J. Cosmet. Sci., **60,** 587–598 (November/December 2009)

Addressing technical challenges associated with the FDA's proposed rules for the UVA *in vitro* testing procedure

OLGA V. DUEVA-KOGANOV, COLLEEN ROCAFORT, STEVEN OROFINO, ULI OSTERWALDER, and JUAN BRITO,
Ciba Corporation, Tarrytown, NY (O.V.D.-K., C.R., S.O., J.B.), and Basel, Switzerland (U.O).

Accepted for publication June 15, 2009. Presented at the Annual Scientific Seminar of the Society of Cosmetic Chemists, New York, December 11, 2008.

Synopsis

The proposed rules of the Food and Drug Administration (FDA) for the UVA *in vitro* testing procedure were applied to the evaluation of various sunscreen formulations and the following technical challenges were observed: when proposed roughened quartz substrates were used, the required coefficient-of-variation criteria were not met, and the dynamic ranges of the available transmittance analyzers were exceeded for sunscreens with high SPF values. In the proposed rules, the FDA requested comment regarding the suitability of other possible substrates. In this research, two modifications to the FDA's proposed rules were evaluated: (a) the use of an alternative substrate, Vitro Skin® N-19 (IMS, Inc.) instead of roughened quartz substrate and (b) an increase in application time from 10 seconds to 30 seconds to ensure a uniform distribution of sunscreen product over the application area of the substrate. These two modifications allowed meeting the required coefficient-of-variation criteria without exceeding the dynamic ranges of the available transmittance analyzers. The modified test conditions were utilized for the evaluation of six commercial sunscreens, which fulfilled criteria of "medium" or "high" categories—based on their UVAI/UV ratios. These findings were in agreement with the statement in the proposed rules that the FDA is aware of the difficulty for current sunscreen formulations to meet the "highest" category and believes that allowing such a category will foster additional research and development in this area. To determine if it was possible to achieve a UVA rating greater than 0.95, two experimental sunscreen prototypes with bisoctrizole (USAN), bemotrizinol (USAN), avobenzone, and octocrylene were tested under the modified test conditions and attained the "highest" category. It should be noted that bisoctrizole and bemotrizinol are being evaluated by the FDA under TEA and are not permitted in the US at this time, but they are approved for use in the rest of the world.

INTRODUCTION

On August 27, 2007 the FDA released the long-awaited proposed rules on UVA protection (1), which offer a comprehensive evaluation of sunscreen product efficacy *in vivo* (SPF and UVA-PF) and *in vitro* (UVAI/UV ratio). The FDA requires using both *in vivo* and *in vitro* UVA radiation testing methods to ensure that the magnitude and breadth of UVA protection is determined. The FDA asks US sunscreen manufacturers to declare, in addition to the SPF, the level of UVA protection, expressed in five categories: "No UVA protection," "Low,"

"Medium," "High," and "Highest." The FDA believes that increasing protection from UVA radiation is beneficial for consumers' health because scientific data demonstrates that UVB and UVA radiation protection is equally important for the skin. The FDA's vision is to reward balanced and photostable UVB/UVA protection. The purposes of this research were: (a) to utilize the FDA's proposed rules for the UVA *in vitro* testing procedure in the evaluation of various sunscreen formulations and to address the discovered technical challenges by modifying this procedure; (b) to evaluate various sunscreens according to the modified procedure; and (3) to determine if it was possible to attain a UVAI/UV ratio greater than 0.95.

METHOD AND MATERIALS

PRE-IRRADIATION DOSE

The FDA proposed to specify a pre-irradiation dose (PID) in terms of "erythemal effective dose" because all solar simulators used by the industry may not have the exact filter combination and spectral transmittance of filters can vary. This dose was calculated by weighing the output spectrum of the solar simulator with the reference action spectrum for erythema as defined by CIE according to the formula:

$$\text{PID (J/m}^2\text{-eff)} = \text{SPF} * 1\ \text{MED} * 2/3$$

where 1 MED = 200 J/m^2-eff. Pre-irradiation criteria were fulfilled utilizing a Weather-O-Meter Ci65A with a Right Light™ inner/quartz outer filter combination recently introduced by Atlas (2), which provides an excellent match to natural sunlight, especially in the UV region (Figure 1).

When the Ci65A spectral power distributions are normalized to 1.57 W/m^2 at 420 nm, the 200 J/m^2-erythemal effective dose (1 MED) is reached within ten minutes. Alternatively, this parameter can be normalized to 1.1 W/m^2 at 420 nm in order to reach 1 MED within 14 minutes. Figure 1 shows that when the irradiation flux is normalized to 1.1 W/m^2

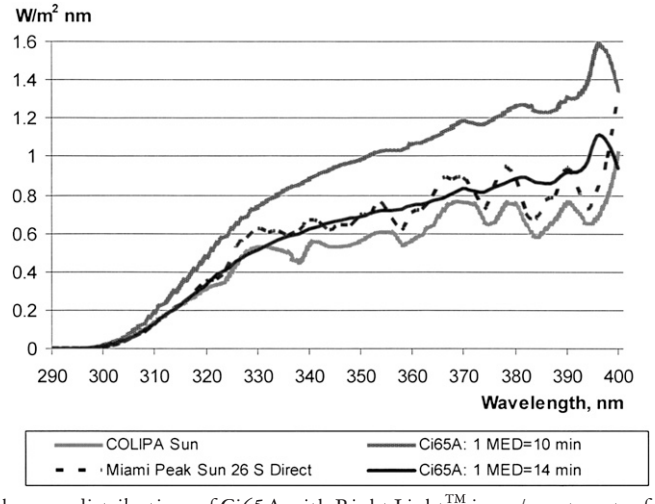

Figure 1. Spectral power distributions of Ci65A with Right Light™ inner/quartz outer filters normalized to 1.57 W/m^2 and 1.1 W/m^2 at 420 nm. COLIPA Sun and Miami Peak Sun 26 S Direct.

at 420 nm, it provides exposure conditions closely matching Miami Peak Sun 26 S Direct and COLIPA sun. In our study the irradiation flux was normalized to 1.57 W/m^2 at 420 nm in order to expedite the pre-irradiation step.

SUBSTRATES

The FDA's proposed rules use optical grade roughened quartz plates as substrates with an application dose of 2 mg/cm^2, which is applied with a gloved finger (pre-saturated with test article) within approximately ten seconds with a very light spreading action. Optical grade roughened quartz substrates with dimensions of 5 cm × 5 cm × 2 mm (Q-Glass) were obtained from the Q-Glass Company (3). According to the manufacturer, Q-Glass plates are roughened on one side in a reproducible manner. It should be noted that the roughness of quartz plates is not specified by the FDA; however, L. Ferrero *et al.* showed that this parameter is important for uniform application and reproducible measurements on roughened substrate (4). In the proposed rules, the FDA requested comment regarding the suitability of other possible substrates, which prompted the evaluation of an alternative substrate, Vitro Skin® N-19 in this study. It was pre-cut in 6.2 cm × 6.2 cm pieces to provide a sufficient area for transmittance measurements at the required 12 locations and pre-hydrated according to reference 5. References (blanks) and substrates with applied test articles were placed on slide mounts, positioned inside the Ci65A, and pre-irradiated simultaneously in order to reach the required PIDs.

TRANSMITTANCE ANALYZERS

Labsphere UV 2000S and Optometrics 290S transmittance analyzers were employed in this study:

- The Labsphere UV 2000S (Figure 2) utilizes a Xenon UV source, 10 watts, with flash radiation. It has an integrating sphere and a photodetector, and it provides a continuous emission spectrum from 290 nm to 400 nm, with sufficient illumination at each wavelength, but not in excess of 0.2 J/cm^2; the dynamic range from 290 nm to 400 nm is at least 2.7 absorbance units.
- The Optometrics SPF-290S transmittance analyzer has a Xenon UV source, 125 watts, with an integrating sphere, a monochromator, and a photomultiplier; the dynamic range from 290 nm to 400 nm is 2.5 absorbance units.

MEASUREMENTS AND CALCULATIONS

The determination of the UVAI/UV ratio according to the FDA's proposed methodology consists of two consecutive parts. The first part requires conducting spectral transmittance measurements in order to calculate the value of mean transmittance and its standard deviation from 290 nm to 400 nm at 5-nm increments, and the second part requires determining the coefficient of variation. At least 12 measurements of transmitted spectral irradiance are required for reference without sunscreen: [C(λ)1,C(λ)2…C(λ) 12], and for the substrate with applied sunscreen: [P(λ)1,P(λ)2…P(λ) 12]. These calculations generate 23 transmittance values with associated standard deviations, one for each 5-nm

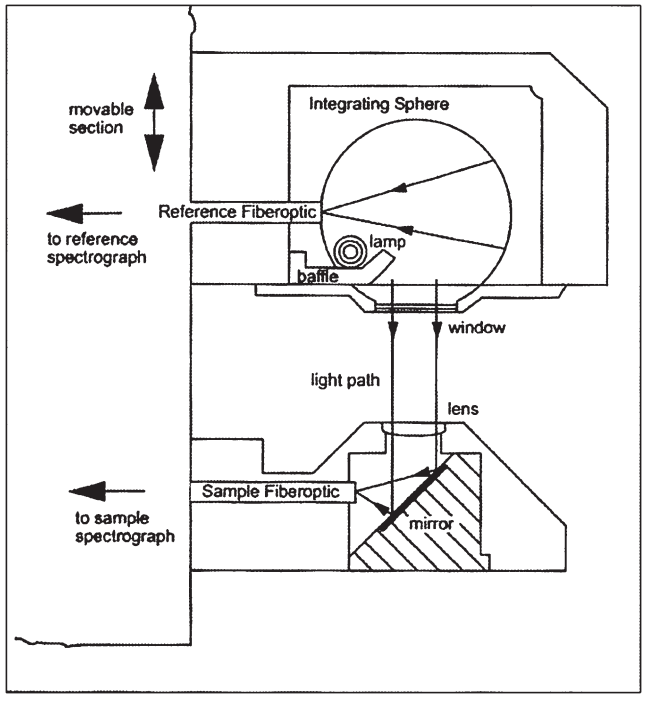

Figure 2. Optical design of Labsphere UV 2000S transmittance analyzer (courtesy of Labsphere).

increment from 290 nm to 400 nm. The value of mean transmittance and its standard deviation are calculated according to the following equations:

$$\overline{T(\lambda)} = \frac{\sum_1^n P(\lambda)/n}{\sum_1^n C(\lambda)/n} \qquad \text{and} \qquad s = \sqrt{\left[\frac{\overline{P(\lambda)} \times s(C(\lambda))}{(C(\lambda))^2}\right]^2 + \left[\frac{s(P(\lambda))}{C(\lambda)}\right]^2}$$

Standard deviations of reference s(C(λ)) and sample s(P(λ)) are also calculated accordingly:

$$s(C(\lambda)) = \sqrt{\frac{\sum_1^n \left(C(\lambda) - \overline{C(\lambda)}\right)^2}{(n-1)}} \qquad \text{and} \qquad s(P(\lambda)) = \sqrt{\frac{\sum_1^n \left(P(\lambda) - \overline{P(\lambda)}\right)^2}{(n-1)}}$$

The coefficient of variation (CV) is determined by dividing the standard deviation by the mean and expressing the resulting value as a percentage. The CV provides an indication of the uniformity of the sunscreen layer, and this value should be less than 10%. At least five repetitions are used for each test article.

It should be noted that when measurements are taken on the Labsphere UV 2000S, they can be extracted as transmittance, absorbance, or mPF values. The Labsphere UV 2000S measures transmittance values in the wider range of 250-450 nm, and the special calculating template was created to extract only the required transmittance values from 290 nm to 400 nm at intervals of 5 nm. The Optometrics SPF 200S provides an option to measure transmittance values from 290 nm to 400 nm at intervals of 5 nm, but the values can only

be extracted in mPF format and a different calculating template was needed to convert mPF values to transmittance values.

The second part of this method is dedicated to the calculation of the actual UVAI/UV ratio and UVA category. This requires converting the transmittance average values for each wavelength to the absorbance average values using the following equation: $A(\lambda) = -\log T(\lambda)$. The index of UVA protection is calculated as the area per unit wavelength under the UVAI portion of a plot of absorbance, $A(\lambda)$ versus wavelength, divided by the area per unit wavelength under the entire UV portion of the curve. The areas of the UVAI and UV sections of the curve are calculated according to these equations:

$$\int_{340}^{400} A(\lambda)d(\lambda)B(\lambda) / \int_{340}^{400} d(\lambda) \qquad \text{and} \qquad \int_{290}^{400} A(\lambda)d(\lambda)B(\lambda) / \int_{290}^{400} d(\lambda)$$

The integrals in these formulas are calculated using Simpson's rule for irregular areas, with the assumption that the biological action spectrum factor, $B(\lambda)$, is equal to 1 for all wavelengths.

The FDA is proposing that test results for each *in vitro* or *in vivo* test be categorized according to UVA rating categories (Table I). It is proposing that the overall UVA radiation category for use in product labeling be the lowest category determined by the *in vitro* and *in vivo* test results. Manufacturers of products that do not obtain a minimum UVA protection either *in vivo* or *in vitro*, or who choose not to make UVA claims or run tests, are required to label the product "No UVA Protection." Each overall UVA protection category corresponds to and (on product labeling) may be used with the graphical representations in the form of solid "stars" illustrated in Table II.

TEST ARTICLES

Six commercial and two experimental test articles containing various sunscreen actives were utilized. Two experimental sunscreen prototypes contained bisoctrizole (USAN), bemotrizinol (USAN), avobenzone, and octocrylene. It should be noted that bisoctrizole and bemotrizinol are being evaluated by the FDA under TEA and are not permitted in the US at this time, but they are approved in the rest of the world.

Experimental test articles: formulations and manufacturing procedures

(A) Experimental sunscreen N (Table III)

- Technical data: pH value = 5.0-6.0; viscosity (Brookfield DV-II + T-F @3rpm) = 130,000–190,000 cps.

Table I
UVA Rating Categories

Category	*In vitro* result	*In vivo* result
Low	0.20 to 0.39	2 to under 4
Medium	0.40 to 0.69	4 to under 8
High	0.70 to 0.95	8 to under 12
Highest	Greater than 0.95	12 or more

Table II
Graphical UVA Rating Based on Category

Combined category rating	Star rating
Low	★☆☆☆
Medium	★★☆☆
High	★★★☆
Highest	★★★★

Table III
Experimental Sunscreen N

Part	INCI-Name/USAN	Supplier	% w/w (as supplied)
A	Water		q.s
	Disodium EDTA	Fluka	0.10
	PEG-8	Jeen International	1.00
	Butylene glycol	Fluka	2.50
B	Dibutyl adipate	Cognis	3.00
	Steareth-2	Lipo	0.75
	Steareth-20	Lipo	1.00
	Isodecyl neopentanoate	ISP	1.50
	PEG-100 stearate	Lipo	1.75
	Cetearyl alcohol	Croda	2.50
	Bemotrizinole (USAN)	Ciba	2.00
	Octocrylene	ISP	2.30
	Avobenzone	DSM Nutritional Products, Inc.	3.00
	C12-15 alkyl benzoate	Finitex	2.00
	Isononyl isononanoate	Alzo International, Inc.	1.50
	Cetyl lactate	Lipo	0.75
	Diethylhexyl 2,6-naphthalate	Symrise	1.75
	Isopropyl myristate	Cognis	1.50
C	Water		20.00
	Bisoctrizole (USAN)	Ciba	12.00
	Acrylates/C12-22 alkyl methacrylate copolymer	ISP	1.00
D	Sodium acrylates copolymer (and) hydrogenated polydecene (and) PPG-l trideceth-6	Ciba	0.80
E	Cyclopentasiloxane (and) dimethiconol	Dow Corning	0.80
	Isododecane (and) dimethicone corsspolymer-3	Jeen International	0.36
F	Phenoxyethanol (and) ethylhexylglycerin	S&M	0.65
	Fragrance		q.s

- Manufacturing procedure: In a suitable container, Part A ingredients are added and heated to 68°C–72°C. In a side container, ingredients of part B are premixed and heated to 68°C–72°C. When Part A and Part B reach the desired temperature, Part B is slowly added into Part A and mixed well and/or milled if desired. In a separate container, Part C is premixed until uniform. When the main batch is below 50°C, Part C is added and mixed well. Cooling of the batch continues. When the main batch is below 30°C, Part D is added and mixed until it is completely smooth and uniform. An increase of the shear may be necessary to overcome accumulation. Part E is premixed and added to the main batch with continuing mixing. The rest of the ingredients are added and mixed until uniform.

Table IV
Experimental Sunscreen P

Part	INCI-Name/USAN	Supplier	% w/w (as supplied)
A	Water		q.s
	Disodium EDTA	Fluka	0.10
	PEG-8	Jeen International	1.00
	Butylene glycol	Fluka	2.40
B	Dibutyl adipate	Cognis	3.00
	Steareth-20	Lipo	0.80
	Steareth-2	Lipo	0.50
	Isodecyl neopentanoate	ISP	2.00
	PEG-100 stearate	Lipo	2.55
	Bemotrizinole (USAN)	Ciba	2.30
	Octocrylene	ISP	2.00
	Avobenzone	DSM Nutritional Products, Inc.	3.00
	C12-15 alkyl benzoate	Finitex	2.50
	Isononyl isononanoate	Alzo International Inc.	2.00
	Cetyl lactate	Lipo	0.75
	Diethylhexyl 2,6-naphthalate	Symrise	1.75
	Isopropyl myristate	Cognis	1.60
C	Water		20.00
	Bisoctrizole (USAN)	Ciba	7.00
	Acrylates/C12-22 alkylmethacrylate copolymer	ISP	1.00
D	Sodium acrylates copolymer (and) hydrogenated polydecene (and) PPG-1 trideceth-6	Ciba	1.00
E	Cyclopentasiloxane (and) dimethiconol	Dow Corning	0.90
	Isododecane and dimethicone crosspolymer-3	Jeen International	0.50
F	Phenoxyethanol (and) ethylhexylglycerin	S&M	0.80
	Fragrance		q.s

(B) Experimental sunscreen P (Table IV)

- Technical data: pH = 4.75-5.75; viscosity (Brookfield DV II + T-D @ 3rpm) = 20,000–45,000 cps.
- Manufacturing procedure: In a suitable container with an appropriate mixer, ingredients in Part A are added and heated to 68°C–73°C. In a side container, ingredients of Part B are mixed and heated to 68°C–73°C. When Parts A and B are at the indicated temperature, Part B is slowly added into part A and mixed well and/or milled if desired. In a side container, ingredients of Part C are blended until uniform. When the main batch is below 50°C, Part C is added and mixed well. Cooling of the batch continues. When the main batch is below 30°C, Part D is added and mixed well until it is completely smooth and uniform. Ingredients of part E are preblended, added to the main batch, and mixed well. The rest of the ingredients are added separately and mixed until uniform.

EXPERIMENTAL RESULTS AND DISCUSSION

Experimental data are presented in Figures 3-4 and Tables III-V. Figure 3 illustrates potential limitations of the proposed roughened quartz substrate that are apparent even for SPF

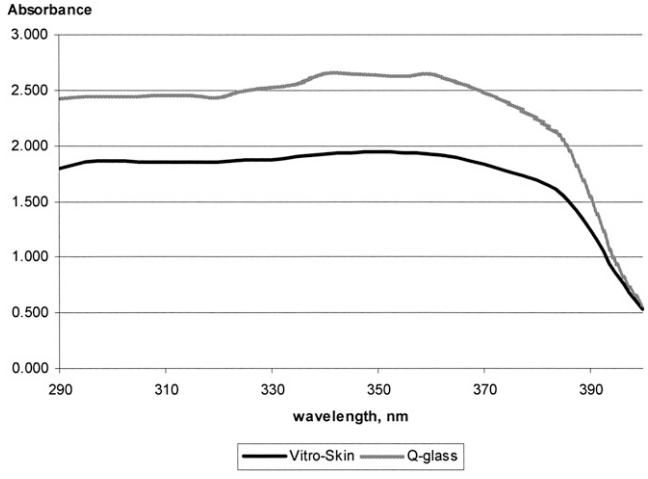

Figure 3. Absorbance spectra of experimental sunscreen P (SPF~30) with "highest" UVA rating (Labsphere UV 2000S; Vitro Skin® N-19; Q-Glass).

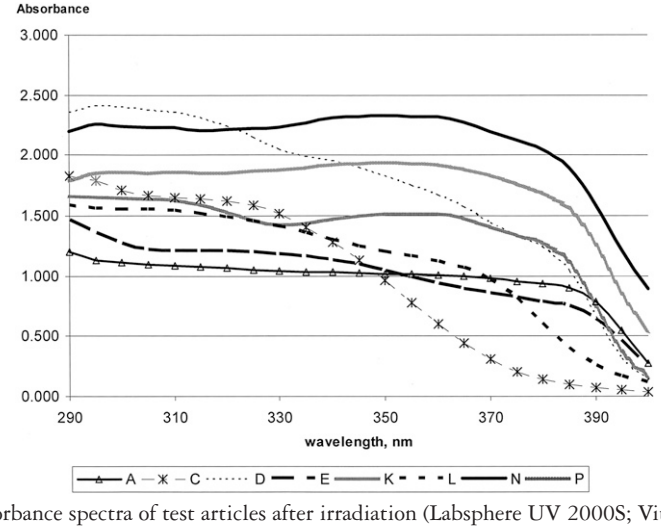

Figure 4. Absorbance spectra of test articles after irradiation (Labsphere UV 2000S; Vitro Skin® N-19).

30 sunscreen, with its absorbance spectrum being close to the dynamic range limits of the transmittance analyzer. These limitations prohibit the evaluation of high SPF sunscreens on a roughened quartz substrate. The utilization of the roughened quartz substrate also creates the following technical problems: CV values were much higher than the required 10% or less for all tested products due to the lack of uniformity. An alternative substrate, Vitro Skin® N-19, worked well with the application dose recommended by the FDA; however, it was found that the application time of ten seconds was not sufficient to evenly apply the sunscreen over a relatively large application area. Thirty seconds of application time seems more reasonable in conjunction with this substrate. It was possible to obtain CV values of 10% or less on the alternative substrate. The surface of Vitro Skin® N-19 is more efficient in de-emulsifying sunscreen emulsions and supporting low spot-to-spot variability during the transmittance measurements compared to the roughened quartz plates proposed by the

Table V
Test Articles and Their Respective UVAI/UV Ratios Obtained with Labsphere UV 2000S and with Vitro Skin® N-19 and Roughened Quartz (Q-glass) Substrates

	Commercial sunscreen products						Experimental	
	A	C	D	E	K Boots Five Star	L	N 2156-16	P 2156-18
Actives	SPF-15	SPF-15	SPF-15	SPF-30	SPF-30	SPF-25	SPF~50	SPF~30
Avobenzone	3		2	3	+	+	3	3
Octocrylene	10			2.35	+	+	2.3	2
Homosalate			10	8		+		
Octisalate			5	4	+	+		
Oxybenzone		5	3	5				
Octinoxate		7.5				+		
Bemotrizinol (USAN)						+	2	2.3
Bisoctrizole (USAN) active							6	3.5
Diethylhexyl butamido triazone					+			
Pre-irradiation dose, MED	10	10	10	20	20	17	33.3	20
Vitro Skin UVAI/UV ratio	0.905-0.926	0.469-0.519	0.750-0.787	0.853-0.862	0.880-0.893	0.734-0.736	0.960-0.964	0.950-0.954
Q-Glass UVAI/UV ratio	0.929			0.912				0.948-0.955
FDA UVA rating	★★★☆ High	★★☆☆ Medium	★★★☆ High	★★★☆ High	★★★☆ High	★★★☆ High	★★★★ Highest	★★★★ Highest

FDA. Absorbance spectra of all test articles obtained on alternative substrate Vitro Skin® N-19 were within the dynamic range of the Labsphere UV 2000S (Figure 4). Figures 3 and 4 also show that the experimental products N and P, with the "highest" UVA rating, produce a characteristic "flat" absorbance spectra.

Results presented in Table V demonstrate that the UVAI/UV ratios of test articles A (SPF 15), E, and P (SPF 30) obtained with the Labsphere UV 2000S on the alternative substrate, Vitro Skin® N-19, are similar to the ratios obtained on roughened quartz plates. However, CV values were much higher than the required 10% or less for products tested on quartz plates. After irradiation, the majority of the US commercial sunscreens tested belong to medium- or high-UVA protection categories. Two experimental sunscreens containing the broad-spectrum photostable actives bisoctrizole and bemotrizinol in conjunction with avobenzone and octocrylene were able to achieve the "highest" UVA rating category.

Data in Table VI show that the UVAI/UV ratios of tested sunscreens obtained on both transmittance analyzers the Labsphere UV 2000S and the Optometrics SPF 290S with Vitro Skin® N-19, were comparable for the majority of test articles; however, in some instances these ratios were slightly higher when the Labsphere UV 2000S was utilized.

Table VI
Test Articles and Their Respective UVAI/UV Ratios Obtained with Optometrics SPF-290 and Labsphere UV 2000S and with Vitro Skin® N-19 as Substrate

	Commercial sunscreen products					
	A	C	D	E	K Boots Five Star	L
Actives	SPF-15	SPF-15	SPF-15	SPF-30	SPF-30	SPF-25
Avobenzone	3		2	3	+	+
Octocrylene	10			2.35	+	+
Homosalate			10	8		+
Octisalate			5	4	+	+
Oxybenzone		5	3	5		
Octinoxate		7.5				+
Bemotrizinol (USAN)						+
Bisoctrizole (USAN) active						
Diethylhexyl butamido triazone					+	
Pre-irradiation dose, MED	10	10	10	20	20	17
Optometrics SPF-290S UVAI/UV ratio	0.857-0.882	0.441-0.475	0.727-0.753	0.823-0.837	0.884-0.891	0.743-0.744
Labsphere UV-2000S UVAI/UV ratio	0.905-0.926	0.469-0.519	0.750-0.787	0.829-0.862	0.880-0.893	0.734-0.736
FDA UVA rating	★★★☆ High	★★☆☆ Medium	★★★☆ High	★★★☆ High	★★★☆ High	★★★☆ High

Table VII
Effect of Irradiation on Vitro Skin® N-19 Tested in Conjunction with Experimental Sunscreen P

Sample description	Irradiated sample and irradiated blank	Irradiated sample and non-irradiated blank
UVAI/UV ratio	**0.9538**	**0.9690**

Ratios obtained on the Optometrics SPF 290S may be lower because this instrument exposes test articles to additional irradiation during the measurements.

EFFECT OF IRRADIATION ON VITRO SKIN® N-19

The effect of irradiation on Vitro Skin® N-19 was tested in conjunction with experimental sunscreen formula P (SPF~30), which was applied to the substrate and irradiated along with a reference. Calculations of the UVAI/UV ratios for this sunscreen were conducted using the irradiated and non-irradiated references to analyze the effect of reference irradiation on the calculated ratios (Table VII). The results presented in Table VII indicate that the effect of irradiation on the Vitro Skin® N-19 (reference) transmittance spectra and on the calculated UVAI/UV ratios is negligible.

CONCLUSIONS

The proposed rules of the Food and Drug Administration (FDA) for the UVA *in vitro* testing procedure were applied for the evaluation of various sunscreen formulations, and the following technical challenges were observed: when proposed roughened quartz substrates were used, the required coefficient-of-variation criteria were not met, and the dynamic ranges of the available transmittance analyzers were exceeded for sunscreens with high SPF values.

In the proposed rules, the FDA requested comment regarding the suitability of other possible substrates, which prompted the evaluation of an alternative substrate, Vitro Skin® N-19. In this research, two modifications to the FDA's proposed rules were evaluated: (a) the use of Vitro Skin® N-19 instead of roughened quartz substrate and (2) an increase in application time from ten seconds to 30 seconds to ensure a uniform distribution of sunscreen product over the application area of the substrate. These two modifications allowed meeting the required coefficient-of-variation criteria without exceeding the dynamic ranges of the available transmittance analyzers.

The modified test conditions were utilized for the evaluation of six commercial sunscreens, which fulfilled criteria of "medium" or "high" categories—based on their UVAI/UV ratios. These findings were in agreement with the statement in the proposed rules that the FDA is aware of the difficulty for current sunscreen formulations to meet the "highest" category and believes that allowing such a category will foster additional research and development in this area.

To determine if it was possible to achieve a UVA rating greater than 0.95, two experimental sunscreen prototypes with bisoctrizole (USAN), bemotrizinol (USAN), avobenzone, and octocrylene were tested under the modified test conditions, and attained the "highest" category. Relevant data regarding the suitability of an alternative substrate, Vitro Skin® N-19, were included in the comments submitted to the FDA by Joseph W. Stanfield (6). It should be noted that bisoctrizole and bemotrizinol are being evaluated by

the FDA under TEA and are not permitted in the US at this time, but they are approved for use in the rest of the world.

ACKNOWLEDGMENTS

We are grateful for the support of our colleagues at Ciba: Joseph Lupia, B. Scott Jaynes, Gustavo Vazquez, Shawn O'Brian, Shiela Loggins, and Ellen Werner.

REFERENCES

(1) Food and Drug Administration, 21 CFR Parts 347 and 352, Sunscreen drug products for over-the-counter human use, proposed amendment of final monograph: Proposed rules, Federal Register, §352.1, **72**(165), 49070–49122 (2007).
(2) Atlas SunSpots®, Material Testing Product and Technology News, **38**(81), 14–15 (2008).
(3) Q-Glass Company, Inc. www.qglass.com
(4) L. Ferrero, M. Pissavini, S. Marguerie, and L. Zastrow, Photochemical behavior assessment of sunscreen preparations by *in vitro* UV spectroscopy, *IFSCC Magazine,* **7**(3), 197–205 (2004).
(5) http://www.ims-usa.com/ittrium/visit?path=A1×66×1y1×a0×1×65y1×c6×1×65y1×cc×1×65
(6) J. W. Stanfield, Substrates for UVA *in vitro* testing. *Docket No. 1978N-0038 RIN No. 0910-AF43,* December 26, 2007, Suncare Research Laboratories, LLC.