

Antiperspirant Testing in the Worldwide Marketplace

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When the concept of antiperspirants hit the market a number of decades ago, the general belief was that there would be a limited market for the product and that the product would inevitably go head to head with deodorants for the lion's share of consumer usage.

However, with the marketplace changes in perception and usage of these products, this industry has entered a new age where antiperspirants are crossing cultural and geographic lines not anticipated in those early days.

The initial antiperspirants were along the lines of a cream, taken from a bottle and applied to the underarm. This rather uncomfortable formulation was followed in the 1950's by the traditional solids, which in turn spawned roll-ons, semi solids and aerosols. These formulations became more and more complex, often incorporating the use of deodorants along with the antiperspirant as consumer needs moved into that direction.

In some countries, deodorants are classified as cosmetic in nature, while the biological changes caused by antiperspirants may have those products fall into the pharmaceutical arena.

In any case, the critical question still applies: Does the formulation work? And, if so, how efficacious is the formula? Therefore, it is imperative that a proper testing program be developed to accurately determine the efficacy of antiperspirants on the market.

One model for this type of efficacy testing may be as follows. This model is based on the tentative FDA monograph of August, 1982, which superseded the initial monograph of October, 1978. It should be noted that this testing is not stand alone. A full program of analytical stability, microbiological safety and quality testing of batches should also be put into place.

Testing Procedure for Efficacy of Antiperspirants

•Prior to the actual testing, a great deal of preparation is required.

•First, a panel is created by randomly selecting from a group of subjects qualified to participate on the study. These subjects have received an annual physical to determine eligibility for study participation.

Subjects who are on certain types of medications or have certain medical conditions such as diabetes, heart disease, respiratory problems or axillary abnormalities, are not eligible to participate in antiperspirant testing.

•Prior to the start of perspiration collections and product applications, subjects participate in the conditioning phase.

The conditioning phase is typically a 17-day dry-out period when no other soaps, antiperspirants or deodorants are used by the subjects, except for those issued by the testing facility. Subjects are instructed not to shave their axillae at least 48 hours prior to entering the study, and for the remainder of the study period.

•After the conditioning phase is complete, the study begins. On the first study day, subjects receive a brief physical by qualified technicians that includes a blood pressure and examination of the axillae for any signs of irritation. Subjects who do not meet blood pressure requirements or show signs of axillary irritation are disqualified at this time.

Each subject is given an individual envelope bearing the subject's name and qualification/subject number. Each envelope contains two loose, unweighed Webril pads and four plastic sandwich bags containing Webril pads, each labeled to match the subject's number and either the word 'RIGHT' A, 'LEFT' A, 'RIGHT' B or 'LEFT' B. Each 'RIGHT' pad is identified by red dots in each corner.

The left pads do not have identifying marks. Subjects acclimate for approximately 30 minutes in an area that is approximately 70BF.

- In unison, the subjects enter the controlled-temperature room maintained at 100°F (\pm 2°F) and 35-40% relative humidity for qualification. Upon instruction from the study personnel, all subjects place the unweighed pads in the axillary vault for a forty-minute acclimation phase.

Upon completion of the acclimation phase, a technician removes and discards the unweighed pads and places the pre-weighed 'Left A' and 'Right A' pads in the appropriate axillary vault for a twenty-minute collection period.

After the twenty-minute collection period, a technician removes the 'A' collection pads and places them in the appropriate plastic bags. The process is then repeated with the pre-weighed 'B' bags for a second twenty-minute collection period.

Both bags are then placed into the appropriate envelope and are carried out of the controlled-temperature room by the subjects and placed in a designated location.

- Post-weights are then calculated to determine qualification. Typically, a minimum of 30 subjects are required to qualify for the study by producing 150mg of perspiration under each axilla for each 20-minute collection period. Those subjects that qualify, will return for supervised axillary washes and test material applications.

- Supervised washing of the axillary area utilizes 4" x 4" gauze pads placed in a solution of mild soap and tepid water.

Subjects will use one pad for each axilla, then discard and move to the next station to rinse each axilla with plain tepid water. A different rinse pad will be used for each axilla. A paper towel is then placed in each axilla to blot the area dry. There is no rubbing. The paper towels are left in place until applications of the test materials.

- A randomized test material application is made to either one or both axillae. Approximately 400mg of the test material is applied by a technician to ensure complete coverage of the axillary vault. There is a one-hour wait post-application prior to dismissal or before entering the controlled-temperature room for perspiration collection.

- Solid test materials can be applied from individual containers. The containers are weighed pre- and post-application to ensure approximately 400mg of the material has been applied.

Semi-solids are measured into a weighing boat for

each subject. The test material is then applied with a finger cot.

Liquids, solutions, and suspensions are drawn up into a 1cc tuberculin syringe. The syringe barrel is used to swab the axillary vault to evenly distribute the test material.

Aerosols are applied as a two-second spray directly from the container. A metronome is used to measure the two seconds. Containers are weighed pre- and post-application and an average amount of application is obtained for the group.

Pump materials are applied as three to four strokes directly from the container.

- The number of applications prior to perspiration collection is the Sponsor's option. Generally, four daily applications (test days two through five) are performed prior to the test perspiration collection on test day five. To determine the efficacy of an antiperspirant at 24 hours after four applications, test material applications would be made on test days one through four.

Also, perspiration collections can be performed at any point during the study period or at a specified number of hours post-application to determine the efficacy of the test material at that particular timeframe.

- To determine that a test material is an effective antiperspirant per the TFM, the product must show a reduction in perspiration of at least 20% in 50% of the population. Descriptive statistics are calculated for the amount of test products used and the amount of perspiration for treated and control axillae at each evaluation.

The geometric mean perspiration is also calculated because the distribution of perspiration is generally assumed to be lognormal. The logarithm of the amount of perspiration will be calculated for treated and control axillae at each evaluation.

The hypothesis that the means of the logarithms of the amount of perspiration are equal for the two conditions is tested using the paired t-test. The ninety-five percent confidence interval for the reduction in perspiration is calculated by taking the antilogarithm of the ninety-five percent confidence interval on the mean reduction in log (perspiration) at each evaluation.

The binomial test is used to test the hypothesis that at least fifty percent of the population will obtain a reduction in perspiration of at least twenty percent.

The Wilcoxon ranked sum test is used to test the hypotheses that the median reduction in perspiration was equal to twenty percent.

Additional Issues

As indicated previously, the above mentioned testing procedure is only designed for efficacy of antiperspirants.

Of equal importance to the developer of these products is the knowledge that, as pharmaceuticals, manufacturing of the product must be performed under strict regulatory guidelines. Further, testing programs for microbiological and analytical stability must be developed under the those guidelines for these types of products.

This process would also have to include the development and validation of stability indicating test methods for each of the products. Ongoing quality testing according to guidelines should also be put into place.

In Conclusion

The development of an effective testing program for the antiperspirant market is critical, not only for regulatory purposes, but to determine the most effective formulation for the marketplace.

The procedure is logistically complex, yet provides an effective methodology to make the proper determinations within the regulatory environment.

Critical issues in Antiperspirant Development and Marketing

1. Determination of formulation

2. Determination of delivery system

a. Aerosol

b. Roll on

c. Stick

d. Soft Stick

3. Production of material according to Regulatory standards

4. Development of testing program

a. Efficacy

b. Analytical Stability

i. Method Development

ii. Method Validation

iii. Accelerated Stability

iv. Room Temperature Stability

c. Microbiological Testing

i. Preservative Efficacy: Plate Count

ii. Production Environmental

d. Batch Release Testing