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PART II

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

Food and Drug Administration

■

SUNSCREEN DRUG PRODUCTS FOR OVER-THE-COUNTER HUMAN DRUGS

Proposed Safety, Effective and Labeling Conditions

lergic skin sensitizers. The Kligman test uses sodium lauryl sulfate to irritate the test site, thereby hastening and accentuating the allergic skin sensitizing potential of a substance.

b. *Effectiveness data.* For proof of effectiveness of sunscreen active ingredients and formulations, the Panel recommends sunscreen product testing procedures for determining the Sun Protection Factor (SPF) value and related labeling claims. (See part III, paragraph D, below—Sunscreen Product Testing Procedures for Determination of the Sun Protection Factor (SPF) Value and Related Labeling Claims.)

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D. SUNSCREEN PRODUCT TESTING PROCEDURES FOR DETERMINATION OF THE SUN PROTECTION FACTOR (SPF) VALUE AND RELATED LABELING CLAIMS

1. *Sunscreen active ingredients contained in sunscreen products.* The active sunscreen ingredients of the product consist of one or more of the ingredients classified as Category I within any established, maximum daily dosage limit and the finished product provides an SPF value of not less than 2.

2. *Sun protection factor (SPF) value.* An SPF value is defined as the UV energy required to produce a minimal erythema dose (MED) on protected skin divided by the UV energy required to produce an MED on unprotected skin. In effect, the SPF value is the reciprocal of the effective transmission of the product viewed as a light filter. The UV light (UVL) energy is measured by various photodetectors as described below.

The SPF value may also be defined by the following ratio:

SPF value = MED (protected Skin (PS))/MED (unprotected skin (US))

where, MED (PS) is the minimal erythema dose for protected skin after application of 2 mg/cm² or 2 μl/cm² of the final formulation of the sunscreen product, and MED (US) is the minimal erythema dose for unprotected skin, i.e., skin to which no sunscreen product has been applied.

The SPF value is the value that can be directly compared between individuals and between products.

3. *Standard sunscreen.*—a. *Laboratory validation.* The use of standard sunscreens for testing purposes permits the direct comparison of results between laboratories to assure uniform evaluation of sunscreen products. Comparing the mean SPF values between laboratories assures that the proper SPF value categorization of a product is maintained. By comparing the standard deviations of the mean SPF values between laboratories, the relative precision of sunscreen testing can be monitored.

A sunscreen preparation containing homosalate was tested by five laboratories in a cooperative trial using solar simulators (ref. *1*). The information accumulated from these studies makes this preparation a suitable standard for use in monitoring the tests for SPF value of sunscreen products. This preparation gave a mean SPF value of 4.24 (standard deviation = 1.14). The Panel, therefore, recommends this sunscreen preparation as a standard sunscreen.

b. *Preparation of the standard homosalate sunscreen.* The standard homosalate sunscreen is prepared from two different preparations (part A and part B) with the following compositions:

PREPARATION OF PART A AND PART B OF THE STANDARD SUNSCREEN

PART A

Ingredients	Percent by weight
Homosalate	8.00
White petrolatum	2.00
Stearic acid	3.00
Stearyl alcohol	2.00
Propylparaben	0.015

PART B

Methylparaben	0.025
Sequestrene Na, (EDTA disodium)	0.05
Sodium lauryl sulfate	0.50
Propylene glycol	12.00
Purified water U.S.P.	72.41

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

c. *Assay of the standard homosalate sunscreen.* 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-absorbing denaturant.

(2) *Preparation of a 1 percent solution of the standard homosalate sunscreen preparation.* Accurately weigh 1 g of the standard homosalate sunscreen preparation into a 100 ml volumetric flask. Add 50 ml 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 the 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 ml of the filtrate. Collect the next 20 ml of the filtrate (second collection).

Add 1 ml of the second collection of the filtrate to a 50 ml 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 nm.

(5) *Calculation of the concentration of homosalate.* 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 to prepare the test solution (1:50), the weight of the sample of the standard homosalate sunscreen preparation (1 g), 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 $\times 50 \times 100/1 \times 172$ = percent concentration by weight.

4. *Light source and light monitoring.*—a. *Artificial light source (solar simulator) and monitoring.* A solar simulator for sunscreen testing shall be defined as a light source having:

(1) A continuous emission spectrum in the UV-B (290 to 320 nm);

(2) Less than 1 percent of its total energy contributed by nonsolar wave-

lengths (wavelengths shorter than 290 nm); and

(3) Not more than 5 percent of its erythemically effective energy contributed by nonsolar wavelengths.

The instrument must be monitored periodically to assure that it delivers the appropriate spectrum described above. The monitoring procedure is described below.

The xenon arc solar simulator is the preferred artificial light source. Test data using other artifical light sources to establish the degree of efficacy at UV-B wavelengths of sunscreens must have corroborating natural sunlight testing for acceptance.

Xenon solar simulators presently utilize xenon arcs from 150 to more than 6,000 watts. For example, to produce 1 MED with a 150-watt lamp requires 120±30 seconds at the exit port of the instrument when the irradiated site is 1 cm in diameter. Depending upon instrumental design, other irradiation sizes and times can be utilized. Solar simulators of 150 watts usually produce 10 or 12 solar constants. A solar constant is the total amount of energy at all wavelengths per square meter, available from the sun, at the Earth's surface. For example, if the MED for a normal subject is 20 minutes of sunlight exposure, then the solar simulator would produce an MED of 2 minutes at 10 solar constants in the same subjects. The more powerful solar simulators can produce up to 40 solar constants. Irradiated sites more than 4 mm in diameter present no difficulty in determining skin erythema.

A solar simulator uses filters to absorb (cut off) the shorter UV wavelengths which do not reach the earth's surface from the sun. The primary filter is a suitable filter of colorless glass, sharp cut in the UV range, with a T_{50} (50 percent transmittance point) cut location approximately at 310 nm±6. Dichroic or heat-absorbing filters are used to reduce unnecessary visible and infrared radiation.

Regardles of the light source employed, some uncertainties in interpreting results of in vivo testing, using sunlight or artificial sources, include:

(i) Between individual investigators reading the minimal erythema dose response (MED) (the minimal perceptible erythema) on skin, the readings vary ±20 percent. However, each individual investigator is remarkably consistent after some experience. To partially overcome the variation between observers, the investigator indoors should use a constant light source like an incandescent or a warm white fluorescent lamp at a fixed distance and read the results on the subject in a room with white or light grey walls. No instrument has proven so reliable and consistent as the human eye, but the investigator may use a color gauge, a reflectometer, or a series of color-correcting red filters of increasing red intensity. The filters are placed over the irradiated site where the correct filter will eliminate the erythema and produce a uniform color. The reliability of reproducing results obtained from such a system of filters would have to be verified. In addition, it would be difficult to translate such data into SPF values unless there could be shown to be a 1:1 correlation between a color filter and a known standard sunscreen.

(ii) The same dose of UV light produces different intensities of erythema in different people. This is why the MED must be determined for each subject whatever the light source.

(iii) Inherent differences in the erythemic exposure-color relationship occur between individuals because the same dose of UV light causes different degrees of erythema depending on the time or reading after exposure.

The advantages of a xenon lamp solar simulator for in vivo testing include the following: The continuous spectrum mimics the sun in the UV range with comparable output over the 290 to 400 nm range; a constant spectrum at a constant angle with high output is obtained; and the lamp produces a stable spectrum over long use.

The disadvantages of using the xenon lamp for in vivo testing include the following: The full solar spectrum output is low in the visible and infrared wavelengths; using the xenon lamp is time consuming if only one test site can be irradiated at a time; and it is difficult to measure the output, but instrumentation is available for this purpose.

The xenon arc solar simulator can be monitored. Calibrated thermopiles (instruments that measure the xenon UV total output by converting it to heat energy) can be used to successfully measure the output of solar simulators. The total energy output (solar and nonsolar) of the xenon lamp solar simulator can be measured by a thermopile which should be accurate to 1 percent. If the thermopile has a window, it should be constructed of quartz. Such devices are accurate to at least 1 percent when properly used. Other devices have been used to measure solar simulators, including photocells, photodiodes, photomultipliers, with and without filters. The basic requirements for a suitable monitoring device are that they be stable for several hours, be sensitive to UV-B radiation, and provide values reproducible daily.

The output of a solar simulator is measured in units of Joules. A Joule (J) is an absolute unit of work or energy equal to 1 million ergs. One Joule (J)=1×10^7 ergs=1 watt-second $=10^6$ microwatt-second=2.4×10^{-4} kilocalories. The UVL intensity of a solar simulator will be reported in J/m².

b. *Natural light source (sunlight) and monitoring.* Testing sunscreen products in sunlight offers several advantages. The test situation more closely approximates the actual ways the sunscreen product will be used by the consumer. The test subject is exposed simultaneously to the full solar spectrum, the heat, and the humidity. Testing of several sunscreen products simultaneously can be done. An estimation of tanning efficacy can be made. Uncontrollable variables in outdoor testing include vagaries of the weather, changing cloud cover, changing radiation intensity with time, changing sun angle to the body surface with time, and variable heat-induced sweating. Monitoring the amount of exposure to natural sunlight is more difficult than for solar simulators. The vagaries of each environment together with the changes in solar altitude with time make timing solar exposure inexact for determing total erythemic exposure. If solar exposures based on time are utilized, the results of 1 day's testing probably cannot be duplicated on another day.

Recently, the Robertson-Berger meter (R-B meter) (ref. *2*) has proved successful in monitoring and reproducing solar erythemic exposures (ref. *3*). An instrument of this type is recommended for monitoring all outdoor studies. Other recording radiometers are in use which permit continuous measurement of the sun's intensity in J/m² (ref. *4*).

The R-B meter records a measure of the cumulative amount of UV radiation that passes through its filters and photosensors after each 30-minute interval. Such 30-minute recordings may range from 0 to slightly over 1,000 depending on the geographical location and the meteorological conditions prevailing at the test location. A count of approximately 400 is estimated to produce one MED on the "typical" Caucasian skin.

5. *General guidelines for all testing procedures.*—a. *Selection of test subjects (male and female).* Only fair-skin volunteers with skin types I, II, and III, using the following guidelines, should be selected:

SELECTION OF FAIR-SKIN SUBJECTS

Skin Type and Sunburn and Tanning History [1]

I—Always burns easily; never tans (sensitive).

II—Always burns easily; tans minimally (sensitive).

III—Burns moderately; tans gradually (light brown) (normal).

[1] Based on first 30 to 45 minutes sun exposure after a winter season of no sun exposure.

IV—Burns minimally; always tans well (moderate brown) (normal).
V—Rarely burns; tans profusely (dark brown) (insensitive).
VI—Never burns; deeply pigmented (insensitive).

A medical history will be obtained from each volunteer with emphasis on the effects of sunlight on his/her skin. To be ascertained are the general health of the individual, the individual's skin type (I, II, or III), whether the individual is taking medication, topical or systemic, that is known to produce abnormal sunlight responses, e.g., declomycin or chlorpromazine, and whether the individual is subject to any abnormal responses to sunlight, such as a phototoxic or photoallergic response.

b. *Test site inspection.* The physical examination should determine the presence of sunburn, suntan, scars, active dermal lesions, and uneven skin tones on the areas of the back to be tested. The presence of nevi, blemishes, or moles will be acceptable if in the physician's judgment they will not interfere with the study results. Excess hair on the back is acceptable if the hair is clipped or shaved.

Some investigators have found a reflectometer useful to ensure uniformity of skin tone to the average skin reflectance in the test areas. Reflectance readings should not vary by more than 5 percent (refs. 4 and 5).

c. *Informed consent.* Legally effective written informed consent must be obtained from each individual.

d. *Test site delineation.*—(1) *Test site area.* A test site area serves as an area for determining the subject's MED after application of either the sunscreen standard or the test sunscreen product, or for determining the subject's MED when the skin is unprotected (control site). The area to be tested is the back between the beltline and the shoulder blade (scapulae) and lateral to the midline. The test site areas may be horizontal or vertical, and rectangular or square. Depending upon the test scheme, each test site area for applying a product or standard control should be a minimum of 50 cm^2 e.g., 5×10 cm. The test sites are outlined with ink. If the person is to be tested in an upright position, the lines should be drawn on the skin with the subject upright. If the subject is to be tested while prone, the markings should be made with the subject prone. Change of position between marking and testing can change the test area as much as 40 percent.

(2) *Test subsite area.* Each test site area is divided into at least three test subsite areas that are at least 1 cm^2 Usually four or five subsites are employed. Each test subsite area within a test site area is subjected for a time interval, in a series of time intervals, in which the test site area is exposed for the determination of the MED as described below.

e. *Application of test materials.* To insure standardized reporting and to define a product's SPF value, the application of the product will be expressed on a weight basis per unit area which establishes a standard film. The Panel recommends that the test sunscreen product and the sunscreen standard application be 2 mg/cm^2 or 2 ul/cm^2 For some products, lesser amounts may be justified based on intended usage.

The specific gravity of the product is determined according to standard techniques. In testing situations, it is easier to accurately measure volumes for applications. Most sunscreen products have a specific gravity near unity. The 50 cm^2 test site area previously recommended above would require 100 mg of a product or 100 ul (assuming a specific gravity of 1 to obtain a standard 2 mg/cm^2 test application.

For oils and most lotions, the viscosity is such that the material can be applied with a volumetric syringe. For creams, heavy gels, and butters, the product is warmed slightly so that it can be applied volumetrically. On heating, care must be taken so as not to alter the product's physical characteristics, especially separation of the formulations. Pastes and ointments should be weighed, then applied by spreading on the test site. Numerous investigators have obtained more reproducible results by spreading a product using a finger cot than by spreading with a glass or plastic rod.

f. *Waiting period.* Before exposing the test site areas after applying a product, a waiting period is employed. This waiting period will be at least 15 minutes, or depending upon the product's labeling to the consumer, the waiting period before testing will be the amount of time specified on the labeling.

g. *Number of subjects.* The Panel recommends that groups of at least 20 subjects be used for each test panel. One reason for the panel's decision is that the MED testing is done in 25 percent increments of exposure. The 25 percent exposure increments are reasonably close to the standard deviations observed in test results (ref. 5). The standard error for a 20-subject test panel would be 25 percent divided by the square root of 20, i.e.,

$$\text{Standard error} = (25 \text{ percent})/\sqrt{20}$$

The Panel agreed that a sunscreen product categorizes itself if the mean of the SPF test values fall within the limits of a PCD as described elsewhere in this doecument (see part II, paragraph A.7. above—Categories of sunscreen products.) The standard error should not exceed ± 5 percent of the mean. An appropriate number of additional subjects should be used to determine the PCD, if a PCD does not fall within the limits of the standard error.

6. *Specific guidelines for all testing procedures.* The Panel has provided the following table of specific testing procedures which are discussed more fully below.

Summary of Sunscreen Testing Procedures for Determining Product labeling

Type of test	Light source	Total test time (min)
SPF Value	A	(2)
SPF Value	N	(2)
Sweat Resistance	A	30
Water Resistance	A	40
Waterproof	A	80

[1] A=artificial light source, N=natural light source.
[2] Variable.

The Panel has not proposed tests to determine if a sunscreen product is water resistant, sweat resistant or waterproof, using a natural light source (sunlight), for several reasons.

There are three major difficulties with testing sunscreen products outdoors for water resistance, sweat resistance, and waterproof claims. These are the lack of protection of the subject's untreated skin against sunburn during the long exposures, the determination of the quantity of sunlight striking the skin when immersed and penetrating the wet stratum corneum, and the maintenance of the protective template on the test site during water immersion. The exposed skin outside the test sites can be protected by applying sunscreens between water immersions. Wet clothing usually transmits significant amounts of UVL.

The Panel believes the testing of sunscreen products for water resistance, sweat resistance, and waterproof claims is easier and more reproducible in an indoor pool. The Panel believes that water immersion is a more severe test of a sunscreen product than is sweating. It, therefore, recommends that the claim "Resists removal by sweating" is appropriate if the product proves water resistant or waterproof in the tests described below.

Because of the difficulties inherent in sunlight water resistance, waterproof and sweat resistance testing for substantivity discussed above, the Panel does not recommend that this method of testing be required. It does recommend that ways to test for substantivity of sunscreen products against water immersion and during copious sweating in natural sunlight be developed.

a. *Determination of SPF value using artificial light source.* This test determines the SPF value of a sunscreen

product after UV-A and UV-B irradiation of the skin.

A series of UV light exposures (units of time) are administered to the subsites on each volunteer with the solar simulator. One series of exposures is administered to the untreated, unprotected skin to determine the volunteer's inherent MED. The time intervals selected are a geometric series represented by $(1.25)^n$, where in each exposure time interval is 25 percent greater than the previous time. The reason for using the geometric sequence of UV exposure is to maintain the same relative uncertainity (expressed as a constant percentage), independent of the volunteer' sensitivity to UV light, regardless of whether the subject has a high or low MED. One example is the time intervals of 1, 1.25, 1.56, 1.96, and 2.44 minutes. This series would be suitable for a normal person exposed to the 150-watt xenon lamp solar simulator. Usually, the MED of a person's unprotected skin is determined the day prior to testing a product.

The protected test sites (standard and/or test sunscreen product) usually are exposed to UV light the next day. The exact series of exposures to be given is determined by the MED of the unprotected skin. For example, for the 8 percent homosalate standard sunscreen with an SPF of 4, the time intervals to be selected are 4, 5, 6.24, 7.84, and 9.76 minutes for a person with an MED of 1.56 minutes on the unprotected skin.

Specifically, what is needed is a series of exposures of the sites in which the lower exposure times produce no effect on the skin. Also, at 16 to 24 hours later, the longer exposure times should produce light and moderately red exposure sites. The MED is the time of exposure that produces the minimally perceptible erythema at 16 to 24 hours postexposure. The SPF of the test sunscreen is then calculated from the exposure time interval required to produce the MED of the protected skin, and from the exposure time interval required to produce the MED of the unprotected skin (control site), i.e.,

SPF value = Exposure time interval (MED (PS))/Exposure time interval (MED (US).)

b. *Determination of SPF value using natural light source (sunlight).* This test determines the SPF value of a suncreen product in sunlight.

Applications will dry in at least 15 minutes or longer as specified on the labeling. Common practice utilizes an opaque template or grid of opaque materials to cover the test sites to control the time exposures of the subsites to the sun after the product has dried. The remainder of the back is covered with heavy toweling or other opaque materials when a suncreen is applied to the exposed parts of the subject's skin during the test. The subject will lie in the prone position in direct sunlight for a predetermined period of time. The day of sun exposure may not be the same for all subjects. However, sun exposure of individual subjects will be completed during one continuous exposure period. Sun exposure of all subjects must be completed within 2 weeks for any one test and must be conducted at the same geographical location for any one test. During each exposure, the sun intensity will be measured continuously by a recording radiometer or a recording R-B meter. Empirically, approximately 6×10^4 Joules/m^2, as measured by a recording radiometer, will evoke 1 MED in skin types I and II subjects when read 16 to 24 hours later. Using the recording R-B meter, 400 counts are equivalent to 1 MED in skin type III subjects (ref. 3), and MED's as low as 200 counts may be expected of skin type I. Duration of sun exposure will be documented in Joules/m^2 or in R-B counts. Temperature and humidity will be measured in R-B meter counts. Temperature and humidity will be measured at the beginning, the end, and at the maximal sun intensity for the exposure period. Descriptive comments about wind and cloud conditions will be made at times, but the primary measure of variations in cloud cover during exposure will be the continuous radiometer or R-B meter record.

At preestablished exposure times as determined by the meter reading, the subsite areas of the test site area will be exposed so that graded exposures will be obtained. Identical sequence of exposures will be administered to all test sites.

The Panel has reviewed several suggested test protocols of varying design that effectively determine the SPF of a sunscreen product. One example test protocol follows. It assumes a subject of skin type I with an MED of 15 minutes, 4.5×10^4 Joules/m^2, or 300 R-B meter counts (ref. 3). The study is a controlled test of a sunscreen product, a standard sunscreen product, and an untreated control.

With the protective template in place, the approximate dose of sun exposure of individual subsites within the treated and unprotected test sites were as follows:

Robertson-Berger Meter Counts (exposure Count Intervals) (Ref. 3). 160, 213, 283, 376, 501, 666, and 886.

The R-B meter count intervals selected are a geometric series represented by $(1.33)^n$, wherein each exposure count interval is 33 percent greater than the previous exposure count interval. For the unprotected subsite, usually a miximum of 800 R-B meter counts assures 3 MED's in skin types I and II, and 2 MED's in normal skin type III subjects. Greater exposures increase the risk of severe sunburn, but provide little additional useful data.

For test and standard sunscreen products with different SPF values, the dose of exposure will vary accordingly. Often a pilot study is performed in three to six subjects to obtain the approximate SPF of a new product.

The SPF value of the test sunscreen using the R-B meter is calculated as follows:

SPF value = exposure count interval (MED (PS))/exposure count interval (MED (US)).

c. *Determination of sweat resistance using artifical light source.* This test determines the sweat resistance and substantivity of a sunscreen product after 30 minutes of copious sweating to substantiate the claim of sweat resistance. The claim as appropriate will be allowed if the sunscreen product retains the same PCD, as described elsewhere in this document, after the sweat test as before the sweat test. (See part II, paragraph A.7. above Categories of sunscreen products.)

The Panel concludes that a 30-minute period of copious sweating induced under controlled environmental conditions is an appropriate test for determinng sweat resistance and substantivity claims of a sunscreen product. If a subject fails to sweat profusely, he will be dropped from the study and another subject selected. The MED of the unprotected test site area on each subject is determined using the solar simulator. Usually the next day, the SPF of the test sunscreen product is determined for each subject using the solar simulator. The same day or the next day the test sunscreen product is applied. The subjects sit quietly in a controlled environment at a temperature of 35 to 38° C (95 to 100° F) and a relative humidity of 70 to 80 percent. To prevent evaporative cooling of the skin with resulting decreased sweating, there should be little air movement. A few subjects may require an air temperature of 105° F, with a relative humidity of 60 percent. For safety purposes, older persons should not be used. All subjects exposed to heat stress should have their pulse and temperature taken every 15 minutes. If a subject's pulse exceeds 160 counts per minute, and oral temperature of 38.9° C (102° F) or a rectal temperature of 39.2° C (102.5° F), the subject's participation must stop.

The 30-minute test period begins when the subject starts to sweat profusely, drops or rivulets of sweat running down the test site. Most subjects will sweat profusely within 10 minutes, but a few may take up to 20 minutes to develop copious sweating. After the

30-minute period of heavy sweating, the subject leaves the controlled environment, permits the test site area to air dry, and then the postsweating SPF of the sunscreen product is determined. The test sunscreen product must permit delivery of sweat through the film. No standard sweat resistant product is available as yet.

If the test sunscreen product retains the same PCD after the sweat test as before the sweat test, the claim of "sweat resistant" will be allowed.

d. *Determinating if a sunscreen is water resistant or waterproof using artifical light source.* This test determines the water resistance of a sunscreen product after 40 minutes of moderate activity (swim and play activity) in water (swimming pool) to substantiate the claim of water resistance, and after 80 minutes of moderate activity to substantiate the claim of waterproof. The claims as appropriate will be allowed if the sunscreen product retains the same PCD, as described elsewhere in this document, after the test as before the test. (See part II., paragraph A.7. above—Categories of sunscreen products.) Because it is impossible to produce even, controlled sweating among individuals, the Panel recommends that the claim "resists removal by perspiration" is appropriate if the product proves water resistant or waterproof in the water test. The Panel believes that water immersion is a more severe test of a sunscreen product than is sweating.

No water resistant or waterproof standard sunscreen product is available; so a standard sunscreen product is not used in the test.

The Panel concludes that a 20-minute period of moderate activity in the water in a swimming pool after the application of the test sunscreen product, followed by a 20-minute rest period, then a second 20-minute period of moderate activity is an appropriate test for determining water resistance and substantivity claims of a sunscreen product. The test site areas are then exposed to the solar simulator. The pool and air temperature and the relative humidity should be recorded. A sample schedule of a water test for a water-resistant sunscreen product is as follows:

9:30—Apply sunscreen product (followed by the waiting period after application of the sunscreen product indicated on the product labeling).
10:00—20 minutes moderate activity.
10:20—Rest period
10:40—20 minutes moderate activity
11:00—Conclude water test (air dry test sites without toweling).
11:10—Begin solar simulator exposure to test site area in the manner described above.

A sample schedule of a water test for a waterproof sunscreen product is as follows:

9:30—Apply sunscreen product (followed by the waiting period after application of the sunscreen product indicated on the product labeling).
10:00—20 minutes moderate activity.
10:20—Rest period.
10:40—20 minutes moderate activity.
11:00—Rest period.
11:20—20 minutes moderate activity.
11:40—Rest period.
12:00—20 minutes moderate activity.
12:20—Conclude water test (air dry test sites without toweling).
12:30—Begin solar simulator exposure to test sites in the manner described above.

Sunscreen active ingredients dissolve much more slowly in seawater than in freshwater because seawater contains about 3 percent salts. Therefore, a freshwater pool (21 to 32° C) should be used. The Panel recommends that this substantivity test should be conducted in an indoor pool to diminish the risk of exposure to natural sunlight during the conduct of the test, especially in skin types I and II.

The solar simulator-exposed test site areas are read at 16 to 24 hours after exposure determine the SPF for the subjects as described above. The Panel believes that a sunscreen product that can withstand 80 minutes of water immersion can reasonably claim to be waterproof. The Panel chose the 20-minute water periods because some unpublished marketing data revealed that the average person goes into the water 3.6 times for an average duration of 21 minutes per immersion at the beach or pool (Ref. 4).

7. *Response criteria.* After UVL exposure to natural or artificial sources is completed, all immediate responses are recorded. These include several types of typical responses such as the following.

a. An immediate darkening or tanning, typically grayish or purplish in color, fading in 30 to 60 minutes, and attributed to photo-oxidation of existing melanin granules;

b. Immediate reddening, fading rapidly, and viewed as a normal response of capillaries and venules to heat, visible and infrared radiation; and

c. An immediate generalized heat response, resembling prickly heat rash, fading in 30 to 60 minutes, and apparently caused by heat and moisture generally irritating to the skin's surface.

After the immediate responses are noted, each subject shields the exposed area from further UV radiation for the remainder of the test day. The MED is determined 16 to 24 hours after exposure.

Specifically, these tests depend upon determining the light energy corresponding to a minimally perceptible erythema of a subject's skin at 16 to 24 hours postexposure for each series of exposures. To determine the MED somewhat more intense erythemas usually must also be produced. The goal is to have some exposures that produce absolutely no effect, while of those exposures that produce an effect, the maximal exposure should be no more than twice the total energy of the minimal exposure. The maximum exposure anticipated in these tests corresponds to what most individuals would describe as a light to moderate sunburn.

8. *Rejection of test data.* These tests occasionally fail, and must be discarded. There are only the following two technical reasons for rejection of test data.

a. Sometimes the exposure series fails to elicit an MED response on either the treated or unprotected skin sites. In either event, that test is a technical failure and must be discarded. If the subject reacts to one or more exposure on the unprotected control site, but not on the treated site, then a minimal estimate of the SPF can be obtained.

b. The responses on the treated sites are randomly absent, which indicates the product was not spread evenly. Therefore, no assessment of protection is possible.

9. *Treatment of data.* The SPF value will be calculated for each test of a sunscreen product as follows:

a. *Calculation of the SPF value from data obtained in tests using a solar simulator.* The measurement units in tests using a solar simulator to obtain MED's for calculation of the SPF value are time units, usually seconds. The following is an example of the calculation of the SPF value from MED's obtained using a solar simulator:

SPF value = Exposure time interval (MED(PS))/Exposure time interval (MED(US))

SPF value = 180 seconds (MED(PS))/60 seconds (MED(US))

Therefore the SPF value = 3.

The PCD for a sunscreen product with an SPF value of 3 would be categorized as a minimal sun protection products because the SPF value of 3 is more than a value of 2 and less than an SPF value of 4.

b. *Calculation of the SPF value from data obtained in tests using a recording radiometer or a Robertson-Berger meter*—(1) *Recording radiometer.* The measurement units in tests using a recording radiometer are energy units, Joules/m^2. The following is an example of the calculation of the SPF value from MED's obtained using a recording radiometer:

SPF value = Joules/m^2 (MED(PS))/Joules/m^2(MED(US))

SPF value = 28×10^4 Joules/m^2 (MED(PS))/6×10^4 Joules/m^2(MED(US))

Therefore, the SPF value = 4.6.

The PCD for a sunscreen product with an SPF value of 4.6 would be categorized as a moderate sun protection product because the SPF value of 4.6 is more than a value of 4 and less than an SPF value of 6.

(2) *Robertson-Berger meter (R-B meter).* The measurement units in tests using a Robertson-Berger meter are counts. The following is an example of the calculation of the SPF value from MED's obtained using a Robertson-Berger meter:

SPF value = Exposure count interval (MED(PS))/Exposure count interval (MED(US))

SPF value = 2,600 counts (MED(PS))/400 counts (MED(US))

Therefore, the SPF value = 6.5.

The PCD for a sunscreen product with an SPF value of 6.5 would be categorized as an extra sun protection product because the SPF value of 6.5 is more than a value of 6 and less than an SPF value of 8.

REFERENCES

(1) OTC Volume 060169.
(2) Proceedings of the Third Conference on Climatic Impact Assessment Program, February 26-March 1, 1974, DOT, TSC-OST 74-15.
(3) Measurement of Ultraviolet Radiation in the United States and Comparisons with Skin Cancer Data, U.S. Department of Health, Education, and Welfare, National Institutes of Health (DHEW No. 76-1029), November 1975.
(4) OTC Volume 060158.
(5) OTC Volume 060166.

The Food and Drug Administration has determined that this document does not contain an agency action covered by 21 CFR 25.1(b) and consideration by the agency of the need for preparing an environmental impact statement is not required.

Therefore, under the Federal Food, Drug, and Cosmetic Act (secs. 201, 502, 505, 701, 52 Stat. 1040-1042 as amended, 1050-1053 as amended, 1055-1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321, 352, 355, 371) and the Administrative Procedure Acts (secs. 4, 5, and 10, 60 Stat. 238 and 243 as amended (5 U.S.C. 553, 554, 702, 703, 704) and under authority delegated to him (21 CFR 5.1)), the Commissioner proposes that subchapter D of chapter I of title 21 of the Code of Federal Regulations be amended by adding new part 352, to read as follows:

PART 352—SUNSCREEN PRODUCTS FOR OVER-THE-COUNTER HUMAN USE

Subpart A—General Provisions

Sec.

Subpart B—Active Ingredients

Subpart C—Testing Procedures

Subpart D—Labeling

AUTHORITY: Secs. 201, 502, 505, 701, 52 Stat. 1040-1042 as amended, 1050-1053 as amended, 1055-1056 as amended by 70 Stat. 919 and 72 Stat. 948 (21 U.S.C. 321, 352, 355, 371) (5 U.S.C. 553, 554, 702, 703, 704).

Subpart A—General Provisions

§ 352.1 Scope.

An over-the-counter sunscreen product in a form suitable for topical administration is generally recognized as safe and effective and is not misbranded if it meets each of the following conditions and each of the general conditions established in § 330.1 of this chapter.

§ 352.3 Definitions.

(a) *Product category designation (PCD).* A labeling designation for sunscreen products to aid in selecting the type of product best suited to the individual's complexion (pigmentation) and desired response to ultraviolet (UV) light.

(1) *Mineral sun protection product.* Sunscreen products that provide an SPF value of 2 to under 4, and offer the least protection, but permit suntanning.

(2) *Moderate sun protection product.* Sunscreen products that provide an SPF value of 4 to under 6, and offer moderate protection from sunburning, but permit some suntanning.

(3) *Extra sun protection product.* Sunscreen products that provide an SPF value of 6 to under 8, offer extra protection from sunburning, and permit limited suntanning.

(4) *Maximal sun protection product.* Sunscreen products that provide an SPF value of 8 to under 15, offer maximal protection from sunburning, and permit little or no suntanning.

(5) *Ultra sun protection product.* Sunscreen products that provide an SPF value of 15 or greater, offer the most protection from sunburning, and permit no suntanning.

(b) *Sunscreen active ingredient.* An active ingredient that absorbs at least 85 percent of the light in the UV range at wavelengths from 290 to 320 nanometers, but transmits UV light at wavelengths longer than 320 nanometers. Such agents permit tanning in the average individual and also permit some reddening (erythema) without pain.

(c) *Sunscreen opaque sunblock.* An opaque sunscreen active ingredient that reflects or scatters all light in the UV and visible range at wavelengths from 290 to 777 nanometers and thereby prevents or minimizes suntan and sunburn.

(d) *Sun protection factor (SPF) value.* An SPF value is defined as the UV energy required to produce a minimal erythema dose (MED) on protected skin divided by the UV energy required to produce a MED on unprotected skin. In effect, the SPF value is the reciprocal of the effective transmission of the product viewed as a light filter. The SPF value may also be defined by the following ratio:

SPF value = MED (protected skin (PS)/MED (unprotected skin (US)).

Where MED (PS) is the minimal erythema dose for protected skin after application of 2 milligrams per square centimeter or 2 microliters per square centimeter of the final formulation of the sunscreen product, and MED (US) is the minimal erythema dose for unprotected skin, i.e., skin to which no sunscreen product has been applied.

Subpart B—Active Ingredients

§ 352.10 Sunscreen active ingredients.

The active ingredients of the product consist of the following when used within the topical dosage limits established and the finished product provides a minimum SPF value of not less than 2 as measured by the testing procedure in subpart C of this part:

Aminobenzoic acid 5 to 15 percent.
Cinoxate 1 to 3 percent.
Diethanolamine *p*-methoxycinnamate 8 to 10 percent.
Digalloyl trioleate 2 to 5 percent.
Dioxybenzone 3 percent.
Ethyl 4-[bis(hydroxypropyl)] aminobenzoate 1 to 5 percent.
2-Ethylhexyl 2-cyano-3, 3-diphenylacrylate 7 to 10 percent.
Ethylhexyl *p*-methoxycinnamate 2.0 to 7.5 percent.
2-Ethylhexyl salicylate 3 to 5 percent.
Glyceryl aminobenzoate 2 to 3 percent.
Homosalate 4 to 15 percent.
Lawsone 0.25 percent with dihydroxyacetone 3 percent.
Menthyl anthranilate 3.5 to 5 percent.
Oxybenzone 2 to 6 percent.
Padimate A 1 to 5 percent.
Padimate O 1.4 to 8.0 percent.
2-Phenylbenzimidazole-5-sulfonic acid 1 to 4 percent.
Red petrolatum 30 to 100 percent.
Sulisobenzone 5 to 10 percent.
Titanium dioxide 2 to 25 percent.
Triethanolamine salicylate 5 to 12 percent.

§ 352.20 Combinations of sunscreen active ingredients.

Two or more sunscreen active ingredients identified in § 352.10 may be combined within the topical dosage limits established: *Provided*, The finished product provides a minimum SPF value of not less than 2 as measured by the testing procedures in subpart C of this part.

Subpart C—Testing Procedures

§ 352.40 Standard sunscreen.

(a) *Laboratory validation.* A standard sunscreen shall be used concomitantly in the testing procedures for determining the SPF value of a sunscreen product to assure the uniform evaluation of sunscreen products. The standard sunscreen shall be an 8 percent homosalate preparation with a mean SPF value of 4.24 (standard deviation = 1.14).

(b) *Preparation of the standard homosalate sunscreen.* The standard homosalate sunscreen is prepared from two different preparations (preparation A and preparation B) with the following compositions:

COMPOSITION OF PREPARATION A AND PREPARATION B OF THE STANDARD SUNSCREEN

PREPARATION A

Ingredients	Percent by weight
Homosalate	8.00
White petrolatum	2.00
Stearic acid	3.00
Stearyl alcohol	2.00
Propylparaben	0.015

PREPARATION B

Methylparaben	0.025
Sequestrene Na, (EDTA disodium)	0.05
Sodium lauryl sulfate	0.50
Propylene glycol	12.00
Purified water U.S.P.	72.41

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

(c) *Assay of the standard homosalate sunscreen.* 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 absorbing denaturant.

(2) *Preparation of a 1 percent solution of the standard homosalate sunscreen preparation.* Accurately weight 1 gram of the standard homosalate sunscreen preparation into a 100 milliliter volumetric flask. Add 50 milliliter of the assay solvent. Heat on a steam bath and mix well. Cool the solution to room temperature (15 to 30° FC). Then dilute the solution to volume with the 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 milliliters of the filtrate. Collect the next 20 milliliters of the filtrate (second collection). Add 1 milliliter 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) *Calculation of the concentration of homosalate.* 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 to prepare the test 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 × 50 × 100/1 × 172 = percent concentration by weight.

§ 352.41 Light source and light monitoring.

(a) *Artificial light source (solar simulator).* A solar simulator for sunscreen testing shall be defined as a light source having continuous emission spectrum in the UV-B (290 to 320 nanometers) with less than 1 percent of its total energy contributed by nonsolar wavelengths (wavelengths shorter than 290 nanometers) and not more than 5 percent of its erythemically effective energy contributed by nonsolar wavelengths. The instrument must be monitored periodically to assure that it delivers the appropriate spectrum.

(b) *Natural light source (sunlight).* Sunlight more closely approximates the actual ways the sunscreen product will be used by the consumer. The test subject is exposed simultaneously to the full solar spectrum. However, uncontrollable variables in outdoor testing include vagaries of the weather changing cloud cover, changing radiation intensity with time, changing sun angle to the body surface with time, and variable heat-induced sweating. A suitable meter should be used for monitoring all outdoor studies.

§ 352.42 General testing procedures.

(a) *Selection of test subjects (male and female).* Only fair-skin volunteers with skin types I, II, and III using the following guidelines shall be selected:

SELECTION OF FAIR SKIN SUBJECTS

Skin Type and Sunburn and Tanning History[1]

I—Always burns easily; never tans (sensitive).
II—Always burns easily; tans minimally (sensitive).
III—Burns moderately; tans gradually (light brown) (normal).
IV—Burns minimally; always tans well (moderate brown) (normal).
V—Rarely burns; tans profusely (dark brown) (insensitive).
VI—Never burns; deeply pigmented (insensitive).

A medical history shall be obtained from each volunteer with emphasis on the effects of sunlight on their skin. To be ascertained are the general health of the individual, the individual's skin type (I, II, or III), whether the individual is taking medication, topical or systemic, that is known to produce abnormal sunlight responses, and whether the individual is subject to any abnormal responses to sunlight, such as a phototoxic or photoallergic response.

(b) *Test site inspection.* The physical examination shall determine the presence of sunburn, suntan, scars, active dermal lesions, and uneven skin tones on the areas of the back to be tested. The presence of nevi, blemishes, or moles will be acceptable if in the physician's judgment they will not interfere with the study results. Excess hair on the back is acceptable if the hair is clipped or shaved.

(c) *Informed consent.* Legally effective written informed consent must be obtained from each individual.

(d) *Test site delineation.*— (1) *Test site area.* A test site area serves as an area for determining the subject's MED after application of either the sunscreen standard or the test sunscreen product, or for determining the subject's MED when the skin is unprotected (control site). The area to be tested shall be the back between the beltline and the shoulder blade (scapulae) and lateral to the midline. Each test site area for applying a product or the standard sunscreen shall be a minimum of 50 square centimeter, e.g.,

[1] Based on first 30 to 45 minutes sun exposure after a winter season of no sun exposure.

5×10 centimeter. The test site areas are outlined with ink. If the person is to be tested in an upright position, the lines shall be drawn on the skin with the subject upright. If the subject is to be tested while prone, the markings shall be made with the subject prone.

(2) *Test subsite area.* Each test site area shall be divided into at least 3 test subsite areas that are at least 1 square centimeter. Usually 4 or 5 subsites are employed. Each test subsite are within a test site area is subjected for a time interval, in a series of time intervals, in which the test site area is exposed for the determination of the MED.

(e) *Application of test materials.* To insure standardized reporting and to define a product's SPF value, the application of the product shall be expressed on a weight basis per unit area which establishes a standard film. Both the test sunscreen product and the standard sunscreen application shall be 2 milligrams per square centimeter or 2 microliters per square centimeter. For oils and most lotions, the viscosity is such that the material can be applied with a volumetric syringe. For creams, heavy gels, and butters, the product shall be warmed slightly so that it can be applied volumetrically. On heating, care shall be taken so as not to alter the product's physical characteristics, especially separation of the formulations. Pastes and ointments shall be weighed, then applied by spreading on the test site area. A product shall be spread by using a finger cot.

(f) *Waiting period.* Before exposing the test site areas after applying a product, a waiting period of at least 15 minutes is required.

(g) *Number of subjects.* Groups of at least 20 subjects shall be used for each test panel. A sunscreen product categorizes itself if the mean of the SPF test values falls within the limits of a PCD. The standard error shall not exceed ± 5 percent of the mean. An appropriate number of additional subjects shall be used to determine the PCD, if a PCD does not fall within the limits of the standard error.

(h) *Response criteria.* After UVL exposure to natural or artificial sources is completed, all immediate responses shall be recorded. These include several types of typical responses such as the following: An immediate darkening or tanning, typically greyish or purplish in color, fading in 30 to 60 minutes, and attributed to photo-oxidation of existing melanin granules; immediate reddening, fading rapidly, and viewed as a normal response of capillaries and venules to heat, visible and infrared radiation; and an immediate generalized heat response, resembling prickly heat rash, fading in 30 to 60 minutes, and apparently caused by heat and moisture generally irritating to the skin's surface. After the immediate responses are noted, each subject shall shield the exposed area from further UV radiation for the remainder of the test day. The MED is determined 16 to 24 hours after exposure. Testing depends upon determining the light energy corresponding to a minimally perceptible erythema of a subject's skin at 16 to 24 hours postexposure for each series of exposures. To determine the MED, somewhat more intense erythemas must also be produced. The goal is to have some exposures that produce absolutely no effect, while of those exposures that produce an effect, the maximal exposure should be no more than twice the total energy of the minimal exposure.

(i) *Rejection of test data.* Test data shall be rejected if the exposure series fails to elicit an MED response on either the treated or unprotected skin sites or if the responses on the treated sites are randomly absent, which indicates the product was not spread evenly.

§ 352.43 Determination of SPF value using artificial light source.

A series of UV light exposures (units of time) are administered to the subsite areas on each volunteer with a solar simulator. One series of exposures shall be administered to the untreated, unprotected skin to determine the volunteer's inherent MED. The time intervals selected shall be a geometric series represented by $(1.25)^n$, wherein each exposure time interval is 25 percent greater than the previous time to maintain the same relative uncertainty (expressed as a constant percentage), independent of the volunteer's sensitivity to UV light, regardless of whether the subject has high or low MED. One example is the time intervals of 1, 1.25, 1.56, 1.96, and 2.44 minutes. This series would be suitable for a normal person exposed to the 150-watt xenon lamp solar simulator. Usually, the MED of a person's unprotected skin is determined the day prior to testing a product. The protected test sites (standard sunscreen and/or test sunscreen product) usually are exposed to UV light the next day. The exact series of exposures to be given shall be determined by the MED of the unprotected skin. For example, for the 8 percent homosalate standard sunscreen with an SPF value of 4.24, the time intervals to be selected are 4, 5, 6.24, 7.84, and 9.76 minutes for a person with an MED of 1.56 minutes on the unprotected skin. A series of exposures of the sites in which the lower exposure times produce no effect on the skin is required. Also, at 16 to 24 hours later, the longer exposure times should produce light and moderately red exposure sites. The MED is the time of exposure that produces the minimally perceptible erythema at 16 to 24 hours postexposure. The SPF value of the test sunscreen is then calculated from the exposure time interval required to produce the MED of the protected skin, and from the exposure time interval required to produce the MED of the unprotected skin (control site) as follows:

SPF value = Exposure time interval (MED (PS))/exposure time interval (MED (US))

§ 352.44 Determination of SPF value using natural light source (sunlight).

An opaque template or grid of opaque materials shall be used to cover the test sites in order to control the time exposures of the subsite areas to the sun after the product has dried. The remainder of the back shall be covered with heavy toweling or other opaque materials when a sunscreen is applied to the exposed parts of the subject's skin during the test. The subject shall lie in the prone position in direct sunlight for a predetermined period of time. The day of sun exposure may not be the same for all subjects. However, sun exposure of individual subjects shall be completed during one continuous exposure period. Sun exposure of all subjects shall be completed within 2 weeks for any one test and shall be conducted at the same geographical location for any one test. During each exposure, the sun intensity shall be measured continuously by a recording radiometer or a recording Robertson-Berger meter. Duration of sun exposure shall be documented in Joules per square meter or in Robertson-Berger meter counts. Temperature and humidity shall be measured at the beginning, the end, and at the maximal sun intensity for the exposure period. Descriptive comments about wind and cloud conditions shall be made at times, but the primary measure of variations in cloud cover during exposure will be the continuous radiometer or Robertson-Berger meter record. At preestablished exposure times as determined by the meter reading, the subsite areas of the test site area shall be exposed so that graded exposures will be obtained. Identical sequence of exposures shall be administered to all test sites. The SPF value of the test sunscreen product using the Robertson-Berger meter is calculated as follows:

SPF value = Exposure count interval (MED(PS))/Exposure count interval (MED(US))

§ 352.45 Determination of sweat resistance using artificial light source.

A 30-minute period of copious sweating induced under controlled environmental conditions shall determine sweat resistance and substantivity claims of a sunscreen product. A subject that fails to sweat profusely shall

be dropped from the study and another subject selected. The MED of the unprotected test site area on each subject shall be determined using the solar simulator. Usually the next day, the SPF of the test sunscreen product is determined for each subject using the solar simulator. The standard sunscreen is not used in this test. The same day or the next day the test sunscreen product is applied. The subjects sit quietly in a controlled environment at a temperature of 35 to 38° C (95 to 100° F) and a relative humidity of 70 to 80 percent. To prevent evaporative cooling of the skin with resulting decreased sweating, there should be little air movement. A few subjects may require an air temperature of 41° C (105° F) with a relative humidity of 60 percent. For safety purposes, older people should not be used. All subjects exposed to heat stress should have their pulse and temperature taken every 15 minutes. If a subject's pulse exceeds 160 counts per minute, an oral temperature of 38.9° C (102° F), or a rectal temperature of 39.2° C (102.5° F), his/her participation shall stop. The 30-minute test period begins when the subject starts to sweat profusely, drops or rivulets of sweat running down the test site. Most subjects will sweat profusely within 10 minutes, but a few may take up to 20 minutes to develop copious sweating. After the 30-minute period of heavy sweating, the subject leaves the controlled environment, permits the test site area to air dry, and then the postsweating SPF of the test sunscreen product is determined. The test sunscreen product must permit delivery of sweat through the film. If the test sunscreen product retains the same PCD after the sweat test as before the sweat test, the claim of "sweat resistant" will be allowed.

§§ 352.46 Determining if a sunscreen is water resistant or waterproof using artificial light source.

The standard sunscreen is not used in the tests. An indoor fresh water pool (23 to 32° C) shall be used in these testing procedures.

(a) *Procedure for testing the water resistance of a sunscreen product.* A 20-minute period of moderate activity in the water in a swimming pool after the application of the test sunscreen product followed by a 20-minute rest period, then a second 20-minute period of moderate activity shall be used to determine the water resistance and substantivity claims of a sunscreen product. The test site areas are then exposed to the solar simulator. The pool and air temperature and the relative humidity shall be recorded.

The following procedure shall be used for the water resistance test:

(1) Apply sunscreen product (followed by the waiting period after application of the sunscreen product indicated on the product labeling).

(2) 20 minutes moderate activity in water.

(3) 20 minute rest period.

(4) 20-minutes moderate activity in water.

(5) Conclude water test (air dry test sites without toweling).

(6) Begin solar simulator exposure to test site areas in the manner described above.

A sunscreen product that can withstand 40 minutes of water immersion may claim to be water resistant.

(b) *Procedure for testing the waterproof claim of a sunscreen product.* The following procedure shall be used for the waterproof test:

(1) Apply sunscreen product (followed by the waiting period after application of the sunscreen product indicated on the product labeling).

(2) 20 minutes moderate activity in water.

(3) 20-minute rest period.

(4) 20 minutes moderate activity in water.

(5) 20-minutes rest period.

(6) 20 minutes moderate activity in water.

(7) 20-minutes rest period.

(8) 20 minutes moderate activity in water.

(9) Conclude water test (air dry test sites without toweling).

(10) Begin solar simulator exposure to test site areas in the manner described above.

The solar simulator-exposed test site areas shall be read at 16 to 24 hours later to determine the SPF for the subjects as described above. A sunscreen product that can withstand 80 minutes of water immersion may claim to be waterproof.

Subpart D—Labeling

§ 352.50 Labeling of sunscreen products.

(a) *Statement of identity.* The labeling of the product contains the established name of the drug(s) identified under § 352.10 and identifies the product as a "sunscreen."

(b) *Indications.* The labeling of the product contains a statement of the indications under the heading "Indication(s)" and is limited to one or more of the following phrases:

(1) *For all (minimal, moderate, extra, maximal, and ultra) sunscreen products.* (i) "Sunscreen to help prevent sunburn."

(ii) "Filters (or screen) out the sun's burning rays to prevent sunburn."

(iii) "Screens out the sun's harsh and often harmful rays to prevent sunburn."

(iv) "Overexposure to the sun may lead to premature aging of the skin and skin cancer. The liberal and regular use over the years of this product may help reduce the chance of these harmful effects."

(v) "Overexposure to the sun may lead to premature aging of the skin and skin cancer. The liberal and regular use over the years of this product may help reduce the chance of premature aging of the skin and skin cancer."

(2) *Additional indications.* In addition to the indications provided above in § 352.50(b)(1), the following may be used:

(i) *For minimal sunscreen products:* (*a*) "Affords minimal protection against sunburn."

(*b*) "Prolongs exposure time before sunburn occurs."

(*c*) "Permits tanning (or suntanning) and reduces chance of (or minimizes) sunburning."

(*d*) "Helps prevent sunburn on limited exposure of untanned skin."

(*e*) "Helps to protect the skin against sunburn while permitting tanning."

(*f*) "Allows you to stay in the sun two times longer than without sunscreen protection."

(*g*) "Provides two times your natural protection from sunburn."

(ii) *For moderate sunscreen products.* (*a*) "Affords moderate protection against sunburn."

(*b*) "Prolongs exposure time before sunburn occurs."

(*c*) "Permits tanning (or suntanning) and reduces chance of (or minimizes) sunburning."

(*d*) "Helps prevent sunburn on moderate exposure of untanned skin."

(*e*) "Allows you to stay in the sun four times longer than without sunscreen protection."

(*f*) "Provides four times your natural protection from sunburn."

(iii) *For extra sunscreen products.* (*a*) "Affords extra protection against sunburn."

(*b*) "Prolongs exposure time before sunburn occurs."

(*c*) "Permits limited tanning (or suntanning) and reduces chance of (or minimizes) sunburn."

(*d*) "Helps prevent sunburn."

(*e*) "For sun-sensitive skin."

(*f*) "Extra protection against sunburn for blondes, redheads and fair-skinned persons."

(*g*) "Allows you to stay in the sun six times longer than without sunscreen protection."

(*h*) "Provides six times your natural protection from sunburn."

(iv) *For maximal sunscreen products.* (*a*) "Affords maximal protection against sunburn."

(*b*) "Prevents sunburn and limits tanning."

(*c*) "For sun-sensitive skin."

(*d*) "Maximal protection against sunburn for blondes, redheads and fair-skinned persons."

(e) "Allows you to stay in the sun eight times longer than without sunscreen protection."

(f) "Provides eight times your natural protection from sunburn."

(v) *For ultra sunscreen products.* (a) "Affords the most protection against sunburn."

(b) "Prevents tanning and sunburn."

(c) "For highly sun-sensitive skin."

(d) "Greatest protection against sunburn for blondes, redheads, and fair-skinned persons."

(e) "Provides the highest degree of sunburn protection and permits no tanning."

(f) "Provides the highest degree of sunscreen protection and permits no tanning."

(3) *For all (maximal and ultra) sunscreen products that contain sunscreen opaque sunblock ingredients.* "Reflects the burning rays of the sun."

(c) *Warnings.* The labeling of the product contains the following warnings under the heading "Warnings:"

(1) *For all (minimal, moderate, extra, maximal, and ultra) sunscreen products.* The labeling of all sunscreen products contains the following warnings:

(i) "For external use only, not to be swallowed."

(ii) "Avoid contact with the eyes."

(iii) "Discontinue use if signs of irritation or rash appear."

(2) *Specific warnings.*—(i) *For sunscreen products providing an SPF value of 2 to under 4:* "Use on children under 2 years of age only with the advice of a physician."

(ii) *For sunscreen products providing an SPF value of 4 or greater:* "Use on children under 6 months of age only with the advice of a physician."

(iii) *For sunscreen products containing lawsone 0.25 percent with dihydroxyacetone 3 percent.* (a) "This is a two lotion product. Do not mix the contents of the two solutions. Use both solutions, for use of one alone will not provide protection."

(b) "Use only on skin free of rash and abrasions."

(c) "May stain clothing when freshly applied."

(d) *Directions for use.* The labeling of the product shall contain the following statement under the heading "Directions:"

(1) (i) For sunscreen products providing a minimum SPF value of 2 to under 4 for adults and children over 2 years of age: Apply liberally before sun exposure and reapply after swimming or after excessive sweating. There is no recommended dosage for children under 2 years of age except under the advice and supervision of a physician.

(ii) For sunscreen products providing a minimum SPF value of 4 for adults and children over 6 months of age: Apply liberally before sun exposure and reapply after swimming or after excessive sweating. There is no recommended dosage for children under 6 months of age except under the advice and supervision of a physician.

(2) *For all (minimal, moderate, extra, maximal, and ultra) sunscreen products*—(i) *That satisfy the water resistant testing procedures.* "Apply liberally before sun exposure and reapply after 40 minutes in the water or after excessive sweating."

(ii) *That satisfy the waterproof testing procedures.* "Apply liberally before sun exposure and reapply after 80 minutes in the water or after excessive sweating."

(iii) *That satisfy the sweat resistance testing procedures.* "Apply liberally before sun exposure and reapply after 30 minutes of excessive sweating."

(3) *For sunscreen products containing lawsone 0.25 percent with dihydroxyacetone 3 percent.* Products are composed of two separate formulations. Solution 1 contains 3 percent dihydroxyacetone and Solution 2 contains 0.25 percent lawsone.

(i) Products providing a minimum SPF value of 2 to under 4 for adults and children over 2 years of age: Apply liberally before sun exposure as follows: *First application.* The evening prior to sun exposure: Apply Solution 1. Wait 15 minutes then apply Solution 2 to the same areas of skin. Wait until dried. Then repeat application of solutions alternately as before until a total of three applications of both lotions have been applied. Leave on skin without washing. *Repeated application.* After first day apply one application of each lotion. Reapply after swimming or after excessive sweating. There is no recommended dosage for children under 2 years of age except under the advice and supervision of a physician.

(ii) Products providing a minimum SPF value of 4 for adults and children over 6 months of age: Apply liberally before sun exposure as follows: *First application.* The evening prior to sun exposure: Apply Solution 1. Wait 15 minutes then apply Solution 2 to the same areas of skin. Wait until dried. Then repeat application of solutions alternately as before until a total of three applications of both lotions have been applied. Leave on skin without washing. *Repeated application.* After first day, apply one application of each lotion. Reapply after swimming or after excessive sweating. There is no recommended dosage for children under 6 months of age except under the advice and supervision of a physician.

(e) *Statement on product performance*—(1) *Labeling claims for Product Category Designation (PCD).* The following appropriate labeling statement shall be prominently placed on the principal display panel of the products:

(i) Products containing active ingredient(s) that provide an SPF value of 2 to under 4: "Minimal Sun Protection Product (SPF 2)—Stay in the sun twice as long as before without sunburning."

(ii) Products containing active ingredient(s) that provide an SPF value of 4 to under 6: "Moderate Sun Protection Product (SPF 4)—Stay in the sun 4 times as long as before without sunburning."

(iii) Products containing active ingredient(s) that provide an SPF value of 6 to under 8: "Extra Sun Protection Product (SPF 6)—Stay in the sun 6 times as long as before without sunburning."

(iv) Products containing active ingredient(s) that provide an SPF value of 8 to under 15: "Maximal Sun Protection Product (SPF 8)—Stay in the sun 8 times as long as before without sunburning."

(v) Products containing active ingredient(s) that provide an SPF value of 15 or greater: "Ultra Sun Protection Product (SPF 15)—Stay in the sun 15 times as long as before without sunburning."

(2) *Labeling claims related to the product performance.* One or more of the following labeling claims for sunscreen products that satisfy the sunscreen product testing procedures identified in § 352.40 may be used.

(i) *For all (minimal, moderate, extra, maximal, and ultra) sunscreen products*—(a) *That satisfy the water resistance testing procedures.*

(1) "Water resistant."

(2) "Retains its sun protection for at least 40 minutes in the water."

(3) "Resists removal by sweating."

(b) *That satisfy the waterproof testing procedures.*

(1) "Waterproof."

(2) "Retains its sun protection for at least 80 minutes in the water."

(3) "Resists removal by sweating."

(c) *That satisfy the sweat resistance testing procedures.*

(1) "Retains its sun protection for at least 30 minutes of heavy sweating."

(2) "Sweat resistant."

(3) *Labeling guide for recommended sunscreen product use.* The Panel recommends that the following compilation of skin types and PCD's be appropriately included in labeling as a guide:

RECOMMENDED SUNSCREEN PRODUCT GUIDE

Sunburn and tanning history	Recommended sun protection product
Always burns easily; never tans	Maximal. Ultra.
Always burns easily; tans minimally	Extra.
Burns moderately; tans gradually	Moderate.
Burns minimally; always tans well	Minimal.
Rarely burns; tans profusely	Minimal.

Interested persons are invited to submit their comments in writing (preferably in quadruplicate and identified with the Hearing Clerk docket number found in brackets in the heading of this document) regarding this proposal on or before November 24, 1978. Such comments should be addressed to the Office of the Hearing Clerk (HFA-305), Food and Drug Administration, Room 4-65, 5600 Fishers Lane, Rockville, Md. 20857, and may be accompanied by a supporting memorandum or brief. Comments replying to comments may also be submitted on or before December 26, 1978. Comments may be seen in the above office between 9 a.m. and 4 p.m., Monday through Friday.

In accordance with Executive Order 12044, the economic effects of this proposal have been carefully analyzed, and it has been determined that the proposed rulemaking does not involve major economic consequences as defined by that order. A copy of the regulatory analysis assessment supporting this determination is on file with the Hearing Clerk, Food and Drug Administration.

Dated: August 8, 1978.

SHERWIN GARDNER,
Acting Commissioner of Food and Drugs.

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