. If it is not after 20 subjects then the entire test is rejected, and has to be reassessed.

2.1. Inclusion criteria

- Male and female healthy subjects (a medical examination is performed prior to the test).
- Age: between 18 and 60.
- Type: Caucasian.
- Skin type: II III or IV according to Fitzpatrick classification
- With an ITA° value comprised in the following range: 20°• ITA° • 41°.

Colorimetric ITA values and skin Colour Categories are defined by the colorimetric descriptors of Chardon et al. (1990) using the CIE (1976) L*a*b* colour space:

Very Light	-	ITA° values		> 55°
Light	-	ITA° values	from	> 41 to 55°
Intermediate	-	ITA° values	from	> 28 to 41°
Tan (or Matt)	-	ITA° values	from	> 10 to 28°

where: ITA° = [Arc Tangent ((L* - 50) / b*)] 180 / 3.1416

- Subjects who have not been involved in any sun test since less than two months (no remaining marks on the back).

- Subjects who have not had sun exposure on the back area for at least 2 months prior to the study

- Absence of sunburn, suntan, scars, or active dermal lesions on the areas of the back tested.

- Test area must be uniform in colour, without nevi, blemishes or solar lentigo and without excessive hairs.

- Subjects aware of the test procedure and having signed an informed consent form.

2.2. Non Inclusion criteria

- Subjects who do not fit the previous inclusion criteria.

- Pregnant or lactating women,

- Past history of allergy, photoallergic, phototoxic, or other abnormal responses to sunlight,

- Past history of allergies or sensitivity to cosmetic products, toiletries, sunscreens and/or topical drugs,

- Known allergy to latex,

- Subjects with dermatological problems on the test area

- Subjects having used self tanning products on the back in the previous month

- Subjects accustomed to using tanning beds

- Subjects taking medication with photosensitizing potential, drugs and/or dietary supplements able to induce skin colouring, corticoids, currently or during the month before the test

- Subjects taking anti-histaminic or anti-inflammatory drugs, currently or within the week before the test

3. STANDARD SAMPLE

A standard sample [5% de butyl méthyl dibenzoyl méthane (BMDM), 3% d'éthyl hexyl methoxycinnamate (EHMC)] proposed by JCIA will be used in every study to confirm the reliability of the results obtained for the test samples.

The mean UVA-PF value of the standard preparation has to be 3.75 (standard deviation 1.01) according to the JCIA, and 4.5 (standard deviation 0.5) from our experience.

The test will be validated if the mean value obtained for the standard product lies within the indicated range and if the statistical criterion (see below) is fulfilled.

This standard should be used for testing of products with expected UVA-PF between 3 and 8.

For products with expected UVA-PF >8, a standard product with a higher UVA-PF should be used (in process of development)

4. SOLAR SIMULATOR

The source of UVA radiation must be obtained from a 150 or 300 watts xenon lamp (of which the spectrum encompasses UV up to visible light), typically is a Multiport 601 Solar Simulator, (SOLAR LIGHT), fitted with a SCHOTT WG 335 (3mm) and a SCHOTT UG 11 (1mm) optical cut-off filters to eliminate wavelengths below 320 nm (UVB) and above 400 nm (visible light and infrared), and yield the whole UVA spectrum. (The wavelengths corresponding to infrared rays are eliminated by a dichroic filter).

Furthermore, the ratio of UVA I (340-400 nm) and UVA II (320-340 nm) has to be as close as possible to that of the sunlight (UVAII / UVAI=8-20%).

The spectrum has to be controlled annually by an expert and the certificate of compliance should be accessible.

5. TEST AREA

The back is the chosen anatomical region for the test area. The individual test sites should be delineated, within the region between the scapula line and the waist, on either side of the spinal column.

6. PRODUCT QUANTITY AND APPLICATION

The application of the products has to be made according to the procedure described in the International SPF test method 2003 (CD Rom provided), on areas of at least 30 cm^2 (at most 60 cm^2) located between the scapula line and the waist.

The volunteers shall be laid down, on the belly. The room must be temperate (temperature between 18°C and 26°C).

Areas are delineated using a template and a special skin marker, a distance of 1 cm is necessary between each test site. The number of sites has to be restricted to six.

Products and standard are applied evenly with a finger cot, at a dose of 2 mg / cm^2 ± 2.5% (if necessary, in case of uneven application, application may be repeated without finger cot, on a new area).

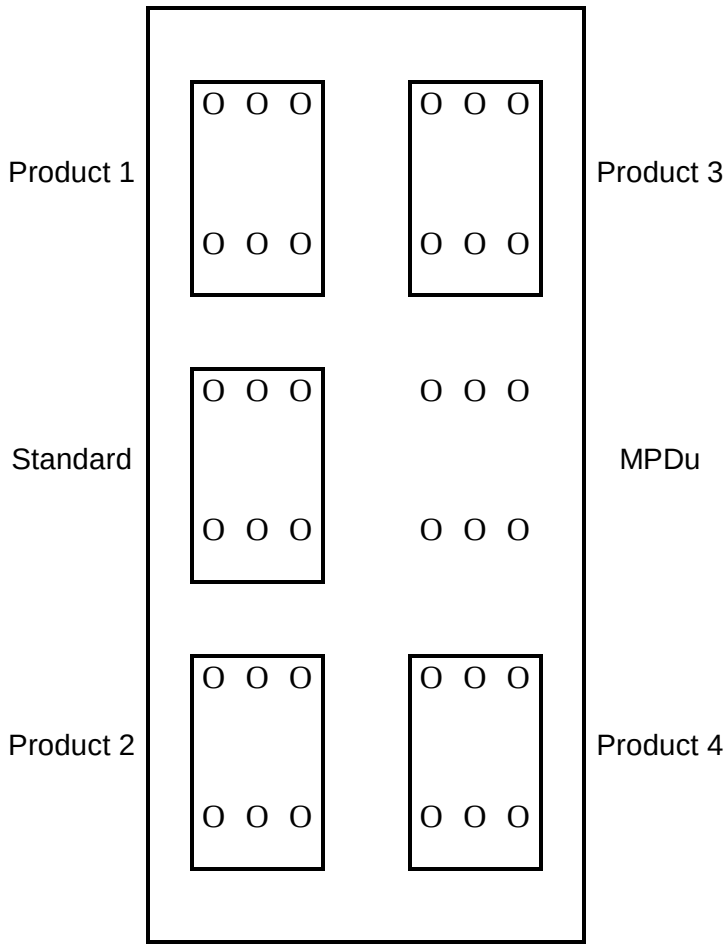
The amount of product to be applied is weighed in a syringe or in an another device such as a watch glass. A method of weighing by loss must be used.

The product is then dispensed in small droplets over the whole test site. Product shall be gently spread with circular and then linear movements (up and down), without excessive pressure.

The spreading time shall be from 20 to 50 seconds.

The location of the products on the sites has to be randomized on the subjects panel.

Example of repartition:



7. DETERMINATION OF THE MINIMAL PIGMENTING DOSE

The determination of the unprotected minimal pigmenting dose (MPDu) and protected minimal pigmenting dose (MPDp) should be made on the same day.

7.1. Position of subjects

The position should be the same for product application, for UV exposure and for MPD assessment. Prone position is recommended.

7.2. Determination of the minimal pigmenting dose on the unprotected area (MPDu)

When a Mlultiport Solar Light lamp is used UV radiation is conducted by six light guides enabling the delivery of 6 independent doses of ultraviolet radiation of identical spectrum and different intensity onto spots of 8 mm diameter each.

The UVA flux of each optical fiber is determined by the operator to obtain a geometric progression of 25% (1, 1.25, …).

The range of doses generally used for the determination of the MPDu is approximatively :

8 - 10 - 12 - 15 - 19 - 25 J/cm²

Usually, it takes between 4 to 7 minutes to achieve the MPDu (for a 300 Watts Multiport lamp), whatever the skin color is.

The luminous flux, expressed in mW/cm², of each of the 6 fibers is measured with a UV- meter PMA 2100 SOLAR LIGHT fitted with a photosensitive cell with an optimal sensitivity in UVA.

The unprotected area (without test product) has to be exposed after the exposure of all the protected areas, to respect the waiting time of 2 to 4 hours for the determination of the MPD.

7.3. Determination of the minimal pigmenting dose on the product test areas (MPDp)

The exposure is performed between 15 and 30 minutes after the application of the products, the volunteers being in the same position as for the product application (prone position).

The range of UVA flux (25% geometric progression) for the determination of MPD of areas where products are being tested will be identical to that used for the unprotected area.

The exposure time is calculated by the investigator by multiplying the exposure time required to achieve the MPDu by the expected UVA PF of the tested product.

Exposure time and flux values delivered on each area shall be reported in the case report form.

8. PRODUCT REMOVAL

After UV exposures, standard and test products may be removed gently, using a cotton or cellulose pad with a neutral lotion to eliminate traces of pigments or coloured products which could interfere with the pigmentation evaluation.

9. MPD ASSESSMENT PROCEDURE

The MPD is evaluated visually.

The MPD should be assessed when the persistent pigment darkening response is stable, i.e. 2 to 4 hours after the UVA exposure on the last site which is the unprotected area.

Visual evaluation should be performed in a blind manner by a qualified observer under standardised, sufficient and uniform illumination conditions (white lamps, industry type, delivering at least 500 Lux over the examination plane), the subject lying down in prone position.

The minimal pigmenting dose (MPD) corresponds to the lowest UVA dose inducing an unambiguous minimal pigmentation with delimited borders.

The data shall be rejected under the following circumstances:

- No pigmenting response on any spots
- All spots are marked
- Random pigmenting response that does not follow the logical sequence of the test.

10. CALCULATIONS OF THE UVA PROTECTION FACTOR AND STATISTICS

The UVA Protection Factor (UVA-PF) is calculated for each volunteer as the ratio of the minimal UVA dose necessary to induce the minimal darkening effect on the skin protected by the product (MPDp) and on the minimal UVA dose necessary to induce the minimal darkening effect on the unprotected skin (MPDu):

UVA-PFi=MPDpi/MPDui

Where MPD is the Minimal Pigmenting Dose necessary to see the unambiguous minimal pigmentation with delimited borders, 2 to 4 hours after exposure.

10.1. Statistics

Standard deviations (s) and standard errors to the mean (SEM) are determined for the studied product and for the standard preparation.

SEM = s /• n

Where:

n = Number of subjects in the test

s = Standard deviation

The UVA-PF value is determined from a minimum of 10 subjects.

The standard error (SEM) must lie within 10% of the measured PFA value (mean value) for the product and for the standard product.

If not, the number of subjects shall be increased until the statistics is met. If the criterion is not fulfilled after 20 subjects then the entire test shall be rejected.

If the mean value of the standard product is not in the expected range, the test shall be rejected.

10.2. Collection and validation of data

Individual results (MPDp and MPDu) as well as colorimetric informations of subjects at the time of the test will be recorded by the study technician (subject case report forms and computerised data base) and validated by the trial manager.

All individual data and means will be available for an easy consultation at any time.

11. PROTOCOL DEVIATIONS

The test must be carried out according to the protocol established, under the responsibility of the investigator.

All deviations from the protocol (e.g. deviation from inclusion criteria, missing examination, change in quantity of product applied) will be reported in the Case Report Form (CRF) and the study report.

12. EARLY TERMINATION OF THE STUDY

Any exit from the study or premature termination of the study, for any reason (withdrawal, incident during testing, intolerance reaction) will be reported the Case Report Form (CRF) and the study report.

Annex 3:

Determination of the critical wavelength (λ_c)

Critical wavelength is one of the parameters describing the extent to which sun protection products can be considered to give broad-spectrum protection against also UVA radiation.

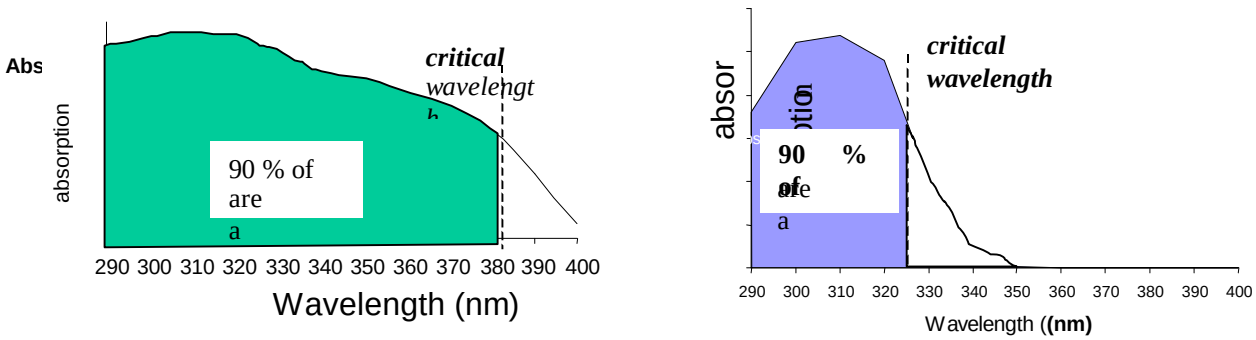
With a background in the absorption curve (from 290 – 400 nm), the critical wavelength is defined as the point where 90% of the area of UV radiation is absorbed/reflected by the product.

Determination of the critical wavelength using an *in vitro* method was elaborated by Diffey (Diffey, 1994)

In Figures 1a and 1b, the absorption spectra for two products are shown graphically. With a background in the mentioned criterion for critical wavelength (≥ 370 nm), Figure 1a shows a broad-spectrum product with λ_c = 380 nm. Figure 1b shows a product with only UVB protection, where λ_c = 327 nm.

Broad-spectrum product **UVB product**

Figures 1a and 1b: The figures show absorption spectra with critical wavelengths for two



sun protection products. Figure 1a: Broad-spectrum product. Figure 1b: a typical "UVB product"

Method:

The practical aspects of the described method for determination of critical wavelength are similar to the *in vitro* determination of SPF factor (Diffey, 1994).

The analyses can be carried out using, for example, an SPF-290S Analyser equipped with an «Integrating Sphere», which collects any light spreading from the sample. The amount of cream used for testing should be 2 mg/cm^2. Otherwise, usual techniques in connection with such instrumental methods are used.

The critical wavelength is determined by the following equation:

$$0{,}9 = \frac{\int_{290}^{\lambda_C} Log_{10} MPF_\lambda}{\int_{290}^{400} Log_{10} MPF_\lambda}$$

• = Wavelength (nm)

λ_C = Critical wavelength

MPF = Monochromatic Protection Factor.

Background documents

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