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Representing the personal care products industry

E. Edward Kavanaugh
President

November 17, 1992

William E. Gilbertson, Pharm.D.
Director
Monograph Review Staff
Office of Over-the-Counter Drugs
Food and Drug Administration
7520 Standish Place
Rockville, Maryland 20855

Re: Docket No. 78N-0038

Dear Dr. Gilbertson:

As you may recall, The Cosmetic, Toiletry, and Fragrance Association (CTFA) and its members agreed to undertake round-robin testing in an effort to determine whether independent laboratories, operating under a single protocol consistent with the testing guidelines issued in FDA's Sunscreen Panel Report, could obtain replicable results when testing a relatively high SPF formulation on a blinded basis. In addition, our members intended to use the testing as a means of identifying an unbranded OTC sunscreen formulation that might serve as a SPF 15 control in the event that further standardized testing is necessary in the future. Seven laboratories, all represented on CTFA's Sunscreen Task Force, conducted testing on three formulations:

Formulation A: 8 percent octyl dimethyl PABA, 5 percent ethylhexyl p-methoxycinnamate, and 4 percent oxybenzone (with a "known" SPF of approximately 15);

Formulation B: 7 percent octyl dimethyl PABA and 3 percent oxybenzone (with a "known" SPF of approximately 15); and

Formulation C: 8 percent homosalate (with a "known" SPF of approximately 4).

As discussed in detail in the attached report, the mean SPF values for all seven labs were 16.5, 16.3 and 4.4 for Formulations A, B and C, respectively. Individual laboratory means ranged from 15.6 to 18.5 for Formulation A, from 15.3 to 18.4 for Formulation B, and from 4.1 to 5.0 for Formulation C. In our opinion, these results demonstrate that different laboratories, operating under one protocol, can obtain valid, reproducible results when testing high SPF sunscreen formulations and that the proposed SPF testing guidelines are capable of evaluating high SPF products (with SPFs of 15 and above). Finally, Formulation B was preferred for testing purposes over Formulation A because it is a less complex formula to manufacture and it produced slightly more consistent results.

On another matter, some time ago you requested that CTFA and its members undertake an effort to develop an appropriate, standardized, validated testing procedure for measuring OTC sunscreen drug products' protection against ultraviolet A (UVA) radiation. CTFA and our members agree that a sound UVA testing methodology is of considerable importance because UVA radiation contributes not only to sunburn but also to premature aging, wrinkling, and certain forms of cancers. Furthermore, as knowledge and concern about skin cancer, photoaging and other deleterious effects caused by over-exposure to the sun increases, consumers understandably are interested in knowing whether their own sunscreens provide significant UVA protection. For these reasons, we applaud FDA's efforts to arrive at an appropriate methodology.

Following your request, our Sunscreen Task Force met on a number of occasions to debate and analyze a variety of UVA testing methodologies. After considerable discussions, two methodologies were subjected to additional research, and under CTFA auspices a number of members conducted round-robin clinical testing on the two methods. When the testing was completed, the results and their implications were reviewed by the Task Force members and several outside consultants. On the basis of that review, it now appears that there is no consensus among CTFA members as to a preferred or "standard" method for measuring UVA protection. Furthermore, it is likely that one or more Task Force members may favor adoption of a methodology different from the two tested under CTFA auspices. In hindsight, the lack of consensus among our members is not surprising, since throughout the world there are similar strongly held differences of opinion as scientists from many nations and backgrounds attempt to identify the optimal method for measuring UVA protection.

Accordingly, at this time it does not appear that CTFA, as an organization, will be in a position to recommend to FDA a single method for measuring UVA protection. We are confident, however, that the data produced in our testing will be made available for FDA's review as the agency considers this important issue, because it is quite likely that CTFA members will be submitting data to support the

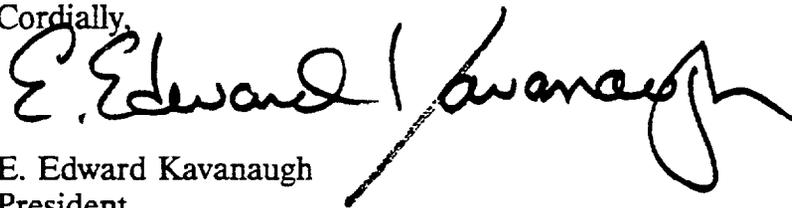
methodology they believe to be appropriate. CTFA takes no position on the merits of any particular methodology submitted by individual companies.

Despite our members' lack of consensus on one methodology to recommend to FDA, we should point out that it is well-documented that many currently-marketed OTC sunscreen products do block a significant portion of UVA rays. Thus, the absence of agreement on a testing methodology should not detract from one very important fact: U.S. sunscreen manufacturers currently are producing highly protective OTC sunscreen products and they are undertaking considerable research efforts in order to provide even more protective products in the future.

For your information, CTFA worked with representatives of the Nonprescription Drug Manufacturers Association (NDMA) in these efforts.

Please do not hesitate to contact us if you have questions or if we can be of additional assistance.

Cordially,

A handwritten signature in black ink, appearing to read "E. Edward Kavanaugh". The signature is written in a cursive style with a long, sweeping underline that extends to the right.

E. Edward Kavanaugh
President

Enclosure

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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

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 to 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

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 (A and B) and the homosalate standard sunscreen (HMS) described in the FDA Proposed Monograph on OTC Sunscreens¹. 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 octyldimethyp PABA, 5 percent ethylhexyl p-methoxycinnamate, and 4 percent oxybenzone
2. B: 7 percent octyldimethyp 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
Skilman, NJ

Schering-Plough HealthCare Products
Memphis, TN

Testing procedures were those outlined in the FDA Proposed Monograph on OTC Sunscreens¹: 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/cm²; 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 al².

Data were analyzed by ANOVA and Tukey's Honestly Significant Difference (HSD) Test³. 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 substantially lower than those of the other laboratories. The lower SPF values were attributed to excessive rubbing during product application⁴ 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 earlier¹.

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

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