C T F A

THE COSMETIC, TOILETRY, AND FRAGRANCE ASSOCIATION

July 20, 1998

E. EDWARD KAVANAUGH
PRESIDENT

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John D. Lipnicki
Division of OTC Drug Products (HFD-560)
Center for Drug Evaluation and Research
Food and Drug Administration
9201 Corporate Boulevard
Rockville, Maryland 20850

Re: Docket No. 78N-0038

Dear Mr. Lipnicki:

Recently you requested certain materials that were part of CTFA's submissions in 1992 and 1994 regarding the CTFA High SPF Standard. Those materials were submitted to the docket on November 17, 1992 and May 5, 1994 respectively, and we are pleased to provide you with additional copies of those materials (attached).

In addition, we are submitting a method of preparation and a method of analysis for the High SPF Standard (SPF 15) formulation submitted by CTFA to FDA. This information is necessary to properly prepare the formulation for use in SPF testing.

Please feel free to contact us if you need further information.

Sincerely,

Thomas J. Donegan, Jr.
Vice President-Legal and General Counsel

enclosures

78N-0038

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CTFA HIGH SPF STANDARD:

SUPPLEMENT TO FINAL REPORT

ORIGINAL REPORT

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Representing the personal care products industry

E. Edward Kavanaugh
President

HIGH SPF STANDARD EVALUATION

HIGH SPF TASK FORCE

COSMETIC, TOILETRY, AND FRAGRANCE ASSOCIATION

OCTOBER 1992

The Cosmetic, Toiletry, and Fragrance Association
1101 17th Street, N.W. • Suite 300 • Washington, D.C. 20036 • (202) 331-1770 • Fax (202) 331-1969

Introduction and Objectives

As a project of the CTFA High SPF Task Force, seven laboratories determined the static sun protection factor (SPF) of 2 proposed SPF 15 control sunscreen formulations and the homosalate standard sunscreen (HMS) described in the FDA Proposed Monograph on OTC Sunscreens[1]. Objectives were to determine interlaboratory variability of SPF for the formulations and to select a formulation to serve as a high SPF control.

Materials and Methods

Formulations contained the following active ingredients:

1. A: 8 percent octyldimethyl PABA, 5 percent ethylhexyl p-methoxycinnamate, and 4 percent oxybenzone

2. B: 7 percent octyldimethyl PABA and 3 percent oxybenzone

3. HMS: 8 percent homosalate

Formulation A was provided by Van Dyk Company, Belleville, NJ, and Formulations B and HMS were provided by Schering-Plough HealthCare Products, Memphis, TN.

Participating laboratories included the following:

Avon Products
Suffern, NY

BioSearch Laboratories
Philadelphia, PA

Bristol-Myers Squibb
Buffalo, NY

Harrison Research Laboratories
Maplewood, NJ

Hill Top Laboratories
Cincinnati, OH

Johnson & Johnson Consumer Products
Skillman, NJ

Schering-Plough HealthCare Products
Memphis, TN

Testing procedures were those outlined in the FDA Proposed Monograph on OTC Sunscreens[1]: subjects were males and females with skin types I, II and III; sunscreens were applied to the mid-back with an application density of 2 mg/cm^2; ultraviolet doses were given in 25 percent increments and ultraviolet sources were xenon arc lamp solar simulators with UG-11 or UG-5 visible light blocking filters and WG320 UVC-blocking filters. Spectral calibrations had been performed for each lamp and each met the requirements proposed by Sayre, et al[2].

Data were analyzed by ANOVA and Tukey's Honesty Significant Difference (HSD) Test[3]. Statistically significant differences were defined as those having a p-value ≤ 0.05 and clinically significant differences were defined as those greater than or equal to one exposure increment (25 percent).

Results

A total of 153 subjects yielded SPF values for one or more formulations and all subjects provided written informed consent.

Results for all subjects are summarized in Table 1. The mean SPF values were 16.5, 16.3 and 4.4 for formulations A, B and HMS, respectively. Individual subject data for each laboratory are presented in Table 2.

One laboratory submitted SPF results that were significantly lower than those of the other laboratories. The lower SPF values were attributed to excessive rubbing during product application[4] and the test was repeated for all 3 formulations. In the following analyses the original data were replaced with data from the repeated tests.

Results for HMS were consistent with those reported earlier[1].

None of the differences observed between A and B or among laboratories were considered clinically significant. That is, the differences were small in terms of perceptible degree of protection.

A repeated measures analysis of variance (ANOVA) was performed to evaluate formulation (A and B) and laboratory effects on SPF. In this analysis data were omitted for 13 subjects who did not have SPF values for both A and B. Laboratory effects were significant ($p=0.035$) but formulation effects ($p=0.635$) and the formulation-laboratory interaction ($p=0.794$) were not significant.

ANOVAs were also performed for each formulation to examine differences among laboratories. These analyses showed significant differences among laboratories for A ($p=0.046$) and HMS ($p=0.023$), but not for B ($p=0.158$). To further examine laboratory differences, Tukey's HSD test was performed for A and HMS. For A, significant differences were observed between laboratories 2 and 5 ($p=0.046$) and for HMS significant differences were observed between laboratories 2 and 5 ($p=0.012$) and laboratories 4 and 5 ($p=0.037$).

Conclusions

The consensus of the Task Force was that Formulation B was preferable over Formulation A as an SPF 15 control due to its less complex formula and slightly more consistent results.

It was concluded that Formulation B is an appropriate SPF 15 control sunscreen formulation.

It was also concluded that different laboratories, operating under one protocol, can obtain valid, reproducible results when testing high SPF Sunscreens.

REFERENCES

1. US Food and Drug Administration. Sunscreen drug products for over-the-counter human use. Federal Register 1978; 43:38206-69.

2. Sayre RM, Cole C, Bilheimer W, Stanfield J, Ley R. Spectral comparison of solar simulators and sunlight. Photodermatol Photoimmunol Photomed 1990; 7:159-65.

3. Kirk RE. Experimental Design. Belmont CA, Brooks Cole 1982.

4. Sayre RM, Powell J, Rheins LA. Product application technique alters the sun protection factor. Photodermatol Photoimmunol Photomed 1991; 8:222-4.

Table 1. POOLED SPF RESULTS FOR ALL LABORATORIES

	A	B	HMS
Mean SPF	16.5	16.3	4.4
Std Dev	3.64	3.43	0.84
Std Err	0.30	0.28	0.07
% SEM	1.8	1.7	1.6
n	147	146	144
Max Lab Mean	18.5	18.4	5.0
Min Lab Mean	15.6	15.3	4.1

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TABLE 2. INDIVIDUAL SUBJECT SPF DATA BY LABORATORY

	Lab 1			Lab 2			Lab 3			Lab 4 (Original)			Lab 4 (Repeat)			Lab 5			Lab 6			Lab 7		
	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS
	23.4	18.8	5.0	18.8	18.8	5.0	15.0	15.0	5.0	12.1	15.1	4.0	23.4	23.4	6.3	15.0	20.0	4.0	19.0	15.2	5.3	18.7	15.0	5.0
	19.5	19.5	4.0	12.2	15.0	4.0	18.8	18.8	5.0	9.6	9.6	4.0	15.1	15.1	4.0	23.5	23.5	5.0	15.2	15.2	4.2	12.1	15.1	4.0
	15.0	15.0	4.0	18.5	23.1	4.0	15.0	15.0	4.0	12.0	12.0	4.0	23.4	18.8	6.3	18.8	18.8	5.0	15.1	18.9	4.2	15.0	18.8	5.0
	23.4	18.7	5.0	18.8	18.8	5.0	18.8	18.8	4.0	12.0	12.0	4.0	15.0	18.8	3.2	9.6	9.6	3.2	15.2	19.0	5.3	9.7	9.7	5.0
	15.0	18.7	5.0	15.0	12.0	4.0	15.0	18.8	5.0	18.8	12.0	4.0	15.0	15.0	4.0	23.5	23.5	5.0	23.8	19.0	4.2	23.4	15.0	5.0
	15.0	15.0	3.2		19.5	5.2	15.0	18.8	5.0	15.0	12.1	4.0	15.0	15.0	4.0	18.8	23.5	5.0	12.2	9.7	3.4	15.0	12.0	4.0
	15.0	23.4	4.0	11.5	11.5	3.1	12.0	15.0	3.2	12.0	12.0	4.0	15.0	23.4	5.0	18.5	23.1	3.9	12.1	15.2	4.2	12.0	15.0	3.2
	19.5	19.5	4.0	18.8	18.8	4.0	15.0	15.0	5.0	18.9	15.1	4.0	15.0	15.0	3.2	18.8	18.8	6.2	19.1	12.2	3.4	9.6	9.6	3.2
	15.0	12.0	3.2	18.5	15.0	4.0	15.0	15.0	4.0	15.0	15.0	4.0	15.1	12.1	3.2	18.8	23.5	3.2	15.1	12.0	3.3	12.0	23.4	6.2
	14.6	14.6	4.0	15.0	15.0	4.0	12.0	18.8	5.0	15.0	15.0	4.0	15.0	15.0	4.0	23.4	18.8	6.3	15.1	15.1	3.3	9.7	12.1	4.0
	15.0	15.0	5.0	12.0	12.0	3.2	12.0	12.0	4.0	12.0	12.0	3.2	15.0	15.0	4.0	15.0	18.8	5.0	15.3	15.3	4.2	23.4	18.8	5.0
	18.4	15.1	4.0	18.8	20.0	5.0	18.8	18.8	5.0.	15.0	12.0	3.2	18.8	18.8	4.0	15.0	15.0	6.3	15.1	15.1		15.1	15.1	3.2
	15.0	18.7	5.0	12.0	12.0	3.2	15.0	18.8	5.0	15.0	15.0	5.0	18.8	18.8	4.0	15.0	15.0	5.0		15.2	5.2	18.8	23.4	6.2
	18.4	14.7	3.7	18.8	23.4	5.0	18.8	15.0	5.0	12.0	12.0	4.0	15.0	15.0	4.0	18.8	12.0	5.0	15.3	15.3	4.2	18.8	18.8	4.0
	23.4	18.7	5.0	12.2	15.0	4.0	15.0	15.0	4.0	18.8	15.0	4.0	12.0	15.0	4.0	12.0	12.0	5.0	15.2	15.2	4.2	18.8	29.3	5.0
	15.0	12.0	4.0	15.0	15.0	5.0	18.8	15.0	4.0	12.0	15.0	4.0	12.0	15.0	3.2	18.8	18.8	5.0		15.1	4.2	15.1	12.1	3.2
	18.7	18.7	4.0	18.8	15.0	5.0	18.8	12.0	3.2	15.0	15.0	4.0	9.6	12.0	3.2	18.8	18.8	5.0		15.2	4.2	18.7	18.7	5.0
	15.0	18.7	5.0	15.0	15.0	3.2	15.0	15.0	3.2	18.8	15.0	4.0	23.4	15.0	4.0	23.1	23.1	6.2		18.9	3.4	12.0	23.4	
	14.8	14.8	3.1	12.0	12.0	4.0	15.0	15.0	5.0	12.0	12.0	3.2	15.0	23.4	5.0	18.8	18.8	5.0		19.1	6.5	12.0	12.1	4.0
	15.0	12.0	4.0	15.0	12.2	3.3	18.8	18.8	5.0	12.0	12.0	3.2	12.0	15.0	5.0	23.5	15.0	5.0		15.2	4.2	15.0	15.0	5.0
				15.0	12.2	3.3													15.1		4.2	18.9	15.1	3.2
				9.8	12.0	5.0													15.2			18.8	12.0	4.0
				15.0	15.0	3.2													15.2			18.8	18.8	
																			13.9			15.0	18.8	
																			15.3					
																			15.2					
Mean SPF	17.2	16.7	4.2	15.3	15.6	4.1	15.9	16.2	4.4	14.2	13.2	3.9	15.9	16.7	4.2	18.4	18.5	5.0	15.6	15.6	4.3	15.7	16.5	4.4
Std Dev	3.18	3.07	0.66	3.02	3.63	0.75	2.43	2.34	0.70	2.84	1.73	0.42	3.84	3.46	0.92	3.91	4.27	0.89	2.52	2.50	0.80	4.04	4.87	0.94
Std Err	0.71	0.69	0.15	0.64	0.76	0.16	0.54	0.52	0.16	0.64	0.39	0.09	0.86	0.77	0.21	0.88	0.95	0.20	0.56	0.56	0.18	0.82	0.99	0.20
% SEM	4.1	4.1	3.5	4.2	4.9	3.8	3.4	3.2	3.5	4.5	2.9	2.4	5.4	4.6	4.9	4.8	5.1	4.0	3.6	3.6	4.2	5.3	6.0	4.6
n	20	20	20	22	23	23	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	24	24	21

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ABSTRACT

Seven laboratories determined the static SPF values of 2 proposed SPF 15 control sunscreen formulations (A and B) and the homosalate standard sunscreen (HMS) in a total of 153 subjects.

Formulation A contained 8 percent octyldimethyl PABA, 5 percent ethylhexyl p-methoxycinnamate and 4 percent oxybenzone and Formulation B contained 7 percent octyldimethyl PABA and 3 percent oxybenzone.

For A the mean SPF was 16.5 (n=147, S.E.= 1.8% of the mean), for B the mean SPF was 16.3 (n=146, S.E.= 1.7% of the mean) and for HMS the mean SPF was 4.4 (n=144, S.E.= 1.6% of the mean).

Results for all laboratories placed both A and B in the SPF 15 product category, with laboratory means ranging from 15.6 to 18.5 and from 15.3 and 18.4, for A and B, respectively. Likewise HMS was placed in the SPF 4 category, with means ranging from 4.1 to 5.0. Differences among laboratories were not considered clinically significant, although they were statistically significant for A (p=0.046) and HMS (p=0.023). Differences between A and B were not significant (p=0.653).

Formulation B was preferred over A due to its less complex formula and slightly more consistent results. It was concluded that B is an appropriate SPF 15 control sunscreen and that different Laboratories, operating under one protocol, can obtain valid reproducible results when testing high SPF Sunscreens.

Introduction and Objectives

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Formulations contained the following active ingredients:

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Results for HMS were consistent with those reported earlier[1].

None of the differences observed between A and B or among laboratories were considered clinically significant. That is, the differences were small in terms of perceptible degree of protection.

A repeated measures analysis of variance (ANOVA) was performed to evaluate formulation (A and B) and laboratory effects on SPF. In this analysis data were omitted for 13 subjects who did not have SPF values for both A and B. Laboratory effects were significant ($p=0.035$) but formulation effects ($p=0.635$) and the formulation-laboratory interaction ($p=0.794$) were not significant.

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Conclusions

The consensus of the Task Force was that Formulation B was preferable over Formulation A as an SPF 15 control due to its less complex formula and slightly more consistent results.

It was concluded that Formulation B is an appropriate SPF 15 control sunscreen formulation.

It was also concluded that different laboratories, operating under one protocol, can obtain valid, reproducible results when testing high SPF Sunscreens.

REFERENCES

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Table 1. POOLED SPF RESULTS FOR ALL LABORATORIES

	A	B	HMS
Mean SPF	16.5	16.3	4.4
Std Dev	3.64	3.43	0.84
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Max Lab Mean	18.5	18.4	5.0
Min Lab Mean	15.6	15.3	4.1

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TABLE 2. INDIVIDUAL SUBJECT SPF DATA BY LABORATORY

	Lab 1			Lab 2			Lab 3			Lab 4 (Original)			Lab 4 (Repeat)			Lab 5			Lab 6			Lab 7		
	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS	A	B	HMS
	23.4	18.8	5.0	18.8	18.8	5.0	15.0	15.0	5.0	12.1	15.1	4.0	23.4	23.4	6.3	15.0	20.0	4.0	19.0	15.2	5.3	18.7	15.0	5.0
	19.5	19.5	4.0	12.2	15.0	4.0	18.8	18.8	5.0	9.6	9.6	4.0	15.1	15.1	4.0	23.5	23.5	5.0	15.2	15.2	4.2	12.1	15.1	4.0
	15.0	15.0	4.0	18.5	23.1	4.0	15.0	15.0	4.0	12.0	12.0	4.0	23.4	18.8	6.3	18.8	18.8	5.0	15.1	18.9	4.2	15.0	18.8	5.0
	23.4	18.7	5.0	18.8	18.8	5.0	18.8	18.8	4.0	12.0	12.0	4.0	15.0	18.8	3.2	9.6	9.6	3.2	15.2	19.0	5.3	9.7	9.7	5.0
	15.0	18.7	5.0	15.0	12.0	4.0	15.0	18.8	5.0	18.8	12.0	4.0	15.0	15.0	4.0	23.5	23.5	5.0	23.8	19.0	4.2	23.4	15.0	5.0
	15.0	15.0	3.2		19.5	5.2	15.0	18.8	5.0	15.0	12.1	4.0	15.0	15.0	4.0	18.8	23.5	5.0	12.2	9.7	3.4	15.0	12.0	4.0
	15.0	23.4	4.0	11.5	11.5	3.1	12.0	15.0	3.2	12.0	12.0	4.0	15.0	23.4	5.0	18.5	23.1	3.9	12.1	15.2	4.2	12.0	15.0	3.2
	19.5	19.5	4.0	18.8	18.8	4.0	15.0	15.0	5.0	18.9	15.1	4.0	15.0	15.0	3.2	18.8	18.8	6.2	19.1	12.2	3.4	9.6	9.6	3.2
	15.0	12.0	3.2	18.5	15.0	4.0	15.0	15.0	4.0	15.0	15.0	4.0	15.1	12.1	3.2	18.8	23.5	3.2	15.1	12.0	3.3	12.0	23.4	6.2
	14.6	14.6	4.0	15.0	15.0	4.0	12.0	18.8	5.0	15.0	15.0	4.0	15.0	15.0	4.0	23.4	18.8	6.3	15.1	15.1	3.3	9.7	12.1	4.0
	15.0	15.0	5.0	12.0	12.0	3.2	12.0	12.0	4.0	12.0	12.0	3.2	15.0	15.0	4.0	15.0	18.8	5.0	15.3	15.3	4.2	23.4	18.8	5.0
	18.4	15.1	4.0	18.8	20.0	5.0	18.8	18.8	5.0.	15.0	12.0	3.2	18.8	18.8	4.0	15.0	15.0	6.3	15.1	15.1		15.1	15.1	3.2
	15.0	18.7	5.0	12.0	12.0	3.2	15.0	18.8	5.0	15.0	15.0	5.0	18.8	18.8	4.0	15.0	15.0	5.0		15.2	5.2	18.8	23.4	6.2
	18.4	14.7	3.7	18.8	23.4	5.0	18.8	15.0	5.0	12.0	12.0	4.0	15.0	15.0	4.0	18.8	12.0	5.0	15.3	15.3	4.2	18.8	18.8	4.0
	23.4	18.7	5.0	12.2	15.0	4.0	15.0	15.0	4.0	18.8	15.0	4.0	12.0	15.0	4.0	12.0	12.0	5.0	15.2	15.2	4.2	18.8	29.3	5.0
	15.0	12.0	4.0	15.0	15.0	5.0	18.8	15.0	4.0	12.0	15.0	4.0	12.0	15.0	3.2	18.8	18.8	5.0		15.1	4.2	15.1	12.1	3.2
	18.7	18.7	4.0	18.8	15.0	5.0	18.8	12.0	3.2	15.0	15.0	4.0	9.6	12.0	3.2	18.8	18.8	5.0		15.2	4.2	18.7	18.7	5.0
	15.0	18.7	5.0	15.0	15.0	3.2	15.0	15.0	3.2	18.8	15.0	4.0	23.4	15.0	4.0	23.1	23.1	6.2		18.9	3.4	12.0	23.4	
	14.8	14.8	3.1	12.0	12.0	4.0	15.0	15.0	5.0	12.0	12.0	3.2	15.0	23.4	5.0	18.8	18.8	5.0		19.1	6.5	12.0	12.1	4.0
	15.0	12.0	4.0	15.0	12.2	3.3	18.8	18.8	5.0	12.0	12.0	3.2	12.0	15.0	5.0	23.5	15.0	5.0		15.2	4.2	15.0	15.0	5.0
				15.0	12.2	3.3													15.1		4.2	18.9	15.1	3.2
				9.8	12.0	5.0													15.2			18.8	12.0	4.0
				15.0	15.0	3.2													15.2			18.8	18.8	
																			13.9			15.0	18.8	
																			15.3					
																			15.2					
Mean SPF	17.2	16.7	4.2	15.3	15.6	4.1	15.9	16.2	4.4	14.2	13.2	3.9	15.9	16.7	4.2	18.4	18.5	5.0	15.6	15.6	4.3	15.7	16.5	4.4
Std Dev	3.18	3.07	0.66	3.02	3.63	0.75	2.43	2.34	0.70	2.84	1.73	0.42	3.84	3.46	0.92	3.91	4.27	0.89	2.52	2.50	0.80	4.04	4.87	0.94
Std Err	0.71	0.69	0.15	0.64	0.76	0.16	0.54	0.52	0.16	0.64	0.39	0.09	0.86	0.77	0.21	0.88	0.95	0.20	0.56	0.56	0.18	0.82	0.99	0.20
% SEM	4.1	4.1	3.5	4.2	4.9	3.8	3.4	3.2	3.5	4.5	2.9	2.4	5.4	4.6	4.9	4.8	5.1	4.0	3.6	3.6	4.2	5.3	6.0	4.6
n	20	20	20	22	23	23	20	20	20	20	20	20	20	20	20	20	20	20	20	20	20	24	24	21

CTFA HIGH SPF STANDARD:

SUPPLEMENT TO FINAL REPORT

LETTER ROM DR. GILBERTSON

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NOV 30 1992

E. Edward Kavanaugh
President
The Cosmetic, Toiletry, and Fragrance Association
1101 17th Street, N.W.
Suite 300
Washington, DC 20036-4702

Re: Docket No. 78N-0038
Comment No. C111

Dear Mr. Kavanaugh:

Thank you for your letter dated November 17, 1992 regarding the standardized testing of high SPF sunscreens and the development of generally recognized testing methodologies for UVA sunscreens. I appreciate your Association's continuing interest in these matters.

We have done a preliminary review of the information you provided. In order to fully evaluate your data, our Office will need additional information, i.e., copies of all cited material, the complete formulation of each proposed control standards A and B, and all raw data results for each individual subject (including the low SPF results that were not used because of "excessive rubbing" and the data from the 13 subjects that was not included in the final analyses because the subjects did not have SPF values for both test formulations). As you may know, these raw data should be purged of individual subject's names and initials used to identify the subjects. That information may be submitted now or following publication of the tentative final monograph.

Regarding my request that CTFA develop an appropriate, standardized, validated testing procedure for measuring an OTC sunscreen drug product's ability to protect against UVA radiation, I appreciate your efforts to achieve a consensus methodology. I am hopeful that several UVA testing procedures will be submitted to the agency after the tentative final monograph for OTC sunscreen drug products is published. The agency will evaluate all methods submitted and choose an

appropriate UVA testing method for the OTC sunscreen drug product's monograph.

Thank you again for your continuing assistance.

Sincerely yours,

William E. Gilbertson, Pharm.D.
Director
Monograph Review Staff
Office of OTC Drug Evaluation
Center for Drug Evaluation and Research

CTFA HIGH SPF STANDARD:

SUPPLEMENT TO FINAL REPORT

INDIVIDUAL LAB DATA AND OVERALL RESULTS

CTFA High SPF Standard: Supplement to Final Report										
Lab 1 Subject Data							**Lab 2 Subject Data**			
Subject	Initial	Final	SPF				(Not Available)			
Number	MED	MED	A	B	C					
1	12	12	23.40	18.80	5.00					
2	12	12	19.50	19.50	4.00					
3	19	19	15.00	15.00	4.00					
4	12	12	23.40	18.70	5.00					
5	19	19	15.00	18.70	5.00					
6	15	15	15.00	23.40	4.00					
7	19	19	15.00	15.00	3.20					
8	15	19	19.50	19.50	4.00					
9	24	30	15.00	12.00	3.20					
10	12	12	15.00	15.00	5.00					
11	19	24	14.60	14.60	4.00					
12	15	19	18.40	15.10	4.00					
13	19	19	15.00	18.70	5.00					
14	15	19	18.40	14.70	3.70					
15	12	12	23.40	18.70	5.00					
16	19	19	15.00	12.00	4.00					
17		8	18.70	18.70	4.00					
18	24	19	15.00	18.70	5.00					
19	19	24	14.80	14.80	3.10					
20	12	12	15.00	12.00	4.00					
Average	16.47	17.20	17.21	16.68	4.21					
SD	3.99	5.32	3.18	3.07	0.66					
n	19	20	20	20	20					

CTFA High SPF Standard: Supplement to Final Report										
Lab 3 Subject Data										
Subject	Age	Sex	Skin	Final	SPF					
Number			Type	MED	A	B	C			
1	45	F	II	10.00	15.00	15.00	5.00			
2	43	F	II	10.00	18.75	18.75	5.00			
3	49	M	I	12.50	15.00	15.00	4.00			
4	39	F	I	8.00	18.75	18.75	4.00			
5	38	M	II	12.50	15.00	18.75	5.00			
6	23	F	II	12.50	15.00	18.75	5.00			
7	62	F	II	12.50	12.00	15.00	3.20			
8	43	F	II	12.50	15.00	15.00	5.00			
9	36	F	III	15.60	15.00	15.00	4.00			
10	53	F	II	12.50	12.00	18.75	5.00			
11	55	F	II	12.50	12.00	12.00	4.00			
12	55	M	I	6.40	18.75	18.75	5.00			
13	49	M	I	8.00	15.00	18.75	5.00			
14	49	F	II	12.50	18.75	15.00	5.00			
15	19	M	II	10.00	15.00	15.00	4.00			
16	33	M	I	8.00	18.75	15.00	4.00			
17	60	M	II	8.00	18.75	12.00	3.20			
18	27	M	I	8.00	15.00	15.00	3.20			
19	24	F	II	15.60	15.00	15.00	5.00			
20	44	F	II	10.00	18.75	18.75	5.00			
Average	42.30			10.88	15.86	16.20	4.43			
SD	12.41			2.62	2.41	2.31	0.70			
n	20			20	20	20	20			

CTFA High SPF Standard: Supplement to Final Report

Lab 4 Original Panel Subject Data								Lab 4 Final Panel Subject Data						
Subject Number	Age	Sex	Final MED	SPF A	B	C		Subject Number	Age	Sex	Final MED	SPF A	B	C
1	37	F	69	12.1	15.1	5		1	55	F	60	>23.4	>23.4	6.3
2	36	F	85	9.6	9.6	4		2	64	F	93	>15.1	>15.1	4
4	39	F	65	12	12	4		6	33	F	48	>23.4	18.8	>6.3
5	27	F	48	12	12	4		9	24	F	60	15	>18.8	3.2
7	35	M	68	18.8	12	4		18	32	F	60	15	15	4
8	47	F	58	15	12.1	4		23	35	F	48	15	15	4
9	25	F	73	12	12	4		24	60	F	60	15	23.4	5
10	38	F	61	18.9	15.1	4		25	45	M	52	15	15	3.2
11	54	F	60	15	15	4		26	58	F	62	15.1	12.1	3.2
12	48	F	52	15	15	4		27	28	F	81	15	15	4
13	33	F	55	12	12	3.2		28	64	F	60	15	15	4
14	48	F	75	15	12	3.2		29	62	F	60	18.8	18.8	4
15	47	F	65	15	15	5		30	22	F	48	18.8	18.8	4
16	23	F	75	12	12	4		39	32	F	70	15	15	4
17	62	F	60	18.8	15	4		31	48	F	60	12	15	4
18	57	F	75	12	15	4		32	28	F	65	12	15	3.2
19	41	F	48	15	15	4		33	42	F	60	9.6	12	3.2
20	29	F	60	18.8	15	4		34	46	F	65	23.4	15	4
22	40	F	75	12	12	3.2		35	27	F	48	15	23.4	5
23	31	F	60	12	12	3.2		36	43	F	60	12	15	5
Average	39.85		64.4	14.2	13.2	3.9			42.4		61.0	15.1	16.3	4.1
SD	10.72		10.0	2.8	1.7	0.5			14.2		11.0	3.1	3.3	0.8
n	20		20	20	20	20			20		20	17	17	19

CTFA High SPF Standard: Supplement to Final Report										
Lab 5 Subject Data										
Subject	Age	Sex	Skin	Initial	Final	SPF				
Number			Type	MED	MED	A	B	C		
1	21	M	II	16	16	15.00	20.00	4.00		
2	20	F	I-II	13	13	23.50	23.50	5.00		
3	22	F	I	10	10	18.80	18.80	5.00		
4	22	F	II	16	20	9.60	9.60	3.20		
5	24	F	I	8	8	23.50	23.50	5.00		
6	18	M	I-II	13	13	18.80	23.50	5.00		
7	18	M	II	16	13	18.50	23.10	3.90		
8	19	M	II	16	16	23.40	<9.6	5.00		
9	22	F	I-II	13	13	18.80	18.80	6.20		
10	48	F	III	13	13	18.80	23.50	3.20		
11	41	F	II	16	16	23.40	18.80	6.30		
12	31	F	II	16	16	15.00	18.80	5.00		
13	22	F	II	16	16	15.00	15.00	6.30		
14	21	F	I-II	13	13	15.00	15.00	5.00		
15	21	M	II	16	16	18.80	12.00	5.00		
16	19	F	I-II	13	13	12.00	12.00	5.00		
17	18	F	I-II	13	13	18.80	18.80	5.00		
18	22	F	I-II	13	13	>23.5	>23.5	>6.2		
19	21	F	II	16	16	18.80	18.80	5.00		
20	19	F	II	16	13	23.10	23.10	6.20		
21	20	F	I	10	10	18.80	18.80	5.00		
22	21	F	I-II	13	13	23.50	15.00	5.00		
Average	23.18			13.86	13.77	18.61	18.52	4.97		
SD	7.49			2.36	2.60	3.97	4.27	0.86		
n	22			22	22	21	20	21		

CTFA High SPF Standard: Supplement to Final Report										
Lab 6 Subject Data										
Subject	Age	Sex	Skin	Initial	Final	SPF				
Number	(yr)		Type	MED	MED	A	B	C		
1	53	F	II	150	180	19.03	15.23	5.25		
2	45	F	II	100	125	15.20	15.20	4.20		
3	25	F	II	120	150	15.10	18.88	4.17		
4	60	M	II	180	180	15.23	19.03	5.25		
5	73	F	III	150	180	23.79	19.03	4.21		
6	38	F	III	180	180	12.18	9.74	3.36		
7	54	F	II	191	191	12.14	15.18	4.19		
8	19	M	I	120	120	19.07	12.20	3.37		
9	43	F	I	100	100	15.09	12.04	3.33		
10	34	F	II	100	100	15.09	15.07	3.34		
11	35	F	II	270	173	15.29	15.29	4.22		
12	36	F	II	130	130	15.08	15.08			
13	62	F	III	240	190		15.15	5.22		
14	48	F	II	175	112	15.25	15.25	4.20		
15	41	F	II	192	153	15.18	15.18	4.18		
16	43	F	I	180	144		15.14	4.17		
17	48	F	II	150	120		15.16	4.18		
18	30	F	II	150	150		18.90	6.53		
19	66	F	II	120	120		19.09	3.37		
20	45	F	I	120	120		15.20	4.19		
21	50	F	II	240	153	15.06		4.15		
22	33	M	II	200	200	15.20				
23	57	F	III	170	170	15.17				
24	35	M	IV	200	220	13.89				
25	21	F	II	180	180	15.25				
26	46	M	III	200	160	15.25				
Average	43.85			165.7	153.9	15.63	15.55	4.25		
SD	13.47			45.28	32.83	2.51	2.49	0.80		
n	26			26	26	20	20	20		

Lab 7 Subject Data										
Subject	Age	Sex	Skin	Height	Weigh	Final	SPF			
Number	(yr)		Type	(in)	(lb)	MED	A	B	C	
1	37	F	II	66	160	20	18.70	15.00	5.00	
2	20	F	II	66	118	31	12.10	15.10	4.00	
3	26	F	II	61	115	20	15.00	18.75	5.00	
4	43	F	III	66	111	31	9.70	9.70	5.00	
5	37	F	II	64	143	16	23.40	15.00	5.00	
6	35	F	II	67	180	25	15.00	12.00	4.00	
7	34	F	III	69	120	39	12.00	15.00	3.20	
8	24	F	II	66	125	39	9.60	9.60	3.20	
9	41	F	III	68	134	25	12.00	23.40	6.24	
10	30	F	I	62	115	31	9.70	12.10	4.03	
11	41	F	III	69	155	25	23.40	18.80	5.00	
12	27	F	II	62	133	31	15.10	15.10	3.20	
13	19	F	II	65	135	25	18.80	23.40	6.20	
14	23	M	I	71	157	25	18.80	18.80	4.00	
15	37	F	I	63	153	16	18.80	29.30	5.00	
16	21	F	III	68	180	31	15.10	12.10	3.20	
17	40	F	II	68	150	25	18.70	18.70	5.00	
18	34	F	III	65	128	25	12.00	23.40	6.20	
19	22	F	I	66	148	25	12.00	15.10	4.00	
20	32	M	II	72	195	25	15.00	15.00	5.00	
21	20	F	II	63	110	31	18.90	15.10	3.20	
22	24	F	I	65	170	20	18.80	12.00	4.00	
23	32	F	II	64	110	25	18.80	18.80		
24	23	F	I	65	176	20	15.00	18.80		
Average	30.08			65.88	142.5	26.08	15.68	16.67	4.49	
SD	7.76			2.787	25.35	6.05	4.035	4.79	0.99	
n	24			24	24	24	24	24	22	

CTFA High SPF Standard: Supplement to Final Report

Overall Results

FORMULA	A	B	C
AVERAGE	16.38	16.66	4.41
SD	3.45	3.59	0.85
N	122	121	122
SE	0.31	0.33	0.08
SE%	1.91%	1.96%	1.74%

CTFA HIGH SPF STANDARD:

SUPPLEMENT TO FINAL REPORT

FORMULAS

CTFA High SPF Standard: Supplement to Final Report

Formula A: Van Dyk Standard

Ingredient	Percent by Weight
Benzophenone-3	5.00
Octyldimethyl PABA	5.00
Octyl Methoxycinnamate	8.00
Carbomer 940	10.00
Cetyl Alcohol	0.50
Dimethicone 200	0.50
DMDM Hydantoin	0.30
Glycerin	3.00
Glyceryl Stearate	2.00
Methylparaben	0.30
Polysorbate 20	2.00
Stearic Acid	3.00
Stearyl Alcohol	0.50
Triethanolamine	2.00
Water	57.90
	100.00

Formula B: Plough Standard

Ingredient	Percent by Weight
Benzophenone-3	3.00
Octyldimethyl PABA	7.00
Benzyl Alcohol	0.50
Cocoa Butter	2.00
Glyceryl Monosterate	3.00
Lanolin	4.50
Methylparaben	0.30
Propylparaben	0.10
Sorbitol Solution	5.00
Stearic Acid	2.00
Triethanolamine	1.00
Water	71.60
	100.00

Formula C: Homosalate Standard

Ingredient	Percent by Weight
Homosalate	8.00
Edetate Sodium	0.05
Lanolin	5.00
Methylparaben	0.10
Propylene Glycol	5.00
Propylparaben	0.05
Stearic Acid	4.00
Triethanolamine	1.00
Water	74.30
White Petrolatum	2.50
	100.00

Spectral comparison of solar simulators and sunlight

Sayre RM, Cole C, Billhimer W, Stanfield J, Ley RD. Spectral comparison of solar simulators and sunlight.
Photodermatol Photoimmunol Photomed 1990: 7: 159–165.

In evaluating sunscreen efficacy, spectral distribution of the irradiation sources can influence the sun protection factor (SPF). The purpose of this investigation was to examine the uniformity of ultraviolet (UV) spectral irradiance of solar simulators used in various SPF testing laboratories, compare them with natural sunlight UV radiation (UVR), and recommend performance limits to ensure that the variability of radiation sources in the UVB region minimally affects SPF estimates. The critical portion of the solar erythemogenic spectrum was identified as the UVB portion, defined as the region between 280 and 320 nm. The spectral irradiance of 26 solar simulators and other UV sources was measured and compared with a summer noon solar spectrum measured in Albuquerque, NM. Proposed spectral limits were developed as a 6-nm "acceptance band" centered on this standard spectrum normalized at 320 nm. The results indicated that the xenon-arc solar simulators currently used in the United States in testing sunscreens either meet the proposed standard solar spectrum or can be readily modified with available UV filters to meet this standard. The devices that have spectral characteristics not resembling sunlight fail to meet the proposed standard and should not be used for sunscreen SPF testing.

R. M. Sayre[1], C. Cole[2], W. Billhimer[3], J. Stanfield[4], R. D. Ley[5]

[1]Schering-Plough HealthCare Products, Memphis, Tennessee, [2]Johnson & Johnson Consumer Products, Skillman, New Jersey, [3]Hill Top Research, Cincinnati, Ohio, [4]Westwood Pharmaceuticals, Buffalo, New York, [5]Lovelace Medical Foundation, Albuquerque, New Mexico, USA

Key words: sunlight; solar simulator; spectrum; sun protection factor; ultraviolet light; sunscreen

C. A. Cole, Schering-Plough HealthCare Products, Memphis, TN 38151, USA

Accepted for publication July 27, 1990

Progress in photobiology has depended on the availability of light sources capable of providing appropriate and sufficient radiation. Early photobiological investigations were limited to experiments with mercury-arc lamps and the carbon-arc lamps, which have inherent deficiencies and limitations. Fluorescent light sources, particularly in the UV portion of the spectrum, became available in the middle of the century, which was a great step forward for photobiological studies. About the same time, xenon-arc lamps became available but were limited by the large amount of infrared radiation emitted. These lamps also required bulky and expensive power supplies and were by no means portable (1).

It wasn't until 1969 that a light-weight, portable, and inexpensive solar simulator became available for dermatologic testing (2). The source designed by Berger (Solar Light, Philadelphia, PA, USA; Model 12S) dealt with the unwanted infrared radiation by incorporating a dichroic mirror that passed infrared and visible radiation, reflecting only the UV portion of the xenon lamp spectrum to the output port. Additional filtration of the beam was accomplished with a UVC blocking filter (Schott WG-320) and an additional visible and IR radiation blocking filter (Schott UG-11). This lamp claimed 10 times solar intensity in the UV portion of the spectrum, and more recent modifications have increased the UV intensity to approximately 50-100 times solar intensity in the UV region. As with any UV light source, the tolerable output intensity is limited by the total energy load imposed upon the skin, whether it is within the desired wavelength regions or not.

Virtually all solar simulators currently used in the United States for SPF testing are manufactured by Solar Light, Oriel (Stamford, CT, USA), Kratos Analytical (now known as Spectral Energy, Hillsborough, NJ, USA) or are individually assembled from components. The majority of the instruments in use are based on a 150-W ozone-free xenon-arc lamp with subsequent filtration (Solar Light). Since the introduction of the original model, several design and component changes have been introduced to improve the uniformity, intensity, and convenience.

Most of the larger xenon-arc lamps have been modified by their owners to make them suitable for SPF testing. The majority of these changes have related to reducing the infrared and visible portions of the spectrum. The result is that wide variance

Table 2. Solar simulators measured

Laboratory	Number, source and supplier	Filters and dichroic mirror
A1,A2	2 150 W xenon-arc Solar Light	1 mm WG-320 1 mm UG-11 400 nm dichroic
B1,B2	2 150 W xenon-arc Solar Light	1 mm WG-320 1 mm UG-11 400 nm dichroic
C1	1 1000 W xenon-arc Kratos Analytical	1 mm WG-320 1 mm UG-11 (1)380 nm dichroic (1)400 nm dichroic
* C2	1000 W configured with	2 mm WG-305
D1,D2	2 150 W xenon-arc Solar Light	1 mm WG-320 1 mm UG-11 400 nm dichroic
* E1	1 (4) 275 W ultra vitalux Osram	part of bulb envelope
F1	1 150 W xenon-arc Solar Light	1 mm WG-320 1 mm UG-11 400 nm dichroic
F2	1 2500 W xenon arc Schoeffel Optical	1 mm WG-320 (1)380 nm dichroic
F3	1 1000 W xenon-arc Kratos Analytical	1 mm WG-320 1 mm UG-11 (2)400 nm dichroics
* G1	1 6500 W xenon-arc	2.0 mm WG-295 only filter
* G2		3.0 mm WG-305 only filter
* G3		0.65 mm WG-320 only filter
* G4		1.0 mm WG-320 only filter
* G5		1.3 mm WG-320 only filter
* G6		2.0 mm WG-320 only filter
* G7		3.0 mm WG-320 only filter
* H1	1 150 W xenon-arc Solar Light	1 mm WG-320 1 mm UG-11 400 nm dichroic
* H2	1 2500 W xenon-arc Kratos Analytical	1 mm WG-320 2 mm UG-11 4-inch water filter 380 nm dichroic mirror
* H3	2500 W configured with	2 mm WG-320
* I1	1 1000 W xenon-arc Kratos Analytical	1 mm WG-320 (2) 550 nm dichroic
J1,J2	2 150 W xenon-arc Solar Light	1 mm WG-320 1 mm UG-11 400 nm dichroic
* K1	1 Dermalight (Dr. Honle Metal Halide) Dermalight Systems	H1 filter (UVC cut-off)

* Comparison source not participating in high SPF standard testing

tative solar simulators approximately matched the solar spectrum for wavelengths shorter than 320 nm. To provide standard spectral limits necessary for comparison for wavelengths shorter than 320 nm, a band around the "standard" sunlight spectrum was defined by shifting the spectrum 3.0 nm towards the UVC region (blue) and 3.0 nm towards the UVA region (red) to create a 6-nm "accept-

Table 3. Solar simulator spectral limits: standard noon solar spectrum (irradiance/irradiance at 320 nm)

Blue limit	150-W xenon SS	1000-W xenon SS	Standard noon sun	Red limit
320	1.000E+00	1.000E+00	1.000E+00	8.140E−01
1.000E−00	9.367E−01	9.303E−01	8.896E−01	7.149E−01
9.413E−01	8.593E−01	8.502E−01	7.725E−01	6.276E−01
8.144E−01	7.673E−01	7.531E−01	6.772E−01	4.960E−01
7.149E−01	6.557E−01	6.426E−01	5.568E−01	3.532E−01
310 6.276E−01	5.283E−01	5.161E−01	4.276E−01	2.649E−01
4.960E−01	4.051E−01	3.968E−01	3.081E−01	1.777E−01
3.532E−01	2.798E−01	2.737E−01	2.290E−01	1.009E−01
2.649E−01	1.676E−01	1.660E−01	1.384E−01	4.686E−02
1.777E−01	8.368E−02	8.255E−02	7.507E−02	1.754E−02
300 1.009E−01	3.207E−02	3.300E−02	2.749E−02	6.387E−03
4.686E−02	9.009E−03	1.037E−02	1.073E−02	2.140E−03
1.754E−02	1.689E−03	2.126E−03	4.000E−03	3.516E−04
6.387E−03	2.042E−04	2.888E−04	9.304E−04	
2.140E−03	2.363E−05	2.927E−05	9.089E−05	
290 3.516E−04	8.120E−06	4.134E−06	9.838E−06	
1.000E−04	5.765E−06		2.060E−06	
1.000E−04	4.759E−06			
1.000E−04				
1.000E−04				
280 1.000E−04				

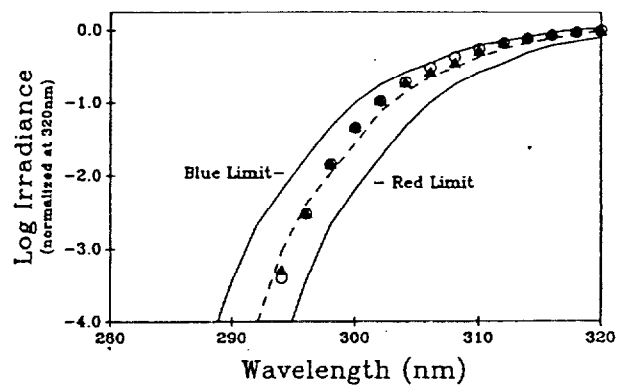

Fig. 1. Log of irradiance (320 nm normalization) of sunlight measured in Albuquerque, NM (----) in June, 1987 at 1200 on a clear day. This spectrum has been shifted 3 nm towards the UVC region to set the "blue limit" and 3 nm towards the UVA region to set the "red limit". The scatter plots represent a 150-W xenon-arc solar simulator (O) (Solar Light Model 12S), and a 1000-W xenon-arc solar simulator (▲) (Kratos).

ance" band. This provided spectral limits relative to the representative summer solar spectrum that could be compared directly with any spectrum measured and normalized to 320 nm. To determine whether a solar simulator spectrum is within the proposed limits, its spectral irradiance values can be compared to the numerical values listed in Table 3 or plotted against the limits seen in Fig. 1.

Compliance with limits

A solar simulator that has any normalized values exceeding the blue limit value or is less than the

both filters cannot meet the proposed standards because it exceeds the proposed red limit.

The importance of the spectroradiometer characteristics for this type of measurement is illustrated in Fig. 6. When the source is measured at 1.5-nm bandpass (SR2), the standard is met; however, when it is measured at 10-nm bandpass (SR4), the same source fails to comply with the standard. Narrower bandpasses tend to yield more accurate values of the irradiance at a given wavelength because they limit the amount of radiation detected from adjacent wavelengths, especially in regions of rapidly changing intensity, as is the case for these solar simulators. Fig. 7 and 9 show spectra from non-xenon-arc UV sources and shows their non-compliance with the proposed standard. Both filtered and unfiltered FS fluorescent sunlamp exceed the blue limits. The Osram Vitalux Lamp shown in Fig. 7 exceeds the proposed blue limit at practically all wavelenghts within the spectral standard. Similarly, the Dermalight (Dr. Honle metal halide lamp) also exceeds proposed limits. None of the evaluated non-xenon-arc sources complied with the proposed limits.

Fig. 8 examined the possible compliance of solar spectra taken at different times of the day and different solar angles. These results indicate that the proposed spectral standard limits are sufficiently broad to accommodate a day's changes in the solar spectrum from approximately 0900 to 1600.

Discussion

The spectral standard

The UVB spectral standard for solar simulators was based upon a noontime solar spectrum for the latitudes in the southern United States in midsummer. This spectrum approaches the highest solar UVB intensity occurring in the continental United States (except perhaps at higher elevations). The noontime spectrum was normalized to 320 nm to allow comparisons of various lamps that operate

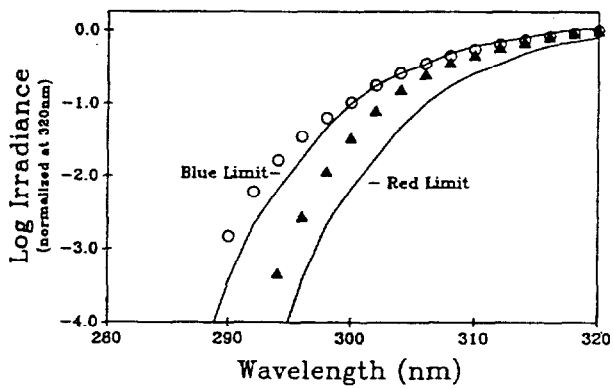

Fig. 6. Log of irradiance of a 1000-W xenon-arc solar simulator without (○) and with (▲) a 1-mm UG11 (Schott Optical) black glass filter in the beam path. The system includes a WG 320 filter, 1 mm thick for both measurements.

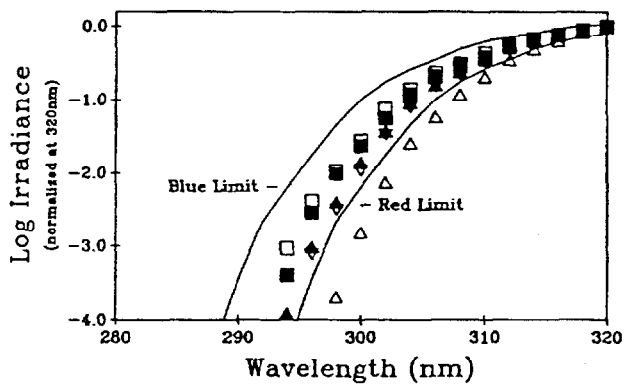

Fig. 8. Log of irradiance of sunlight measured in Albuquerque, NM throughout the day in July 3, 1986. The measurements were made at 0800 (△), 1000 (▲), 1200 (□), 1400 (■) and 1600 (▽). Only the 0800 measurement was out of the range of defined between the blue and red limit region.

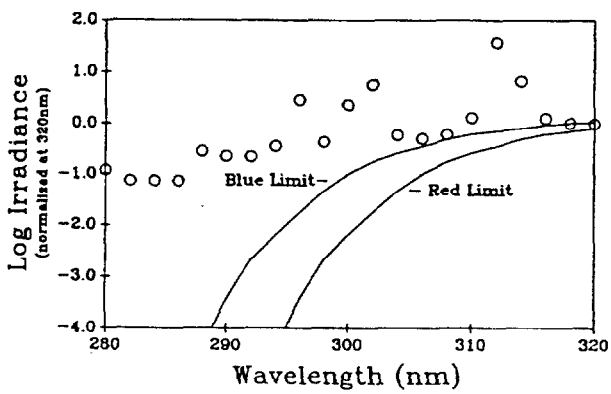

Fig. 7. Log of irradiance of Osram Ultravitalux lamp (○) compared with the blue and red limits for solar simulators.

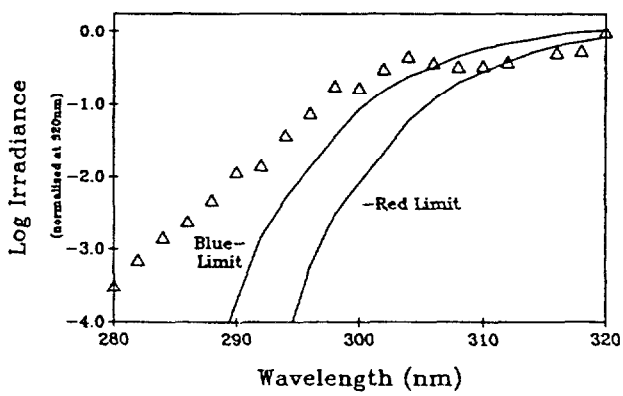

Fig. 9. Log of irradiance of a Dr. Honle metal halide phototherapy lamp with the UVC filter in place as compared with the blue and red limits for solar simulators.

3-mm WG-305 filter is of particular significance, in that a 2-mm WG-305 has been proposed to be necessary for achieving a standardized solar simulator spectrum for France (5). It is important to note that such a filtered xenon-arc solar simulator would exceed the blue limit of the proposed standard at practically all wavelengths.

At 290 nm, a wavelength where most solar simulators meeting the standard would no longer be emitting, the WG-305 spectrum exceeds the allowable limit by a factor of more than 50. At shorter UVC wavelengths, the spectral deviation is even greater. Our data represent a 3 mm filter; the 2 mm required for the French system would allow even greater levels of radiation.

The proposed standard allows direct comparison with specific limits, but by plotting the normalized data on a log scale, as in the figures shown here, an immediate estimate of the magnitude of deviation can be observed.

Fig. 6 showed a comparison of the possible deviation from the proposed red limits of the standard by the simple addition of a UG-11. The deviation of concern in that case amounts to a variance of a few percent beyond the limit. Such a minor deviation probably could not be observed in any biological SPF test (6, 7). However, the deviation caused by using a 2-mm WG-305 instead of a 1- or 2-mm WG-320 would likely be observed in biological SPF testing. The deviation of non-solar sources such as the spectral distribution of the Osram Ultravitalux from the proposed standard is quite obvious (Fig. 7). The Osram Ultravitalux does not resemble sunlight in any respect. It exceeds the proposed standards not only within the normal sunburn range of 290 to 320 nm, but also exceeds the standard limits at shorter wavelengths. This source is used as the DIN testing standard in Germany (8) and is often suggested as being a reasonable representation of sunlight.

Although some sunscreens show comparable SPF values when tested with the Ultravitalux and xenon-arc (9, 10) lamps, these results apparently conflict, as application densities were different for these sources in one test and similar in the other. SPF values for some sunscreens when tested with Dermalight source would be expected to show similar deviations as the Ultravitalux because of the failure to comply with the blue limit (Fig. 9).

Having spectral limits for solar simulators based upon natural sunlight spectra measured with the same spectroradiometer has proven to have several advantages. The most obvious is that all measurements were made with the same precision because equivalent spectroradiometers were used for all critical measurements. The second advantage is that by having reasonably broad spectral limits, more than one solar spectrum is acceptable. Fig. 8 shows solar spectra taken at different times during the day on July 3, 1986 in Albuquerque, New Mexico. Only the 0800 spectrum lies outside the proposed spectral limits.

In summary, choosing a representative solar spectrum as our standard and normalizing the spectrum at 320 nm allows attainable spectral limits to be established. These limits appear not only to incorporate similarly filtered solar simulators but to include many normal solar spectra. At the same time, the proposed spectral limits exclude non-solar-like sources.

Conclusion

We propose a spectral standard for solar simulators used to test sunscreen products. By rigorously controlling the source spectrum, one source of variability will be eliminated in the testing of products. All solar simulators examined in this study that used filtered xenon arcs met or can be modified to meet this spectral standard. Importantly, sources that do not use xenon-arc lamps and sources using improperly filtered xenon-arc lamps will not meet the proposed standard. Fixing the shortwave radiation characteristics is the first step necessary in evaluating the necessity and impact of setting limits on the spectral distribution of the sources in the longwave UVA region for sunscreen testing.

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CTFA HIGH SPF STANDARD:

SUPPLEMENT TO FINAL REPORT

MAY, 1994

SPF Values for Each Subject and Site and Summary Statistics

Subject	(U) 5 Sites	(U) 7 Sites	(O) 5 Sites	(O) 7 Sites
1	5.0	4.0	8	8
2	4.9	5.9	15.4	8.9
3	5.0	4.8	10.0	8.0
4	NA	NA	NA	NA
5	TF	TF	>	-
6	-	>	>	-
7	>	>	-	>
8	>	>	12.5	9.6
9	5.0	5.0	12.5	9.6
10	5.0	4.8	8.0	8.7
11	7.5	7.5	19.5	18.0
12	6.0	5.4	15.6	12.0
13	7.5	6.0	15.7	10.4
14	>	>	12.5	12.0
15	NA	NA	NA	NA
16	6.0	7.2	12.5	14.4
17	6.0	6.8	-	TF
18	6.0	7.5	8.0	10.0
19	9.4	7.5	15.6	10.9
20	6.2	6.2	10.4	10.8
21	9.4	7.5	15.6	14.4
22	9.2	9.2	>	-
23	7.5	6.8	10.0	12.5
24	7.5	5.8	10.0	8.7
25	4.8	5.4	10.0	10.9
26	6.0	4.8	8.0	9.1
Mean	6.5	6.2	12.0	10.9
N	19.0	19.0	19.0	19.0
Std Dev	1.6	1.3	3.2	2.6
S.E.M.	0.4	0.3	0.7	0.6
CV	24.4	21.2	27.0	23.5
CV(SEM)	5.6	4.9	6.2	5.4
UCL	7.3	6.7	13.2	11.9
LCL	5.8	5.7	10.7	9.9
SPF	5.00	5.0	10.0	9.0

NA - Not applicable
TF - Technical failure
'-' - comparison value missing
'>' - greater than expected SPF

Number of Irradiation Subsites and Exposure Increments

CTFA Position

The TFM recommends changing from five exposure sites at equally spaced 25% dose increments to the use of seven exposure sites, two of which are smaller, half-dose increments centered around the expected SPF in order to provide "more precise" SPF values. CTFA-generated data demonstrates that 1) MED's vary by about 13% (data to be submitted 5/12/94) between sites on a subject. Requiring increments lower than this will not give "more precise" SPF numbers, 2) using the same products with both dosing regimens (five sites, equal increments and seven sites, half-dose increments centered around the expected SPF), it was found that mean SPFs did not differ statistically and 3) it is difficult to predict the center exposure, as in product (O) in attached data where the center exposure was incorrectly assumed to be 8.0. The half-dose increments around the 8.0 did not significantly impact in the SPF determination. Therefore, for these reasons, we do not support the use of 7 exposure sites and a change in the increments because it does increase the risk, but not the precision of the test. (see attached data)

Minimum Test Subsite Area (TFM S352.72: page)

Background

The TFM states that ..."each test site area shall be divided into at least three test subsite areas that are at least one square centimeter."

Comment

We propose that the minimum acceptable irradiation area be 8 mm in diameter.

Rationale

Allowing small sites to be used permits lower wattage lamps to be employed, as well as widely used components like liquid light guides which have apertures of 8 mm in diameter. A distinct advantage of irradiating small areas is that more skin area will be available for testing and less skin area is exposed. Setting a lower area limit does not preclude the use of larger irradiation areas and will not affect the accuracy of resulting measurements. Test subsite areas as low as 8 mm in diameter have been successfully validated for use in human SPF testing. (see data attached).

TITLE: Statistical Analysis of SPF Study CR 93-042

A randomized study was conducted on four back sites per subject to compare SPF values obtained using five irradiation sites at equal 25% increments versus the seven recommended (Sunscreen Tentative Final Monograph, May 1993) irradiation sites, two of which are smaller, half dose increments centered around the expected SPF in twenty-six subjects. Two products were tested using each of the two methods; test materials coded (U) and (O); evaluable data for analysis were obtained from 19 subjects.

1. Key Conclusions

Test material coded (U) has an estimated SPF of 5 using both methods. Test material coded (O) has an estimated SPF of 10 when 5 irradiation sites were used to determine SPF, and SPF of 9 when 7 irradiation sites were used to determine SPF. The results of the paired t-test to compare the mean SPF of the individuals using the two methods show that the SPF estimates are comparable for (U). For (O), there is borderline evidence that the two methods produce different SPF values ($p=0.057$).

2. Detailed Findings

The SPF values for each subject, product, and SPF test method are shown on the following page. The results of the paired t-test to compare the mean SPF of the individuals using the two methods are given in the table below for each test material.

Comparison of Methods to Determine SPF

Product	N	Mean Difference	S.E.	t statistic	p-value
(O)	19	-1.21	0.59	-2.04	0.057
(U)	19	-0.31	0.24	-1.30	0.211

3. Study Description

A study was conducted to compare SPF values using five irritation sites at equal 25% increments versus the seven recommended (Sunscreen Tentative Final Monograph, May 1993) irradiation sites, two of which are smaller, half-dose increments centered around the expected SPF. Two products were tested in 26 subjects using each of the two methods; test material coded (U) and (O). Subjects were randomized to one of four treatment sequences, which are listed as follows.

Study Design
Sequences to Which Subjects were Randomized

	Site			
Sequence	1	2	3	4
1	U5	U7	O5	O7
2	U7	O7	U5	O5
3	O5	U5	O7	U7
4	O7	O5	U7	U5

Evaluable data were obtained from 19 subjects.

4. Statistical Methods

The primary objective is to compare the equality of SPF values obtained using five irradiation sites versus the seven recommended by the Sunscreen Tentative Monograph in two products. Therefore, a paired t-test was employed to compare the SPF value obtained using the two methods for each of the products.

MEMORANDUM

TO:	[redacted]	DATE:	March 28, 1994
FROM:	Kathleen K. Wille Laura P. Ragouzis Deanne Guthrie	R/L:	Nondiscretionary
		COPY:	Ken Smiles
TITLE:	Statistical Analysis - Study CR93026-7109-SPF-TKL		

The purpose of this study was to compare Sun Protection Factor (SPF) results of the multi-port solar simulator to the single-port solar simulator and to qualify the multi-port as a valid test machine to determine the Static SPF of Category I - containing sunscreen products.

Two test materials, coded A (with SPF = 15) and O (with SPF = 4) were used in this double blind study with each subject randomized to receive one of the test materials. In addition to the test material, each subject also received a homosalate (HMS) control supplied by the Investigator. According to the protocol, each subject had a test area on the mid to lower untanned back divided into 4 sites. Two of the sites were exposed to the multi-port simulator, one with the test material and one with the HMS control. Similarly, the other two sites were exposed to the single-port simulator with the test material and control.

1. Key Conclusions

For product A, there was no significant difference between multi-port and single-port simulators (p-value = 0.09) in determining SPF. Similarly, for product O, there was also no significant difference between the type of simulator (p-value = 0.32) in determining SPF. In addition, there was no significant difference between multi-port and single-port simulators (p-value = 0.29) in determining SPF for the HMS control. Results from the analyses are presented in Tables 1 through 3.

2. Study Description

The purpose of this study was to compare Skin Protection Factor (SPF) results of the multi-port solar simulator to the single-port solar simulator and to qualify the multi-port as a valid test machine to determine the Static SPF of Category I - containing sunscreen products.

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3. Statistical Methods

The data for each product, as well as the control, were analyzed using a 2-way analysis of variance with instrument type (port) and subject as two factors. A SPF value could not be properly determined for subject 13999 at the single-port site treated with active test material because there was erythema at each subsite; this value is indicated by a '<' flag on the data listing and was not included in the data analysis. For several other subjects receiving Product O, no erythema was observed at any of the subsites, indicating that the MED was underestimated; this is indicated with a '>' on the data listing. For these subjects, the SPF value in the data listing underestimates their true SPF. These values were retained for the analysis. If they were excluded from the analysis, the pattern of missing data would preclude a meaningful statistical analysis. Although including these values may result in an underestimate of the SPF, this allows the analysis to be performed using a conservative measure of SPF.

4. Discussion

Although an apparent trend ($p = 0.09$) exists suggesting a difference in the SPF estimates obtained with the multi-port and single-port instruments, sample size calculations indicate that 211 subjects would be required to reach significance ($\alpha = 0.05$) with 80% power. The monograph allows for 20-25 subjects to determine SPF, thus a differece of the magnitude observed with the two instruments would not be detected under the current regulations for determining SPF.

Table 1

PRODUCT A

Analysis of Variance

SOURCE	DF	SS	F	PROB
Port	1	5.86	4.03	0.0916
Subject	6	42.15	4.82	0.0385

Least Square Means for Simulator

PORT	LSMean	Std Err
Multi	18.14	0.46
Single	16.84	0.46

Table 2

PRODUCT O

Analysis of Variance

SOURCE	DF	SS	F	PROB
Port	1	2.80	1.14	0.3206
Subject	8	62.48	3.19	0.0721

Least Square Means for Simulator

PORT	LSMean	Std Err
Multi	7.87	0.52
Single	8.70	0.58

Table 3

HMS CONTROL

Analysis of Variance

SOURCE	DF	SS	F	PROB
Port	1	0.34	1.22	0.2875
Subject	15	6.11	1.46	0.2346

Least Square Means for Simulator

PORT	LSMean	Std Err
Multi	4.24	0.13
Single	4.04	0.13

STUDY CR-93026-7109-SPF-TKL

		MULTI - PORT		SINGLE - PORT	
PRODUCT	SUBJECT	SPF	HMS CONTROL	SPF	HMS CONTROL
A	11169	15.00	3.31	12.69	3.38
	14105	21.75	4.80	18.00	4.78
	15779	18.00	4.80	18.00	4.78
	17763	18.12	4.00	18.21	4.86
	40020	18.16	4.00	18.00	4.00
	41720	17.81	4.00	18.00	4.00
	42202	18.12	4.83	15.00	4.00
D	9652	6.20	4.00	6.27	4.00
	12423	7.50 >	4.00	12.00	4.10
	13999	10.93	4.00	5.72 <	4.09
	14683	6.00	4.00	9.36	4.00
	15625	7.44 >	4.96 >	4.85	3.23
	16077	10.93	5.00	10.90 >	3.18
	16453	9.37	5.00	9.42	5.00
	17318	5.00	3.20	6.27 >	4.00
	18928	7.44 >	4.00	7.50	3.21

EFFECT OF ERYTHEMA EVALUATION TIME ON SUNSCREEN PRODUCT SPF

ABSTRACT

The SPF of an SPF 30 sunscreen product was determined according to the FDA Proposed Monograph for OTC Sunscreen Products, using erythema evaluations at both 16 and 24 hours.

Subjects were 20 healthy volunteers with Skin Types II or III. Results showed no statistically significant difference, with a power greater than 80 percent to detect a 20 percent difference.

We concluded that erythema evaluations at 16 to 24 hours appear to be appropriate for determining sunscreen SPF.

Introduction

The sun protection factor (SPF) of a sunscreen product is determined as the average of the ratio of the sunscreen-protected minimal erythema dose (MED) of ultraviolet radiation (UV) to the unprotected MED in a panel of at least 20 subjects.

The Proposed Monograph for OTC Sunscreens[1] specified in 1978 that the erythemal responses of sunscreen-protected and unprotected sites for determining sunscreen SPF would be evaluated 16 to 24 hours after administration of UV doses, while the Tentative Final Monograph[2] in 1993 specified evaluations at 22 to 24 hours after administration of UV doses.

This study was conducted between June 15 and November 18, 1993, to determine whether SPF values for a sunscreen with protection in the SPF 30 range were significantly different for evaluations of erythema at 16 and at 24 hours after UV doses. If results for 16 and 24 hours were not significantly different, this would provide evidence that evaluation times between 16 and 24 hours are appropriate and that restricting erythema reading time to 22 to 24 hours is not necessary. A difference of 20 percent is considered a clinically significant difference and statistical significance is defined by a p-value ≤ 0.05.

Objective

The objective was to assess the effect of evaluation time on SPF values determined for an SPF 30 sunscreen product by evaluating erythemal responses at 16 and 24 hours.

Methods and Materials

Subjects

Subjects were selected from volunteers enrolled in ongoing SPF studies, according to the proposed monograph for OTC sunscreens.[1]

Subjects included 14 females and 6 males, ranging in age from 21 to 52 years (mean = 36.3, S.D.= 10.3). Fitzpatrick skin type[3] was II for all subjects except one, whose skin type was III. Original subject MEDs ranged from 8 to 20 seconds (mean = 14.4, S.D.= 3.2). All subjects were in good general health and were taking no medications which might affect the response to UV, as determined by medical history. All subjects provided written, witnessed informed consent. Subject demographic data are shown in Table 1.

Table 1. Subject Demographic Data

Subject No.	Initials	Age	Sex	Skin Type	Original MED (sec)
S23873	LC	37	M	II	16
S24080	CL	47	F	II	16
S24372	AA	22	F	II	16
S24627	TG	44	M	II	10
S24710	BG	44	M	II	13
S24711	KL	33	F	II	13
S25573	ER	43	F	II	16
S25630	JM	41	M	II	16
S25632	DP	52	F	III	16
S25776	LR	52	M	II	13
S25778	BG	43	F	II	10
S25912	BB	21	F	II	16
S25914	SP	47	F	II	16
S26114	DS	29	F	II	13
S26161	ME	34	F	II	10
S26268	SM	24	F	II	20
S26290	MR	28	F	II	8
S26304	SF	23	M	II	13
S26372	CS	24	F	II	20
S26382	CW	37	F	II	16
	Mean	36			Mean 14
	S.D.	10.3			S.D. 3.2

Solar Simulators

Timed UV doses were administered to the mid-back in a series with 25 percent increments (e.g. 8, 10, 13, 16 and 20 seconds), using one of 4 Berger[4] 150 Watt xenon arc lamp solar simulators, which had been calibrated within 3 months using an Optronic Model 742 spectroradiometer and a calibration source traceable to NIST. Each lamp was equipped with a 2 mm dichroic mirror, a 1 mm UVC-

blocking WG320 filter and a 1 mm UG-11 visible- and infrared-blocking filter.

Lamp outputs were routinely checked using a Solar Light Company radiometer, immediately before each test. A typical MED represents a total UV dose of approximately 2.74 J/cm^2.

Sunscreen Products

The SPF 30 sunscreen product contained oxybenzone 4.0%, ethylhexyl-p-methoxycinnamate 7.5%, homosalate 5.0% and octyl salicylate 5.0%.

Seventeen of the 20 subjects were also treated with 8% homosalate standard,[1] and one subject received another test product in addition to the SPF 30 product.

Procedures

On the first day of study participation subjects provided informed consent, completed a medical history and were given a set of UV exposures to determine the original MED. Subjects were instructed to return after approximately 24 hours for evaluation of erythema responses. On the second day, or within one week of the original MED determination, subjects returned for SPF determinations. Test products were applied to 50 cm^2 areas of the mid-back at a dosage of 2 mg/cm^2 and allowed to dry for at least 15 minutes. UV doses were administered to sunscreen-protected and adjacent unprotected sites and subjects were instructed to return at 16 hours and again at 24 hours, for evaluations of erythemal responses.

Erythemal responses were graded by a blinded evaluator under standardized lighting using the following grading scale:

0 = No reaction
0.5 = Minimal response
1.0 = Definite erythema
2.0 = Severe erythema with edema

The UV dose corresponding to the first site of an exposure series with a grade of 1.0 or higher was considered the MED. Subject responses were considered unevaluable if grades were inconsistent with dose (e.g. random progression or missing responses), no erythemal responses were observed or erythemal responses were observed at all sites.

Results

Evaluation Times and SPF Values

The actual elapsed time for the 16 hour evaluation ranged from 13.8 to 17.7 hours (mean = 15.7, S.D.=0.9); the actual elapsed time for the 24 hour evaluation ranged from 22.4 to 24.6 hours (mean = 23.7, S.D.= 0.5). The mean SPF for the test product was 30.46 for 16 hour evaluations and 31.88 for 24 hour evaluations. The difference between means was not significant by student's t test ($p > 0.05$) and the power to detect a 20 percent difference was greater than 80 percent.

The mean SPF of the homosalate standard was 4.24 for 16 hour evaluations and 4.16 for 24 hour evaluations. Both values are within the acceptable range of SPF values for the standard.[1,2] Evaluation times and SPF results are listed by subject in Table 2.

Table 2. Evaluation Times and SPF Values

Subject No.	Initials	16 Hour Evaluation			24 Hour Evaluation		
		Hours	SPF 30	SPF 4	Hours	SPF 30	SPF 4
S23873	LC	16.02	37.50	----	23.70	36.92	----
S24080	CL	16.09	36.93	----	24.09	30.00	----
S24372	AA	15.48	37.50	----	23.42	37.50	----
S24627	TG	15.75	30.00	5.20	23.58	23.08	4.00
S24710	BG	14.98	18.75	4.00	24.00	18.75	5.00
S24711	KL	16.11	30.00	4.93	23.73	24.38	3.25
S25573	ER	16.22	46.88	5.00	24.25	46.16	6.16
S25630	JM	14.13	19.20	3.20	22.80	24.00	5.00
S25632	DP	15.45	19.20	2.55	24.00	24.00	2.55
S25776	LR	15.63	29.73	4.07	24.02	36.94	3.25
S25778	BG	16.26	24.00	>5.00	23.16	24.00	>3.85
S25912	BB	13.82	30.00	5.00	22.43	37.50	4.00
S25914	SP	14.07	37.81	----	23.28	37.81	4.90
S26114	DS	16.00	29.73	5.00	23.07	36.94	5.00
S26161	ME	16.33	30.00	5.00	24.32	37.50	5.00
S26268	SM	16.35	23.78	4.05	23.43	46.89	5.07
S26290	MR	16.25	30.00	5.00	23.97	30.00	4.00
S26304	SF	17.65	37.50	4.00	24.57	24.00	3.23
S26372	CS	16.03	30.72	2.55	23.75	24.00	3.19
S26382	CW	16.05	30.00	4.07	23.50	37.15	4.00
	Mean	15.73	30.46	4.24	23.69	31.88	4.16
	S.D.	0.90	7.23	0.90	0.52	8.23	0.95

CONCLUSION

It was concluded that no clinically or statistically significant differences were seen for 16 or 24 hour evaluation of erythema, for an SPF 30 sunscreen product or for the homosalate standard sunscreen product. Based on these results, evaluations at times ranging from 16 to 24 hours appear to be appropriate.

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SPF 15 STANDARD LOTION

INGREDIENT	PERCENT
Part A	
Lanolin	4.50
Cocoa Butter	2.00
Glyceryl Monostearate	3.00
Stearic Acid	2.00
Padimate O	7.00
Oxybenzone	3.00
Propylparaben	0.10
Part B	
Water	71.60
Sorbitol Solution	5.00
Triethanolamine, 99%	1.00
Methylparaben	0.30
Part C	
Benzyl Alcohol	0.50
Part D	
Water	Q.S.

STEP 01 Into a suitable stainless kettle equipped with a propeller agitator add the ingredients of Part A. Mix with heating to 170 to 180 F, until uniform.

STEP 02 Into a suitable stainless steel manufacturing tank with a counter rotary agitator add the "Water" of Part B and begin mixing and heating to 170 to 180 F. Add the remaining ingredients of Part B and mix until uniform. Maintain temperature at 170 to 180 F.

STEP 03 To the batch of Step 02 at 170 to 180 F, add the oil phase of Step 01 at 170 to 180 F and mix until smooth and uniform. Slowly cool batch to 120 to 130 F.

STEP 04 To the batch of Step 03 at 120 to 130 F add the Benzyl Alcohol of Part C. Mix until uniform. Continue to cool batch to 95 to 105 F.

STEP 05 To the batch of Step 04 at 95 to 105 F, Q.S. to volume using the "Water" of Part D. Mix until uniform. Cool batch to 80 to 90 F.

SUNSCREEN ASSAY (Oxybenzone & Padimate O): AP1290

A. Reagents:

1. Acetic Acid, glacial, ACS grade
2. Isopropanol, HPLC grade
3. Methanol, HPLC grade
4. Oxybenzone, Reference Standard
5. Padimate O, Reference Standard

B. Instrumentation:

Equilibrate a suitable liquid chromatograph to the following or equivalent conditions:

Column :	Ultrasphere ODS 250 x 4.6 mm (5μ) or Supelcosil LC-18 DB 250 x 4.6 mm (5 μ)
Mobile Phase :	85:15:0.5 Methanol:Water:Acetic Acid
Flow Rate :	1.5 mL/min.
Temperature :	Ambient
Detector :	UV Spectrophotometer @ 308 nm
Attenuation :	As needed
Injection Amount :	10 μL

C. Standard Preparation:

1. Accurately weigh about 0.50 g of Oxybenzone, Reference Standard into a 250-mL volumetric flask. Dissolve and dilute to volume with isopropanol. Mix well.

2. Accurately weigh about 0.50 g of Padimate O, Reference Standard into a 250-mL volumetric flask. Dissolve and dilute to volume with isopropanol. Mix well.

3. Accurately pipet 3.0 mL of the Oxybenzone stock solution (C.1.) and 7.0 mL of the Padimate O stock solution (C.2.) into a 100-mL volumetric flask. Dilute to volume with isopropanol and mix well. This is your Standard Preparation.

D. Sample Preparation:

1. Accurately weigh approximately 1.0 g of sample into a 50-mL volumetric flask.

2. Add approximately 30 mL of isopropanol and heat with swirling until the sample is evenly dispersed.

3. Cool to room temperature and dilute to volume with isopropanol. Mix well.

4. Pipet 5.0 mL of the sample solution (D.3.) into a 50-mL volumetric flask and dilute to volume with isopropanol. Mix well.

E. System Suitability:

An HPLC equilibrated to the above conditions would be considered suitable. This system would insure that three replicate injections of the Standard Preparation would yield a relative standard deviation of not more than 2.0% calculated on peak areas for Oxybenzone and Padimate O. The system would also ensure a calculated resolution between the Oxybenzone and Padimate O peaks of not less than 3.0.

F. Analysis:

1. Inject 10 µL of the Standard Preparation in triplicate collecting data for about 15 minutes or until the Padimate O peak has completely eluted. Determine if the system meets the suitability criteria as established above. Elution order: (1) Oxybenzone (2) Padimate O.

2. Similarly inject 10 µL of each Sample Preparation.

3. Calculate the percent of each sunscreen in the sample as follows:

$$\frac{(\text{Smp. Oxybenzone Peak Area})(\text{Std. Oxybenzone Wt. g})(6)}{(\text{Std. Oxybenzone Peak Area})(\text{Smp. Wt. g})} = \text{Oxybenzone \% (w / w)}$$

$$\frac{(\text{Smp. Padimate O Peak Area})(\text{Std. Padimate O Wt. g})(14)}{(\text{Std. Padimate O Peak Area})(\text{Smp. Wt. g})} = \text{Padimate O \% (w / w)}$$

CTFA HIGH SPF STANDARD:

SUPPLEMENT TO FINAL REPORT

REFERENCES

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 × 50 × 100/1 × 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-

EXPERIMENTAL DESIGN: PROCEDURES FOR THE BEHAVIORAL SCIENCES

SECOND EDITION

ROGER E. KIRK BAYLOR UNIVERSITY

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TUKEY'S *HSD* TEST

One of the more widely used a posteriori procedures for evaluating all pair comparisons among means was developed by Tukey (1953). This test, which is ca the *HSD* (*honestly significant difference*) test or *WSD* (*wholly significant differe* test, has been the subject of numerous investigations.* The test sets the exp mentwise error rate at α for the collection of all pairwise comparisons. The b assumptions of normality, homogeneity of variance, and so on, discussed at beginning of Section 3.5 are also required. In addition, the n's in each treatment l must be equal. Alternative procedures for the unequal n and unequal variance c are described later.

Tukey's *HSD* test is based on the sampling distribution of the studenti range statistic which, like the t distribution, was derived by William Sealey Goss The studentized range statistic q is

$$q = \frac{\overline{Y}_{\text{largest}} - \overline{Y}_{\text{smallest}}}{\sqrt{\dfrac{MS_{\text{error}}}{n}}}$$

where $\overline{Y}_{\text{largest}}$ and $\overline{Y}_{\text{smallest}}$ are the largest and smallest of p sample means, MS_{error} is estimator of the unknown common population error variance, and $\sqrt{MS_{\text{error}}/n}$ is standard error of the range of means, denoted by $\sigma_{\overline{Y}}$. The sampling distribution depends on the number of sample means used in computing the range, $\overline{Y}_{\text{largest}} - \overline{Y}_{\text{sma}}$ It is reasonable to expect that on the average the size of the range for, say, t independent samples is larger than that for two samples and increases as the num of samples increases. This increase in the size of the range, $\overline{Y}_{\text{largest}} - \overline{Y}_{\text{smallest}}$, as number of means increases is reflected in the studentized range distribution. Selec percentage points for the distribution of q are given in Appendix Table E.7. To e the table, two values are required: the degrees of freedom for MS_{error} and p, the num of means on which the range, $\overline{Y}_{\text{largest}} - \overline{Y}_{\text{smallest}}$, is based. For a completely randomi design, an estimator of the population error variance is $MSWG$ with $p(n - 1)$ degr of freedom.

The critical difference, $\hat{\psi}(HSD)$, that a pairwise comparison must exceec be declared significant is, according to Tukey's procedure,

$$\hat{\psi}(HSD) = q_{\alpha;p,\nu}\sqrt{\frac{MS_{\text{error}}}{n}}$$

where $q_{\alpha;p,\nu}$ is obtained from Appendix Table E.7 for α level of significance, p mea and ν degrees of freedom associated with MS_{error}. We will illustrate the procedure the data in Table 3.5-1; assume that MS_{error} is equal to 28.8 w $p(n - 1) = 5(10 - 1) = 45$ degrees of freedom. The .01 level of significance wil used. For these data, $\hat{\psi}(HSD)$ corresponding to the .01 level of significance fo two-tailed test is equal to

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* For a summary of research since 1953 and bibliographies see Keselman and Rogan (1977) Miller (1977).

TABLE 3.5-1 Absolute Value of Differences Among Means (MS_{error} = 28.8, p = 5, and n = 10)

	$\overline{Y}_1$	$\overline{Y}_5$	$\overline{Y}_3$	$\overline{Y}_4$	$\overline{Y}_2$
$\overline{Y}_1$ = 36.7	—	3.6	6.7	10.5*	12.0*
$\overline{Y}_5$ = 40.3		—	3.1	6.9	8.4*
$\overline{Y}_3$ = 43.4			—	3.8	5.3
$\overline{Y}_4$ = 47.2				—	1.5
$\overline{Y}_2$ = 48.7					—

*$p < .01$

$$\hat{\psi}(HSD) = q_{.01;5,45}\sqrt{\frac{MS_{error}}{n}} = 4.893\sqrt{\frac{28.8}{10}} = 8.30.$$

A test of the overall null hypothesis that $\mu_1 = \mu_2 = \cdots = \mu_p$ is provided by a comparison of the largest pairwise difference between means, $\hat{\psi} = \overline{Y}_{largest} - \overline{Y}_{smallest}$, with the critical difference $\hat{\psi}(HSD)$. This test procedure, which utilizes a range statistic, is an alternative to the overall F test. For most sets of data, the range and F tests lead to the same decision concerning the overall null hypothesis. However, the F test is generally more powerful. According to Table 3.5-1, the difference between the largest and smallest means is equal to 12.0. Because this difference exceeds $\hat{\psi}(HSD) = 8.30$, the overall null hypothesis is rejected. An examination of Table 3.5-1 indicates that three pairwise comparisons—those starred—exceed the critical difference and hence are declared significant at the .01 level. It should be noted that the values of $q_{\alpha;p,\nu}$ in Appendix Table E.7 are appropriate for testing two-tailed hypotheses; this is true for all of the a posteriori procedures described in Section 3.5.

It is instructive to compare the critical difference for Tukey's *HSD* test with those for the *LSD*, Dunn, and Dunn-Šidák tests. The critical differences are

$$\hat{\psi}(HSD) = q_{.01;5,45}\sqrt{\frac{MS_{error}}{n}} = 4.893(1.697) = 8.30$$

$$\hat{\psi}(LSD) = t_{.01/2,45}\sqrt{\frac{2MS_{error}}{n}} = 2.689(2.400) = 6.45$$

$$\hat{\psi}(D) = tD_{.01/2;10,45}\sqrt{\frac{2MS_{error}}{n}} = 3.520(2.400) = 8.45$$

$$\hat{\psi}(DS) = tDS_{.01/2;10,45}\sqrt{\frac{2MS_{error}}{n}} = 3.519(2.400) = 8.45.$$

As expected, the *LSD* test is the most powerful because at the second stage of the testing procedure it does not control the error rate at α for the collection of tests. The least sensitive procedures in this example are those of Dunn and Dunn-Šidák. They become more powerful relative to Tukey's *HSD* test as the number of comparisons among the p means is reduced. For example, if an experimenter had planned to make only eight instead of all ten pairwise comparisons among means, the critical difference for the Dunn-Šidák procedure would have been only

$$\hat{\psi}(DS) = tDS_{.01/2:8,45}\sqrt{\frac{2MS_{\text{error}}}{n}} = 3.443(2.400) = 8.26$$

which is less than that for Tukey's procedure.

Tukey's procedure can be used to establish $100(1 - \alpha)\%$ simultaneous confidence intervals for all pairwise population contrasts. The confidence interval is given by

$$\hat{\psi}_i - \hat{\psi}(HSD) \leq \psi_i \leq \hat{\psi}_i + \hat{\psi}(HSD)$$

where $\hat{\psi}(HSD) = q_{\alpha;p,\nu}\sqrt{\frac{MS_{\text{error}}}{n}}$

$$\hat{\psi}_i = \overline{Y}_{\cdot j} - \overline{Y}_{\cdot j'}$$

$$\psi_i = \mu_j - \mu_{j'}.$$

The test statistic for Tukey's procedure is

$$q = \frac{\hat{\psi}_i}{\hat{\sigma}_{\overline{Y}}} = \frac{\overline{Y}_{\cdot j} - \overline{Y}_{\cdot j'}}{\sqrt{\frac{MS_{\text{error}}}{n}}}.$$

If $|q| \geq q_{\alpha;p,\nu}$, the null hypothesis, H_0: $\mu_j - \mu_{j'} = 0$, is rejected. Tukey's procedure can also be used with the conventional t statistic (3.2-1) described in Section 3.2.

$$t = \frac{\hat{\psi}_i}{\hat{\sigma}_{\psi_i}} = \frac{\overline{Y}_{\cdot j} - \overline{Y}_{\cdot j'}}{\sqrt{\frac{2MS_{\text{error}}}{n}}}$$

The critical value for this t statistic is $q_{\alpha;p,\nu}/\sqrt{2}$, since $t = q/\sqrt{2}$.

Tukey's procedure can be extended to test nonpairwise contrasts. However, this is not recommended since for this application it is less powerful than Scheffé's procedure, which is described later.

Earlier we noted that Tukey's procedure assumes equal n's. This is necessary in order for the sample means to have the same variance σ^2/n. The procedure also assumes that the p population variances are homogeneous. In the following sections we will describe procedures for evaluating pairwise comparisons that do not require these assumptions.

SPJØTVOLL AND STOLINE'S MODIFICATION OF THE HSD TEST

Over the years a variety of a posteriori procedures have been suggested for evaluating pairwise comparisons when the sample n's are unequal: Dunn (1974), Gabriel (1978b), Hochberg (1974), Kramer (1956), Šidák (1967), Scheffé (1953), Spjøtvoll and Stoline (1973), and Tukey (1953). Ury (1976) compared the procedures of Dunn-Šidák (Šidák, 1967), Hochberg (1974), Scheffé (1953), and Spjøtvoll and Stoline (1973). He concluded that when the n's are similar the preferred procedure was that due to Spjøtvoll and Stoline. When the n's are quite different or a very high

Product application technique alters the sun protection factor

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A number of factors may alter the efficacy of a sunscreen product being tested. Notably among these are (1) the source of ultraviolet (UV) radiation, (2) the filtration of the UV radiation source, (3) such environmental factors as swimming or sweating (4) and/or the amount of product applied. This is the first report in which the technique of product application itself is examined. We find that the act of rubbing the product into the skin appears also to remove product from the skin. In our study, different techniques of product application produced a 25% deviation in product sun protection factor. The variables associated with the application of sunscreening products are discussed.

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Key words: sunscreen; SPF (sun protection factor) testing; product application; test factor

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The adoption of the sun protection factor (SPF) test developed over 13 years ago has provided the sunscreen industry with the means to measure sunscreen effectiveness, and to label sunscreen products (i.e. the SPF) (1). Along with providing the basic protocol for performing the SPF test, a number of factors were identified and defined: these include 1) the types of individuals to be tested (Fitzpatrick skin types I-III) (1–6), 2) the amount of product to be applied (1, 7–9), 3) the ultraviolet (UV) source to be used (10–13) 4) and the statistics to be used to analyze the data (14).

During the ensuing years these factors have been examined by various investigators (2–14). Several investigators have suggested that the major source of test result differences between laboratories that tested identical products was differences in the UV sources used. In fact, there have been statements within the industry that all laboratories should actually use one specific type of solar simulator from one manufacturer. Recent studies have indicated that the variance among similar products tested, using different UV sources, are the result of different spectra being produced (15).

Our work examines another area of variability and appropriately is related to how much a product is tested. Although this area has received extensive review, no examination has been made as to how much specific application factors could alter the SPF. This study examines the consequences of different application procedures during which all other factors (such as human subjects, solar simulators, response scoring and products) remain constant.

Material and methods

Three products were studied. The first was an SPF 4 sunscreen standard that consisted of 8% homosalate in a defined stearic acid lotion. The other two formulas are currently proposed as SPF 15 sunscreen standards: One is a 7% padimate 0 and 3% oxybenzone formula (SPF 15 a); the other is an 8% padimate 0, 5% octyl methoxycinamate and 3% oxybenzone lotion (SPF 15 b).

In this study a 1000-W Kratos filtered xenon-arc solar simulator was used. This solar simulator's spectral distribution was measured using an Optronic 738–740 spectroradiometer calibrated against a 1000-W tungsten standard traceable to the US National Institute of Standards and Testing and determined to comply with the proposed spectral standards for solar simulators (Fig. 1) (13).

The standard sunscreen test protocol (proposed final monograph) was followed in which each human volunteer received a series of controlled exposures, with the test formulas being applied at an application density of 2 mg/cm^2 to a 5 × 10 cm area template to the paraspinal region of the back. All 3 formulas were tested on each volunteer. In the first set of tests, each formula was carefully rubbed uniformly into the entire test area. Fifteen minutes after product application, the test area received an appropriately graded series of light exposures.

For the second set of tests, the same basic procedures were followed, but the products were rubbed into the skin only with brief finger contact, to the extent that no accumulation of product could be observed within the application area. This repre-

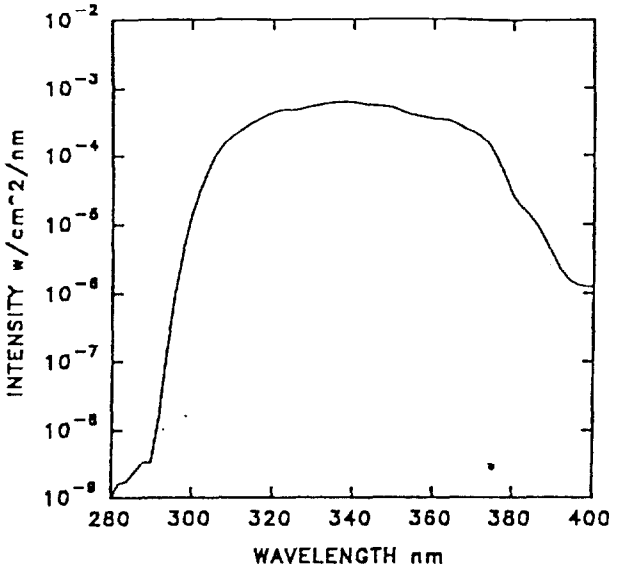

Fig. 1. 1000-W solar simulator spectrum: 1000-W xenon-arc solar simulator filtered with a dichroic mirror and a 1-mm WG-320 (Schott) filter and a 1-mm UG-11 (Schott) filter

sented only 6 passes of the finger across the area to ensure uniform application. Fifteen minutes after product application, the test areas received the appropriate exposures from the solar simulator.

Twenty-four ± 2 hours after exposure the control and treated sites were re-examined and the least exposure producing a uniform faint erythema was used as the minimal erythemal dose (MED). The test product's SPF is the product-treated MED divided by the control MED for each person tested. Twenty individuals were tested in each series.

Results

Table 1 shows the results of all tests performed. Each mean value shown consists of 20 individual tests. Only the 13.2 to 16.7 SPF 15a product test difference was statistically significant ($P<0.05$, Student's t-test). Although the others represent less difference, they do indicate a trend in decreasing SPF as the product is increasingly rubbed into the skin.

Table 1. SPF comparison of rubbed versus not-rubbed product applications

Rubbed	Mean±SD*	Not-rubbed	Mean±SD*
SPF sunscreen		SPF sunscreen	
4	3.9±0.42	4	4.2±0.92
15a	13.2±1.73**	15a	16.7±3.46**
15b	14.2±2.84	15b	15.9±3.84

* Standard deviation. ** $P \leq 0.05$.

Discussion

Our results demonstrate that the manner in which sunscreen products are applied to the skin can alter their effectiveness on the skin. The more a sunscreen product is rubbed into the skin, the lower its SPF. Whether these results are due to actually rubbing the product deeper into the skin or off onto the finger cannot be determined by the studies performed at this time.

Our results indicate that possibly additional directions are necessary within the protocol used to test sunscreen products so that all laboratories perform the fundamental test in the same manner. Clearly the magnitude of the change in SPF produced by simply rubbing the product are as great if not greater than those predicted for different filtration of solar simulators (10, 11). In fact, the application of the product appears to produce change in SPF comparable to those suggested and occasionally determined for different application amounts (7–9).

The differences observed between application techniques indicate that they can play a major role in the variability of test results by affecting the pass/fail criteria. If the exposure procedure produces a 25% uncertainty in results, additional uncertainty can be produced by nonuniform application techniques. Care must also be exercised when more than one person applies products in a laboratory. Additionally, care must be taken when comparing results of different laboratories.

Conclusion

Control of the application technique for sunscreen products is important because deviation in the technique can alter the SPF value as determined for the formula. Failure to adequately control application procedures can alter the overall test variability and test reproducibility. Our work indicates that the application procedures need to be rigorously controlled in test protocols.

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