Technomics Research, LLC

Economic and Statistical Analysis of Healthcare Technology

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Statistical Analysis Plan for

An Evaluation of the Safety and Effectiveness of the N-SWEAT Patch for the Treatment of Primary Axillary Hyperhidrosis or Excessive Axillary Sweating
(SAHARA)

and

The pH SUB-STUDY – An Evaluation of Skin pH for a Subset of Subjects Treated in the Sahara Study

Prepared for

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Contents

1. STATISTICAL CONSIDERATIONS AND GENERAL STATISTICAL ANALYSIS METHODS

This Statistical Analysis Plan (SAP) presents a detailed description of the statistical methods and procedures to be implemented for data analysis in the study and supersedes analyses described in the clinical investigation plan, entitled "An Evaluation of the Safety and Effectiveness of the N-SWEAT Patch for the Treatment of Primary Axillary Hyperhidrosis or Excessive Axillary Sweating (SAHARA)". Deviations from this plan will be considered only if there is statistical justification. Any deviations from this SAP will be substantiated by sound rationale and documented in the clinical report.

This SAP also provides the analysis plan for "The pH SUB-STUDY – An Evaluation of Skin pH for a Subset of Subjects Treated in the Sahara Study". The analysis identified for the sub-study is described in Section 13.

Categorical variables will be summarized by counts and percentages. Continuous variables will be summarized by n, mean, standard deviation, minimum, median and maximum.

When the arithmetic mean is found not to be an appropriate measure of central tendency, alternative statistics will be considered (e.g. median). When the distribution of a variable does not support the use of parametric statistics, nonparametric approaches or data transformations may be implemented. If data transformations are used, they will be specified in the final clinical report.

2. STUDY DESIGN, RANDOMIZATION AND BLINDING

The Sahara Study is a prospective, multi-center, randomized, blinded, pivotal study to evaluate the safety and effectiveness of the N-SWEAT Patch.

Subjects with primary axillary hyperhidrosis or excessive sweating (defined by a score of 3 or 4 on the HDSS), who have provided informed consent and have met the study eligibility criteria, will participate. Up to 120 adult subjects will be enrolled. The first 10 subjects will be treated with the N-SWEAT patch and constitute the roll-in cohort and up to 110 subjects will be randomized to 1 of 2 treatment groups in a 1:1 ratio to receive a single administration of the N-SWEAT Patch or a sham control patch. The randomization will be blocked by investigational center and stratified by HDSS 3 vs. 4 at baseline. Although a sample size of 100 subjects (50 in each group) is the target; up to 10 additional subjects may be enrolled to account for loss to follow up or other missing and critical data.

Randomized subjects will be blinded to their treatment assignment. Site personnel administering the treatment will observe the treatment effect and the disposal process and may be unblinded as a result of their observations. This person will not conduct the follow-up assessments and will not reveal the assumed treatment assignment to the subject, other site personnel, or the investigator at any time during the study follow-up period. Study subjects and study staff will be instructed not to discuss assumptions about the treatment received.

The sponsor will identify those who need to be unblinded in order to conduct the study. All others at the sponsor will remain blinded until the 4 week analysis.

3. COMPANION DOCUMENTS

There are two documents that are companion documents associated with this statistical analysis plan. The first is the endpoint mapping table which provides detailed information on where in the electronic data capture system the data necessary to complete the analyses specified in this plan are captured and the second is the table shell document. The table shell document is prepared for the 4 week analysis.

4. SAMPLE SIZE AND POWER CONSIDERATIONS

The primary effectiveness evaluation is driving the randomized sample size for the trial. The maximum of two scenarios considered required 50 evaluable subjects per randomized group at 4 weeks of follow-up. Increasing that number for up to 10% attrition requires 55 randomized subjects per group or 110 randomized subjects. This number provides at least 80% power for the primary efficacy objective at the two-sided 0.05 significance level.

The trial is also designed to enroll a roll-in cohort of N=10 treatment subjects at one investigational center prior to randomizing any subjects in the trial.

5. STUDY SUCCESS

The Sahara study will be deemed a success with a statistically significantly higher (at the 0.05 two-sided significance level) proportion of patients with HDSS score of 1 or 2 at 4 weeks post-treatment in subjects randomized to treatment vs. sham (primary effectiveness endpoint) accompanied by an acceptable safety profile.

6. ANALYSIS SETS / POPULATIONS

6.1 Roll-in Cohort

The roll-in cohort is an initial cohort of N=10 active treatment subjects enrolled at one investigational site to provide FDA with an initial assessment for safety of the device. Efficacy endpoints for roll-in subjects will be restricted to summary statistics and reported separately..

6.2 Intent-to-Treat Population

The intent-to-treat (ITT) population will include all randomized patients assigned to treatment. In this population, treatment will be based on the treatment to which patients were randomly assigned regardless of which treatment they actually received.

6.3 Safety Population

The safety population is the ITT population plus the roll-in cohort.

6.4 Full Analysis Set

The full-analysis set (FAS) is those ITT subjects that have evaluable data for the endpoint.

6.5 Per-Protocol Set

The Per Protocol Set (PP) will include all randomized subjects in the FAS who did not have any major protocol violations. The DSMB or independent reviewer will identify major protocol violations, if any, prior to data lock and unblinding. If no subjects are excluded from the PP, the PP will not be required. The PP will be used for supporting analyses of efficacy data.

7. TIMING OF ANALYSES

Safety for the Roll-in cohort will be summarized when at least 2 weeks of follow-up is available on the last enrolled roll-in subject.

After the 30th, 60th, and 90th subject from the randomized cohort (active and control) is treated and followed for 7 days, the running safety report will be submitted to FDA. The report will be submitted within 30 days of treatment.

The interval safety report will include:
1. Cumulative frequency tables of all AE reported to date for the active patch, and all the AE reported to date for the sham patch, using the terminology in Table 9 in the investigational plan; and

2. A list of AEs in the recently completed 30-subject cohort, to include the device used (active or control), time to onset, time to resolution, intervention (including OTC product use), whether the AE was procedure- or device-related, and descriptive and photographic data.

Once all subjects complete 4 weeks of follow-up, the data will be summarized for evaluation of the endpoints. At this time, the sponsor will be unblinded to the treatment groups, but the investigators and subjects will remain blinded until study completion. Lastly, the data will be summarized when all subjects complete the study.

8. ASSESSMENT OF COMPARABILITY OF RANDOMIZED GROUPS AND EVALUATION FOR POOLING

8.1 Demographics / Baseline Characteristics and Protocol Administration

Patient disposition will be listed and summarized for the ITT and roll-in data sets by treatment group. Protocol deviations will be collected and summarized by randomized group in the ITT population and roll-in group.

Demographics (age, gender, race/ethnicity) and baseline characteristics (HDSS, GSP, Fitzpatrick skin type, and BMI) will be summarized by treatment group for ITT and roll-in groups.

The randomized groups will be compared at time of randomization for the important demographics and baseline characteristics specified. Should additional important baseline parameters be identified prior to the analysis, they will be evaluated in the same manner. Any of the variables that are significant at a two-sided α=0.05 will be evaluated as covariates or strata variables in the primary effectiveness analysis or as an additional or supporting analysis to the primary effectiveness endpoint and if desired, secondary/observational endpoints as well. Continuous variables will be evaluated both as stratification variables by dichotomizing the subjects into two groups based on the median or other appropriate value and as a continuous variable in the statistical models. Logistic regression analysis may be used for the primary efficacy endpoint should it be desirable to evaluate multiple covariates simultaneously in a statistical model.

8.2 Treatment Characteristics

At a minimum, the duration of patch placement, pain level during treatment and cleaning will be summarized by randomized group for the ITT and roll-in population.

8.3 Evaluation for Pooling

Pooling of the investigational sites will be evaluated for the primary efficacy endpoint. Investigational centers with less than 10 randomized subjects will be combined for this purpose. The Breslow-Day test will be used to assess the treatment by site interaction and if statistically significant at p<0.15, an overall response rate will be evaluated at 4-weeks using CMH test stratified by site. If not statistically significant, the data will be pooled for analysis.

9. HANDLING OF MISSING DATA FOR THE PRIMARY EFFICACY ENDPOINT

A sensitivity analysis to the missing data in the ITT sample will be conducted for the primary efficacy endpoint. The sensitivity analysis will include a best case, worst case and tipping point analysis. The best case analysis will impute successes for subjects randomized to treatment with missing data and failures for subjects randomized to sham with missing data. The worst case analysis will impute failures for subjects randomized to treatment with missing data and success for subjects randomized to sham with missing data. The tipping point analysis completes the matrix of imputations possible between the best case and worst analysis to determine where statistical significance is maintained or lost. If the worst case analysis maintains statistical significance, the tipping point analysis is not necessary.

10. PRIMARY SAFETY ANALYSIS

Subjects Included in Analysis: All subjects in the Safety Population.

Endpoint(s): Local skin reactions and adverse events.

Hypothesis: A single hypothesis test associated with a specific safety endpoint is not being proposed for the primary safety outcome. Rather, the local skin reaction and adverse event profile in total will be reviewed for acceptability.

Primary Statistical Analysis: Number and percent of subjects affected by each DSMB classified event or reaction will be summarized. Subgroups of events/reactions will also be summarized and include but are not limited to serious events, those related to the treatment, and those that are both serious and related to the treatment. Events will additionally be summarized by DSMB determined severity and investigator reported time required for resolution. Treatment related AEs are defined by either a possible, probable, or highly probable relationship to the N-SWEAT Patch or possible, probable, or highly probable relationship to the N-SWEAT Procedure as adjudicated by the DSMB.

Lastly, adverse events will be summarized in subgroups defined by total time of treatment over both axilla, average and maximum pain throughout treatments. Subgroups will be defined by above and below the median for each treatment characteristic.

11. EFFICACY ANALYSIS

11.1 Primary Efficacy

The proportion of subjects with HDSS of 1 or 2 at 4-weeks in subjects randomized to treatment (p_T) will be higher than that in subjects randomized to sham (p_S).

Subjects Included in Analysis: All ITT subjects.

Endpoint(s): The proportion of subjects with HDSS of 1 or 2 at 4 weeks of follow-up.

Hypothesis*:*

H_o*:* The proportion of subjects with HDSS of 1 or 2 at 4-weeks in subjects randomized to treatment (p_T) will be lower than or equal to that in subjects randomized to sham (p_S), $p_T \leq p_S$

H_a*:* The proportion of subjects with HDSS of 1 or 2 at 4-weeks in subjects randomized to treatment (p_T) will be greater than that in subjects randomized to sham (p_S), $p_T > p_S$

Sample Size Rationale: . The sample size and power calculations for the randomized cohort are based on the company's clinical trial data as well as on published data (Glaser et al., 2012). To account for substantial variability in the proportion of responders across various trials, multiple scenarios were considered.

Per definition of the primary endpoint a responder is a patient with HDSS values of 1 or 2 at 4-weeks post treatment. If proportions of responders in the treated vs. sham arms are 85% vs. 60%, respectively, then using PASS 2019, testing two proportions using the Mantel-Haenszel test, 50 patients per arm will be needed to detect the treatment difference with the 80% power at the 0.05 two-sided significance level. If proportions of responders in the

treated vs. sham arms are 73% vs. 44%, then 45 patients per arm will be needed. The evaluable sample size of 50 patients per arm was chosen

Primary Statistical Analysis: The proportion of patients with HDSS of 1 or 2 at 4 weeks post-treatment will be compared between treatment vs. sham using the Cochran-Mantel-Haenszel (CMH) test stratified by baseline HDSS value of 3 vs. 4 in the FAS population. Statistical significance is achieved with two-sided p-value <0.05 equivalent to one-sided p-value < 0.025.

Additional Statistical Analysis: Additional analyses include those summarized in **Section 8.3** Evaluation for Pooling of Data and **Section 9** Handling of Missing Data for the Primary Efficacy Endpoint. The primary statistical analysis will be completed in the PP population as well.

An analysis will also be performed using all available time points with complete follow-up at the time of the analysis. A generalized linear mixed model will be used to compare the proportion of subjects with HDSS of 1 or 2 between randomized groups over time on study. The dependent variable is HDSS of 1 or 2 (Y/N) with independent variables to include randomized group, follow-up time, baseline HDSS and two-way interaction terms. The covariance structure among the compound symmetric, auto-regressive and unstructured that provides the best model fit by the Schwarz BIC criterion will be used.

A hierarchical stepwise backward elimination technique will be used to reduce the model. The two-way interactions will be reviewed first, the two-way interaction with the largest p-value provided that p-value is greater than 0.05 will be removed from the model and the model refit and process repeated until only two-way interactions with p-values < 0.05 are retained. The main effects for any two-way interactions retained in the model must remain in the model as well as the randomized treatment. With that said, the main effects will be evaluated in the same manner as two-way interactions. This analysis will be repeated in the PP population as well.

Additional Statistical Analysis Subjects Randomized to Treatment: Logistic regression will be used to evaluate whether there is relationship between the total time that the patch was on both axilla and the primary efficacy endpoint as well as the average and maximum level of pain during treatment and the primary efficacy endpoint. The treatment characteristic will be evaluated as a continuous variable and a categorical variable dichotomized at the median value.

11.2 Secondary Efficacy

11.2.1 Type I Error Control, Additional Claims and Labeling

Should the primary effectiveness endpoint be found to be statistically significant, additional secondary endpoints will be evaluated for inclusion in the labeling for the device including p-values and 95% confidence intervals. The secondary endpoints are listed in priority order in **Section 11.2.2** Priority Order and Hypothesis Tests and will be evaluated in that order. If statistical significance is achieved for the highest priority endpoint the testing will

move to the next highest until either statistical significance is not reached, or the list has ended. This ordered hypothesis approach permits each hypothesis to be evaluated at two sided α=0.05 or equivalently one-sided α=0.025 and controls the study-wide Type I error at 5%.

Secondary endpoints or additional analysis outside of those that do support additional claims are supportive in nature and not intended to support additional claims. Data may be included in labelling per agreement with the FDA and will be limited to summary statistics (e.g. mean, standard deviation, minimum, median, maximum, number and percent) and will not include 95% confidence intervals or p-values. For more information about the secondary endpoint analyses see **Section 11.2.3** Secondary Objectives.

11.2.2 Priority Order and Hypothesis Tests

These hypothesis tests will be evaluated in the FAS population.

1. **To prove that the mean improvement in QoL scale Bother from baseline to 4-weeks is statistically significantly greater in the treatment group as compared to the sham group.**

***Hypothesis**:*

H_o: The mean improvement in QoL scale Bother from baseline to 4-weeks in subjects randomized to treatment (μ_T) will be lower than or equal to that in subjects randomized to sham (μ_S), $\mu_T \leq \mu_S$.

H_a: The mean improvement in QoL scale Bother from baseline to 4-weeks in subjects randomized to treatment (μ_T) will be greater than that in subjects randomized to sham (μ_S), $\mu_T > \mu_S$.

Success is defined as a statistically significant difference (at the 0.05 two-sided significance level) between least squared means for randomized groups.

2. **To prove that the mean improvement in QoL scale Impact from baseline to 4-weeks is statistically significantly greater in the treatment group as compared to the sham group.**

***Hypothesis**:*

H_o: The mean improvement in QoL scale Impact from baseline to 4-weeks in subjects randomized to treatment (μ_T) will be lower than or equal to that in subjects randomized to sham (μ_S), $\mu_T \leq \mu_S$

H_a: The mean improvement in QoL scale Impact from baseline to 4-weeks in subjects randomized to treatment (μ_T) will be greater than that in subjects randomized to sham (μ_S), $\mu_T > \mu_S$

Success is defined as a statistically significant difference (at the 0.05 two-sided significance level) between least squared means for randomized groups.

3. **To prove that the proportion of patients with improvement of at least 2 grades from baseline to 4-weeks in HDSS is statistically significantly greater in the treatment group as compared to the sham group.**

Hypothesis:

H_o: The proportion of subjects with improvement of at least 2 grades from baseline to 4 weeks in HDSS in subjects randomized to treatment (p_T) will be lower than or equal to that in subjects randomized to sham (p_S), $p_T \leq p_S$

H_a: The proportion of subjects with improvement of at least 2 grades from baseline to 4 weeks in HDSS in subjects randomized to treatment (p_T) will be greater than that in subjects randomized to sham (p_S), $p_T > p_S$

Success is defined as a statistically significant difference (at the 0.05 two-sided significance level) between proportions of patients with at least 2 grade improvement in HDSS from baseline to 4 weeks between randomized group using CMH test stratified by baseline HDSS (3 vs. 4).

4. **Proportion of subjects with at least 50% improvement in gravimetric sweat production (GSP) in subjects treated with the N-SWEAT Patch only at 4-weeks. (GSP will be calculated based on the total sweat produced by both axillae.)**

H_o: The proportion of subjects with at least 50% improvement in gravimetric sweat production (GSP) in subjects randomized to treatment (p_T) is not statistically significantly different from 0, $p_T = 0$.

H_a: The proportion of subjects with at least 50% improvement in gravimetric sweat production (GSP) in subjects randomized to treatment (p_T) is statistically significantly different from 0, $p_T \neq 0$.

Success is defined as a statistically significant result (at the 0.05 two-sided significance level). It is expected that at least 50% of subjects will have at least 50% improvement in gravimetric sweat production from baseline at 4-weeks.

11.2.3 Secondary Objectives

11.2.3.1 To compare the mean improvement over baseline for QOL scale Bother between subjects randomized to treatment as compared to sham

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): QOL scale Bother score

Statistical Analysis: An analysis will be performed using all available time points with complete follow-up at the time of the analysis. A generalized linear mixed model will be used to compare average change in QOL Bother from baseline to follow-up between randomized groups over time on study. The dependent variable change in QOL Bother from baseline to follow-up with independent variables to include randomized group, follow-up time, baseline HDSS and two-way interaction terms. The covariance structure among the compound symmetric, auto-regressive and unstructured that provides the best model fit by the Schwarz BIC criterion will be chosen.

A hierarchical stepwise backward elimination technique will be used to reduce the model. The two-way interactions will be reviewed first, the two-way interaction with the largest p-value provided that p-value is greater than 0.05 will be removed from the model and the model refit and repeated until only two-way interactions with p-values < 0.05 are retained. The main effects for any two-way interaction retained in the model must remain in the model as well as the randomized treatment. That being said, the main effects will be evaluated in the same manner as the two-way interaction terms. This analysis will be repeated in the PP population.

11.2.3.2 To compare the mean improvement over baseline for QOL scale Impact between subjects randomized to treatment as compared to sham

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): QOL scale Impact score

Statistical Analysis: An analysis will be performed using all available time points with complete follow-up at the time of the analysis. A generalized linear mixed model be used to compare average change in QOL Impact from baseline to follow-up between randomized groups over time on study. The dependent variable change in QOL Impact from baseline to follow-up with independent variables to include randomized group, follow-up time, baseline HDSS and two-way interaction terms. The covariance structure among the compound symmetric, auto-regressive and unstructured that provides the best model fit by the Schwarz BIC criterion will be chosen.

A hierarchical stepwise backward elimination technique will be used to reduce the model. The two-way interactions will be reviewed first, the two-way interaction with the largest p-value provided that p-value is greater than 0.05 will be removed from the model and the model refit and repeated until only two-way interactions with p-values < 0.05 are retained. The main effects for any two-way interaction retained in the model must remain in the model as well as the randomized treatment. That being said, the main effects will be evaluated in the same manner. This analysis will be completed in the PP population as well.

11.2.3.3 To compare the proportion of patients with at least a 2 grade improvement in HDSS from baseline between subjects randomized to treatment as compared to sham

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): HDSS.

Statistical Analysis: The proportion of patients with at least a 2 grade improvement in HDSS from baseline to 4 weeks will be compared between treatment vs. sham using the Cochran-Mantel-Haenszel (CMH) test stratified by baseline HDSS value of 3 vs. 4 in the FAS population. Statistical significance is achieved with two-sided p-value <0.05 equivalent to one-sided p-value < 0.025. This analysis will be completed in the PP group as well.

An analysis will be performed using all available time points with complete follow-up at the time of the analysis. A generalized linear mixed model will be used to compare the proportion of subjects with at least 2 grade improvement from baseline to 4 weeks between randomized groups over time on study. The dependent variable is 2 grade improvement over baseline (Y/N) with independent variables to include randomized group, follow-up time, baseline HDSS and two-way interaction terms. The covariance structure among the compound symmetric, auto-regressive and unstructured that provides the best model fit by the Schwarz BIC criterion will be chosen.

A hierarchical stepwise backward elimination technique will be used to reduce the model. The two-way interactions will be reviewed first, the two-way interaction with the largest p-value provided that p-value is greater than 0.05 will be removed from the model and the model refit and repeated until only two-way interactions with p-values < 0.05 are retained. The main effects for any two-way interaction retained in the model must remain in the model as well as the randomized treatment. That being said, the main effects will be evaluated in the same manner as the two-way interactions. This analysis will be completed in the PP group as well.

11.2.3.4 To estimate the proportion of subjects randomized to treatment with at least 50% improvement from baseline to 4 weeks in gravimetric sweat production (GSP)

Subjects Included in Analysis: All FAS subjects randomized to receive the N-SWEAT patch.

Endpoint(s): The average of 2 accurate GSP measurements will be conducted for each Axilla at each time point. The total sweat production at each timepoint will be calculated by summing the average sweat production from both axilla. The percentage change at 4 weeks will be calculated based on the total sweat production at baseline and 4 weeks.

Statistical Analysis: The potential confounding factors of room temperature, room humidity , position during evaluation and time of evaluation will be summarized for baseline and 4 weeks. The difference in temperature, humidity, time of evaluation and whether or not the baseline and 4 week evaluation were performed in the same or different position will be summarized. These factors will be evaluated with respect to their relationship with the endpoint and association with outlying values, if any, using graphical techniques and summary statistics. Depending on this evaluation, outlying values may be excluded from the analysis with justification provided and relationships, if any found, will be summarized.

The proportion of patients with 50% or greater improvement from baseline to 4 weeks will be statistically compared to zero by calculating the Wilson's 95% two-sided confidence interval and comparing the lower bound to zero. If the lower bound is greater than zero, there is statistically

significant evidence that the proportion of subjects with a clinically relevant improvement exists and is greater than 0. This analysis will be completed in the PP population as well.

11.3 Observational Endpoints

Observational endpoints will be summarized at all available time points at the time of analysis. Observational endpoints are supportive in nature and not intended to support additional claims. Data may be included in labelling per agreement with the FDA and will be limited to summary statistics (e.g. mean, standard deviation, minimum, median, maximum, number and percent) and will not include 95% confidence intervals or p-values. Statistical significance will be determined based on a two-sided p-value of 0.05. The p-values for the observational endpoints will not be adjusted for multiplicity and should be interpreted with caution.

11.3.1 To compare the mean improvement over baseline for QoL-7 between subjects randomized to treatment as compared to sham

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): QoL-7 score. The score is calculated by assigning 1 for a yes response and 0 for a no response and summing over the 7 questions.

Statistical Analysis: An analysis will be performed using all available time points with complete follow-up at the time of the analysis. A generalized linear mixed model be used to compare average change in QoL-7 from baseline to follow-up between randomized groups over time on study. The dependent variable change in QoL-7 from baseline to follow-up with independent variables to include randomized group, follow-up time, baseline HDSS and two-way interaction terms. The covariance structure among the compound symmetric, auto-regressive and unstructured that provides the best model fit by the Schwarz BIC criterion will be chosen.

A hierarchical stepwise backward elimination technique will be used to reduce the model. The two-way interactions will be reviewed first, the two-way interaction with the largest p-value provided that p-value is greater than 0.05 will be removed from the model and the model refit and repeated until only two-way interactions with p-values < 0.05 are retained. The main effects for any two-way interaction retained in the model must remain in the model as well as the randomized treatment. That being said, the main effects will be evaluated in the same manner as the two-way interaction terms.

This analysis will be repeated for each of the 7 questions that comprise the QOL-7 and in the PP population.

11.3.2 To compare the proportion of patients with HDSS 1 or 2 at 4 weeks AND at least 50% improvement in GSP at 4 weeks over baseline between subjects randomized to treatment as compared to sham

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): HDSS at follow-up. GSP % change at follow-up compared to baseline. will be calculated as in **Section 11.2.3.4**

Statistical Analysis: The proportion of patients with an HDSS of 1 or 2 at 4 weeks of follow-up AND at least 50% improvement in GSP at 4 weeks over baseline will be compared between treatment vs. sham using the Cochran-Mantel-Haenszel (CMH) test stratified by baseline HDSS value of 3 vs. 4 in the FAS population. Statistical significance is achieved with two-sided p-value <0.05 equivalent to one-sided p-value < 0.025. This analysis will be completed in the PP group as well.

11.3.3 To compare the proportion of patients with HDSS 1 or 2 at 4 weeks AND at least 75% improvement in GSP at 4 weeks over baseline between subjects randomized to treatment as compared to sham

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): HDSS at follow-up. GSP % change at follow-up compared to baseline. will be calculated as in Section 11.2.3.4

Statistical Analysis: The proportion of patients with an HDSS of 1 or 2 at 4 weeks of follow-up AND 75% improvement in GSP at 4 weeks over baseline will be compared between treatment vs. sham using the Cochran-Mantel-Haenszel (CMH) test stratified by baseline HDSS value of 3 vs. 4 in the FAS population. Statistical significance is achieved with two-sided p-value <0.05 equivalent to one-sided p-value < 0.025. This analysis will be completed in the PP group as well.

11.3.4 To compare the duration of efficacy between subjects randomized to treatment as compared to sham

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): HDSS

Statistical Analysis: A Kaplan-Meier product limit method will be used for the analysis. Time 0 will be the treatment date. For subjects who do not respond to treatment, the duration of treatment will be 0. For subjects who do respond to treatment, the event is the first subsequent week of follow-up after the 4 week follow-up in which the subject reported an HDSS of 3 or 4 or censoring from the study either due to drop-out or completing the study without reverting to HDSS 3 or 4. The study groups will be compared using the Log-Rank statistic stratified by HDSS 3 or 4 at baseline.

This analysis will be completed for reversion to the patient's baseline value and in the PP group as well.

11.3.5 To compare mean change from baseline at 4 weeks in GSP between subjects randomized to treatment as compared to sham.

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): The average of 2 accurate GSP measurements will be conducted for each Axilla at each time point. The total sweat production at each timepoint will be calculated by summing the average sweat production from both axilla. The change in GSP at 4 weeks will be calculated by subtracting the total sweat production at baseline from the total value at 4 weeks.

Statistical Analysis: An analysis of variance model will be used to compare average change in total GSP at 4 weeks as compared to baseline between randomized groups. The dependent variable is change in total GSP at 4 weeks as compared to baseline with independent variables to include randomized group, baseline HDSS, and two-way interaction terms.

A hierarchical stepwise backward elimination technique will be used to reduce the model. The two-way interactions will be reviewed first, the two-way interaction with the largest p-value provided that p-value is greater than 0.05 will be removed from the model and the model refit and repeated until only two-way interactions with p-values < 0.05 are retained. The main effects for any two-way interaction retained in the model must remain in the model as well as the randomized treatment. That being said, the main effects will be evaluated in the same manner as the two-way interaction terms. This analysis will be repeated in the PP population.

11.3.6 To compare responses to additional QOL questions from baseline throughout follow-up, as appropriate between subjects randomized to treatment as compared to sham.

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): The responses to the following questions:

Baseline and follow-up: My underarm order bothers me (Not at all, a little bit, a moderate amount, a great deal, an extreme amount.

2 and 4 weeks only: I would recommend this treatment to another person (y/n).

Follow-up only: I can wear clothes that I want to wear (y/n),

Statistical Analysis: These data will be summarized by number and percent in each category by randomized group and follow-up. The data will be summarized in the PP population as well.

12. SPECIFICATION OF SUBGROUPS FOR ANALYSIS

The primary efficacy endpoint will be summarized within subgroups defined by Baseline HDSS, age, gender and race/ethnicity. Adverse events and local skin reactions will be summarized by Fitzpatrick Skin Types. It is important to note that the study is not powered to demonstrate statistical significance within subgroups and therefore it is not an expectation of the analysis that statistical significance be demonstrated with the subgroups.

13. PH SUB-STUDY

13.1 Study Design and Purpose

Up to 25 total Sahara Study subjects undergoing treatment at up to 6 centers participating in the pH sub-study will be included. Select pH Sub-Study centers will commit to enrolling up to 10 subjects each into this pH Sub-Study. Enrollment can be stopped when data have been collected on at least 20 axillae (10 subjects) treated with the N-SWEAT Patch and at least 10 axillae (5 subjects) with HDSS 4 treated with the N-SWEAT patch. Centers will attempt to consent and enroll consecutive subjects into this sub-study; deviations will be documented.

The purpose of the pH Sub-Study is intended to measure the Baseline and Final Skin pH for a subset of subjects treated as part of the Sahara Study. This sub-study is designed to address a question posed by FDA regarding residual NaOH on the skin and its potential role in skin irritation or injury. NaOH is a byproduct of the N-SWEAT Patch interaction with sweat described in Section 3 in the pH sub-study protocol. In summary, the presence of sodium hydroxide results in high pH which at high enough concentrations and exposure time could be associated with skin injury; thus, measuring skin pH is a surrogate for direct measurement of sodium hydroxide concentration on the skin after treatment.

For consistency, the skin pH will be measured in both axillae. Measurements will be taken prior to treatment with the N-SWEAT Patch (or sham) and after the completion of the post-treatment cleaning as described in the Sahara Study protocol.

The pH Sub-study is designed to demonstrate that the Final Skin pH after the N-SWEAT treatment is not consistent with a level that would potentially cause skin injury. Further, the study should illustrate an absence of a significant amount of NaOH. Thus, this study will show that there is minimal risk of sustained skin exposure to significant residual NaOH following treatment with the N-SWEAT Patch.

13.2 Timing of Analysis

Once 20 subjects have been enrolled in the pH Sub-study, a data set will be pulled to determine if at least 10 subjects/20 axilla have been treated with the N-SWEAT Patch with at least 5 subjects/10 axilla having baseline HDSS=4. If these conditions are met, enrolment into the sub-study will cease and the data will be summarized. If these conditions are not met, enrolment will continue until 25 subjects have been enrolled in the pH sub-study and the data will be summarized at this time.

13.3 Demographics / Baseline Characteristics and Treatment Characteristics

Demographics (age, gender, race/ethnicity), baseline characteristics (HDSS, GSP, Fitzpatrick skin type, pre-treatment pH and BMI), and treatment characteristics (at a minimum, the duration of patch placement, pain level during treatment and cleaning) will be summarized by randomized group for the ITT population enrolled in the pH sub-study.

13.4 To summarize the number and percent of subjects and axilla with pH > 11 post treatment and cleaning of the area treated by randomized group

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): pH after treatment and cleaning of the area treated.

Statistical Analysis: The number and percent of axilla with post-treatment pH > 11 per randomized group and per randomized group and baseline HDSS will be summarized. The number and percent of subjects with at least one axilla with post-treatment pH > 11 will be also be summarized for the same groups.

13.5 To summarize the change in pH pre to post-treatment by randomized group.

Subjects Included in Analysis: All FAS subjects will be included in the analysis.

Endpoint(s): pH pre-treatment and after treatment and cleaning of the area treated.

Statistical Analysis: Descriptive statistics for the pH pre- and post-treatment as well as the change (post treatment – pre-treatment) per axilla will be summarized by randomized group and by randomized group and baseline HDSS.