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Dockets Management
Food and Drug Administration, rm 1-23
12420 Parklawn Dr.
Rockville, MD 20857

Subject: Supplement to submission of a Proposed Amendment to Sunscreen Drug Products for Over-the-Counter Human Use; Final Monograph; Rule, 21 CFR Part 352, Subpart D-Testing Procedures, §352.71 Light Sources (solar simulator); Docket number 78N-0038, CP 12 Rapid Precision Testing Laboratories Vol#: 130 Received June 21, 1999 and docket entered June 22, 1999.

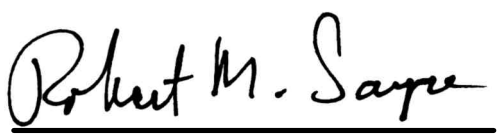
Sirs: This is to advise that the COLIPA Standard for Solar Simulators permits excessive variability of SPF values for certain sunscreen products and could result in confusion to sunscreen users. In my earlier submission of June 18, 1999, I suggested that the COLIPA Standard for Solar Simulators be adopted. Now I must suggest that the previously recommended acceptance range limits of the standard should be narrowed.

The proposed narrowing of the spectral limits for solar simulators would provide a much needed reduction in SPF variability of sunscreen standard reference formulas and consequently limit the variability of SPFs on product labels due to interlaboratory differences in the specific solar simulators used for testing. The current and proposed ranges are:

COLIPA STANDARD	
CURRENT	**NOW PROPOSED**
%COLIPA Effective Irradiance	**% Effective Irradiance**
<290nm (<1.0%)	**<290nm (<0.1%)**
290nm-310nm (46.0%-67.0%)	**290nm-310nm (56.0%-67.0%)**
290nm-320nm (80.0%-91.0%)	**290nm-320nm (86.0%-91.0%)**
290nm-330nm (86.5%-95.0%)	**290nm-330nm (91.0%-95.0%)**
290nm-340nm (90.5%-97.0%)	**290nm-340nm (94.0%-97.0%)**
290nm-350nm (93.5%-99.0%)	**290nm-350nm (97.0%-98.5%)**

The basis for this recommendation follows on the next 5 pages.

Thank you.



Robert M. Sayre, Ph.D.

Basis for recommendations:

By definition we know that a SPF 2 product attenuates 50% and transmits 50% of the erythemic effective radiation impinging upon it in an SPF test while an SPF 20 product attenuates 95% and transmits 5% of the erythemically effective radiation available.

The COLIPA standard for solar simulators provides a series of wavelength regions such as 290-320 nm with a range of amounts of erythemic effective radiation that can be emitted within the limits. This is expressed as a range of erythemic effective radiation as percentages. The remaining fraction beyond the limit is transmitted.

This then allows us to understand specifically what each limit may mean to an SPF test if a product blocked all radiation within the region, as if a perfect cut-off or blocking filter were employed. For example, the limit for 290-310 nm requires between 46% and 67% erythemic effectiveness, if all radiation were blocked within this region then between 54% and 33% of the erythemic effective radiation would be transmitted at wavelengths greater than 320 nm.

This allows us to say that if such a theoretical 310 nm blocking filter were used in a SPF test, for the solar simulator with the minimum of only 46% erythemic effective radiation in the blocked range, the SPF of a filter transmitting the remaining 54% would be 1.9. Whereas for the solar simulator with the maximum of 67% erythemic effective radiation in the blocked range, the SPF of the filter transmitting the remaining 33% at wavelengths longer than 320 nm, the SPF would be 3.0.

This computation can be done at each limit providing a minimum and maximum SPF possible for that limit's cutoff filter. If one imagines a solar simulator that then complies to the standard at either the lower minimum level or upper maximum level, the SPF possible for an ideal cutoff filter for each limit is calculated in the Table below:

COLIPA STANDARD %COLIPA Effective Irradiance	MINIMUM SPF	MAXIMUM SPF
<290nm (<1.0%)	NA	NA
290nm-310nm (46.0%-67.0%)	1.9	3.0
290nm-320nm (80.0%-91.0%)	5.0	11.1
290nm-330nm (86.5%-95.0%)	7.4	20.0
290nm-340nm (90.5%-97.0%)	10.5	33.3
290nm-350nm (93.5%-99.0%)	15.4	100.0

The potential deviations for solar simulators at either the maximum or minimum if the 290-310 range is not really striking. A factor of two difference can hardly be cause for concern. However, for the last range, 290-350 nm, the potential differences in SPF for solar simulators meeting the minimal limits of the standards and those meeting the maximum limits is cause for concern.

The 290-350 nm limit provides an SPF of only 15.4 for complete blockage of all wavelengths shorter than 350 nm for one COLIPA compliant solar simulator but an SPF of 100 for another filtered appropriately. Such a range would clearly cause many to suggest that too

much material may have been tested providing such a misleading result. In this case the filtration of the solar simulators absolutely required different results.

Various individuals have attempted to interpret such differences statistically as random uncertainties. Such testing differences cannot be handled statistically since they belong to the class of systematical uncertainties. No amount of testing or analysis can ever resolve such differences. Any average and for that matter standard deviation depends purely on the number of tests run with each solar simulator. No amount of standardization can ever cause both instruments to produce the same results.

The concerns of my theoretical arguments have been supported by several published studies that demonstrate significant SPF differences between solar simulators used for testing see: Uhlmann B, Mann T, Gers-Berlag H, Alert D, and Sauermann G. "Consequences for sun protection factors when solar simulators deviate from the spectrum of the sun," *Int J Cosmetic Sci, 18:* 13-24, 1996. In this paper two solar simulators were chosen. The first solar simulator just exceeded the COLIPA standard at the high side and the other solar simulator just exceeded the COLIPA standard on the low side. Two products were tested using both solar simulators. One nominally an SPF 4 and the other nominally an SPF 15. The results are summarized in the Table below:

Solar Simulator/SPF	SPF 4	SPF 15
COLIPA LOW	2.61 ± 0.275	7.21 ± 1.704
COLIPA HIGH	4.84 ± 0.809	19.4 ± 5.801

The SPF 15 product showing a range of SPFs varying by a factor of 3 (SPF 7.21 to 19.4) resembles the variability predicted by the range allowed within the COLIPA standard for 290 – 330 nm (86% - 95%) with a predicted SPF range of SPFs 7.4 – 20.0. Both limits reported, for the test solar simulators and test product, would appear statistically consistent with the limits predicted for solar simulators thusly filtered.

The other paper for consideration is Sayre RM, Stanfied J, Bush AJ, and Lott DL. "Sunscreen Standards Tested With Differently Filtered Solar Simulators, Photodermatol Photoimmunol Photomed, (in press). In this paper two solar simulators both meeting the COLIPA Standard were use to test two SPF 15 sunscreen standards (P2 & P3). The results are shown in the table, below:

Solar Simulator / SPF	P2 Standard	P3 Standard
COLIPA LOW Solar Simulator	10.01 ±1.09	9.35 ±2.96
COLIPA HIGH Solar Simulator	14.88 ±1.91	13.88 ±1.74

The results of each Standard Sunscreen are statistically different depending upon which solar simulator was used to test them. Furthermore, the results when using the COLIPA low solar simulator are outside the range of SPFs that COLIPA says should be obtained for the P3 sunscreen standard. A serious question then arises, what value are the test acceptance ranges for a sunscreen standard formula, if a solar simulator meets the standard must produce SPFs outside the accepted ranges?

COLIPA has published limited results on three different ring tests involving either six or seven laboratories testing a series of three sunscreen standards and one commercial SPF 20-25 product. See Appendix XI: Summary of SPF ring tests: SPF of standards, pp 60-1, in COLIPA Task Force, COLIPA Sun Protection Factor Test Method, Brussels, The European Cosmetic, Toiletry and Perfumery Association –COLIPA, 1994. It should be noted there are probably not three independent ring test but only two as one laboratory was deemed not to have applied the product correctly and consequently retested the set of formulas and another was added. COLIPA notes that this produced greater consistency of
The ring tests apparently utilized COLIPA compliant solar simulators using a testing protocol provided in the COLIPA document:

COLIPA LABORATORY RING TESTS -- COMPARISON

Product	RingTest	Mean	Low Lab	High Lab	Range
P1 DIN STD	R1 (n=6)	4.3	3.6	5.7	58%
	R2 (n=6)	3.9	2.6	4.6	77%
	R3 (n=7)	4.2	3.9	4.6	18%
P2 CTFA SPF-15 STD	R1	12.8	11.0	15.2	38%
	R2	12.0	5.8	14.1	143%
	R3	12.7	11.1	14.1	27%
P3 COLIPA SPF-15 STD	R1	14.4	10.6	22.0	108%
	R2	14.7	8.3	18.2	119%
	R3	15.5	14.2	18.2	28%
P4 SPF 20-25 PRODUCT	R1	22.2	12.6	33.8	168%
	R2	21.3	10.0	34.0	240%
	R3	22.4	11.3	33.9	200%

The averages of all laboratories for each product would appear to be remarkably consistent. All laboratories reasonably reproduced in each ring test the SPF of the P1 din standard. Testing of the older CTFA SPF 15 standard produced a wider range of results in the ring tests with the low laboratory reporting an SPF of only 5.8 for this standard and the high laboratory an SPF of 15.2 (a range from low to high of approximately 200%). Tests on the current, slightly higher, COLIPA P3 standard, in the ring tests ranged from a low average SPF of 8.3 to a high reported average of 22.0. This also gives a minimum to maximum range of approximately 200%.

Perhaps the most interesting result was for the SPF 20-25 commercial product. In the ring tests the low response is 10.0 with the high reported average of each ring test being remarkably close to the maximum 34.0 reported. The minimum to maximum range is approximately 250%. Clearly there is little agreement on the testing of standards and even less when an actual midrange SPF product is in fact tested. The product test would suggest that one laboratory's tests would require the product to be labeled less than SPF 10, while the high laboratory would permit this product to be labeled SPF 30 or SPF 30+. This is clearly not acceptable.

While the COLIPA task force discusses the statistics involved in testing, their own description of the ring tests suggests that the variability reported is purely random. Our analysis and subsequent studies demonstrate that much of this supposedly random variability in SPF testing between laboratories may be due to systematic differences in solar simulator filtration permitted by the regrettably wide ranges of the COLIPA standard.

Unless the range of acceptable solar simulators is changed a legitimate conclusion is that the SPF test and product labeling based upon it may of limited value to the consumer who may not be able to count on a particular level of protection being consistently delivered. Should the FDA want to use a solar simulator standard like that based upon the COLIPA Standard, the acceptable ranges need to be narrowed considerably. Based upon this analysis, I would propose the following:

CURRENT COLIPA STANDARD %COLIPA Effective	CURRENT MIN SPF	CURRENT MAX SPF	PROPOSED NARROWED STANDARD % Effective Irradiance	PROPOSED MIN SPF	PROPOSED MAX SPF
<290nm **(<1.0%**)	Unchanged	Unchanged	<290nm (**<0.1%)**	Changed	Changed
290nm-310nm (**46.0%-67.0%)**	1.9	3.0	290nm-310nm (**56.0%-67.0%)**	2.3	3.0
290nm-320nm (**80.0%-91.0%)**	5.0	11.1	290nm-320nm (**86.0%-91.0%)**	7.1	11.1
290nm-330nm (**86.5%-95.0%)**	7.4	20.0	290nm-330nm (**91.0%-95.0%)**	11.1	20.0
290nm-340nm **(90.5%-97.0%)**	10.5	33.3	290nm-340nm (**94.0%-97.0%)**	16.7	33.3
290nm-350nm (**93.5%-99.0%**)	15.4	100.0	290nm-350nm (**97.0%-98.5%)**	33.3	66.7

Narrowing the acceptance ranges by more than 50% correspondingly decreased the SPF range by somewhat less.

Several comments on the impact to the sunscreen industry may need consideration: In the US the majority of sunscreen manufacturing companies and contract testing laboratories use Solar Light Company single port solar simulators. I have examined 40 single port solar simulators, in eight US and Canadian laboratories, measured in the past 12 months. The result is that 7 would require replacing old filters to meet the proposed changes in the standard. The low number ~20% of solar simulators requiring new filtering, In part, is due to the fact that the quality control procedures for filters supplied by Solar Light Company virtually assures that all single port solar simulators are nearly optically identical and the quality maintenance procedures of the testing laboratories. I understand that most testing laboratories periodically replace older filters to maintain the maximum quality of their testing services.

What does this mean?

1. Clearly the COLIPA Standard for solar simulators allows for widely divergent SPF values depending upon the filtration of solar simulators.
2. The expected SPF of sunscreen standards must vary as spectrum of the solar simulator varies.
3. The acceptable range of SPFs of sunscreen standards needs to be sufficiently broad to encompass all acceptable solar simulators
4. The acceptable ranges in a revised ‘COLIPA’ standard need to be narrowed
5. Based upon current COLIPA limits, the same SPF label on products from different manufactures may not provide the same degree of protection.