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# Choosing an expected sun protection factor value

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**Synopsis**

Sun protection factor, SPF, is a measure of the efficacy of a topical sunscreen product; the higher the SPF, the greater the blockage of ultraviolet-induced erythema. While there are several methods to determine SPF, the Food and Drug Administration (FDA) methods are unique. The FDA methods define the label SPF value as the largest whole integer after subtracting an "A" value from the mean SPF. The A value, composed of the product of the upper 5% point of the t-distribution and the standard deviation (SD), divided by $\sqrt{(n)}$, where $n$ equals the number of subjects, has a significant impact on the label SPF value. Two examples explore this impact. Development of strategies to mitigate the impact of A using expected SPF values are explored using historical clinical trial data. A more enlightened choice of expected SPF values is shown to lead to higher label SPF values.

## INTRODUCTION

Sun protection factor (SPF) is a measure of the efficacy of a topical sunscreen product. A higher SPF means greater protection against erythema from ultraviolet (UV) radiation exposure. SPF is calculated by determining the increase in UV dose to perceptible erythema from unprotected skin to sunscreen-protected skin following UV exposure. An SPF of 2 doubles the time to perceptible erythema (e.g., from 10 to 20 min), an SPF of 4 doubles the SPF 2 times (e.g., from 20 to 40 min), an SPF of 8 doubles the SPF 4 times (e.g., from 40 to 80 min), and an SPF of 16 doubles the SPF 8 times (e.g., from 80 to 160 min). Figure 1 shows the nonlinear relationship between SPF and the blockage of UV-induced erythema.

While the difference in percent blockage of UV-induced erythema between an SPF 32 and an SPF 64 is only 1.5% (98.4 – 96.9% = 1.5%), the SPF 64 product will allow the user to expose themselves to UV for twice as long (e.g., 320 min vs. 640 min).

SPF is an important number because it indicates the effectiveness of the product to block UV-induced erythema. Recently, Garzarella and Caswell (1) published data comparing the SPF of test materials with three test methods, International (2,3) versus Australia/NZ (4), International versus Food and Drug Administration (FDA)-Final Monograph (FM)

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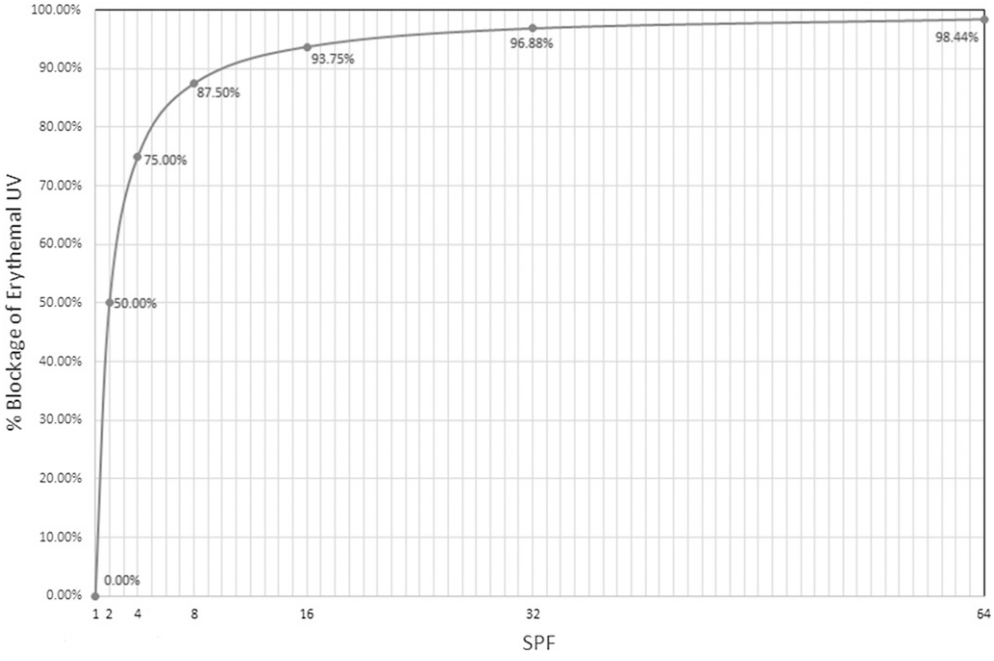


**Figure 1.** Relationship between percentage blockage of UV-induced erythema and SPF value.

(5), and Australia/NZ versus FDA-FM. The statistical analysis for the correlation between International versus Australia/New Zealand, International versus FDA-FM, and Australia/New Zealand versus FDA-FM, were 0.94, 0.99, and 0.95, respectively, illustrating a strong positive correlation between each pair. The difference in least squares mean SPF for each method pair was 0.12, 0.62, and 0.81, respectively, showing no statistically significant differences between the mean SPFs obtained using the different testing methods. The authors concluded that "the procedure discrepancies in FDA-FM, Australia/New Zealand Method, and the International Method are inconsequential; either the differences have no impact on mean SPF value, or, less likely, the differences produce equally and opposite changes in mean SPF, thus cancelling any effects."

Although there is no difference in mean SPF from the various methods, there is a difference in the label SPF, which the consumer sees to make a determination of purchase. In the United States, the FDA regulations dictate the subtraction of an A value from the mean SPF to generate the label SPF. The FDA regulations are the only regulations in which the label SPF differs from the mean SPF. Thus, special consideration must be given when SPF testing for the United States or for other countries that will accept the FDA method.

In testing a formulation for sunscreen efficacy, the first step is to choose an expected SPF value. Typically, a product brief will contain a target label SPF along with several other characteristics of the final product. For successful product development, the label SPF must be achieved, which begins with choosing the correct expected SPF. Several factors need to be considered when choosing an expected SPF for the United States, with the most important being the A factor (5–7). The A value is composed of the product of the upper 5% point of the one-tailed t-distribution and the SD, divided by $\sqrt{(n)}$, where $n$ equals

the number of subjects. The label SPF is the largest whole number after subtracting A from the average SPF. Thus, the average SPF from the clinical trial must be sufficiently large to still meet the target label SPF after the A value has been subtracted.

Historical data of A values have been used to evaluate the chances at 70%, 80%, 90%, and 100% of passing a target label SPF of 15, 20, 30, or 50. Using the results of the analysis herein, one can choose an expected SPF that has a known chance of passing the target label SPF.

## MATERIALS AND METHODS

The methods used to determine these percentage increases involved studying clinical trial data (not shown). With the information provided from those trials, sample SDs were estimated and collaborated to give sample data, which could be used in the calculation of the percentage increase. With that data, sample A values were calculated. A is calculated by multiplying the SD by the critical value on the t-distribution chart at an $\alpha$ level of 0.05, and dividing by the square root of the number of subjects. The 10 calculated A values were examined and the minimum, maximum, and mean were used for further calculations. Using these values, different percent increases were applied to the SPF values to determine what percentage of the clinical trials would pass the intended label SPF value. To determine the actual percent increases, the percent passing was applied to the formula. For example, for SPF 15, the A value to provide 70% passing was 1.32. Therefore, to obtain a label SPF value of 15, the expected SPF value must be at least 16.32, so the subtraction of the A value still results in an SPF of 15. A percentage increase of 8.8% yields this result. This method was continued to find all necessary percentage increases.

## RESULTS AND DISCUSSION

### A VALUE AFFECTS THE LABEL SPF

Unlike other methods, the FDA-FM (5) method and the more recently published FDA Proposed Amendment (6) and FDA Final Rule methods (7) subtract an A value from the mean SPF to calculate the label SPF value. The A value is composed of the product of the upper 5% point of the one-tailed t-value and the SD divided by $\sqrt{n}$, where $n$ equals the number of subjects. This subtraction decreases the average SPF determined by the FDA-FM and FDA Final Rule methods to the label SPF value, which is the largest integer after subtraction. While product briefs frequently seek an SPF with a 5 or 0 at the end, (e.g., 15, 20, 30, etc.) delivering a formulation with the requested label SPF can be difficult due to the variable experimental value of A. There are two examples that exhibit this variability.

*Example 1.* An example of the effect of subtracting A from the average SPF is shown in Table I, where the target label SPF was 50. In this example, the average SPF obtained from the 10 subjects is 52.8. However, subtracting the A value of 4.04 results in a label SPF value of 48, below the target label SPF value of 50.

The A value is dependent on three numbers, one-tailed t-value, SD, and number of subjects. As SPF data from more subjects are added, the one-tailed t-value in the numerator

**Table I**
Typical Data from SPF Testing on 10 Subjects

| | MED (s) | | | SPF | |
|---|---|---|---|---|---|
| | | | Test | | Test |
| Subject no. | Untreated | Standard | Material | Standard | Material |
| 1 | 15 | 245 | 990 | 16.3 | 66.0 |
| 2 | 19 | 310 | 827 | 16.3 | 43.5 |
| 3 | 15 | 281 | 863 | 18.7 | 57.5 |
| 4 | 15 | 225 | 792 | 15.0 | 52.8 |
| 5 | 15 | 245 | 750 | 16.3 | 50.0 |
| 6 | 15 | 245 | 653 | 16.3 | 43.5 |
| 7 | 15 | 245 | 863 | 16.3 | 57.5 |
| 8 | 15 | 281 | 750 | 18.7 | 50.0 |
| 9 | 15 | 245 | 750 | 16.3 | 50.0 |
| 10 | 19 | 356 | 1093 | 18.7 | 57.5 |
| Average SPF ($n$=10) | | | | 16.9 | 52.8 |
| SD | | | | 1.32 | 6.97 |
| Standard error | | | | 0.42 | 2.20 |
| t-Value (one-tailed) | | | | 1.833 | 1.833 |
| A | | | | 0.76 | 4.04 |
| SPF value | | | | 16 | 48 |

MED (s) - Minimal Erythemal Dose (seconds).

decreases, the SD in the numerator decreases, and the number of subjects in the denominator increases. All three values contribute to a decrease in the value of A as subjects are added. An example of this is shown in Table II, which contains the same data as in Table I, only doubled, so that the data from each subject is listed twice. The data for subject 1 is the same data as for subject 11. In this example, the average SPF is 52.8, the same as in Table I. Subtracting the A value of 2.62, results in a label SPF value of 50, which meets the desired target label SPF value. Interestingly, according to the Final Rule, the label SPF of a sunscreen can increase by increasing the number of valid subjects.

Increasing data to 30 subjects by adding the same group of 10 again fails to result in significant additional benefit because the rate of change in the t-value, the SD, and the number of subjects decreases. With data from 30 subjects, the A value reduced from 2.62 to 2.09 and the label SPF remains at 50.

*Example 2.* A second example of the effect of subtracting A from the average SPF occurs when all 10 subjects in the clinical trial to determine SPF return an identical SPF, in this example an SPF of 30. In this instance the SD is zero, so the A value is zero. Subtracting the A value of zero from the average SPF value results in a label SPF value of 30.

If one of the subjects returned an SPF value higher than 30, e.g., 34.5, then the SD would change from zero to 1.42 and the value of A would become 0.82. Subtracting the A value of 0.82 from the average SPF value of 30.5 results in a label SPF value of 29. The label SPF value for the product is 29 despite the fact that not a single subject returned an SPF value below 30. This example shows that, according to the Final Rule, the label SPF value of a formulation can decrease by increasing the individual SPF values of valid subjects.

**Table II**
Typical Data from SPF Testing on 10 Subjects Twice

| | MED (s) | | | SPF | |
|---|---|---|---|---|---|
| | | | Test | | Test |
| Subject no. | Untreated | Standard | Material | Standard | Material |
| 1 | 15 | 245 | 990 | 16.3 | 66.0 |
| 2 | 19 | 310 | 827 | 16.3 | 43.5 |
| 3 | 15 | 281 | 863 | 18.7 | 57.5 |
| 4 | 15 | 225 | 792 | 15.0 | 52.8 |
| 5 | 15 | 245 | 750 | 16.3 | 50.0 |
| 6 | 15 | 245 | 653 | 16.3 | 43.5 |
| 7 | 15 | 245 | 863 | 16.3 | 57.5 |
| 8 | 15 | 281 | 750 | 18.7 | 50.0 |
| 9 | 15 | 245 | 750 | 16.3 | 50.0 |
| 10 | 19 | 356 | 1093 | 18.7 | 57.5 |
| 11 | 15 | 245 | 990 | 16.3 | 66.0 |
| 12 | 19 | 310 | 827 | 16.3 | 43.5 |
| 13 | 15 | 281 | 863 | 18.7 | 57.5 |
| 14 | 15 | 225 | 792 | 15.0 | 52.8 |
| 15 | 15 | 245 | 750 | 16.3 | 50.0 |
| 16 | 15 | 245 | 653 | 16.3 | 43.5 |
| 17 | 15 | 245 | 863 | 16.3 | 57.5 |
| 18 | 15 | 281 | 750 | 18.7 | 50.0 |
| 19 | 15 | 245 | 750 | 16.3 | 50.0 |
| 20 | 19 | 356 | 1093 | 18.7 | 57.5 |
| Average SPF ($n$=20) | | | | 16.9 | 52.8 |
| SD | | | | 1.28 | 6.78 |
| Standard error | | | | 0.29 | 1.52 |
| t-Value (one-tailed) | | | | 1.729 | 1.729 |
| A | | | | 0.50 | 2.62 |
| SPF value | | | | 16 | 50 |

MED (s) - Minimal Erythemal Dose (seconds).

The results of these two examples led us to consider the consequences of the expected SPF value in SPF testing according to the Final Rule.

### EXPECTED SPF VALUE AFFECTS THE LABEL SPF

Consumer Product Testing Company analyzed data from 10 clinical trials evaluating SPF according to the Final Rule (6). The purpose of the analysis was to investigate the relationship between the expected SPF value and the label SPF value using real data from these 10 clinical trials. The expected SPF on these trials were 15, 20, 30, and 50. From these data, we analyzed the SD values that were used to calculate A values, which were subtracted from the average SPF value. The calculated A values were used to forecast expected SPF values. The question we asked was "What Expected SPF value should be

proposed so that subtraction of the A value does not bring the target label SPF value below the desired value?"

To answer this question, data from the 10 clinical trials were analyzed. The expected SPF value was given different percentage increases to examine the effects of obtaining the desired label SPF value. The percentage increase used for examining the expected SPF values ranged from 5% to 15%. Each percentage increase was used in comparing the label SPF value for the 10 clinical trials. From this, a determination could be made of the percentage increase required for the label SPF values of 15, 20, 30, and 50. The data collected from previous clinical trials served as a benchmark in determining the passing rate for label SPF values at 70%, 80%, 90%, and 100%.

Percentage increases were then applied to the expected SPF values to determine how large a percentage increase was needed to obtain the label SPF value with a chance of 70%, 80%, 90%, and 100%. The results from this analysis can be found in Table III.

Table III shows that if the expected SPF of 15 were increased by 8.8%, the clinical trial would have a 70% chance of achieving a label SPF of 15. In other words, increasing the expected SPF from 15 to 16.3 (or 8.8%) gives a 70% chance of reaching a label SPF of 15. Similarly, based on the same 10 clinical trials, if the expected SPF of 15 were increased by 14.4%, from 15 to 17.2, there would be a 100% chance that the label SPF value would remain above 15 after subtraction of the A value.

Using these results, one should carefully choose the expected SPF to maximize the chance of obtaining the desired label SPF. The data in Table III suggest that the expected SPF should be approximately 7% to 9% greater than the desired label SPF, with a slightly higher percentage for lower SPF values and a slightly lower percentage for higher SPF values.

This calculation to achieve a label SPF value decreases the label SPF determined by the FDA-FM and the FDA Final Rule to a value that could be statistically different from the SPF value determined by other methods, likely resulting in identical formulations labeled with different SPF values.

## CONCLUSIONS

In an SPF test according to the FDA-FM or FDA Final Rule, subtraction of the A value from the average SPF results in a reduced label SPF value. To overcome this reduction, the

**Table III**
Percentage Increase in Expected SPF to Achieve the Desired Label SPF

| Percent increase in expected SPF | | | | |
|---|---|---|---|---|
| | Percent passing | | | |
| Label SPF | 70 | 80 | 90 | 100 |
| 15 | 8.8 | 9.6 | 10.2 | 14.4 |
| 20 | 6.7 | 7.9 | 8.5 | 11.4 |
| 30 | 6.1 | 8.4 | 8.7 | 10.6 |
| 50 | 5.9 | 7.4 | 8.1 | 8.7 |

expected SPF must be increased between 7% and 9%. When a label SPF of 15 is desired, the expected SPF should be approximately 16.3 (9% increase). When a label SPF of 30 is desired, the expected SPF should be approximately 32.5 (8.5% increase). Choosing the correct expected SPF value will increase the chance of achieving the desired label SPF.

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