



American Academy of Dermatology

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7188 '00 NOV 30 10:41

October 25, 2000

Robert DeLap, M.D.  
Food and Drug Administration  
9201 Corporate Boulevard, Room S219  
Rockville, MD 20850

NOV 28 2000  
dyp

Dear Dr. DeLap:

Over the years, the American Academy of Dermatology has submitted numerous comments to the administrative record concerning the final monograph on sunscreens, including on September 5, 2000 is response to a reopening of the administrative record on the monograph. In that letter we also provided to the agency, a copy of the proceedings from our February 2000 UVA sunscreen conference.

It has come to our attention that a coalition of sunscreen manufacturers [Bath & Body Works, Inc.; Estee Lauder Companies; Johnson & Johnson Consumer Franchises Worldwide; L'Oreal USA Products, Inc.; Mary Kay, Inc.; and Schering-Plough HealthCare Products, Inc. – Docket Number 78N09938, document number C565, vol. #134] also submitted for your consideration a proposal that addresses the key issues relating to the testing and labeling of products that offer protection against UVA radiation. We are pleased that many of the recommendations put forth in the industry proposal are very similar to the Academy's recommendations. Therefore, we wish to apprise you of our overall support for this initiative; however, we do have two items of difference of which you should be aware.

The American Academy of Dermatology has played an active role in educating the public about sun safety and the use of sunscreens as part of an overall campaign of sun protection. As part of this effort, our public health messages have encouraged all Americans to apply a sunscreen of a sun protection factor (SPF) of 15 or higher. Given the thinning of our protective ozone layer and the continued exposure of Americans occupationally and recreationally to the strongest rays of the sun, we believe more strongly than ever that high SPF sunscreens have an important role to play in preventing erythema and skin cancer.

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We also believe, and it was a recommendation of our conference, that both an *in vitro* and an *in vivo* testing method must be used to measure UVA protection. Critical wavelength is the preferred method of *in vitro* testing for a broad-spectrum claim. The threshold for this claim should be 370 nm. The critical wavelength method must be combined with an *in vivo* method; the latter could be either persistent pigment darkening (PPD), or protection factor in the UVA (PFA). A minimum of 4-fold *increase* in PPD or PFA value in the presence of sunscreen is recommended.

For your information, we are attaching a copy of the industry proposal as well as a copy of the proceedings from the February 2000 conference, which have been approved for publication in the *Journal of the American Academy of Dermatology*, and endorsed by the Academy's Board of Directors.

I would be pleased to answer any questions you may have on this matter. Please do not hesitate to contact me.

Sincerely,

A handwritten signature in cursive script that reads "Richard K. Scher".

Richard K. Scher, M.D.  
President

rs/cah

Enclosures (2)

**AMERICAN ACADEMY OF DERMATOLOGY**  
**CONSENSUS CONFERENCE ON UVA PROTECTION OF SUNSCREENS:**  
**SUMMARY AND RECOMMENDATIONS**

**Washington, D.C., February 4, 2000**

Henry W. Lim, MD, Mark Naylor, MD, Herbert Höningmann, MD, Barbara A. Gilchrest, MD,  
Kevin Cooper, MD, Warwick Morison, MD, Vincent A. DeLeo, MD, Lubomira Scherschun, MD

**Affiliations:**

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The incidence and mortality from skin cancer increases yearly. Of paramount concern is the high incidence rate of cutaneous malignant melanoma. Currently, the efficacy of sunscreens is assessed by sun protection factor (SPF) measurement, which quantifies protection against erythemogenic wavelengths, predominantly in the ultraviolet-B (UVB) spectrum (290 nm -320 nm). While the deleterious effects of UVB radiation exposure are well known, the complete action spectrum for photocarcinogenesis and photoaging, particularly the efficacy of ultraviolet-A (UVA) in humans remains to be elucidated.

Growing indirect evidence suggests a relatively greater role for UVA in chronic sun damage than in acute effects such as sunburn, tanning and vitamin D synthesis, all of which are overwhelmingly attributable to UVB. UVA has several unique characteristics compatible with such a role: 1. It constitutes about 5.0% of the terrestrial profile of sunlight, while UVB only makes up 0.5%; 2. It is not filtered by window glass; 3. It has little temporal flux attenuation; 4. It is relatively unaffected by altitude and atmospheric conditions; and 5. It has deep cutaneous penetration. Therefore, in sunlight reaching the surface of the earth, UVA is almost 20-fold more abundant on average compared to UVB. UVA is present all day and through out the year (although there is variation in the irradiance through out the day and the season of the year), and reaches skin through windows. The probability that each incident photon will reach the dermis is 5 times greater for UVA, so that  $5 \times 20 = 100$  times more UVA than UVB photons reach the dermis, the site of many photoaging changes. Also, it has been shown that UVA radiation causes oxidative damage to guanine bases in DNA indirectly, through a free radical mediated mechanism.

In May 1999 the United States Food and Drug Administration published a sunscreen monograph, but due to the lack of agreed upon methods of measurements, UVA protection by sunscreens was not addressed in the monograph. Because of the concerns of the American Academy of Dermatology (AAD) on this issue, a UVA Sunscreen Working Group was created by Darrell Rigel, MD, then-President of the AAD. This working group (chair: Henry W. Lim, MD; members: Kevin Cooper, MD, Vincent DeLeo, MD, Barbara Gilchrest, MD, Herbert Hönigsmann, MD, Warwick Morison, MD, and Mark Naylor, MD) first convened in New York, New York on July 29, 1999 to review the available *in vivo* and *in vitro* methods of UVA protection. Following this meeting and subsequent telephone conference, the task force recommended that an AAD-sponsored consensus conference be held to provide a forum for discussion on this topic.

The above recommendation was approved by the AAD, and a full-day consensus conference was held in Washington, D.C. on February 4, 2000. Meeting participants included members of the AAD, federal agencies (FDA, Environmental Protection Agency), representatives from the US, UK and European cosmetic and pharmaceutical industry, and representatives from the photobiologic communities (American Society for Photobiology, Photomedicine Society, and The Skin Cancer Foundation).

### **CONFERENCE GOALS**

Five goals provided a discussion framework for the conference participants.

1. To create an open dialogue among members of the medical and scientific communities, federal agency representatives, and industry leaders.

2. To present and discuss the available *in vitro* and *in vivo* methods of UVA sunscreen protection determination.
3. To develop a consensus on the method(s) of determining UVA sunscreen protection.
4. To develop a consensus on consumer labeling of UVA sunscreen protection.
5. To provide recommendations to the United States FDA regarding methods of assessment and labeling of sunscreen products regarding UVA protection.

### **CONFERENCE PROCEEDINGS**

The conference commenced with a welcome and opening remarks from Darrell S. Rigel, M.D. (New York, NY, USA), who stated that the lifetime risk of invasive melanoma in the United States has gone from 1 in 1500 in 1935, to 1 in 250 in 1980, and it has now reached 1 in 74 in 2000. The AAD has advocated the use of sunscreens as a component of the total sun protection measures. While there is an effective way of measuring protection from UVB, there is not a standardized method to measure UVA blocking efficacy.

The conference organizer, Henry W. Lim, MD (Detroit, MI, USA), outlined the genesis and the purpose of the consensus conference. He indicated that the conference was organized to facilitate a discussion among members of the AAD, industry, and photobiology community, with the aim of generating a consensus and providing a recommendation to the FDA. This was followed by Barbara A. Gilchrest, M.D. (Boston, MA, USA), who reviewed the biological effects of UVA radiation. She emphasized that rational testing and labeling for UVA sunscreen protection is made difficult by the present lack of information regarding the action spectra for the

most significant forms of photodamage for normal skin. That is, the UV wavelengths principally responsible for melanoma and photoaging are unknown. In human, the efficacy of UV in causing sunburn has been determined experimentally; it decreases exponentially with wavelength from 300 nm to 400 nm. Formation of DNA photoproducts, such as thymine dimers, also determined in human volunteers, has an identical action spectrum. In combination with available epidemiologic and animal data and with the well-established role of photoproducts in DNA mutations and subsequent malignancy, this action spectrum strongly implicates UVB wavelengths in photocarcinogenesis, at least in development of squamous cell carcinomas, and suggests that UVA plays a relatively insignificant role. However, the lack of a direct linear correlation between sun exposure and melanoma risk, the recognized ability of UVA to cause at least some oxidative DNA damage through generation of free radicals, lack of identified "UVB signature mutations" in melanomas (due perhaps to present ignorance of the critical genes mutated during development of melanoma), and experiments in one species of fish and in opossums have lead some authorities to hypothesize a disproportionately large role for UVA in melanoma than in other forms of skin cancer. Only new insights into melanoma pathogenesis will resolve this important question. The situation is equally problematic for photoaging, in that experiments in imperfect animal models have yielded conflicting data regarding the relative ability of UVA and UVB to cause "aging" and there are no established short-term biomarkers for either dermal or epidermal photoaging changes that might permit experimental determination of an action spectrum in human. In contrast to the above questions, however, many idiopathic photodermatoses and drug-induced photosensitivities have well-studied action spectra, in many

instances peaking in the UVA I (340-400 nm) range. Persons with these disorders, however, constitute only a small portion of sunscreen users.

John Lipnicki, a representative from the FDA (Rockville, MD, USA), briefed the attendees about the government's priorities and concerns. Specifically, FDA requested that "broad spectrum" claims should be supported by evidence of significant and meaningful absorption across the UVB/UVA spectrum, and should not be misleading, confusing, or provide a false sense of security. Applicable test data must be relevant to product labeling, and an indication on a sunscreen label must be clinically meaningful.

The next section of the conferences focused on the available *in vivo* and *in vitro* methods of testing UVA protection. *In vivo* methods discussed were immediate pigment darkening (IPD), persistent pigment darkening (PPD), and protection factor in the UVA (PFA, or APF) determination, while the *in vitro* method was the critical wavelength ( $\lambda_c$ ) determination.

Christopher Irwin from Procter & Gamble (Cincinnati, OH, USA) explained immediate pigment darkening method of UVA assessment (1). This *in vivo* response is a transient brownish-gray skin coloration that occurs and fades within minutes of UVA exposure. Fitzpatrick skin types III, IV and V are used for this test; dose requirement ranges from 1-5 J/cm<sup>2</sup>. It requires a single visit and a short irradiation time; however, its major limitation is the transient nature of the end point, which requires an immediate reading.

Dominique Moyal, PhD, from L'Oreal Research (Clichy, France) presented the persistent pigment darkening method (2,3). This technique measures melanin photo-oxidation after UVA exposure. This technique is also valid for assessing photostability. Subjects with skin types II,

III and IV can be used for this testing. The end point of pigment darkening is stable between 2 to 24 hours after irradiation. UVA dose needed ranges from 8-25 J/cm<sup>2</sup>; as such, it requires high intensity light source and up to one hour of irradiation time in sunscreen protected skin.

Curtis Cole, PhD, from Johnson and Johnson (Skillman, NJ, USA) explained method of the determination of protection factor in the UVA (PFA) (4). Similar to the persistent pigment darkening method, reading is done at 24 hours. The end point is either erythema or tanning; as such, subjects with skin phototype I - IV can be used.

*In vitro* critical wavelength ( $\lambda_c$ ) determination method was discussed by Brian Diffey, PhD (Newcastle, UK). Critical wavelength is defined as the wavelength below which 90% of sunscreen's UV absorbance occurs(5,6). In this method, sunscreen is applied on a substrate, and UV absorbance is then measured from 290 to 400 nm. Therefore, this is a measurement of the breadth or the width of UV protection, while *in vivo* measurement such as SPF is a reflection of the amplitude or the depth of protection. For a given sunscreen preparation, an increase in the SPF would result in an increase in absorbance at the UVB range, hence a decrease in the critical wavelength value; therefore, to maintain the same critical wavelength value, a more efficient UVA filter needs to be added into the preparation.

Patricia Agin, PhD, from Schering-Plough (Memphis, TN, USA), and J Frank Nash, PhD, from Procter and Gamble (Cincinnati, OH, USA) discussed several options in communicating UVA protection efficacy of products to consumers. These include UVA protection factor (which would be a number), qualitative measures (minimal, moderate, and maximal protection), or a pass/fail system (a threshold that all products must pass to make the "broad spectrum" claim).

International experience with sunscreen testing methods and labeling procedures was the topic of the subsequent section of the conference. James Ferguson, M.D. (Dundee, Scotland, UK) explained the Boots UVA Star System used in the UK since 1992. This is an *in vitro* measurement of the ratio of the product's UVA (320-400 nm) absorbance over its UVB (290-320 nm) absorbance. The UVA star labeling is placed in the back of product. Herbert Hönigsmann, M.D. (Vienna, Austria), indicated that both SPF and PPD numbers are used in products sold in Austria. Robin Marks, MD (Melbourne, Australia) described the Australian/New Zealand Standard, which has been in use since 1983 (7,8). This Standard, based on *in vitro* testing, specifies that a "broad spectrum" claim can be made if the product fulfill either one of the criteria: 1. 8  $\mu\text{m}$  layer of the product does not transmit more than 10% of radiation between 320 to 360 nm, or 2. 20  $\mu\text{m}$  layer of the product does not transmit more than 1% of radiation between 320 to 360 nm. In addition, all broad spectrum products must have an SPF of not less than 4. This is accompanied by widespread effort of public education. Heiner Gers-Barlag, PhD, from Beiersdorf AG (Hamburg, Germany) explained that Australian Standard is used currently in Germany.

Following the above presentation, the approximately eighty participants were assigned to one of three discussion break-out groups. Each group was asked to specifically address questions regarding UVA sunscreen protection determination method(s) and labeling. Three group leaders, Kevin Cooper, M.D., Vincent DeLeo, M.D., and Mark Naylor, M.D. directed the discussion groups.

The recommendations from the discussion groups were further discussed by the AAD

UVA Sunscreen Task Force after the conference. The following are the final recommendations for UVA protection of sunscreens of the American Academy of Dermatology:

1. Sunscreen UVB protection, as reflected by SPF should be the primary consideration for sunscreen policy.
2. *In vitro* critical wavelength method is a criterion for broad-spectrum claim. The threshold for this claim should be 370 nm.
3. The critical wavelength method must be combined with an *in vivo* method; the latter could be either persistent pigment darkening (PPD), or protection factor in the UVA (PFA). A minimum of 4-fold *increase* in PPD or PFA value in the presence of sunscreen is recommended.
4. Only sunscreens that fulfill the above *in vitro* and *in vivo* criteria could be labeled as "broad spectrum."
5. No sunscreen which has only UVA protection may claim "broad spectrum" sunscreen.
6. An increase in the SPF must be accompanied with a proportional increase in the UVA protection value. It is recommended these "proportional" values be determined jointly by the FDA and the industry.
7. A threshold, pass/fail labeling for broad spectrum/UVA protection is recommended. Therefore, sunscreens fulfilling the above criteria would be labeled simply as "broad spectrum." This would minimize confusion to the consumers. The specifics of the threshold (critical wavelength, PPD/PFA value, and the UVA/UVB proportionality)

could be displayed in fine prints on the back of the container.

8. More funding should be provided for radiation biology research to help elucidate UVA mechanisms of injury.

In summary, the AAD recommends using a sunscreen with SPF 15 or higher and meeting the UVA protection criteria described above.

## **CONCLUSIONS**

AAD consensus conference concerning UVA protection of sunscreens provided a setting for interaction between members of AAD, industry, government agencies and photobiology community. It is hoped that the recommendations developed at the conference will assist the United States FDA in completing the final sunscreen monograph. The goal of these recommendations is to establish standardized, effective, yet practical, UVA sunscreen testing methods and provide labeling that is understandable to consumers. Ultimately, public education on sun avoidance, the use of protective clothing and hat, and the use of broad spectrum sunscreens with an SPF of at least 15 should reduce the incidence of skin cancer in the United States.

## ACKNOWLEDGMENT

The time and effort of the speakers who participated at the conference are gratefully acknowledged: Patricia Agin, PhD (Memphis, TN, USA), Cutis Cole, PhD (Skillman, NJ, USA), Kevin Cooper, MD (Cleveland, OH, USA), Vincent A. DeLeo, MD (New York, NY, USA), Brian Diffey, PhD (Newcastle, UK), James Ferguson, MD (Dundee, Scotland), Heiner Gers-Barlag, PhD (Hamburg, Germany), Barbara A. Gilchrest, MD (Boston, MA, USA), Herbert Hönigsmann, M.D. (Vienna, Austria), Christopher Irwin (Cincinnati, OH, USA), Henry W. Lim, MD (Detroit, MI, USA), John Lipnicki, MD (Rockville, MD, USA), Robin Marks, MD (Victoria, Australia), Dominique Moyal, PhD (Clichy, France), J. Frank Nash, PhD (Cincinnati, OH, USA), Mark Naylor, MD (Oklahoma City, OK, USA), and Darrell Rigel, MD (New York, NY, USA).

Administrative support for this conference was provided Cheryl Hayden and her staff at the AAD; their effort is greatly appreciated.

## REFERENCES

1. Kaidbey KH, Barnes A. Determination of UVA protection factors by means of immediate pigment darkening in normal skin. *J Am Acad Dermatol* 1991;25:262-266.
2. Chardon A, Moyal D, Hourseau C. Persistent pigment darkening response as a method of evaluation of ultraviolet A protection assays. In: Lowe NJ, Shaath NA, Pathak MA, eds. *Sunscreens: Development, Evaluation and Regulatory Aspects*. 2<sup>nd</sup> Edition. Marcel Dekker, Inc. New York, p. 559-582, 1997.
3. Stanfield JW, Edmonds SH, Agin PP. An evaluation of methods for measuring sunscreen UVA protection factors. In: Lowe NJ, Shaath NA, Pathak MA, eds. *Sunscreens: Development, Evaluation and Regulatory Aspects*. 2<sup>nd</sup> Edition. Marcel Dekker, Inc. New York, p. 559-582, 1997.
4. Cole C. Multicenter evaluation of sunscreen UVA protectiveness with the protection factor test method. *J Am Acad Dermatol* 1994;30:729-736.
5. Diffey BL. A method for broad spectrum classification of sunscreens. *International Journal of Cosmetic Science* 1994;16:47-52.
6. Diffey BL, Tanner PR, Matts PJ, Nash JF. In vitro assessment of the broad-spectrum ultraviolet protection of sunscreen products. *J Am Acad Dermatol*, in press.
7. Sunscreen products - Evaluation and classification. Australian/New Zealand Standard. AS/NZ 2604-1997. Sydney: Standards Australia/Standards New Zealand. 1997.
8. Marks R. Summer in Australia: Skin cancer and the great SPF debate. *Arch Dermatol* 1995;131:462-464.



## Schering-Plough HealthCare Products

August 30, 2000

Dockets Management Branch (HFA-305)  
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**RE: Docket 78N-0038: Sunscreen Drug Products for Over the Counter  
Human Use: Final Monograph, Re-Opening of Administrative  
Record**

The Food and Drug Administration (FDA) has extended the effective date for the final monograph for over-the-counter (OTC) sunscreen drug products and has reopened the administrative record for rulemaking to allow for comment on key technical and labeling issues related to sunscreen products. These issues were outlined by FDA in the June 8, 2000 Federal Register. The FDA intends to publish a comprehensive final monograph on OTC sunscreen drug products by December 31, 2001. The Agency has requested interested parties to provide specific types of data and information which would allow identification and adoption of a standard UVA testing procedure, along with a clear way to present UVA protection information in labeling to consumers.

Contained herein is a proposal developed by an industry group that addresses the key issues relating to the testing and labeling of products that offer UVA protection. This industry group includes manufacturers of sunscreen products designed for use during outdoor activities (e.g. sport and beach use) as well as everyday use (e.g. makeup and foundations). These companies are responsible for the development, manufacture and sale of a majority of the Branded sunscreen-containing products that make SPF and UVA protection label claims. Letters from each individual company supporting this proposal are attached to this document.

Schering-Plough HealthCare Products has been a leader in the development, testing and study of sunscreen products, and has contributed greatly over the years to the development of appropriate sunscreen drug product regulation. We continue to support the promotion of responsible sun safety through our products, their labeling and advertising.

In response to FDA's request for information and data on UVA testing methods and labeling, Schering-Plough HealthCare Products, along with the aforementioned industry group, has developed the enclosed proposal that includes a comprehensive approach to measuring sunscreen UVA protection and provides clear communication of both SPF and UVA protection to consumers and professionals. The proposal addresses three important issues that have been considered by FDA in an attempt to develop rulemaking involving sunscreen products that claim UVA protection. These are (1) *in vivo* and *in vitro* testing of sunscreen UVA performance, (2) UVB/UVA proportionality for sunscreen products, and (3) communication of UVA performance on sunscreen-containing product labels.

This proposal assures not only proportionality of UVA to UVB protection levels in sunscreen products, but also ensures broadness of absorbance for all products making UVA protection claims. UVA/UVB proportionality is an important concept supported by both the American Academy of Dermatology and the FDA to ensure that sunscreens which offer protection from UVB radiation also offer appropriate and relative protection from UVA radiation, both of which contribute to short- and long-term skin damage. At the October 26, 1999 feedback meeting between the Agency and CTFA, as well as in subsequent written communications, FDA asked industry for specific information on the proportionality needed between SPF and UVA protection. Thus, this proposal also assures that higher SPF products contain proportionally increasing levels of UVA protection as the SPF increases based both on the magnitude and the broadness of UVA protection. The proposed approach also supports communication of the level of UVA protection in a simple, integrated format consistent with existing SPF labeling.

In support of this proposal, we have included the results of testing the UVA efficacy of seven prototype sunscreen formulations with SPFs from 4 to 30, composed of a wide variety of active ingredients. We, along with the other companies whose letters are supplied with this submission, support the testing and labeling proposals provided in these documents and hope that this information will assist your completion of a comprehensive final monograph.

Previously, the Cosmetic, Toiletry and Fragrance Association (CTFA) submitted comments addressing FDA questions and issues relating to the testing and labeling of sunscreen products, specifically Sun Protection Factor (SPF) testing and labeling. Importantly, those comments addressed the issue of labeling products with SPF greater than 30, along with additional sunscreen indications beyond sunburn (e.g. photoaging). Schering-Plough HealthCare Products participated in the development of those comments and, notwithstanding the proposal herein, strongly supports those earlier submissions on SPF testing and labeling.

Should the Agency have any questions or comments on the information contained in this submission, please direct them to the undersigned.

Sincerely,

Handwritten signature of Mark B. Gelbert in cursive script.

Mark B. Gelbert, PhD, JD  
Vice President, Scientific Affairs  
Schering-Plough HealthCare Products Inc.

Desk Copies: Dr. Ganley  
Dr. Wilkin  
Dr. Katz  
Mr. Lipnicki



August 30, 2000

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
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Rockville, MD 20852

**RE: Docket 78N-0038: Sunscreen Drug Products for Over the Counter Human Use: Final Monograph, Re-Opening of Administrative Record**

The Agency has requested interested parties to provide specific types of data and information which would allow identification and adoption of a standard UVA testing procedure, along with a clear way to present UVA protection information in labeling to consumers. At the October 26, 1999 feedback meeting between the Agency and CTFA, as well as in subsequent written communications, FDA has also asked industry for specific information on the proportionality needed between SPF and UVA protection.

Enclosed is a proposal for testing sunscreen products for Ultraviolet A (UVA) efficacy and also for labeling the UVA protection provided by these products. This proposal identifies a way to evaluate UVA protection based on the concepts of proportionality and quantitative measurement of efficacy, providing the basis for clear communication of protection to consumers. In support of this proposal, we have included the results of testing the UVA efficacy of seven prototype sunscreen formulations with SPFs from 4 to 30, composed of a wide variety of active ingredients.

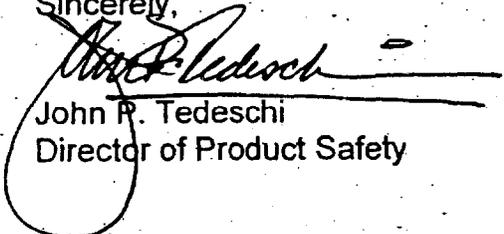
These data illustrate that proportional UVA protection cannot be guaranteed solely by measuring the broadness of absorbance; a measurement of the magnitude of protection is also required to fully and accurately describe the protection provided. This conclusion is consistent with the opinion of the American Academy of Dermatology, who have recommended that an increase in the SPF of a sunscreen must be accompanied by proportional increase in the UVA protection values, and that these "proportional" values should be determined by the FDA and the industry.

Page 2

The proposal presented in this document offers a way to create a comprehensive approach to sun protection which assures not only proportionality of UVA to UVB protection levels but also ensures breadth of absorbance for products making UVA protection claims. More importantly, in light of concerns expressed by the Agency that high SPF products may increase sun exposure and consequently UVA exposure, this proposal also ensures that high SPF products contain proportionally increased levels of UVA protection, coinciding with the view expressed by the American Academy of Dermatology. This approach also supports communication of the level of UVA protection in a simple, integrated format consistent with existing SPF labeling.

We, along with the other companies whose letters are supplied with this submission, support the testing and labeling proposals provided in these documents and hope that this information will assist your completion of a comprehensive final monograph.

Sincerely,



John R. Tedeschi  
Director of Product Safety

cc: J. Grieve  
G. Kort  
G. Ziets

Estée Lauder Companies  
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August 30, 2000

Dockets Management Branch (HFA-305)  
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ESTÉE  
LAUDER  
COMPANIES

RE: Docket 78N-0038: Sunscreen Drug Products for Over the Counter  
Human Use: Final Monograph, Re-Opening of Administrative  
Record

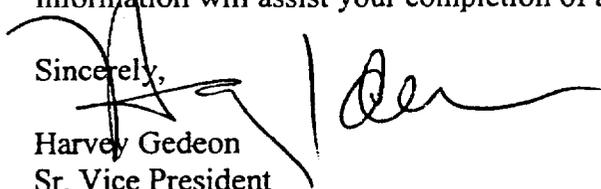
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In support of this proposal, we have included the results of testing the UVA efficacy of seven prototype sunscreen formulations with SPFs from 4 to 30, composed of a wide variety of active ingredients.

We, along with the other companies whose letters are supplied with this submission, support the testing and labeling proposals provided in these documents and hope that this information will assist your completion of a comprehensive final monograph.

Sincerely,

  
Harvey Gedeon  
Sr. Vice President  
Research and Development



August 30, 2000

WILLIAM C. EGAN  
GROUP FRANCHISE CHAIRMAN  
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RE: Docket 78N-0038: Sunscreen Drug Products for Over the Counter  
Human Use: Final Monograph, Re-Opening of Administrative Record

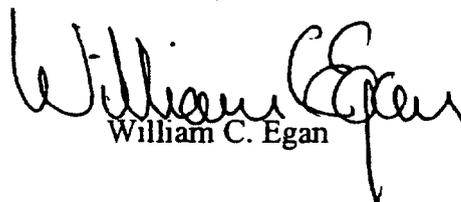
The Agency has requested interested parties to provide specific types of data and information which would allow identification and adoption of a standard UVA testing procedure, along with a clear way to present UVA protection information in labeling to consumers. At the October 26, 1999 feedback meeting between the Agency and CTFA, as well as in subsequent written communications, FDA has also asked industry for specific information on the proportionality needed between SPF and UVA protection.

Enclosed is a proposal for testing sunscreen products for Ultraviolet A (UVA) efficacy and also for labeling the UVA protection provided by these products. This proposal identifies a way to evaluate UVA protection based on the concepts of proportionality and quantitative measurement of efficacy, providing the basis for clear communication of protection to consumers. In light of concerns expressed by the Agency that high SPF products may increase sun exposure and consequently UVA exposure, this proposal also ensures that high SPF products contain proportionally increased levels of UVA protection, coinciding with the view expressed by the American Academy of Dermatology. This approach also supports communication of the level of UVA protection in a simple, integrated format consistent with existing SPF labeling.

In support of this proposal, we have included the results of testing the UVA efficacy of seven prototype sunscreen formulations with SPFs from 4 to 30, composed of a wide variety of active ingredients.

We, along with the other companies whose letters are supplied with this submission, support the testing and labeling proposals provided in these documents and hope that this information will assist your completion of a comprehensive final monograph.

Sincerely,

  
William C. Egan



August 30, 2000

Dockets Management Branch (HFA-305)  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, MD 20852

RE: Docket 78N-0038: Sunscreen Drug Products for Over the Counter  
Human Use: Final Monograph, Re-Opening of Administrative  
Record

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These data illustrate that proportional UVA protection cannot be guaranteed solely by measuring the broadness of absorbance; a measurement of the magnitude of protection is also required to fully and accurately describe the protection provided. This conclusion is consistent with the opinion of the American Academy of Dermatology, who have recommended that an increase in the SPF of a sunscreen must be accompanied by proportional increase in the UVA protection values, and that these "proportional" values should be determined by the FDA and the industry.

The proposal presented in this document offers a way to create a comprehensive approach to sun protection which assures not only proportionality of UVA to UVB protection levels but also ensures breadth of absorbance for products making UVA protection claims. More importantly, in light of concerns expressed by the Agency that high SPF products may increase sun exposure and consequently UVA exposure, this proposal also ensures that high SPF products contain proportionally increased levels of UVA protection, coinciding with the view expressed by the American Academy of Dermatology. This approach also supports communication of the level of UVA protection in a simple, integrated format consistent with existing SPF labeling.

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Sincerely,

A handwritten signature in cursive script that reads "A. John Penicnak".

A. John Penicnak, Ph.D.  
Senior Vice President, Corporate Scientific  
L'ORÉAL USA Products, Inc.

cc: J. Sullivan, General Counsel, L'ORÉAL USA, Inc.

MARY KAY<sup>®</sup>

August 30, 2000

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Sincerely,



Carolyn B. Wills  
Manager, Regulatory Affairs & Compliance

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**Balancing UVA and UVB Protection:  
Proportionality, Quantitative Measurement of Efficacy, and Clear  
Communication to Consumers**

8/30/00

**Balancing UVA and UVB Protection:  
Proportionality, Quantitative Measurement of Efficacy, and Clear  
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**Balancing UVA and UVB Protection:  
Proportionality, Quantitative Measurement of Efficacy, and Clear  
Communication to Consumers**

**Executive Summary**

The Food and Drug Administration (FDA) has extended the effective date for the final monograph for over-the-counter (OTC) sunscreen drug products and has reopened the administrative record for rulemaking to allow for comment on key technical and labeling issues related to sunscreen products. These issues were outlined by FDA in the June 8, 2000 Federal Register. The FDA intends to publish a comprehensive final monograph on OTC sunscreen drug products by December 31, 2001.

Contained herein is a proposal developed by an industry group that addresses the key issues relating to the testing and labeling of products that offer UVA protection. This industry group includes manufacturers of sunscreen products designed for use during outdoor activities (e.g. sport and beach use) as well as everyday use (e.g. makeup and foundations). The following companies have contributed to and strongly support this proposal on UVA testing and labeling:

Bath & Body Works, Inc.  
Estee Lauder Companies  
Johnson & Johnson Consumer Franchises WorldWide  
LORÉAL USA Products, Inc.  
Mary Kay, Inc.  
Schering-Plough HealthCare Products, Inc.

These companies are responsible for the development, manufacture and sale of a majority of Branded sunscreen-containing products that make SPF and UVA protection label claims.

Previously, the Cosmetic, Toiletry and Fragrance Association (CTFA) submitted comments addressing FDA questions and issues relating to the testing and labeling of sunscreen products offering UVB protection, specifically Sun Protection Factor (SPF) testing and labeling. Importantly, those comments addressed the issue of labeling products with SPF greater than 30, along with additional sunscreen indications beyond sunburn (e.g. photoaging). The industry group, made up of the companies above, participated in the development of those comments and, notwithstanding the proposal herein, strongly supports those earlier submissions.

In response to FDA's request for information on UVA testing methods and labeling, the industry group above has developed a proposal that includes a comprehensive approach to measuring sunscreen UVA protection and providing clear communication of both SPF and UVA protection to consumers and professionals. The proposal addresses three important issues that have been considered by FDA in an attempt to develop rulemaking involving sunscreen products that claim UVA protection. These are (1) *in vivo* and *in*

*vitro* testing of sunscreen UVA performance, (2) UVB/UVA proportionality for sunscreen products, and (3) communication of UVA performance on sunscreen-containing product labels.

This proposal assures not only proportionality of UVA to SPF protection levels in sunscreen products, but also ensures broadness of absorbance for all products making UVA protection claims. UVA/UVB proportionality is an important concept supported by both the American Academy of Dermatology and the FDA to ensure that sunscreens which offer protection from UVB radiation also offer appropriate and relative protection from UVA radiation, both of which contribute to short- and long-term skin damage. Thus, this proposal also assures that higher SPF products contain proportionally increasing levels of UVA protection as the SPF increases, based both on the magnitude and the broadness of UVA protection. This coincides with the views expressed by the American Academy of Dermatology. The proposed approach also supports communication of the level of UVA protection in a simple, integrated format consistent with existing SPF labeling.

In summary, this proposal makes the following specific recommendations on sunscreen testing and labeling:

***UVA Testing:***

1. An *in vivo* measurement of the "quantity" of UVA protection provided by a product is needed in addition to a measurement of broadness to fully assess product performance in the UVA range. Broadness of absorbance alone does not fully measure UVA protection or describe product performance in the UVA range. This proposal recommends the adoption of the Protection Factor A (PFA) method and/or the Persistent Pigment Darkening (PPD) method for measuring the quantity of UVA protection provided by a sunscreen product. These methods and their capabilities are described herein.
2. In addition to the amplitude of UVA protection, any sunscreen product labeled for UVA protection must demonstrate absorbance to or above 360 nm. This assessment can be accomplished using standard methods.

***UVA/UVB Proportionality:***

3. UVA protection should increase proportionally with higher SPFs; this can be assured through the use of defined ratios of UVA to SPF protection.
4. Using a sliding scale of minimum UVA efficacy guarantees commensurate UVA protection at each SPF based on a fixed ratio: there is proportional UVA/UVB protection at every SPF. This minimum or "basic" UVA protection should be based on a PFA:SPF ratio of 0.20. Additional UVA protection for products that desire to claim "extra" UVA protection" would require a PFA:SPF ratio of 0.25.

5. Once again, broadness of absorbance is guaranteed for both “basic” and “extra” levels of UVA protection through the requirement that all products that make UVA claims demonstrate absorbance to or above 360 nm.

***Sunscreen Labeling:***

6. SPF should retain preeminence on the principal display panel, and should continue to be the primary driver of consumer product selection.
7. UVA labeling should also be displayed on the principal display panel in terms of simple text descriptors, using wording that will allow consumers to identify and select a product with the level of SPF and UVA protection that suits their Skin Type and sun protection needs.
8. UVA protection claims should be allowed for sunscreen products with SPF's of 4 and higher.
9. Two distinct categories of UVA protection are warranted. Sunscreen products can be formulated to provide basic, proportional UVA/UVB protection, or to exceed that requirement to provide extra UVA protection for those who want or need additional protection. A higher category of UVA protection assures that products which claim “extra” UVA protection deliver that benefit at each SPF.
10. An example of the information contained on the sunscreen product principal display panel, including UVA protection, would include:
  - SPF
  - UVA (select one of the following, as appropriate)
    - “UVA protection” (i.e., meets minimum requirement for UVA/UVB proportionality and exhibits  $\geq 360$  nm absorbance)
    - “Extra UVA protection” (i.e., exceeds minimum requirement for proportional UVA/UVB protection; exhibits absorbance  $\geq 360$  nm)
11. Professional labeling can be provided to physicians that will allow them to select or recommend sunscreen products for their patients’ needs, based on more detailed information describing the quantity (protection factor) and the broadness of protection.

This industry group respectfully submits these recommendations and the supporting detail provided herein and strongly recommends that they be incorporated into the comprehensive final monograph on OTC sunscreen drug products anticipated to publish by December 31, 2001.

## **Balancing UVA and UVB Protection: Proportionality, Quantitative Measurement of Efficacy, and Clear Communication to Consumers**

### **Introduction**

In 1996, industry (via CTFA) submitted to FDA an in vitro UVA test method called Critical Wavelength (1). That method measured the broadness of the protection provided by a sunscreen product, but did not address either the magnitude of protection or the issue of the appropriate proportionality of UVA to UVB protection. The importance of assessing the quantity of UVA protection provided by sunscreen products was highlighted by the Agency in correspondence relating to Citizen Petition 8, docket 78N-0038 (2,3). In that correspondence, the Agency asked for additional UVA protection data beyond Critical Wavelength to support the UVA efficacy of certain combinations of sunscreen active ingredients with avobenzone. The data that the Agency requested was to be based on the in vivo Protection Factor A (PFA) test method (4).

The importance of proportionality was raised at the October 26, 1999 feedback meeting between CTFA and the Agency. At that meeting, FDA asked industry to comment on the requirement for proportionality between the SPF and UVA protection. The request for information on this point was made again in the FDA letter to CTFA of March 20, 2000. The importance of the proportionality of UVA to UVB was also addressed by the American Academy of Dermatology (5) in their April 26, 2000 press statement on UVA:

“The AAD recommends that an increase in the SPF of a sunscreen must be accompanied by a proportional increase in the UVA protection value. These "proportional" values should be determined jointly by the FDA and the industry.”

The final element that must be considered for a comprehensive approach to sun protection is the clear communication of both SPF and UVA protection information. The American Academy of Dermatology has recommended maintaining the SPF as the primary indicator of overall sunscreen performance. In 1996, CTFA submitted market research to the Agency (6) that showed that the best way to communicate UVA protection to the consumer was in the form of simple text descriptors, as opposed to utilizing additional numbers or graphics on the package label. This finding continues to be important, and is consistent with the concept of maintaining the SPF as the primary indicator of the protection provided by the sunscreen product.

In the Federal Register notice of June 8, 2000 (7), the Agency asked for industry input concerning professional labeling and, in particular, what information that labeling might contain. Based on adoption of the proposal herein, voluntary professional labeling information could provide details beyond those needed for consumer labeling concerning the quantity and broadness of the UVA protection offered by a product, along with information on other product performance characteristics that might be pertinent only to physicians. This information would allow physicians to recommend sunscreen products for specific needs and conditions, based on individual evaluation of their patients. However, such professional labeling cannot take the place of clear and comprehensible information on the label for consumers.

The proposal presented in this document offers a way to create a comprehensive approach to sun protection which assures not only proportionality of UVA to UVB protection levels but also ensures breadth of absorbance for products making UVA protection claims. More importantly, in light of concerns expressed by the Agency that high SPF products may increase sun exposure and consequently UVA exposure, this proposal also ensures that high SPF products contain proportionally increased levels of UVA protection, coinciding with the view expressed by the American Academy of Dermatology above. This approach also supports communication of the level of UVA protection in a simple, integrated format consistent with existing SPF labeling.

### **Background on the Requirements for UVA/UVB Proportionality**

The primary use of sunscreen products is to prevent sunburn and other forms of UV damage to skin. According to Urbach (8), the ratio of damage from the UVB and UVA components in sunlight over a day is 80% UVB and 20% UVA. Of the 20% due to UVA (320-400 nm), 62% of the damage risk has been ascribed to the shorter UVA II wavelengths (320-340 nm). Diffey (9) and Cole (23) have described a similar relationship of UVB to UVA (4B: 1A ratio) for UV-induced biological effects on the skin. Therefore, to provide proportional protection against both UVA and UVB, a sunscreen must protect against the 80/20 ratio of UVB and UVA in incident sunlight.

The overall SPF is a composite of the UV protection provided by the sunscreen product in both the UVB and UVA. The biological response of the skin to sunlight can be expressed as  $MED = MED_B + MED_A$ , where one Minimal Erythral Dose (MED) is composed of the contribution to sunburn from both the UVB and UVA wavelengths present in sunlight at any point in time. Using the 4:1 UVB: UVA relationship above, we can calculate the minimum UVA blockage needed to provide UVA/UVB protection for any SPF level. Table 1 describes the number of MEDs resulting from UVB radiation and UVA radiation reflecting that relationship. This table also illustrates the corresponding UVA blockage needed at each SPF to provide minimum protection in the UVA against sunburn and other forms of UVA induced damage based on the 4B: 1A ratio of incident sunlight.

While there are >30 sunburning MEDs per day possible for Fitzpatrick (10) Skin Type I's in the United States, a liberal estimate of the total UVA MEDs available per day is 4-6 UVA MEDs, delivered at a fairly constant rate of 1/2 MED/hr in the summer (11, 12). However, it is shortsighted to consider only the acute effects of either UVA or UVB. Suberythral doses and chronic doses of UVA as well as UVB have been shown to produce measurable damage in the skin. Therefore, considering only the total number of UVA MEDs available per day may underestimate the ability of UVA to contribute to and exacerbate long-term UVB-induced skin damage, including skin cancer and photoaging.

Action spectra for UV damage to skin are also key elements to be considered in determining a method for confirming the UVA protection provided by sunscreens. If the action spectra for other known forms of damage are compared to the action spectrum for sunburn (Figure 1), it is easy to see why a test method for assessing UVA protection must include the effects of the shorter wave UVA as well as the longer wave UVA. In vivo responses to UVA radiation, which can be measured

in clinical tests using light sources which include only UVA wavelengths (320–400 nm), can be used to substantiate protection across the UVA spectrum (Figures 2A and 2B).

### **Protection Minimums for Proportional UVA/UVB Protection**

Based on Table 1, a PFA of  $\geq 2$  in the UVA is needed at incident levels of 10 MEDs of sunlight and above. At levels below 10 MEDs, there is not a requirement for a PFA of 2 to prevent erythema from UVA, as the UVA component of erythema is one MED or less at those levels. Nevertheless, it is desirable to incorporate measurable UVA protection at all SPF levels; therefore, a minimum of a PFA of 2 should be a requirement even at low SPF levels for products that claim to protect against UVA as well as UVB.

The UVA wavelengths from 320 to 340 nm have been recognized as wavelengths that can contribute significantly to the development of skin cancer. Studies by Kelfkens et. al. (13) have shown that short-wave UVA (< 340 nm) is 5 times more efficient in producing skin cancer than the longer wavelength UVA. This is important in light of suggestions that the measurement of sunscreen UVA effectiveness be limited only to a description of its longwave UVA protection (i.e., to only its broadness) or that only one “pass-fail” level of UVA protection be recognized.

From an active ingredient perspective, to block the UVA contribution to sunburn and skin cancer, the absorbance of products of SPF 10 and above must extend beyond the UVA II (320–340 nm) to be effective. This is often achieved through the inclusion of oxybenzone or other UVA absorbers. For higher SPF products, the UVA absorbance must extend into the UVA I region, to or above 360 nm, to achieve the UVA/UVB balance needed at those SPF levels. This can be achieved by including combinations of UVA absorbers or by increasing the content of one or more active ingredients as needed. Products which provide proportional UVA/UVB protection should be readily identifiable to consumers, along with those products that include “extra” UVA protection.

### **Beyond the Minimum Balance Requirements: Extra UVA Protection**

Based on today’s technologies, products can be created such that more UVA protection is provided at any SPF level than is required from a sunburn protection standpoint. This can be done either to provide extra protection against other forms of potential UVA damage beyond sunburn, or as a consequence of extending the spectrum of absorbance through the inclusion of certain active ingredients which absorb well into the UVA I (i.e., >360 nm). While the action spectrum for photoaging effects appears to be very similar to the action spectrum for sunburn for some biological endpoints such as dermal elastosis (14, 15), there have been other studies which have shown that longwave UVA (> 340 nm) may contribute in different ways to premature skin aging. Studies by Lowe et. al. (16) and Lavker et. al. (17) suggest that repeated exposure to suberythemal doses of UVA may result in long term damage, resulting in increased photoaging of the skin. The regular use of sunscreens with effective UVA and UVB protection may help to protect against these cumulative, long-term forms of skin damage, as well as the more acute effects.

Honigsmann has suggested that a PFA of 3 (67% UVA blocked) be incorporated into every sunscreen product above SPF 10 (18). However, it appears from Table 1 that if only one protection factor was to be set for all UVA claims purposes, it would mandate more UVA protection than is scientifically or medically justifiable in lower SPF products (SPF 2-8), while allowing less UVA protection than is actually needed for adequate UVA protection at SPF's of 12 and above. We propose that the minimum requirement for products that provide "extra UVA protection" should be a PFA of 3. From there, UVA protection that increases as SPF increases can be incorporated into products based on UVA protection factors determined in vivo, in combination with broadness of protection. Broadness of absorbance alone does not guarantee proportionality of UVA to UVB.

### **Identification and Communication of Two Distinct Levels of UVA Protection**

Based on specific ratios of UVA to UVB, categories of UVA protection can be defined to recognize products which provide a basic, proportional UVA/UVB protection, and an "extra UVA protection" level based. Breadth of absorbance (i.e., the product absorbs to or above 360 nm<sup>\*</sup>) could also be determined to ensure that the broadness of protection was appropriate to support a UVA protection claim at any SPF level. This could be measured using the critical wavelength method (1), or by a spectrophotometric assessment of the absorbance spectrum.

The means to ensure UVB/UVA proportionality as SPF rises is shown in Table 2. To determine the level of UVA protection needed at any SPF, the SPF would be multiplied by 0.20. For example, an SPF 20 product would require a PFA of 4 to qualify as a sunscreen providing proportional UVA/UVB protection. Table 2 also illustrates the increased UVA protection that would be required for formulations that would qualify for "extra UVA protection" in comparison to the level of UVA protection present in formulas that exhibit basic, proportional UVA/UVB protection. To qualify for the higher level of claim, a PFA to SPF factor of 0.25 must be reached. An SPF 40 product would require a PFA of 8 for proportional UVA/UVB protection, and a PFA of 10 or more to qualify for "extra" UVA protection labeling.

Using the UVB to UVA relationships shown in Table 2, a product could qualify as providing proportional UVA/UVB protection, or could qualify for the "extra UVA protection" claim (for example, for products which include avobenzone). This method of assessing and communicating protection would serve (along with SPF as the primary indicator of product efficacy) to easily identify products which provide the higher level of protection from UVA and UVB, for the most sun sensitive consumers and for dermatology recommendations. It would also serve to allow those who prefer a lower SPF product to identify and select a product based on their Skin Type or needs. Not every consumer will want or need only products with "extra" UVA protection. A selection of affordable, balanced UVA/UVB protection products will continue to remain important, and there should be a readily identifiable UVA claim for the proportional protection that they provide. This proposal would recognize the basic UVA protection provided by products which do not choose to utilize avobenzone or zinc oxide, but which do exhibit good UVA protection nonetheless.

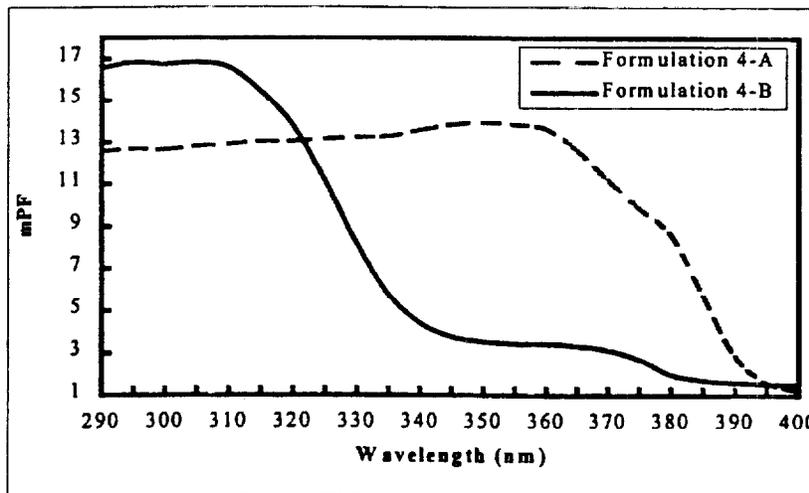
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\* according to the TFM, p. 28233

The existence of two distinct levels of UVA protection will not only allow consumer choice, but will also challenge industry to strive to meet the higher category by developing new technologies and new types of formulations. The “extra UVA protection” category would present true formulation challenges within the limitations of the active ingredient combinations currently allowed, especially at high SPF. As future technologies are identified and our knowledge of the effects of UVA progress, this strategy also provides the flexibility to consider higher levels of sun protection, without altering the familiar labeling that consumers will have come to expect on sunscreen products.

**The Need to Measure Both Breadth and Quantity of Protection**

Critical Wavelength and similar *in vitro* methods primarily measure the broadness of UVA absorbance. They do not quantitatively measure the magnitude of protection. This has been illustrated in previous submissions to the docket that showed that two sunscreens with similar critical wavelengths could have very different UVA absorbance curves and thus provide different protection for consumers. The figure and table below (from reference 22) demonstrate that two formulations with the same SPF can have different absorption curves and very different levels of UVA protection. Similar findings from a recently conducted study confirm these observations and will be discussed below. To have a complete understanding of the UVA protection provided by a sunscreen product, both broadness of absorbance and magnitude of UVA protection must be assessed.



**Monochromatic Protection Factor Curves of Two Prototype Formulations**

| Product Code | SPF ( <i>in vivo</i> ) | $\lambda_c$ (nm) | UVA <sub>e</sub> PF |
|--------------|------------------------|------------------|---------------------|
| 4-A          | 7.5                    | 379              | 10.2                |
| 4-B          | 7.4                    | 372              | 5.2                 |

From the above discussion these important points can be made:

1. A minimum 50% UVA efficacy (a PFA of 2) is appropriate for products below SPF 12 that wish to make basic UVA protection claims. Higher SPF products should contain correspondingly higher UVA protection levels to provide proportional UVA/UVB protection.
2. A sliding scale of minimum UVA efficacies can be proposed so that commensurate UVA protection is guaranteed at each SPF based on the PFA:SPF ratio of 0.20 (i.e., ensuring that a product provides proportionally balanced protection at every SPF).
3. In addition, a higher category of protection based on a higher ratio (PFA:SPF = 0.25) would assure that products which claim "extra" UVA protection on their labeling deliver that benefit from the perspective of both the magnitude of UVA protection as well as through the breadth of absorbance. For that higher classification, a minimum PFA of 3 would be required at SPFs below 12, with UVA protection rising with SPF.
4. Broadness of absorbance can be guaranteed for both the "basic" and "extra" levels of UVA protection through the requirement that all products that make UVA claims must demonstrate absorbance to or above 360 nm.

**Testing of Formulations to Evaluate the Reproducibility of the Protection Factor A (PFA) and Persistent Pigment Darkening (PPD) UVA Test Methods, with Additional Assessment of Broadness of Absorbance**

CTFA sponsored a study in which seven prototype products representing a wide variety of sunscreen formulation vehicles and active ingredients were used to test the reproducibility of the PFA (4) and PPD (19, 20) in vivo UVA test methods between laboratories. This test also served to compare the results obtained by using these methods to determine if the two methods could be used interchangeably to measure UVA protection. In addition, the formulas were evaluated to determine if they met the sunscreen monograph criterion of absorbing to or above 360 nm. The in vitro method used to assess the broadness of absorbance was the CTFA method previously submitted to the FDA in RPT 9 (1). The seven prototype products are provided in Appendix 1.

The protocols for the PFA and PPD (JCIA\*) tests are provided in Appendices 2 and 3. In the PFA method, erythema from UVA is evaluated at 16-24 hr post-exposure. In the PPD (JCIA) method, persistent pigment darkening is assessed 2-4 hr post-exposure. Both methods utilize a xenon-arc solar simulator, filtered with a 3-mm WG335 filter, which includes both the UVA II (320-340 nm) and the UVA I (340-400 nm) (Figure 2A). The main difference in the two test methods (other than post-exposure results reading time) lies in the Skin Types of the subjects tested. Skin Types I, II and III are used for PFA; Skin Types II, III and IV are used for PPD. The biological response spectra for the in vivo test endpoints (erythema or pigment darkening/tanning) when tested with this light source are shown in Figure 2B.

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\* Japan Cosmetic Industry Association

Two laboratories conducted both the PFA and the PPD test procedures to determine the in vivo UVA protection provided by each of the seven prototype formulations. One laboratory included an evaluation of the persistent pigment darkening results (PPD) at 2, 3 and 4 hours post-exposure. Information on the testing laboratories that participated in this study is included with Appendix 1.

Two laboratories also assessed the broadness of absorbance using the Critical Wavelength method as submitted by CTFA in 1996 (1). One laboratory provided data on the critical wavelength both before and after sample pre-irradiation. The other laboratory provided data based both on the labeled SPF of the samples and on the “mean” (average) SPF of the formulations (however, no differences in critical wavelengths were observed).

### **Testing Results**

The individual in vivo test data are provided in Appendices 4 and 5 for the PFA and PPD results, respectively. The data for the critical wavelengths determined are included in Appendix 6.

The data summary in Table 3 shows that for each sunscreen tested, the UVA protection values determined by the two in vivo test methods (PFA and PPD) were comparable, which confirms the results of earlier studies (11, 21). These data also demonstrate that clinical test methods for assessing UVA protection can be used to obtain reliable, reproducible results. Similar conclusions were made based on the multi-center study published on the PFA method by Cole (4). Comparison of the PFA results from the two laboratories and for the PPD results from the two laboratories are shown in Figures 3A and 3B. A comparison of the PPD results obtained at 2, 3 and 4 hours post exposure to the PFA data from the same laboratory is shown in Figure 4 and Table 4. The correlation of the PPD and PFA results for the seven products is shown in Figure 5.

Six of the seven products met the “broadness” criterion (i.e., absorbance  $\geq 360$  nm); however, they exhibited a large range of protection levels in vivo, as determined by the PFA and PPD methods. Only formula E, which contained 7% octyl methoxycinnamate with no added UVA absorber, did not provide a minimum UVA protection value of 2. Additionally, formula E did not exhibit absorption to or above 360 nm. These results are shown in Table 3, Figures 6A and 6B.

Based on the data provided, we suggest that the formulation for product A be used as a control formulation for UVA testing. This formulation is the same SPF 15 formulation submitted by CTFA as a “high SPF” control formulation for SPF testing (for which SPF data and methods validation have already been provided to FDA by CTFA, on 11/17/92 and 3/6/00 respectively).

### **Discussion**

Six of the seven formulas would qualify for UVA labeling based on the criterion of absorbance to or beyond 360 nm, based on the proposed UVA protection classification system described in this document. Formula E did not qualify for UVA labeling based on the criterion of absorbance to or above 360 nm, nor did it meet the minimum UVA protection level (PFA or PPD) needed to fulfill the proportionality requirement for basic balanced protection, and thus would not qualify

for any UVA labeling under the proposed plan.

Formula A (SPF 15) would qualify as a product providing basic, proportional UVA protection, based on meeting the requirements of a PFA: SPF factor of 0.20, with absorbance to  $\geq 360$  nm. This formulation had a PFA or PPD value of 3 and absorbance to  $\geq 360$  nm.

Formula I (SPF 12) appears to be borderline. While it absorbs beyond 360 nm, the PFA values just barely meet the requirements (PFA of 2.4) for the basic level of UVA protection. The PPD results for this formula would not meet the requirement.

Formulas F, G, H and J would qualify as formulas that provide "extra" UVA protection at their SPF level based on the required ratio of a PFA: SPF factor of at least 0.25, as well as exhibiting absorbance to or above 360 nm.

The results (Figure 4) from the study on persistent pigment darkening (PPD/JCIA) which included reading of results at 2, 3 and 4 hr post-exposure show that the biological response is constant over that time period. While the standard time for reading PPD results is 2-4 hours post-exposure, the data show that this response appears to be very stable, and that PFA and PPD results are comparable. The data shown in Figures 3A and 3B illustrate that the differences between the two laboratories for each endpoint were also small, for both PFA and PPD.

A comparison of the in vivo UVA protection values to the in vitro broadness of absorbance (critical wavelength) shows that it is possible to create formulas with a range of SPF's which can provide significant amounts of UVA protection as measured by the magnitude of protection (PFA or PPD) and by broadness of absorbance. However, the data also show that it is not possible to predict the magnitude of UVA protection from either the SPF or from the broadness of absorbance (Critical Wavelength) at a specific SPF. As shown in Figures 7A and 7B, when comparing formula I and formula G (both SPF 12 formulations), we can see that formula G has a PFA or PPD value of 4 (blocks 75% of the UVA damage risk), while formula I has a PFA or PPD value of just over 2, which would block just over 50% of the UVA risk. Despite its zinc oxide content, Formula I falls slightly short in the PPD test for the minimum protection needed to provide proportional UVA/UVB protection at that SPF (i.e., it did not reach the required PPD: SPF factor of 0.20).

The data are also relevant to questions raised about the need to assess both the magnitude and the broadness of UVA protection. As shown above and in Table 3, it is apparent that two sunscreens with the same SPF can exhibit different levels of UVA protection. Therefore, the argument that PFA or PPD results are redundant with the information provided by the SPF is not accurate. This is also highlighted by Figure 2B, which shows that the predominant biological response of these in vivo test methods is due to the UVA I portion of the spectrum (340-400nm). This again illustrates that the proposed in vivo test methods do not solely test UVA II and therefore are not "redundant" with SPF test results.

It is not possible to predict the level of UVA protection from the SPF alone, or to predict the quantity of UVA protection solely from the broadness of the protection (see results for product I, above, and in Table 3). Comparing the level of protection using the results of either the PFA or

the PPD test method to the broadness of absorbance (as measured by Critical Wavelength) documents the absence of a correlation between broadness and magnitude of protection as both the SPF and Critical Wavelength values increase. This finding supports the recommendation of the American Academy of Dermatology, which concluded that measuring broadness alone is not sufficient to accurately describe product performance in the UVA.

### **Conclusions and Recommendations**

1. SPF should retain preeminence on the principal display panel, and should continue to be the primary driver of consumer product selection. UVA labeling should also be displayed on the principal display panel in terms of simple text descriptors, using wording that will allow consumers to identify and select the sunscreen product with the level of SPF and UVA protection that suits their Skin Types and sun protection needs.
2. UVA protection claims should be allowed for sunscreen products with SPFs of 4 and higher. UVA protection should increase proportionally with higher SPFs, which can be assured through the use of defined ratios of SPF to PFA or PPD (see Table 2). A minimum of a PFA of 2 (blocks 50% of the UVA) should be a requirement even at low SPF levels (SPF < 12) for products that claim to protect against UVA as well as UVB.
3. Sunscreen products can be formulated to provide proportional UVA/UVB protection at each SPF level, or to exceed that requirement to provide increased UVA protection for those who want or need extra UVA protection. Therefore, two distinct categories of UVA protection are warranted.
4. "Broadness" of absorbance alone does not fully measure UVA protection or describe product performance in the UVA. A measure of the "quantity" of UVA protection provided by a product is needed in addition to an assessment of broadness of absorbance.
5. The PPD and PFA *in vivo* tests provide comparable results. Either method can produce reliable, reproducible data to measure the "quantity" of UVA protection. For practical purposes, having the option available of conducting testing for which the results can be read at 2-4 hours (PPD) or at 16-24 hours (PFA) may be important. For each product, the test method would be selected in advance; all testing for that formulation would be conducted using one method only. An advantage of the PFA method (4) is that it allows inclusion of Skin Type I subjects, who are those most in need of sun protection and who produce sunburn when exposed to UVA, whereas the PPD method can only be conducted on darker skin types, who produce pigmentation. The PPD test, however, may offer convenience for some laboratories, and with its acceptance as the Japan Cosmetic Industry Association (JCIA) method, may support ongoing efforts for global harmonization.
6. Voluntary professional labeling can be provided to physicians that will allow them to select or recommend sunscreen products for their patients' needs, based on more detailed information describing the quantity (protection factor) and the broadness of protection.

## **Communication of SPF and UVA Protection in Labeling**

An example of the information contained on the principal display panel might include:

- SPF (and water resistance, as appropriate)
- UVA (select one of the following, as appropriate)
  - “UVA protection” (meets minimum requirement for UVA/UVB proportionality and exhibits  $\geq 360$  nm absorbance)
  - “Extra UVA protection” (exceeds minimum requirement for proportional UVA/UVB protection; exhibits absorbance  $\geq 360$  nm)

**TABLE 1**

**AT EACH SPF: WHAT IS REQUIRED FOR PROPORTIONAL PROTECTION?**

| <b>MEDs Incident</b> | <b>SPF Required</b> | <b>UVA MEDs</b> | <b>UVB MEDs</b> | <b>Minimum PFA Required</b> |
|----------------------|---------------------|-----------------|-----------------|-----------------------------|
| 2                    | 2                   | 0.4             | 1.6             | 1                           |
| 4                    | 4                   | 0.8             | 3.2             | 1                           |
| 8                    | 8                   | 1.6             | 6.4             | 1.6                         |
| 12                   | 12                  | 2.4             | 9.6             | 2.4                         |
| 15                   | 15                  | 3               | 12              | 3                           |
| 20                   | 20                  | 4               | 16              | 4                           |
| 25                   | 25                  | 5               | 20              | 5                           |
| 30                   | 30                  | 6               | 24              | 6                           |
| 35                   | 35                  | 7               | 28              | 7                           |
| 40                   | 40                  | 8               | 32              | 8                           |
| 50                   | 50                  | 10              | 40              | 10                          |

**TABLE 2**

**Providing Proportional Protection:**

**Examples of UVA Protection Values at Increasing SPFs**

| <b>SPF</b>     | <b>UVA Protection</b>        |                    | <b>Extra UVA Protection</b>  |                    |
|----------------|------------------------------|--------------------|------------------------------|--------------------|
|                | <b>PFA:SPF factor = 0.20</b> |                    | <b>PFA:SPF factor = 0.25</b> |                    |
|                | <b>% UVA Blocked</b>         | <b>Minimum PFA</b> | <b>% UVA Blocked</b>         | <b>Minimum PFA</b> |
| <b>&lt; 12</b> | 50%                          | <b>2</b>           | 66%                          | <b>3</b>           |
| <b>12</b>      | 60%                          | <b>2.4</b>         | 66%                          | <b>3</b>           |
| <b>15</b>      | 66%                          | <b>3</b>           | 75%                          | <b>4</b>           |
| <b>25</b>      | 80%                          | <b>5</b>           | 84%                          | <b>6.25</b>        |
| <b>30</b>      | 83%                          | <b>6</b>           | 87%                          | <b>7.5</b>         |
| <b>40</b>      | 88%                          | <b>8</b>           | 90%                          | <b>10</b>          |
| <b>45</b>      | 89%                          | <b>9</b>           | 91%                          | <b>11.25</b>       |
| <b>50</b>      | 90%                          | <b>10</b>          | <b>≥92%</b>                  | <b>≥12.5</b>       |

**TABLE 3**

**TEST VALUE COMPARISONS**

| Sample - Testing Lab | Active Ingredients, SPF   | PPD (JCIA, ref. 20) | PFA (Cole, ref. 4) | Critical Wavelength (CTFA Method, ref. 1) |
|----------------------|---|---------------------|--------------------|---|
| J - TKL              | 10% Octocrylene,<br>6% Oxybenzone,<br>5% Octyl Salicylate,<br>3% Avobenzone<br>SPF 30 | 14.07               | 13.00              |   |
| J - CPT              |   | 10.80               | 12.19              | 379.6 nm                                  |
| J - IMSI             |   |                     |                    | 380 nm                                    |
| A - TKL              | 7% Padimate O,<br>3% Oxybenzone<br>SPF 15   | 3.18                | 3.23               |   |
| A - CPT              |   | 3.24                | 3.70               | 360 nm                                    |
| A - IMSI             |   |                     |                    | 362 nm                                    |
| I - TKL              | 6% Octyl<br>Methoxycinnamate,<br>4% Zinc Oxide<br>SPF 12                              | 2.18                | 2.59               |   |
| I - CPT              |   | 2.27                | 2.36               | 370.4 nm                                  |
| I - IMSI             |   |                     |                    | 374 nm                                    |
| G - TKL              | 7% Octyl<br>Methoxycinnamate,<br>3% Avobenzone<br>SPF 12                              | 4.65                | 4.4                |   |
| G - CPT              |   | 3.88                | 4.73               | 376.8 nm                                  |
| G - IMSI             |   |                     |                    | 379 nm                                    |
| F - TKL              | 5% Oxybenzone<br>SPF 9  | 2.95                | 3.43               |   |
| F - CPT              |   | 3.23                | 3.66               | 360 nm                                    |
| F - IMSI             |   |                     |                    | 362 nm                                    |
| E - TKL              | 7% Octyl<br>Methoxycinnamate<br>SPF 8   | 1.58                | 1.79               |   |
| E - CPT              |   | 1.72                | 1.75               | 336 nm                                    |
| E - IMSI             |   |                     |                    | 355 nm                                    |
| H - TKL              | 20% Zinc Oxide<br>SPF 4   | 3.57                | 4.01               |   |
| H - CPT              |   | 3.98                | 4.34               | 380 nm                                    |
| H - IMSI             |   |                     |                    | 381 nm                                    |

**TABLE 4**

**COMPARISON OF MEAN PPD AND PFA VALUES FROM ONE LABORATORY**

| PRODUCT | 2-HOUR PPD RESULT | 3-HOUR PPD RESULT | 4-HOUR PPD RESULT | 16-24 HR PFA RESULT |
|---------|-------------------|-------------------|-------------------|---------------------|
| A       | 3.24              | 3.16              | >3.16*            | 3.61                |
| E       | 1.72              | 1.60              | 1.64              | <1.64*              |
| F       | 3.23              | 3.06              | 3.06              | 3.66                |
| G       | 3.88              | 3.78              | 3.86              | 4.73                |
| H       | 3.98              | 4.35              | 4.43              | 4.34                |
| I       | 2.27              | 2.27              | 2.31              | 2.36                |
| J       | 10.8              | 10.8              | 10.57             | 12.2                |

\*Data sets include 1-2 inexact values

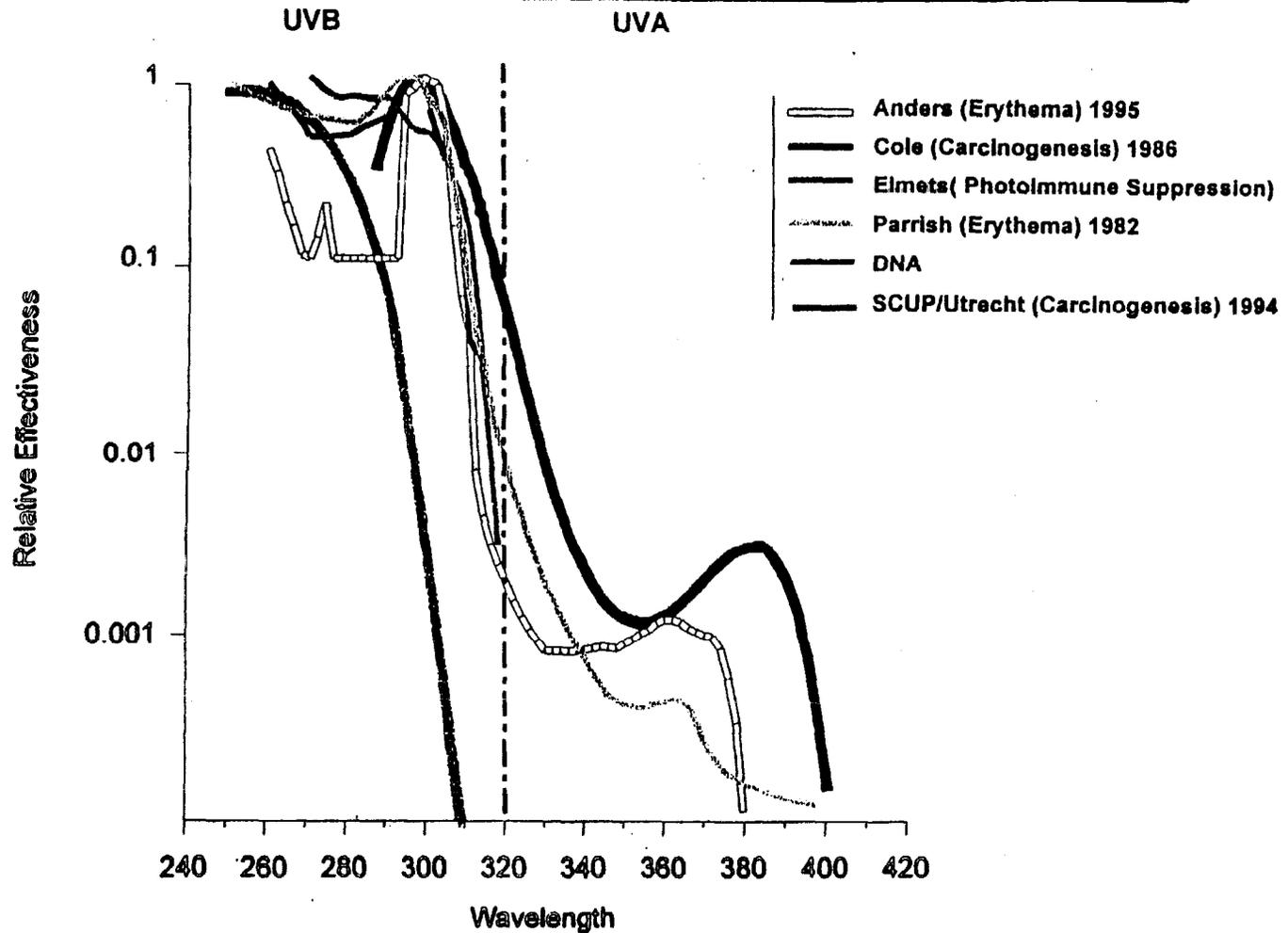
## REFERENCES

1. CTFA/NDMA taskforce report on Critical Wavelength determination for the evaluation of the UVA efficacy of sunscreen products. April 9, 1996. Docket 78N-0038, RPT 9.
2. Letter 167, Docket 78N-0038 to T.S. Elliott, April 8, 1999.
3. Letter 169, Docket 78N-0038 to T.S. Elliott, November 2, 1999.
4. Cole, C. Multicenter evaluation of sunscreen UVA protectiveness with the Protection Factor A test method. *J Am Acad Dermatol* 1994; 30; 729-736.
5. American Academy of Dermatology, Press Release April 20, 2000: available at "<http://www.aad.org/PressReleases/futuresunscreen.html>".
6. CTFA/NDMA. Sunscreen UVA Labeling, Market Research Study Report, Docket 78N-0038, February 6, 1996.
7. Food and Drug Administration. Sunscreen Drug Products for Over-the-Counter Human Use; Final Monograph; Extension of Effective Date; Reopening of Administrative Record. *Fed. Reg.* 65; 36319-36324, June 8, 2000.
8. Urbach F. Ultraviolet A transmission by modern sunscreens: is there a real risk? *Photodermatol Photoimmunol Photomed* 1993; 9; 237-241.
9. Diffey, Brian. Human exposure to ultraviolet radiation. *Seminars in Dermatology* 1990; 9; 2-10.
10. Fitzpatrick T. The validity and practicality of sun-reactive skin types I through IV. *Arch Dermatol* 1988; 124; 869-71.
11. Kaidbey K, Gange RW. Comparison of methods for assessing photoprotection against ultraviolet A in vivo. *J Am Acad Dermatol* 1987;16; 346-53.
12. Sayre RM, Agin PP. A method for the determination of UVA protection in normal skin. *J Am Acad Dermatol* 1990; 23; 429-40.
13. Kelfkens G, de Gruijl FR, van der Leun JC. Tumorigenesis by short-wave ultraviolet A. *Carcinogenesis* 1991; 12; 1377-1382.
14. Kligman LH, Sayre RM. An action spectrum for ultraviolet induced elastosis in hairless mice: quantification of elastosis by image analysis. *Photochem Photobiol* 1991; 53; 237-242.
15. Wulf HC, Poulsen T, Davies RE, Urbach F. Narrow band UV radiation and induction of dermal elastosis and skin cancer. *Photodermatol* 1989; 6; 44-51.

16. Lowe NJ, Meyers DP, Wieder JM, Luftman D, Bourget T, Lehman MD, Johnson AW, Scott IA. Low doses of repetitive UVA induce morphological changes in human skin. *J Invest Dermatol* 1995, 105; 739-743.
17. Lavker RM, Gerberick GF, Veres D, Irwin CJ, Kaidbey KH. Cumulative effects from repeated exposures to suberythemal doses of UVB and UVA in human skin. *J Am Acad Dermatol* 1995; 32; 53-62.
18. Honigsmann H. UVA and human skin. *J Photochem Photobiol B*: 1989; 4; 229.
19. Chardon A, Moyal D, Hourseau C. Persistent pigment darkening response as a method for evaluation of ultraviolet A protection assays. In: Lowe NJ, Shaath NA, Pathak MA, eds. Sunscreens: Development, Evaluation and Regulatory Aspects. New York, NY: Marcel Dekker, Inc. 559-582, 1997.
20. Japan Cosmetic Industry Association. Measurement Standards for UVA Protection Efficacy, 1998.
21. Stanfield JW, Edmonds SH, Agin PP. An evaluation of methods for measuring sunscreen UVA protection factors. In: Lowe NJ, Shaath NA, Pathak MA, eds. Sunscreens: Development, Evaluation and Regulatory Aspects, 2nd edition. Marcel Dekker, Inc., New York, NY, 537-557, 1997.
22. L'Oreal Research/Cosmair Cosmetics Corp. Comment C545, Docket 78N-0038, May 15, 1998.
23. Cole CA and Van Fossen R. Testing UVA Protective Agents in Man. In: Biological Responses to Ultraviolet A Radiation, F. Urbach, ed. Valdenmar Publishing Co., Overland Park, KS, 1992, pp. 335-345.

Figure 1

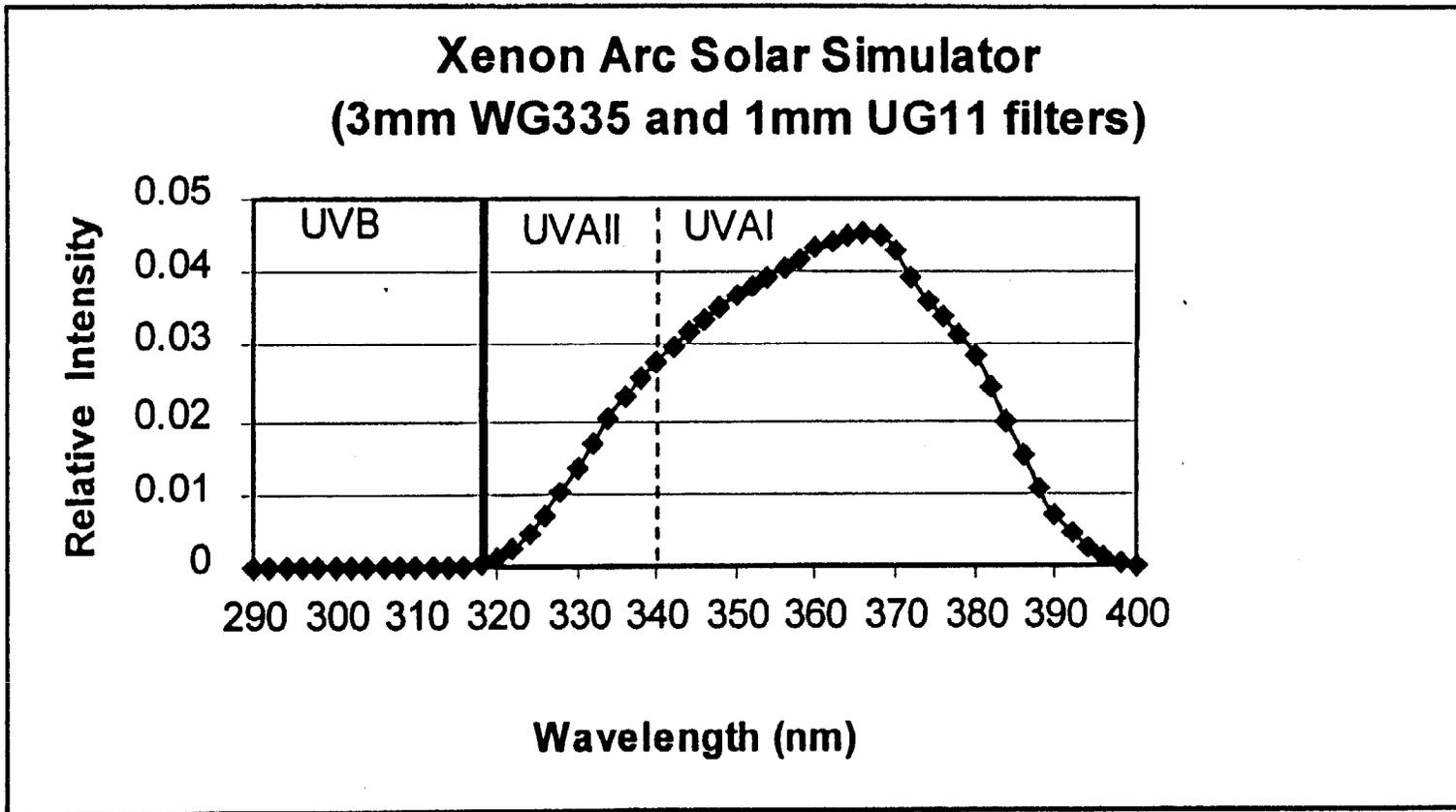
# Comparison of UV Action Spectra



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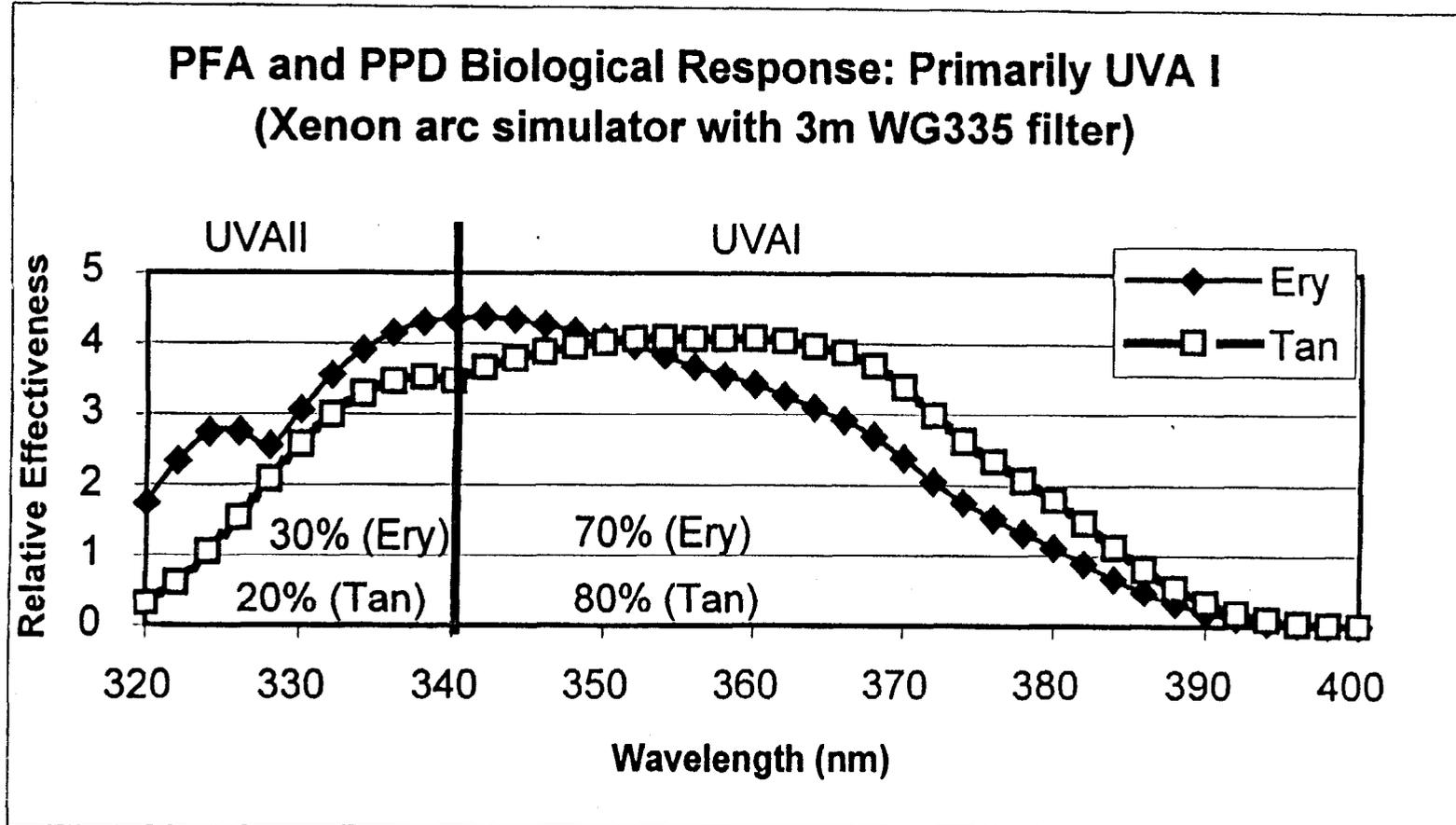
Based on the comparison of the action spectrum for sunburn to the action spectra for other known forms of UV damage shown above, it is important to include the effects of the shorter wave UVA as well as the longer wave UVA into any assessment of sunscreen UVA protection.

**Figure 2A**



Spectral distribution of the UVA source used in both the PFA and PPD test methods. Less than 2% of the biological response results from the UVB contained in the source.

Figure 2B



The action spectra for erythema (ery  $\blacklozenge$ ) (CIE) and for Persistent Pigment Darkening (tan  $\square$ ), when cross multiplied with the WG335 3mm filtered xenon arc solar simulator, clearly show that the predominant biological response is due to the UVA I portion of the spectrum (340-400nm). This illustrates that the proposed *in vivo* test methods do not solely test UVA II and therefore are not "redundant" with SPF test results.

Figure 3A: Comparison of Mean PFA Results From Two Laboratories

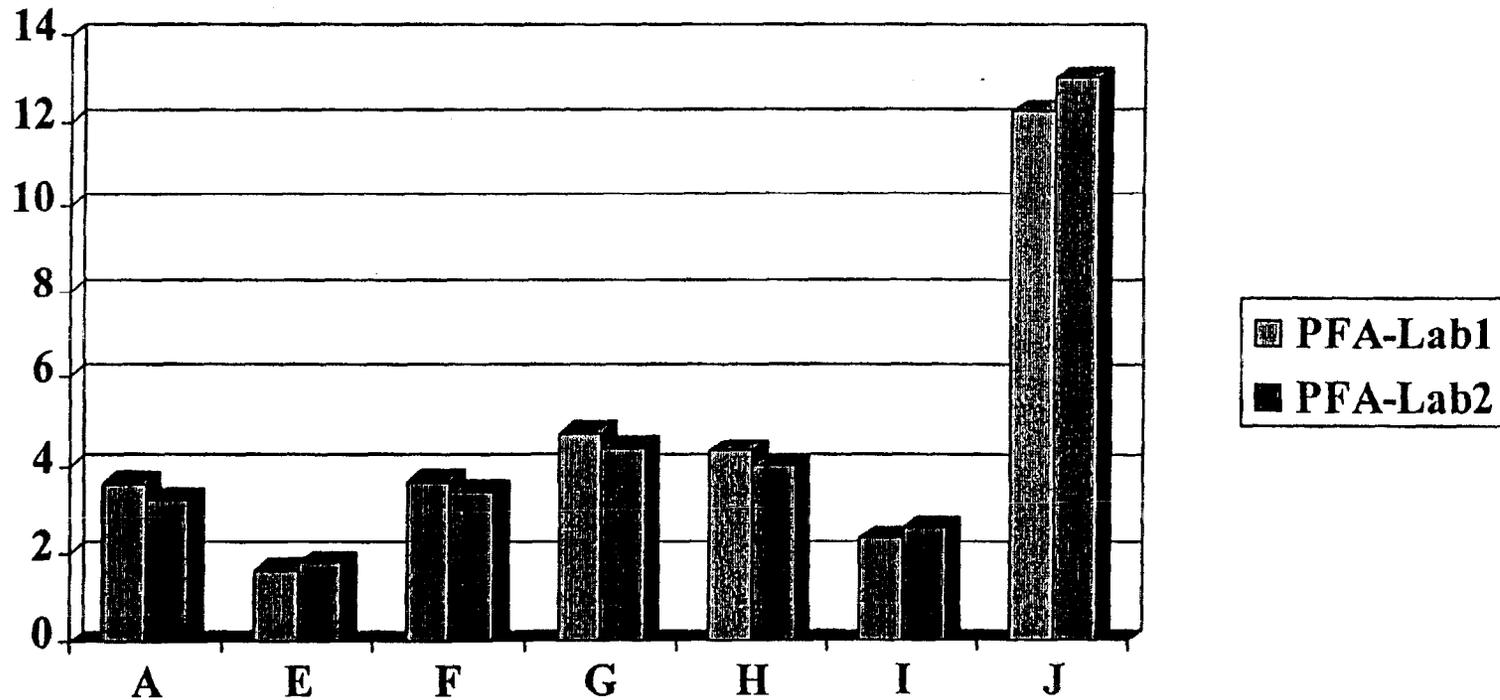


Figure 3B: Comparison of Mean PPD Results From Two Laboratories

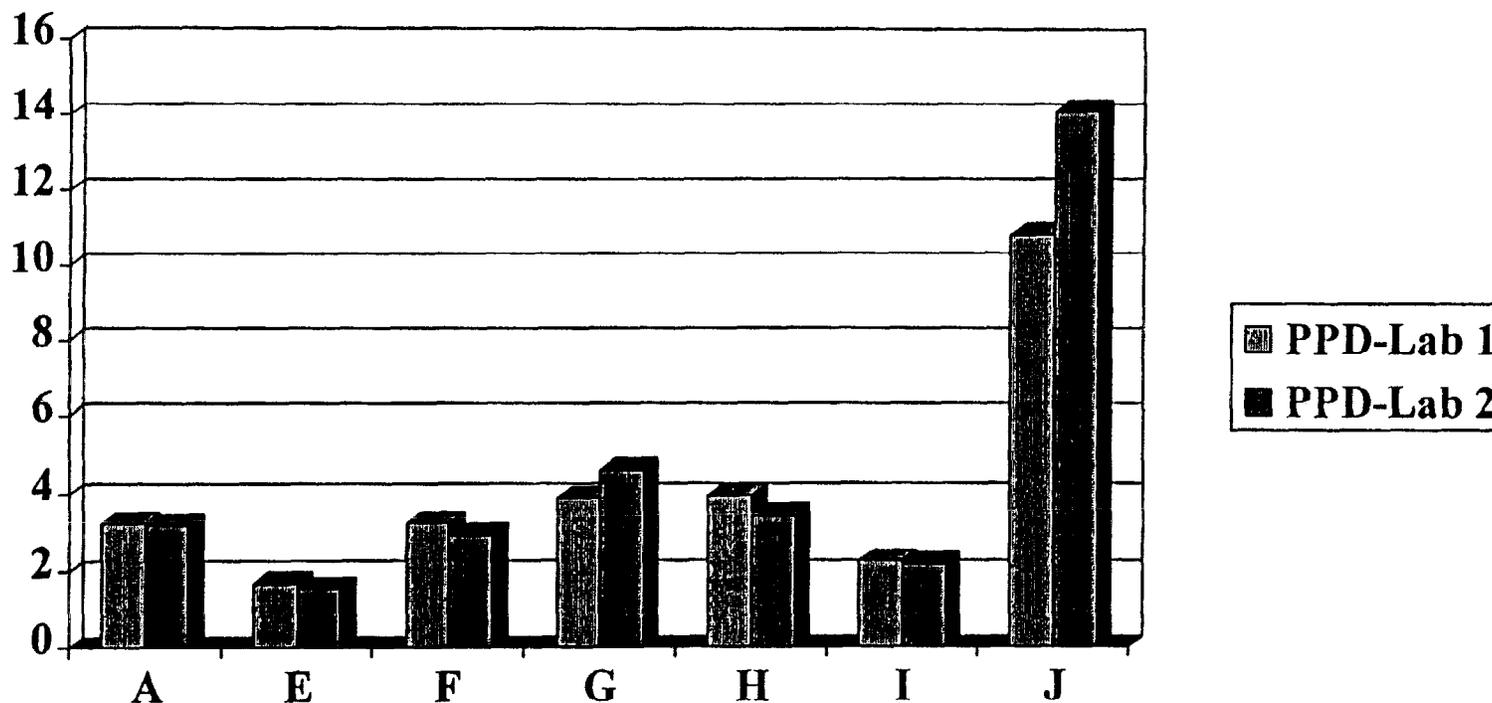


Figure 4: Comparison of Mean PPD and PFA Values From One Laboratory

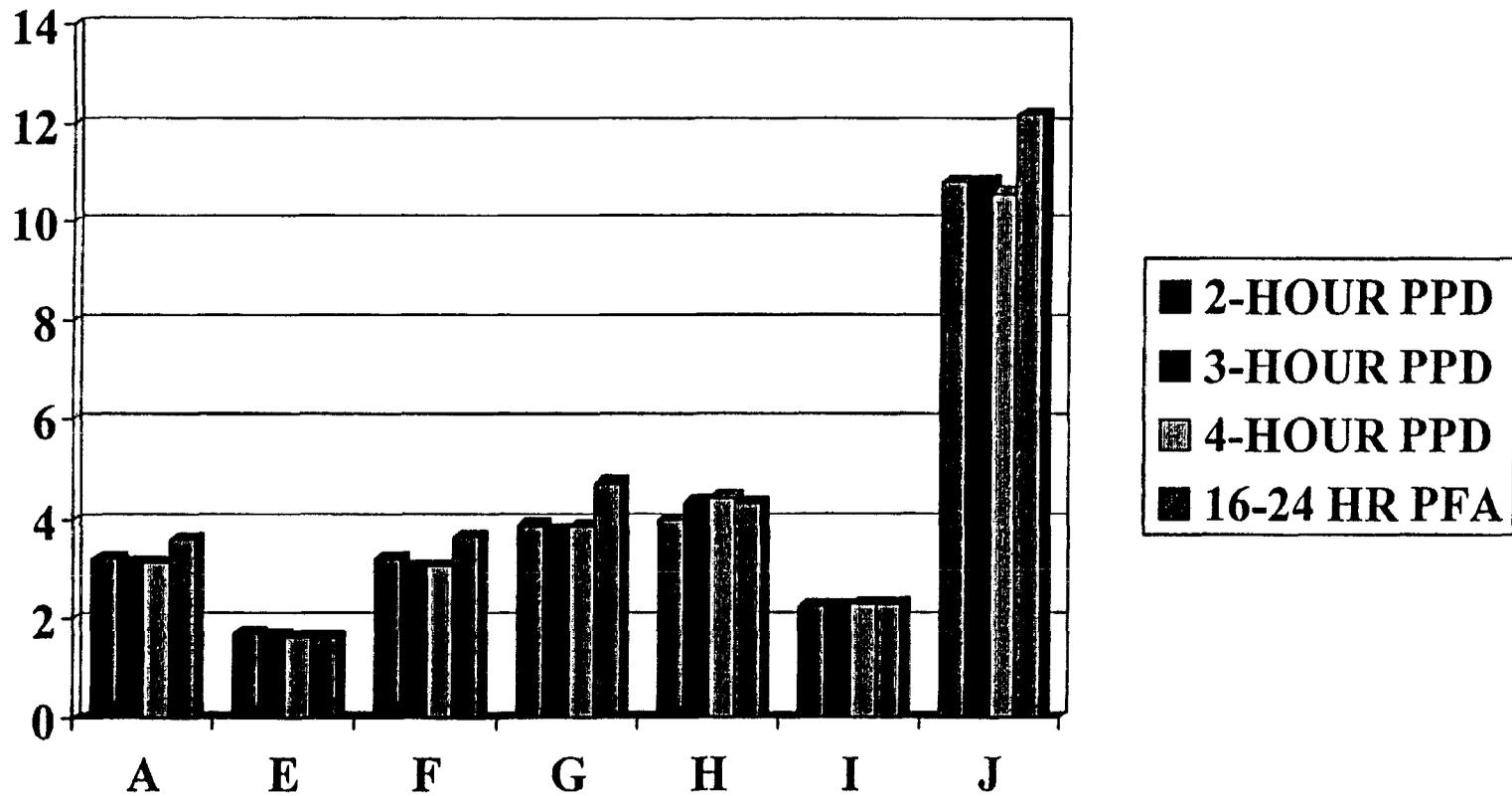
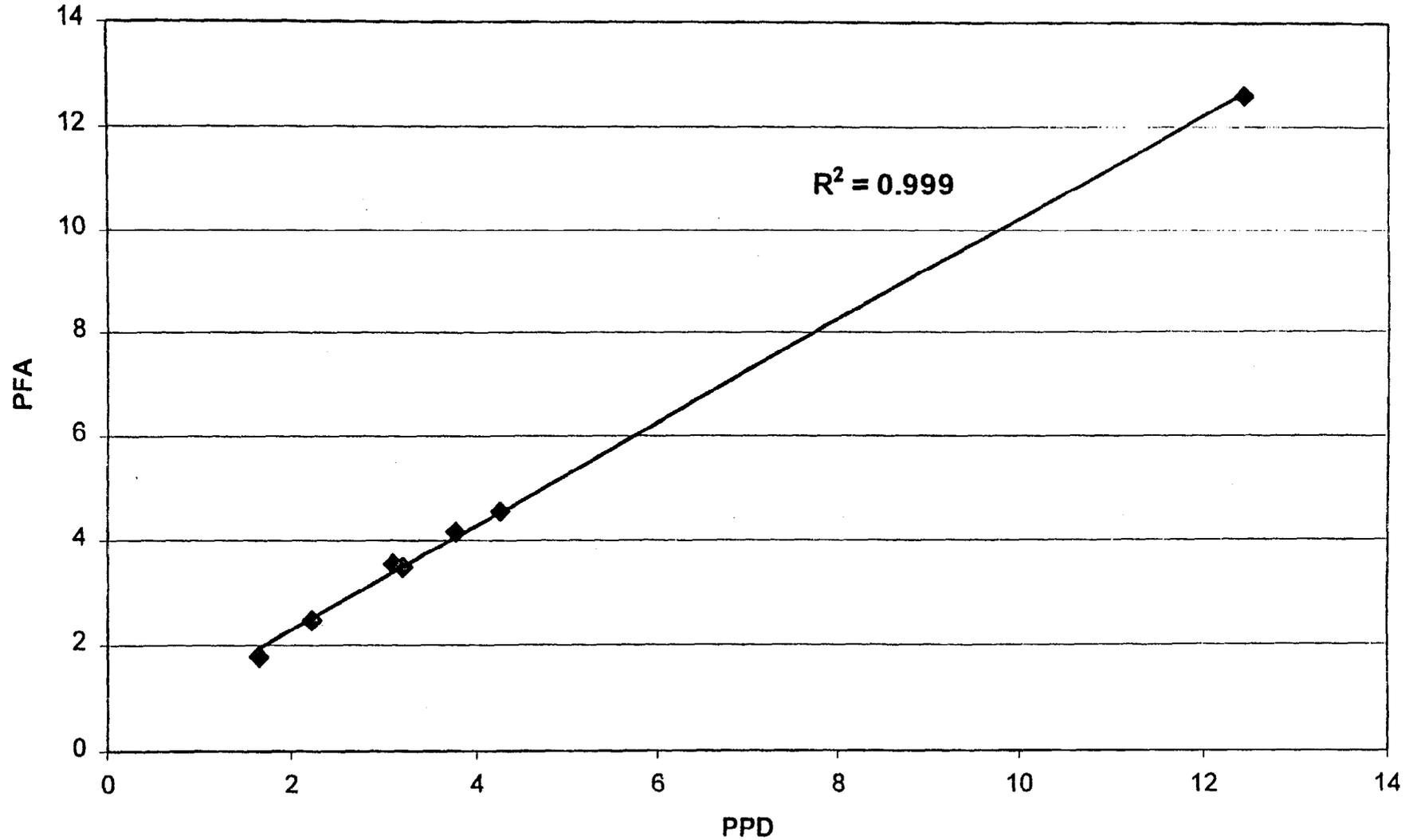


Figure 5: Correlation between Mean PPD and PFA Values



For each sunscreen tested, the PPD and PFA in vivo tests provided comparable results. These two in vivo methods can be used interchangeably to produce reliable data to measure the "quantity" of UVA protection.

Figure 6A

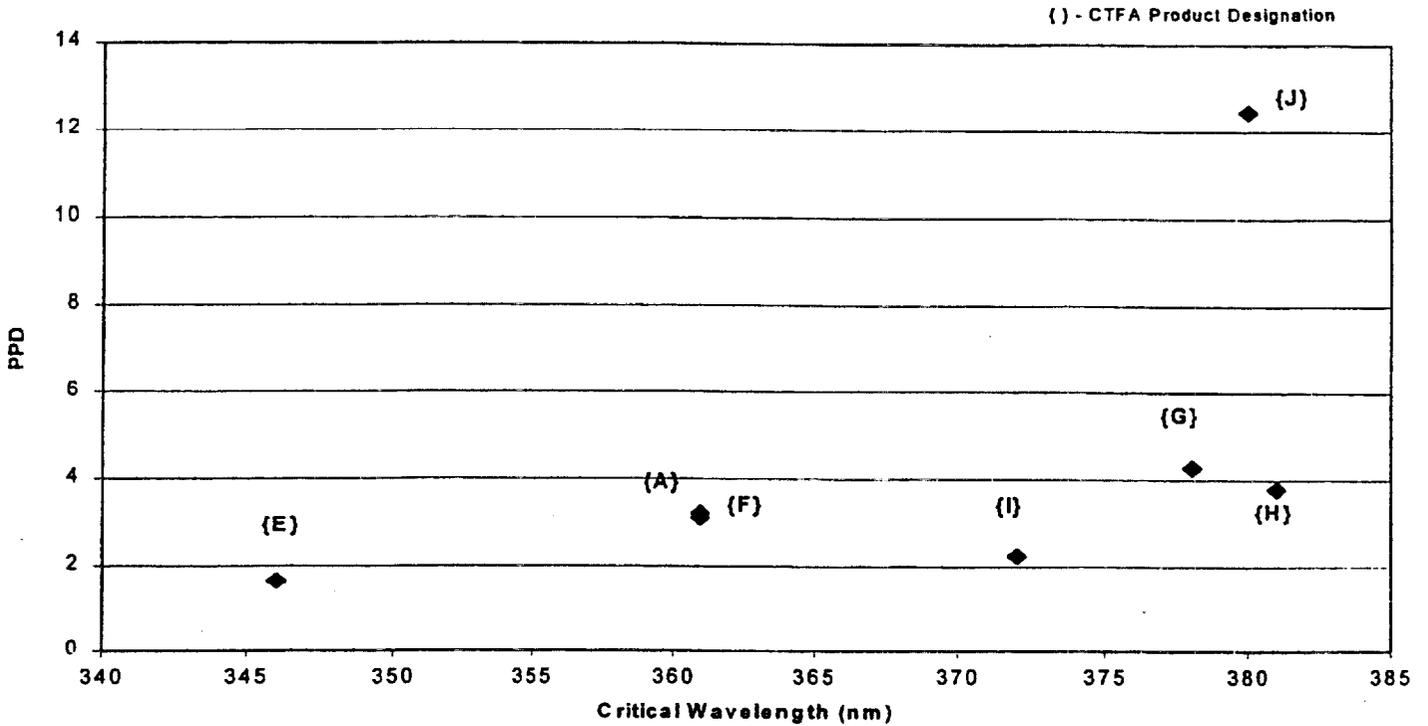
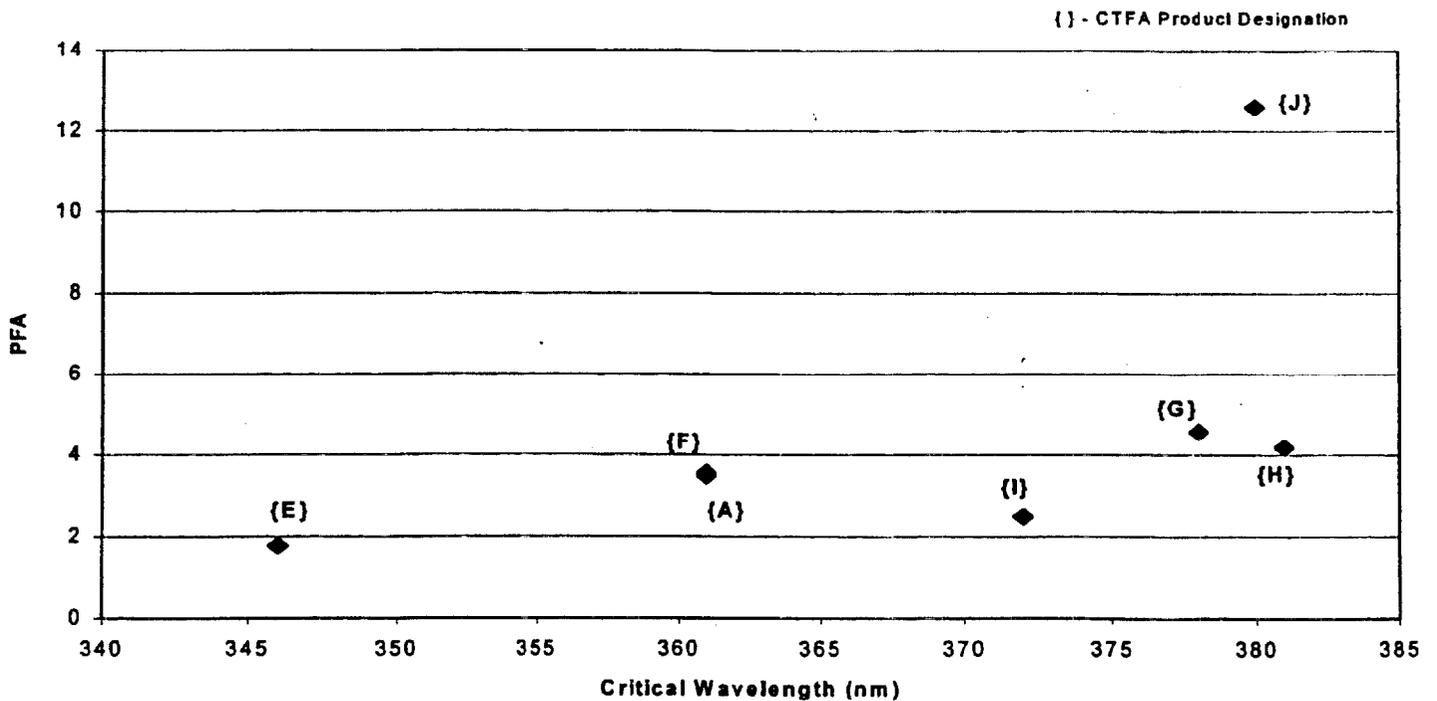


Figure 6B



"Broadness" of absorbance alone (as measured by Critical Wavelength) does not measure the quantity of UVA protection or fully describe sunscreen product performance in the UVA.

Figure 7 A

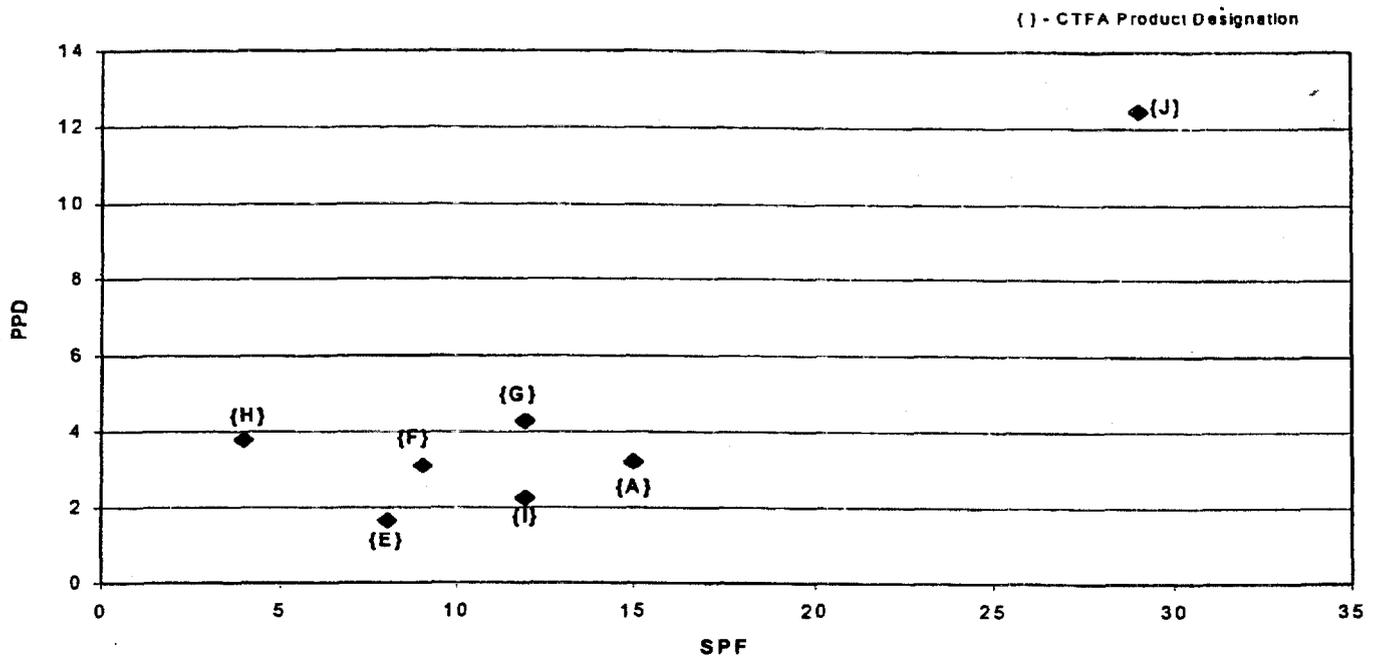
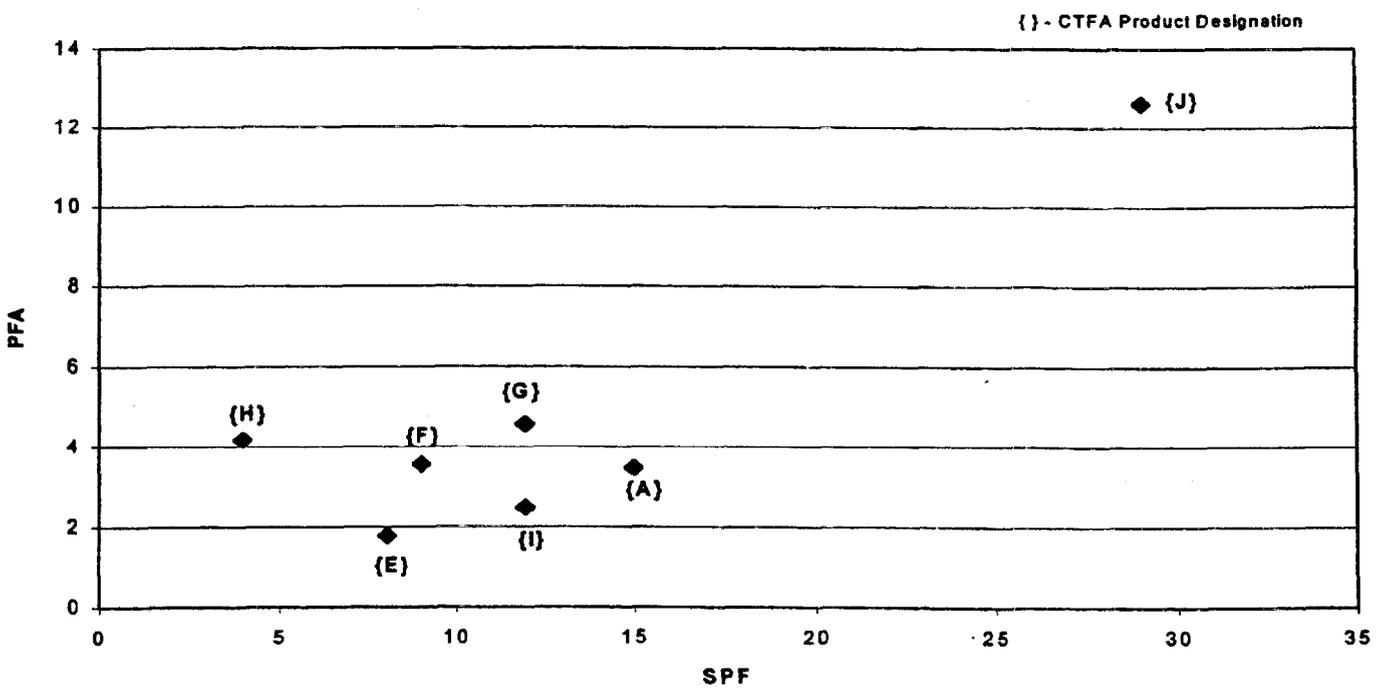


Figure 7 B



Sunscreens with the same SPF can exhibit different levels of UVA protection. Therefore, the argument that PFA or PPD results are redundant with the information provided by the SPF is not correct.