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Division of Dockets Management  
Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, MD 20857

Re: **Docket No. 1978N-0064**  
Antiperspirant Drug Products for Over-the-Counter Human Use; Final Monograph; Partial Stay; Reopening of the Administrative Record  
Response to FDA Request for Comments (Federal Register: October 15, 2004)

Dear Sirs:

Reference is made to the Federal Register Notice of October 15, 2004 regarding the reopening of the administrative record for the OTC antiperspirant drug products and the request for comments related to the claims of enhanced antiperspirant duration. This letter and the attached documents are being submitted in response to the request for comment.

Numark Laboratories markets an antiperspirant, Certain Dri<sup>®</sup> (aluminum chloride 12%) in accordance with 21 CFR Part 350 – Antiperspirant Drug Products for Over-the-Counter Human use. Shortly following the publication of the Federal Register notice of October 15, 2004, Numark Laboratories initiated a clinical trial with the Certain Dri<sup>®</sup> product to produce data to support enhanced duration of effectiveness claims for submission to the Docket in accordance with the Notice. The conduct of the study incorporated the following conditions:

- The study design was in accordance with the antiperspirant testing guidelines referenced in 21 CFR 350.60;
- The test materials included aluminum chloride 12%, as listed in 21 CFR 350.10;
- The study is a randomized, placebo controlled clinical trial;
- The subject panel reflects consumer demographics (equal numbers of men and women, etc.), to demonstrate the enhanced duration of effectiveness is applicable to the entire consumer population.

This study was initiated on January 27, 2005 at Essex Testing Clinic, Inc. in Verona, NJ. Due to unforeseeable circumstances, the completion of the study has been delayed. The study site has informed us that during the course of the study there were difficulties in maintaining the temperature and humidity conditions specified in the protocol. Subsequently, the location of the study was moved to Consumer Product Testing Company in Fairfield, NJ. As such, we respectfully submit the attached initial comment as preliminary information in response to the FDA request for comment, with expectations that this comment will be supplemented with a full report on or about June 30, 2005. The Protocol (Attachment A) is herewith.

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In addition, Numark Laboratories provides the following point-by-point response to FDA's request for comments on the labeling related to products having enhanced duration claims as follows:

**FDA point:** How often to apply the product

**Numark response:** The application schedule of an antiperspirant product would be provided in the Directions of the product labeling. The time to reapplication would be based on the clinical trial data demonstrating antiperspirant effectiveness beyond 24 hours, whether it be 48 hours or more. Thus, suggested language in the Directions section might state: Apply to the underarms at bedtime. Use every day at beginning of use for 7 days. Thereafter, apply every other day or as needed.

**FDA point:** The effect of bathing or showering before the duration of effect period ends

**Numark response:** The effect of bathing or showering should be provided in the Directions of the product labeling. Suggested language might state: It will not wash off the next day, even after bathing or showering.

**FDA point:** Whether any other special labeling should apply to products with a duration of effect greater than 24 hours

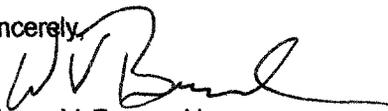
**Numark response:** Assuming the frequency of application is stated clearly in the Directions section of the labeling, there would be no need for any other special labeling for such a product.

**FDA point:** Whether there should be any limit on the enhanced duration claim and whether there are any potential safety issues if a product with enhanced duration of action is reapplied more frequently than directed (e.g., an antiperspirant labeled as providing 48 hours of sweat protection applied every 24 hours).

**Numark response:** When the clinical trial data support an enhanced duration claim, there is no basis to impose limits on the claim. With regard to the safety there is a rationale for the safety of the proposed product use based on the available scientific literature independent of the study in question. Additionally, as a product is applied less frequently due to enhanced duration of effectiveness, the safety profile will be enhanced.

If there are any questions or comments associated with this submission, please contact Wayne Brozynski at (732) 417-1870.

Sincerely,



Wayne V. Brozynski  
Vice President, Operations

**TITLE:** Clinical Efficacy Evaluation of an Antiperspirant Formulation After Four Daily Applications and Perspiration Collections at Baseline, Day Four, Day Six and Day Seven to Support Claims for Enhanced Duration of Effect.

**OBJECTIVE:** To determine the antiperspirant effectiveness of a test material forty-eight (48) and seventy-two (72) hours after four (4) consecutive applications, exceeding the minimum requirements of the FDA recommended procedure outlined in the Antiperspirant Drug Products for Over-the-Counter Human Use; Final Monograph of Monday, June 9, 2003 (effective date: December 9, 2004).

**TESTING FACILITY:** Consumer Product Testing Company, Inc.  
70 New Dutch Lane  
Fairfield, New Jersey 07004

**INVESTIGATORS:** *Principal Investigator:*  
Michael Traudt, Ph.D.  
Senior Director, Clinical Evaluations

Joy Frank, R.N.  
Executive Vice President,  
Clinical Evaluations

**PROPOSED SCHEDULE:** Proposed study initiation and termination dates to be established prior to the start of testing.

**ETHICS:** **Ethical Conduct of the Study:**

This study will be conducted in accordance with the intent and purpose of Good Clinical Practice regulations described in Title 21 of the U.S. Code of Federal Regulations (CFR), the Declaration of Helsinki and Consumer Product Testing Company (CPTC) Standard Operating Procedures (SOP's).

**Subject Information and Consent**

This study will be conducted in compliance with CFR Title 21, Part 50 (Informed Consent of Human Subjects). Informed consent will be obtained from each subject in the study and documented in writing before participation in the study. A copy of the Informed Consent will be provided to each subject.

**TEST MATERIAL(S):**

*Supply & Identification:* Test material(s) will be supplied by the sponsor and are identified by a CPTC study number and client identification code.

*Storage:* Test material(s) will be stored in a secure area and, unless otherwise specified, are stored at ambient temperature and humidity in the containers in which they are received.

*Disposition:* All used/unused test material(s) remaining at the conclusion of the study will be disposed of two months after the final report of the study is issued or returned to the Sponsor at their request.

**INCLUSION CRITERIA:**

- a. Approximately thirty (30) male and/or female volunteers, in general good health, between the ages of 18 and 65 years.
- b. History of stable and normal blood pressure (Systolic range = 100 – 160 mm Hg; Diastolic range = 60 – 90 mm Hg) and must not be taking any antihypertensive medications.
- c. Must produce at least 100 mg of perspiration under each axilla during each of two (2) twenty (20) minute baseline collection periods.
- d. Females must not be pregnant, lactating, or planning on becoming pregnant during the course of the study.
- e. Absence of any axillary irritation.
- f. Completion of a Medical History Form and the understanding and signing of an Informed Consent Form.
- g. In compliance with all pre-study requirements and considered capable of following directions.

**EXCLUSION CRITERIA**

- a. Known sensitivity or intolerance to antiperspirants or deodorants (Medical History, Consent).
- b. Frequent user of antihistamines or anticholinergics (Medical History, Consent).
- c. History of heart disease, asthma, diabetes or mastectomy (Medical History, Consent).
- d. Any axillary abnormalities that would preclude participation (Consent, Visual Examination).

**TEST ROOM CONDITIONS:** Controlled by the Johnson Control Medisys System with a DX-100 controller and maintained at:

Temperature: 100<sup>0</sup> F ( $\pm 2^0$ )

Humidity: 30 - 40%

**TEST SITES:** Right and left axillae.

**TEST PROCEDURE:** This study will be performed to satisfy the requirements as set forth in "Guidelines for Effectiveness Testing of Over-The-Counter Antiperspirant Drug Products". These guidelines are in accordance with the Final Monograph (final rule) for Over-The-Counter Antiperspirant Drug Products, published in the Federal Register on June 9, 2003 (68 FR 34273).

Pre-test Qualification:

- a. A minimum of thirty (30) subjects will be randomly selected from a group of acceptable subjects qualified for participation in the study. The participants will be required to abstain from the use of antiperspirants for seventeen (17) days prior to the start of the study. During this time, deodorants (Original Right Guard Sport Deodorant®) and soaps (Camay® Classic) supplied by Consumer Product Testing Company will be used exclusively. Use of all other deodorants, antiperspirants and soaps will be prohibited.
- b. Subjects will be instructed not to shave their axillae at least 48 hours prior to the start of the study.

Controlled Collection:

- a. Prior to entering the controlled-temperature room, each subject will have their blood pressure taken and will acclimate for approximately 15 minutes in an area that is approximately 70°F. Any subject not meeting blood pressure requirements, (Systolic range = 100 – 160 mm Hg; Diastolic range = 60 – 90 mm Hg), will be disqualified at this time.
- b. The controlled-temperature room will be maintained at a temperature of 100<sup>0</sup> F ( $\pm 2^0$ ) with a relative humidity of 30-40% (percent) by the Johnson Control Medisys System with a DX-100 controller. Entry of subjects into the controlled-temperature room will be conducted in unison.
- c. Each subject will have an envelope bearing his or her name and qualification/subject number. Each envelope will contain:

**TEST PROCEDURE (cont'd):**

Two (2) loose, un-weighed Webril pads and:

Four (4) plastic sandwich bags containing pre-weighed 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" bag will contain a Webril pad identified by red dots in each of two corners.

Controlled Collection (cont'd):

Each "LEFT" bag will contain a Webril pad without identifying marks.

The combined plastic bags and pads are weighed prior to the subsequent perspiration collection.

- d. Upon instruction from study personnel, all subjects will place the unweighed pads in the axillary areas for a forty (40) minute warm-up period. During this time, subjects are allowed to move freely while seated in their chairs.
- e. At the end of the forty (40) minute warm-up period, a clinical technician will remove and discard the unweighed pads and place the pre-weighed "RIGHT" A and "LEFT" A pads into the appropriate axillary vault. Subjects are now required to sit erect with both feet on the floor and arms at their sides. After the twenty (20) minute collection period, a clinical technician will remove the "A" collection pads and place them in the appropriate plastic bags. The process will then be repeated with the pre-weighed "RIGHT" B and "LEFT" B pads. After completion of collection "B", 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.
- f. Post-weights of the pads are then calculated to determine the eligibility of each subject to meet minimum required perspiration output (100mg) in both axillae. Subjects not meeting inclusion criteria for perspiration production will be excluded from the study phase at this time.

Test Phase:

- a. Subjects who meet all the qualifying requirements will have a:
  1. Supervised washing of the axillary vault utilizing 4"x4" gauze pads placed in a solution of mild soap (such as Camay<sup>®</sup> Classic) and tepid water. Subjects will use one pad for each axilla, then discard and move to the next

**TEST PROCEDURE (cont'd):**

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 application of the test material.

Test Phase (cont'd):

2. Randomized test material/placebo control application (as described below) made to both axillae. Half the subjects will receive the test material application in the right axillae and the left axillae will receive the placebo control. The remaining subjects will have the reverse test material/placebo control allocation.
  3. There will be a one (1) hour wait post-application, then dismissal of the subjects.
- b. On Days Two and Three, only application of the test material/placebo control will be conducted, utilizing the following sequence:
- Acclimation, as described previously.
  - Supervised axillary wash, as described previously.
  - Test material/placebo control application, as described below.
  - One (1) hour wait post-application, then dismissal.
- c. On Day Four, test material/placebo control application and perspiration collection will be conducted, utilizing the following sequence:
- Acclimation, as described previously.
  - Supervised axillary wash, as described previously.
  - Test material/placebo control application, as described below.
  - One (1) hour wait post-application.
  - Enter the controlled-temperature room for a forty (40) minute warm-up and two (2) subsequent twenty (20) minute perspiration collection periods, as described previously.
  - Leave the controlled-temperature room and dismissal.

**TEST PROCEDURE (cont'd): Test Phase (cont'd):**

- d. On Day Six and Day Seven perspiration collection is performed, utilizing the following sequence:

Acclimation, as described previously.

Enter the controlled-temperature room for a forty (40) minute warm-up and two (2) subsequent twenty (20) minute perspiration collection periods, as described previously.

Leave the controlled-temperature room and dismissal.

- e. The study is completed on Day Seven (7).

**Product Application:**

The test material and placebo control will be applied by a clinical technician to ensure complete coverage of the axillary vault.

- a. For **liquid, solution or suspension** materials, approximately 400 mg will be applied with a 1cc syringe. The syringe barrel will be used to swab the axillary vault to uniformly distribute the test material.
- b. **Solid** materials will be applied directly from the container to the axilla. The container will be weighed prior to and post-application to ensure that approximately 400 mg of the material has been applied.
- c. **Semi-solid** materials will be applied with a finger cot. Approximately 400 mg ( $\pm$  10mg) of the test material will be measured into a weighing boat for each subject. The material will then be applied by a clinical technician to ensure even coverage of the axillary vault.
- d. **Aerosol** materials will be applied as a two (2)-second spray directly from the container. A metronome will be used to measure the two (2) seconds. Containers will be weighed pre- and post-application and an average amount will be obtained for the group.
- e. **Pump** materials will be applied as three (3) to four (4) strokes directly from the container or, if supplied as bulk material, will be applied as described for liquid, solution or suspension materials.

**ADVERSE EVENTS:**

Subjects will be instructed to notify the Clinical Laboratory immediately of any adverse reactions. Subjects will be evaluated by the Study Director and, if necessary, referred to the physician for medical intervention. If indicated, subjects will be removed from the study. The Sponsor will be notified immediately of such occurrences.

**REPORTING:**

A comprehensive final report describing all procedures used and a summary of all results will be presented at the termination of the study.

**STATISTICS:**

Descriptive statistics will be calculated for the amount of test product used and the amount of perspiration. Descriptive statistics for the amount of perspiration will be calculated for treated and placebo control axillae at each evaluation. The percent reduction in perspiration at the treated axillae will be calculated for each subject as:

$$\text{Percent Reduction} = 100 * \frac{((\text{PlaceboControlAmount}) - (\text{TreatedAmount}))}{\text{PlaceboControlAmount}}$$

Descriptive statistics will be calculated for the percent reduction in perspiration.

The efficacy of the antiperspirant will be tested as described in the "Guidelines for Effectiveness Testing of OTC Antiperspirant Drug Products" using the Wilcoxon Signed Rank Test.

*For Antiperspirant Efficacy Claims:*

The percent reduction in perspiration will be calculated for each subject. The Wilcoxon Signed Rank Test will be used to test the hypothesis that the median reduction in perspiration was equal to or greater than twenty percent.

*For Extended Duration of Effect Claims:*

Requires a minimum of one application and two controlled collections post-application (i.e. one hour post-application and then forty-eight hours and seventy two hours post-application for seventy-two hour effectiveness claims, respectively.

The level of significance for all statistical tests will be  $P \leq 0.05$ . All statistical calculations will be performed using the STATA statistical software package for personal computers.

