Minutes of OTC Sunscreen Final Regulation Public Feedback Meeting
October 26, 1999

Meeting time: 2:30pm

Location: Parklawn Conference Room D
5600 Fishers Lane
Rockville, MD 20857

Meeting Chair: Linda M. Katz, M.D., M.P.H.
Deputy Director, Division of Over-the-Counter Drug Products
Center for Drug Evaluation and Research,
Food and Drug Administration

Meeting Recorder: Elizabeth Yuan
Regulatory Project Manager

FDA Participants:
Robert DeLap, M.D., Office Director, ODEV
Jonathan Wilkin, M.D.,Division Director, DDDDP
Linda M. Katz, M.D., M.P.H., Deputy Director, DOTCDP
Wilson DeCamp, Ph.D., Chemistry Team Leader, DDDDP
Gerald Rachanow, J.D., R.Ph., Regulatory Counsel, DOTCDP
John Lipnicki, Team Leader, DOTCDP
Donald Dobbs, Interdisciplinary Scientist, DOTCDP
Katharine Freeman, Interdisciplinary Scientist, DOTCDP
R. Srinivasan, Ph.D., Statistician, DDDDP
Ramzy Labib, M.D., Ph.D., Medical Officer, DDDDP
Paul Brown, Ph.D., Pharmacologist, DDDDP
Sharon Miller, Optical Engineer, CDRH

External Participants:
Thomas. J. Donegan, Jr., Vice President-Legal & General Counsel, CTFA
Patricia Agin, Ph.D. Schering Plough Healthcare Products
Kenneth Marenus, Ph.D., Estee Lauder Companies

1. Meeting Opening-
The meeting was opened by Dr. Linda M. Katz, Deputy Director, Division of OTC Drug Products, FDA at 2:30 pm.

a) Standard Sunscreens
- Necessary attributes of standard sunscreens
- Discussion of specific standard sunscreen data received by the agency
  - Single laboratory data (Schering-Plough, Hawaiian Tropic)
  - SPF 15 standard sunscreen data (CTFA)

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- Need for data to demonstrate that multiple laboratories can prepare, assay, and utilize the standard
- Discussion of different standards for SPF ranges
- Use of high-performance liquid chromatography (HPLC) to assay the standard
  - Validation data needed
  - Information about the detection of ultraviolet radiation-absorbing impurities

b) Solar Simulator Specifications
- Spectral power distribution table
  - COLIPA table of "percent erythemal contribution"
  - Discussion concerning the lowering of the COLIPA below-290 nm wavelength percent erythemal contribution to 0.1 or 0.01
- Limit on wavelengths longer than 400nm
  - Thermal overloading of the skin
  - Discussion of using limits on total irradiance for all wavelengths
  - Discussion of a specification for a total irradiance limit (e.g., 1250 or 1500 watts/meter^2)
- Exposure dose intervals
  - Discussion of the adequacy of the current exposure dose format for high SPFs

c) Number of Test Subjects for High-SPF Testing
- Potential for variability of responses when testing SPF values over 30

d) Labeling of high-SPF OTC sunscreen drug products
- Consumer perceptions and use
- CTFA February 11, 1997 consumer comprehension data relative to SPF values
- Use of high SPF values in professional labeling
- Statements relating to use of high-SPF products
- UVB/UVA proportionality
- Practical limits in SPF testing (how high is "high")
- CTFA suggestions for communicating in labeling the level of sun protection

2. <u>CTFA Presentation</u>

3. Discussion, Conclusions, and Summation

The following information needs to be submitted to the FDA:
- Validation data/methods used
- Summary of questions to this meeting
- Supporting data requested from the January 1998 UVA meeting
- Any additional data

The meeting was adjourned at 4:43pm, EST.

Minutes prepared by: _____

Chair concurrence: _____

Sunscreen Working Group Meeting- SPF Issues
10/26/99
Sign-In

Name (please print)	Title	Organization
Katharine A. Freeman	Microbiologist	FDA/HFD-560
Donald Dobbs	Biologist	" "
Mark Naylor	Dermatologist	Amer. Acad. of Derm.
Cheryl A. Hayden	Asst. Dir. Fed. Affairs	AAD
Sybil Mead	News Editor	"The Rose Sheet"
Dotty Giordano	Reporter	"The Rose Sheet"
Eve Bachrach	~~[illegible]~~ General Counsel	CHPA
CONSTANCE BULAWKA	Compliance Officer	FDA/CDER/HFD-312
Wilson De Camp	Chemistry T/L	FDA/CDER/HFD-540
Abby Jacobs	Pharm/TOXTL	FDA CDER/HFD-540
Bob James	~~FDA~~ Br. Chief	FDA/CDRH HFZ 134
Brad Wellens	Director DLNDC	FDA/CDER/HFD-310
Daiva Shetty	MO	FDA/CDER/DOCDP
Rae Jones	FDA	FDA/PA
Brett Kay	~~[illegible]~~ Program Assoc.	NCL
Russell Campbell	Consumer Affairs	FDA/OC/OCA
DAN KERAVICH	Proj. Manager	FDA

Sunscreen Working Group Meeting- SPF Issues
10/26/99
Sign-In

Name (please print)	Title	Organization
Dennis L. Lott	Exec. Dir. Tech Affairs	TRLI (Hawaiian Tropic)
Mark Gelbert	VP, Scientific Affairs	Schering Plough HealthCare
Cheryl Sanzare	Dir Drug Reg Affairs	L'Oréal / Cosmair Cosmetics Corp
Chris Corbett	Ass. General Counsel	Cosmair / L'Oréal
Ramzy S. Labib	M.O. DDDDP/CDER	CDER / FDA
Paul Brown	Pharm/Tox Reviewer	CDER/FDA

Sunscreen Working Group Meeting- SPF Issues
10/26/99
Sign-In

Name (please print)	Title	Organization
SALEH A. TURUJMAN	Review Chemist	ONDC III/CDER/FDA
Mark Rosengarten	Director of Reg/Biomed Affairs	Playtex Products Inc
Elizabeth H. Anderson	Assistant General Counsel	The Cosmetic, Toiletry, and Fragrance Assoc.
Steven Rogers	V.P. Marketing & Sales	SunSmart, inc.
John Ameling	Section Head RA	Procter & Gamble
Irwin Butensky	SR VP, Biomedical & Admin Affairs	Playtex
Tom Donegan	CTFA	CTFA
Cheri Jones	V.P. Reg Affs	Obagi Medical Products
Jeff Noshit	Senior Counsel	Porter Novelli
JONATHAN WILKIN	DIR, DDMP	[illegible]

Sunscreen Working Group Meeting

2:30-4:30pm,
October 26, 1999
Parklawn Conference Room D

Agenda

- FDA Presentations
- CTFA Presentation
- General Discussion/Public Comments

FDA presentations

- Introduction
- Standard Sunscreens
- Solar Simulator Specifications
- Number of Test Subjects for High-SPF Testing
- Labeling of High-SPF OTC Sunscreen Drug Products

Introduction

Standard Sunscreens

- Necessary attributes of standard sunscreens
- Discussion of specific standard sunscreen data received by the agency
  - Single laboratory data (Schering-Plough, Hawaiian Tropic)
  - SPF 15 standard sunscreen data (CTFA)
- Discussion of different standards for SPF ranges
- Use of high-performance liquid chromatography (HPLC) to assay the standard
  - Validation data needed
  - Information about the detection of ultraviolet radiation-absorbing impurities

Solar Simulator Specifications

- Spectral power distribution table
  - COLIPA table of "percent erythemal contribution"
  - Discussion concerning the lowering of the COLIPA below 290nm wavelength percent erythemal contribution to 0.1 or 0.01
- Limit on wavelengths longer than 400nm
  - Thermal overloading of the skin
  - Discussion of using limits on total irradiance for all wavelengths
  - Discussion of a specification for a total irradiance limit (e.g., 1250 or 1500 watts/meter^2)
- Exposure dose intervals
  - Discussion of the adequacy of the current exposure dose format for high SPFs

Number of Test Subjects for High-SPF Testing

Potential for variability of responses when testing SPF values over 30

Labeling of High-SPF OTC Sunscreen Drug Products

- Consumer perceptions and use
- CTFA February 11, 1997 consumer comprehension data relative to SPF values
- Use of high SPF values in professional labeling
- Statements relating to use of high-SPF products
- UVB/UVA proportionality
- Practical limits in SPF testing (how high is "high"
- CTFA Suggestions for communicating in labeling the level of sun protection

Standard Sunscreens

Paul C. Brown, Ph.D.
Pharmacology/Toxicology Reviewer
Division of Dermatologic and Dental Drug Products

Standard Sunscreens:

General comments:

- Current Standard is SPF 4.47
- Higher standard may assist in assuring accurate and reproducible measurement of higher SPF formulations

Desirable properties of sunscreen standards:

- Low level of variation from lab to lab. The SPF of the standard should be measured reproducibly from one lab to the next.
- Sensitivity to experimental error. The standard should be capable of detecting errors in the SPF determination procedure if they occur.
- Ease of preparation with a reasonable degree of accuracy.

Comments on specific standard sunscreen data received by the agency:

- CTFA study of two SPF 15 standards in seven laboratories.
  - SPF 15 standards could be measured by several laboratories with reasonably low levels of variation
  - Sensitivity to experimental error and ease of preparation not addressed

- Schering-Plough study of SPF 15, 30 and 45 sunscreen products and Hawaiian Tropic study of SPF 15, 30 and 50 sunscreen products
  - Results indicate that the assay can differentiate products with SPF values of 15 and higher with a low level of variation between subjects.
  - However these studies do not address the need for a high SPF standard since variability from laboratory to laboratory and sensitivity to experimental error were not evaluated.

Conclusions:

- In order to adequately evaluate a new sunscreen standard, the standard should be prepared, assayed and used in SPF tests in multiple independent laboratories.
- The suitability of the analytical method should also be addressed.

Conclusions (Cont.):

- The agency is also interested in comments on the need for additional standard sunscreens with SPF values higher than 15 as well as the use of specific standard sunscreens for specific SPF ranges.

HPLC Assay Methods for SPF Sunscreen Standards

Wilson H. DeCamp
Chemistry Team Leader
Division of Dermatological and Dental Drug Products

A Narrow Focus

- HPLC Methods proposed by CTFA for SPF4 and SPF15 standards (May 5, 1994)
- Replacement of or alternates for the published method?
- Other assay methods may be simpler or more appropriate

Assay Method Summary Homosalate SPF 4 standard

- 21 CFR 352.70(c)
- Spectrophotometric method
- solvent: 1% acetic acid in ethanol
- dilution: 1 gram to 100 mL
- absorbance measured at 306 nm
- reference absorbance value defined as 172 (based on "large number of batches of raw homosalate")

Proposed Method Summary Homosalate SPF 4 standard

- HPLC system
- USP L1 column
- Eluent: methanol:water:acetic acid (85:15:0.5)
- Ambient temperature
- Flow rate: 1.5 mL/min
- Detector: 308 nm

Assay Method Summary Homosalate (bulk), USP 24

- GC system
- USP G27 packing
- FID
- 70°C, Increasing to 220°C
- response compared to USP Homosalate RS

Proposed SPF 15 Reference Standard Formulation

- Padimate O: 7.00%
- Oxybenzone: 3.00%
- Lanolin: 4.50%
- Cocoa Butter 2.00%
- Glyceryl Monostearate: 3.00%
- Stearic Acid: 2.00%
- Propylparaben: 0.10%
- Sorbitol Solution: 5.00%
- Triethanolamine: 1.00%
- Methylparaben: 0.3%
- Benzyl Alcohol: 0.50%
- Water: q.s. ad 100%

Proposed Method Summary
Proposed SPF 15 standard

- HPLC system
- USP L1 column
- Eluent: methanol:water:acetic acid (85:15:0.5)
- Ambient temperature
- Flow rate: 1.5 mL/min
- Detector: 308 nm

Assay Method Summary
Oxybenzone (bulk), USP 24

- Spectrophotometric method
- solvent: methanol
- dilution: 100mg to 100 mL, then 1 mL to 100 mL
- absorbance measured at 285 nm
- reference standard: USP Oxybenzone RS

Assay Method Summary
Padimate O (bulk), USP 24

- Non-aqueous titration method
- solvent: acetic anhydride
- titrant: 0.1 N perchloric acid
- endpoint: potentiometry

Assay Method Summary Padimate O Lotion, USP 24

- HPLC system
- USP L1 column
- Eluent: methanol:water:acetic acid (85:15:0.5)
- Ambient temperature
- Flow rate: 1.5 mL/min
- Detector: 308 nm

Typical Method Validation Issues

- Accuracy
- Precision (Repeatability, Intermediate Precision)
- Specificity
- Detection Limit
- Quantitation Limit
- Linearity
- Range
- Robustness

Example of M.V. Questions Accuracy

- Is the analyte actually what is detected by the method?
- Are the detection conditions optimal for the analysis?
- How is the suitability of the system verified?

Example of M.V. Questions Specificity

- Do other components of the drug product interfere?
- Are synthesis impurities and degradation products identified?

Example of M.V. Questions Linearity

- How does the method respond at concentrations well above or below the label claim?
- Does the concentration vs. response curve intersect the origin?

M.V. Package Contents

- Samples (submitted as listing with contact address)
- Methods
- Data

M.V. Package Contents: Samples

- Drug Substance
- Drug Product
- Internal Standards
- Non-USP Reference Standards
- Impurities
- Degradation Products
- Unusual Reagents

M.V. Package Contents: Methods

- Detailed Description
- Sample Preparation
- Assay Conditions
- Sample Calculation
- Acceptance Criteria

M.V. Package Contents: Data

- Drug Product Composition
- Applicant's Validation Studie(s)
- COA's for Samples
- Material Safety Data Sheets

M.V. Procedure

- Three copies submitted to FDA
- FDA assigns two laboratories
- One laboratory requests samples
- Reports returned to FDA
- Comments on methods forwarded to submitter

Solar Simulators - Existing Specs

- Continuous emission spectrum (290 - 400 nm)
- Similar to sunlight at sea level, 10° zenith angle
- Less than 1% of total energy < 290 nm
- Less than 5% of total energy > 400 nm

Solar Simulator - Proposed Specs

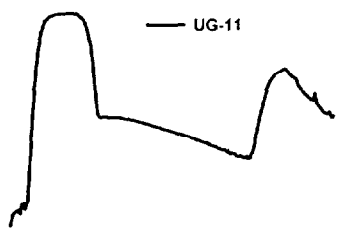
Wavelength Range (nm)	% Cumulative EER
< 290	< 0.1 or 0.01
290 – 310	46 – 67
290 – 320	80 – 91
290 – 330	86.5 – 95
290 – 340	90.5 – 97
290 - 350	93.5 - 99

What about $\lambda > 350$ nm?

- UG-5 filter transmits more UVAI (340 - 400 nm) radiation vs UG-11 filter (plot)
- Chardon et al* report that use of UG-11 vs UG-5 would have greatest impact on sunscreens which rely primarily on UVB absorption
- How to remove excess Visible and IR radiation?

- Sunscreen efficacy can vary with the solar spectrum and the standard for solar simulators. A.M Chardon, FJ Christiaens, JC Dowdy and RM Sayre, pres. at ESP 1999.

SOLAR SIMULATORS



What about $\lambda > 400$ nm?

- Original FDA definition (< 5% of total output) not practical
- Better to place limit on total irradiance to avoid overheating of subject's skin and potential failure of dose reciprocity
- Total Irradiance < 1500 W/m² [or 1250 W/m²]
- Sayre Citizen's Petition data indicates that 50% of tested Solar Simulators can meet this limit, and others could be easily modified

Exposure Dose Intervals

- MED (Unprotected Skin): geometric series of 5 exposures; dose $\Delta = (1.25)^n$
- MED (Protected Skin): geometric series of 5 plus additional 2 centered around expected SPF

SPF < 8: 0.64X, 0.80X, 0.90X, 1.00X, 1.10X, 1.25X & 1.56X
8 <SPF <15: 0.69X, 0.83X, 0.91X, 1.00X, 1.09X, 1.20X & 1.44X
SPF > 15: 0.76X, 0.87X, 0.93X, 1.00X, 1.07X, 1.15X, 1.32X

All values multiplied by MED (US)

X = expected SPF of product

Number of Test Subjects for High SPF Testing

Rajagopalan Srinivasan, Ph.D
Team Leader
Division of Biometrics III
CDER, FDA

Background

- 21CFR 352.72(g) states:
  - "A test panel shall consist of not more than 25 subjects. From this panel, at least 20 subjects must produce valid data for analysis"
  - Statistics Consult dated March 4, 1998 supported the above statement based on the data provided.

Reasons:

- The Method of Statistical Testing using a lower one-sided 95% confidence interval or a one-sided t-test with $\alpha = 0.05$ is a conservative method for categorizing observed SPF measurements in to PCD determinations.
- The SPF is determined to be largest whole number that is excluded by a lower one-sided 95% confidence interval.

Question: Are the current SPF Test Methods able to produce accurate and reproducible SPF values for sunscreen products with SPFs>30?

METHOD OF ANALYSIS

- Two protocols that were used for testing these formulations have been reviewed
- Data summaries are shown in Tables 1, 2 and 3 provided by Schering-Plough Healthcare Products

Goals of the Review

- To demonstrate that the current existing SPF test methodologies can produce accurate and reproducible results for high SPF formulations and,
- To provide data which address the Agency's questions concerning information on the number of test subjects needed and the variability of the data.

Three high SPF formulations were tested according to the 1993 TFM and /or the 1978 PM

- Formula 1: SPF > 30 lotion
- Table 1 compares the data obtained by testing the SPF > 30 lotion by either the 1993 TFM method or by the 1978 PM.
- Based on the data provided, the SPF calculated by both the methods is larger than 30 and the variability is within the acceptable level of 5% of the mean.

High SPF formulations testing (contd.)

- Formula 2: SPF > 40 lotion
- Table 2 include three panels of SPF test results with SPF > 40.
- Based on the data provided, the SPF calculated by both the methods is larger than 40 and the variability is within the acceptable level of 5% of the mean.

High SPF formulations testing (contd.)

- Formula 3: SPF > 40 lotion (Second Formulation)
- Table 3 include two panels of SPF test results with SPF > 40.
- Based on the data provided, the SPF calculated by both the methods is larger than 40 and the variability is within the acceptable level of 5% of the mean.

Conclusions

- The data in Tables 1, 2 and 3 provided by Schering-Plough suggest that the number of subjects (20-25) seems sufficient for the purpose of obtaining valid data for high SPF Products.
- However, if the variability is higher than the acceptable level of 5% of the mean, the number of subjects could be larger than 25.

TA 1

SPF TEST SUMMARY REPORT

FORMULA: SPF > 30 Lotion
Active Ingredients: OXYBENZONE, HOMOSALATE, OCTYL SALICYLATE, OCTYL METHOXYCINNAMATE, AVOBENZONE

Protocol: 1993 Tentative Final Monograph Method
Description: VERY WATER RESISTANT SPF

Subject	MED	Ctl MED		Actual SPF
1	609	16		38.06
2	312	16		19.50
3	488	16		30.50
4	240	10		24.00
5	300	8		37.50
6	750	25		30.00
7	469	13		36.08
8	488	16		30.50
9	750	20		37.50
10	600	25		24.00
11	938	20		46.90
12	938	25		37.52
13	<480	25		<19.20
14	750	20		37.50
15	>938	20		>46.90
16	1172	25		46.88
17	1453	39		37.26
18	1463	31		47.19
19	750	20		37.50
20	1163	31		37.52
21	744	20		37.20
22	938	25		37.52

TEST SUMMARY

Mean SPF: 35.53 **FM SPF: 32**
Number Tested: 22 Number Calculated: 20
Standard Deviation: 6.55
Percent Standard Error of Mean: 5.3

Protocol: 1978 Proposed Monograph Method
Description: WATERPROOF SPF

Subject	MED	Ctl MED		Actual SPF
1	720	16		45.00
2	<461	13		<35.46
3	900	20		45.00
4	576	16		36.00
5	<608	16		<38.00
6	560	16		35.00
7	920	20		46.00
8	800	20		40.00
9	744	16		46.50
10	1006	31		32.45
11	560	16		35.00
12	805	20		40.25
13	599	13		46.08
14	700	20		35.00
15	651	16		40.69
16	644	16		40.25
17	455	13		35.00
18	700	20		35.00
19	700	20		35.00
20	805	25		32.20
21	599	16		37.44
22	609	25		24.36
23	599	20		29.95

TEST SUMMARY

Mean SPF: 37.72 **FM SPF: 35**
Number Tested: 23 Number Calculated: 21
Standard Deviation: 5.89
Percent Standard Error of Mean: 3.4

TABLE 2
SPF TEST SUMMARY REPORT

FORMULA: SPF >40 Lotion
Active Ingredients: OXYBENZONE, HOMOSALATE, OCTYL-METHOXYCINNAMATE, OCTYL SALICYLATE

Protocol: 1978 Proposed Monograph Method
Description: WATERPROOF SPF (Panel 1)

Subject	MED	Ctl MED		Actual SPF
1	624	13		48.00
2	960	20		48.00
3	960	20		48.00
4	960	16		60.00
5	768	16		48.00
6	499	13		38.38
7	<614	20		<30.70
8	960	20		48.00
9	<492	25		<19.68
10	960	20		48.00
11	768	20		38.40
12	768	20		38.40
13	768	16		48.00
14	<768	25		<30.72
15	960	20		48.00
16	<768	25		<30.72
17	1200	20		60.00
18	960	20		48.00
19	1200	20		60.00
20	1500	25		60.00
21	960	16		60.00
22	768	20		38.40
23	1200	25		48.00
24	768	20		38.40
25	<319	13		<24.54

TEST SUMMARY
Mean SPF: 48.60 **FM SPF: 45**
Number Tested: 25 Number Calculated: 20
Standard Deviation: 7.86
Percent Standard Error of Mean: 3.7

Protocol: 1978 Proposed Monograph Method
Description: WATERPROOF SPF (Panel 2)

Subject	MED	Ctl MED		Actual SPF
1	1406	20		70.30
2	1125	25		45.00
3	900	16		56.25
4	900	20		45.00
5	576	16		36.00
6	900	20		45.00
7	900	20		45.00
8	720	20		36.00
9	720	16		45.00
10	900	25		36.00
11	1125	25		45.00
12	720	16		45.00
13	1125	20		56.25
14	1758	25		70.32
15	1125	25		45.00
16	1125	25		45.00
17	1406	25		56.24
18	720	20		36.00
19	1125	25		45.00
20	1125	25		45.00

TEST SUMMARY
Mean SPF: 47.42 **FM SPF: 44**
Number Tested: 20 Number Calculated: 20
Standard Deviation: 9.91
Percent Standard Error of Mean: 4.8

Protocol: 1993 Tentative Final Monograph Method
Description: VERY WATER RESISTANT SPF

Subject	MED	Ctl MED		Actual SPF
1	1744	31		56.26
2	1125	25		45.00
3	783	16		48.94
4	1488	25		59.52
5	828	16		51.75
6	783	20		39.15
7	<461	16		<28.81
8	1488	25		59.52
9	1125	20		56.25
10	1125	25		45.00
11	576	16		36.00
12	<681	20		<34.05
13	1035	20		51.75
14	978	20		48.90
15	<851	20		<42.55
16	<851	25		<34.04
17	1604	39		41.13
18	<851	31		<27.45
19	783	20		39.15
20	1488	25		59.52
21	900	20		45.00
22	1369	25		54.76
23	1190	20		59.50
24	900	16		56.25
25	720	16		45.00

TEST SUMMARY
Mean SPF: 49.92 **FM SPF: 46**
Number Tested: 25 Number Calculated: 20
Standard Deviation: 7.68
Percent Standard Error of Mean: 3.4

TABLE 3
SPF TEST SUMMARY REPORT

FORMULA: SPF >40 Lotion
Active Ingredients: OXYBENZONE, OCTYL SALICYLATE, OCTOCRYLENE, OCTYL METHOXYCINNAMATE

Protocol: Tentative Final Monograph Method (Panel 1)
Description: VERY WATER RESISTANT SPF

Subject	MED	Ctl MED		Actual SPF
1	1000	20		50.00
2	<605	20		<30.25
3	<605	31		<19.52
4	1058	16		66.13
5	783	16		48.94
6	595	13		45.77
7	<855	20		<42.75
8	978	20		48.90
9	770	16		48.13
10	1485	25		59.40
11	736	20		36.80
12	685	16		42.81
13	685	16		42.81
14	1327	25		53.08
15	1056	25		42.24
16	685	16		42.81
27	1320	39		33.85
18	800	16		50.00
19	1056	20		52.80
20	845	20		42.25
21	1056	25		42.24
22	845	16		52.81
23	598	10		59.80

TEST SUMMARY

Mean SPF: 48.08
Number Tested: 23
Standard Deviation: 7.91
Percent Standard Error of Mean: 3.8

FM SPF: 45
Number Calculated: 20

Protocol: Tentative Final Monograph Method (Panel 2)
Description: VERY WATER RESISTANT SPF

Subject	MED	Ctl MED		Actual SPF
1	800	20		40.00
2	1000	25		40.00
3	598	13		46.00
4	1000	20		50.00
5	870	20		43.50
6	1323	25		52.92
7	952	16		59.50
8	1035	20		51.75
9	1294	20		64.70
10	1035	20		51.75
11	>950	16		>59.38
12	626	16		39.13
13	1204	25		48.16
14	828	20		41.40
15	626	13		48.15
16	950	20		47.50
17	1035	20		51.75
18	963	20		48.15
19	673	13		51.77
20	900	20		45.00
21	1604	31		51.74

TEST SUMMARY

Mean SPF: 48.64
Number Tested: 21
Standard Deviation: 6.43
Percent Standard Error of Mean: 3.0

FM SPF: 46
Number Calculated: 20

John D. Lipnicki

Interdisciplinary Scientist/
Team Leader ("Team 2")
Division of OTC Drug Products

SPF Rating System

A concept difficult to explain

- In the limited space on a product label
- In plain language

2

SPF - "What it is"

- The UV energy required to produce an MED on protected skin divided by the UV energy required to produce an MED on unprotected skin.
- SPF value = MED (protected skin (PS))/MED (unprotected skin (US)), where MED (PS) is the minimal erythema dose for protected skin after application of 2 milligrams per square centimeter 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.

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SPF Information

- Erythemal-effective energy reduction
  - SPF 2 = 50%, SPF 30 = 96.7%, SPF 98.3%
- Erythemal-effective energy transmission
  - SPF 2 = 50%, SPF 30 = 3.3%, SPF 58 = 1.7%
- Sunburn prevention
- Product comparison

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Information Not Provided

- Suberythemal doses
- Erythemal "peaks and valleys"
- Nonerythemal UVR
- Biochemical or microscopic

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High-SPF Labeling Concerns

- Consumer perception
- Consumer understanding
- Consumer use

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SPF Perception

- What relationship do consumers see between the series of integers?
  - e.g., is SPF 50 twenty times "better" than SPF 30?
- 2/11/97 feedback to CTFA label comprehension data
  - poor understanding of differences between or importance of SPF and UVA

Consumer Understanding

- The average sunscreen consumer may ascribe more to high SPF values than is clinically relevant.
- This is especially important in the context of using the SPF value to increase "burn time."

Consumer Understanding

- Factors not addressed in high-SPF labeling
  - Suberythemal doses of erythemogenic wavelengths
  - Different (i.e., nonerythemogenic) wavelengths
  - Product absorption spectra - same SPF but different spectra

Consumer Understanding

- Variability - sunscreens (including those with high SPF values) cannot promise a precise result
  - Individuals
  - Absorption spectra and substantivity of different products
  - Exposure conditions
  - Conditions of use (application/reapplication)

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Consumer Use

- Historical explanation of SPF: "allows you to stay in the sun [SPF value]-times longer than without sunscreen" [without burning]
- SPF = UVB perception

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Consumer Use

- CTFA April 16, 1999 citizen petition
  - "...use of sunscreens that focus on exposure to UVB radiation rather than UVA radiation will give consumers a false sense of security and may encourage them and their children to remain in the sun for longer, more dangerous periods of time"

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Consumer Use

- Although the "historical" increased exposure without burning message is true, it omits the previous essential information
- High-SPF values without additional labeling may encourage the use of sunscreens as a safe way to prolong sun exposure

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High-SPF Labeling

- UVB/UVA proportionality
- Additional information
- SPF Limits

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Need for UVB/UVA Proportionality

- Consumers who use high-SPF products to prolong sun exposure may receive increased doses of UVA
- Different sunscreen products with different actives, concentrations, and vehicles provide different amounts and ranges of UVA protection

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January 27, 1999 "UVA" Feedback Meeting

- UVB/UVA proportionality in high-SPF products
- Agency requested information on
  - UVB/UVA proportionality (relative to SPF)
  - appropriate labeling claims
  - UVA test methodologies
- Second request in July 1999 letter

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CTFA April 16, 1999 Citizen Petition

- "...consumers will mistakenly assume that sunscreen products are effective equally against both [UVA and UVB radiation]"

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Additional Information for High-SPF Labeling

- Increasing SPF values without additional information may mislead consumers
- Should convey an appropriate message
  - sun avoidance is best.....
- Possibly clinical relevance based upon individual and/or use
- Use of high-SPF values in professional labeling

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Sun Alert Message

- "Limiting sun exposure, wearing protective clothing, and using sunscreens may reduce the risks of skin aging, skin cancer, and other harmful effects of the sun."
- Sunscreen use alone will not prevent all of the possible harmful effects of the sun for all consumers.
- Without adequate labeling, high SPF numbers may dilute this message.

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"How High Is High" - Practical Limits

- Increased chemical load to skin
- Extremely small increases in laboratory measurements versus large actual-use variations between individuals, products, and conditions of use
- Solar simulator limitations
- Others?

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Conclusion

- The foregoing are concerns and ideas identified at this time.
- We look forward to expeditiously receiving your comments and suggestions.

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SPF TESTING

Methods and Conclusions

Patricia Agin PhD
Schering-Plough HealthCare Products
October 26, 1999

SPF Test Method

- Day 1: Test for Minimal Erythemal Dose (MED) using series of 5 UV exposures (25% increments)
- Day 2: Read MED results; plan control and test site exposure series
- Outline test sites; apply products 2mg/cm^2
- Air dry at least 15 minutes
- Complete water exposures for substantive products as required
- Deliver UV exposures to test sites
- Read results at 22-24 hr
- Calculate subject's SPF for each product tested

HIGH SPF TEST REPORT CONCLUSIONS

- Current test methods can accurately determine SPFs >30
- The data are reproducible from test to test
- 20-25 subjects are adequate
- "TFM" exposure increments (series of 7 with 2 half-increments) do not appear to add significant improvement in precision of results compared to1978 method

Recommendations

- Adopt solar simulator specifications as submitted by CTFA in 1994 (i.e., COLIPA)
- Retain 1500 watts/meter^2 as upper energy limit
- Adopt SPF 15 control formulation, with the understanding that it is only a methodology control
  - Control formulas with higher SPFs are not needed and would not be practical to use
  - Methods validation information will be provided
- Eliminate decreased exposure increments/half increments

Benefits of High SPF Sunscreens

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Problems with the SPF Cap

- High exposure groups will benefit from SPFs >30
- High risk groups may benefit from SPFs >30
- Will Lead to an Arrest in Sunscreen Development
- Best current formulations will be withdrawn

Annual MEDs in Selected U.S. Cities

Source: Hole GE, Johnson AW, Cheney MC, Znaiden A. Cumulative lifetime UVR exposure in the United States and the effect of various levels of sunscreen protection.

Two-Year SPF Comparison[1]

SPF	Cumulative MEDs (2 yr)	Absolute Reduction
0	1453	
30	48	96.7%
60	24	98.3%

[1]Daily Ideal Use; Fort Worth, TX., 10% Total UV

Net Effect of Higher SPF Sunscreen Use

25%

2.4

- Conclusion: Higher SPFs yield greater net protection

Autier P, Dor JF, S Ng, *et al.* Sunscreen Use and Duration of Sun Exposure: a Double-Blind, Randomized Trial. *J Natl Cancer Inst.* 1999;91:1304-1309.

High Risk Individuals

- Individuals with actinic keratoses or skin cancer
- Individuals at high risk for melanoma
- Individuals with outdoor occupations
- Individuals who desire minimal photoaging

Do SPF 30 Sunscreens Provide Complete Protection For Photosensitive Indivduals?

- Porphyrias
- Lupus erythematosis
- Xeroderma pigmentosa
- Polymorphous light eruption
- Answer: NO!

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Sunscreen Effects: Acute *vs.* Chronic

- Acute effects (e.g. SPF) are easy to measure
- Chronic effects are more important
  - Cancer Prevention
  - Photoaging Prevention

Sunscreen Effects: Acute *vs.* Chronic

- Chronic targets are harder to hit
- Chronic targets will likely require sunscreens at or beyond current technology for maximum effect
- Proposed FDA regulations are not conducive to developing better molecules & formulations

Arrest in American Sunscreen Developement

- Some of best coverage of UVA is high SPF
- Best products on market today will dissappear
- American sunscreen development handicapped now by outdated monograph system will fall even further behind

Problems with the SPF Cap

- High exposure groups will benefit from SPFs >30
- High risk groups may benefit from SPFs >30
- Will Lead to an Arrest in Sunscreen Development
- Best current formulations will be withdrawn

UVA Coverage

- Some of the best UVA coverage in American market comes from high SPF preparations (¡ 45 SPF)