A Single-Center Clinical Trial to Evaluate the Efficacy and Tolerability of Hair Essentials™ Dietary Supplement for Women with Androgenic Alopecia (Ludwig I and II)

Study conducted by Thomas J. Stephens & Associates, Inc.
for

Natural Wellbeing Distribution Inc.

GENERAL INFORMATION

Natural Wellbeing Distribution Inc.	HT1000
Test:	A Single-Center Clinical Trial to Evaluate the Efficacy and Tolerability of a Natural Supplement for Women with Androgenic Alopecia (Ludwig I and II)
Test Material:	Active Supplement HT1000
Testing Start Date:	May 6, 2014
Testing End Date:	September 5, 2014

SUMMARY
This 90-day clinical usage study was conducted for Natural Wellbeing Distribution Inc. to assess the efficacy and tolerability of Hair Essentials when used by women with thinning and shedding hair, and female pattern hair loss/androgenic alopecia (Ludwig I and II). A total of 26 women completed the study.

During the course of the study, subjects took 3 capsules of the test material (Active Supplement HT1000) daily as directed. Clinical evaluations were conducted at visit 1 (baseline), visit 2 (day 3), visit 3 (day 45), visit 4 (day 48 [day 45 + 3 days]), visit 5 (day 90), and visit 6 (day 93 [day 90 + 3 days]). Subjects participated in the following procedures at the indicated visits:

- Scalp shave and tattoo
  The Investigator or designee selected a target area of approximately 1 cm^2, approximately 1-2 cm lateral to the scalp, mid-line approximately half the distance between the forehead hairline and the vertex. The hair within the selected target area was shaved and dyed, and a dot tattoo was performed in the target scalp area at baseline, day 45, and day 90.

- Hair wash and shed hair count
  A trained clinician washed each subject's hair and used cheese cloth to catch any hairs lost from the scalp during the shampooing process day 3 and day 48. Once the cheesecloth was dry, the shed hairs were counted.

- Investigator rating
  The Investigator or trained grader rated hair loss/shedding/thinning, hair growth, impression of scalp hair coverage, and overall perception of treatment benefit at day 45 and day 90.

- Subject rating
  Subjects rated the size of bald spot (if applicable), appearance of hair, growth of hair, slowing of hair loss/decreased shedding, and satisfaction with (a) hairline at the front of the head, (b) hair on the top of the head, and (c) hair overall as an overall improvement from baseline at day 45 and day 90.

- Subject self-assessment questionnaire
  Subjects completed a self-assessment questionnaire regarding their hair condition and life quality/emotional wellbeing at baseline and day 90.

- Imaging procedures
  A digital macro photograph image was taken of the target area at baseline, day 3, day 90, and day 93 using a Nikon SLR D7000 camera (Nikon Corporation, Tokyo, Japan). Standardized global photographs were taken of the superior scalp and scalp vertex at baseline, day 45, and day 90 using a Nikon D100 camera (Nikon Corporation, Tokyo, Japan) with Canfield Epiflash (Canfield Imaging Systems, Fairfield, New Jersey) system.

Overall Conclusions
Overall results from this clinical usage study indicate that the Sponsor's test material (Active Supplement HT1000) was effective in improving hair loss parameters as indicated by Investigator and subject ratings under the conditions of this test. The results from this clinical usage study indicate that the Sponsor's test material was effective in improving Investigator rating scores for hair loss/shedding/thinning, hair growth, impression of scalp hair coverage, and overall perception of treatment benefit after 45 and 90 days of use. In addition, the test material was effective in improving subject rating scores for slowing of hair loss/decreased shedding, growth of hair, size of bald spot (if applicable), appearance of hair, satisfaction with hairline at the front of the head, satisfaction with hair on the top of the head, and satisfaction with hair overall as an overall improvement from baseline after 45 and 90 days of use. Results from the self-assessment questionnaire indicate that a statistically significant proportion of subjects selected favorable responses for inquiries regarding hair condition and life quality/emotional wellbeing.

TEST MATERIAL DESCRIPTIONS
Appendix VIII presents the test material description. Each test material was stored in accordance with the protocol and labeled with the assigned test material identification number (TMIN) and Sponsor identification (Sponsor ID).

INSTITUTIONAL REVIEW BOARD
Prior to subject enrollment for the study, the protocol, informed consent form and recruitment materials for this study were reviewed and approved by IntegReview Institutional Review Board (IRB) on April 22, 2014. All revised documents were reviewed and approved prior to implementation. IntegReview IRB, located in Austin, Texas, is a duly constituted IRB under title 21 Code of Federal Regulations (CFR) Parts 50 and 56. Copies of the IRB letters are included in Appendix V.

DATA QUALITY ASSURANCE
The Sponsor was permitted to perform site visits during the course of the study and inspect all case report forms and other documentation directly associated with the study. The Sponsor did not perform any study related site visits.

Stephens independent Quality Assurance Unit monitored the study conduct and audited the study documents, data and clinical study report. Data review and analyses was performed by an independent data committee. The data committee consists of selected representatives from clinical services, quality assurance and the statistical department of Stephens & Associates. When requested, it was the responsibility of the independent data committee to send any interim data reports to the Sponsor.

SUBJECT DISPOSITION AND DEMOGRAPHICS
A summary of subject disposition information is included in Table 1. The demographic information for the per-protocol (PP) population is presented in Table 2. For applicable parameters, the number of subjects in each category is listed with the percentage of total subjects in parentheses. Refer to Appendix VII for a copy of the Screening/Enrollment Log.

TABLE 1: SUBJECT DISPOSITION

	All Subjects
	n
Enrolled Subjects	34
Completed Subjects (PP Population)	26
Discontinued Subjects	8
Reason for Discontinuation	
Subject requested withdrawal	2
Lost to follow-up	4
Investigator decision	2

SUBJECT DISPOSITION AND DEMOGRAPHICS (continued)

TABLE 2: SUMMARY OF DEMOGRAPHIC INFORMATION – PP POPULATION

	All Subjects	
N	26	
Age (Years)		
Mean	54.3	
Standard Deviation	7.9	
Minimum	37	
Median	55.0	
Maximum	65	
	n	*(%)*
Sex		
Female	26	(100.0)
Ethnicity/Race		
Asian	9	(34.6)
Black or African American	3	(11.5)
Hispanic or Latino	3	(11.5)
White	10	(38.5)
Mixed	1	(3.8)
Ludwig		
I	18	(69.2)
II	8	(30.8)

ADVERSE EVENTS

Table 3 provides a brief summary of the AEs reported or observed during the study. Complete copies of the Adverse Event Forms are included in Appendix IX.

TABLE 3: NON-SERIOUS ADVERSE EVENTS

Subject	Adverse Event (Location if applicable)	Date Started	Date Ended	Severity	Relationship	Outcome
012	Rash (entire body)	18 May 2014	24 May 2014	Mild	Possible	Resolved
018	Dizziness	27 May 2014	15 July 2014	Mild	Unlikely	Resolved
	Anxiety	27 May 2014	15 July 2014	Mild	Unlikely	Resolved
	Headache	17 June 2014	15 July 2014	Mild	Unlikely	Resolved
030	Gastroenteritis Viral	28 July 2014	1 Aug 2014	Mild	Unlikely	Resolved
033	Pharyngitis streptococcal	20 Aug 2014	25 Aug 2014	Mild	Unlikely	Resolved

PROTOCOL AMENDMENTS

No planned changes to the study procedures or analyses as specified in the protocol occurred during the course of the study.

PROTOCOL DEVIATIONS

The following protocol deviations were recorded over the course of the study:

- Subject 026 did not wash her hair within 24 hours of the day 45 study visit.
- Subject 026 did not take 3 pills per day for the first 12 days of the study.

Protocol deviations were signed by the Investigator and forwarded to the Sponsor. Refer to Appendix IV for a detailed and signed copy of the Protocol Deviation.

PROCEDURES AND METHODS

Prior to the start of the study, potential subjects were screened over the telephone for eligibility criteria. Women between the ages of 35 and 65 years with self-perceived thinning and shedding hair were scheduled for eligibility screening at the clinic. The prospective subjects were advised to wash their hair with their regular shampoo and hair product within 24 hours prior to the baseline visit.

At visit 1 (baseline), prospective subjects read and signed an IRB-approved informed consent form, after the nature of the study was explained and any study-related questions were answered. Prospective subjects that signed this initial paperwork were assigned a screening number and evaluated for presentation of female pattern hair loss/androgenic alopecia (Ludwig I and II). In addition, a brief physical was completed, including examination of organ systems, pulse, and blood pressure of each prospective subject.

Each prospective subject completed a pregnancy test and completed an eligibility and health questionnaire, which also determined their suitability for entry into the study. Qualified subjects were enrolled into the study and assigned a 3-digit subject number.

The Investigator or designee selected a target area (approximately a 1 cm^2) approximately 1-2 cm lateral to the scalp mid-line approximately half the distance between the forehead hairline and the vertex. The target area was demarcated by the use of 2 small black dot tattoos.

Subjects participated in the following procedures:

- **Imaging Procedures**
  Standardized Global Photographs
  Subjects' hair was parted along the midline and combed to show the hair thinning conditions. Each subject's head was positioned on a headstand facing the camera at a fixed distance. A Nikon D100 camera (Nikon Corporation, Tokyo, Japan) with Canfield Epiflash system was used to take photos of the superior scalp and scalp vertex.

- **Scalp Shave and Tattoo**
  The target area selected by the Investigator or designee was located and the hair within the selected area was trimmed with electric hair clippers. The clipped hairs were trimmed to approximately 1 mm in length using 4" curved scissors. The area was cleaned of any trimmings by using compressed air and the area was looked at using a magnifying loupe to ensure all hairs in the area had been trimmed to 1 mm and the clippings had been removed from the area. Individuals with oily scalps had their scalps blotted with a Kim wipe and an alcohol wipe if necessary.

  All hairs within the shaved site were dyed using Roux Lash & Brow Tint in Black to ensure visibility in video microscopy images. The dying procedure was followed according to package instructions and the skin was cleaned to ensure that the dye could not be seen on the skin during the video microscopy.

  A dot tattoo was performed in the target scalp area by a trained tattoo technician. Two tattoo dots were performed to ensure proper alignment of the photography equipment. While wearing gloves, the technician cleansed the scalp area with an alcohol swab before and after tattoo procedures. The location of the tattoo was measured and recorded on the Tattoo Record Form.

- **Imaging Procedures**
  Macro Photographs
  A macro photograph was taken of the target area of each subject. Several drops of hair gel were applied onto the contact plate using a syringe. The contact plate was positioned over the target area on the scalp in a single motion, first touching the scalp with the bottom side of the contact plate and then raising the camera until the lens barrel was perpendicular to the surface. The 2 tattoo dots were lined up along the edge of the contact plate. The image area was inspected before the image was taken. The macro photograph was taken with a Nikon SLR D7000 camera (Nikon Corporation, Tokyo, Japan) and after the image was taken the area was wiped with a soft cloth or Kim Wipe to remove residual gel.

PROCEDURES AND METHODS (continued)

- **Self-Assessment Questionnaire**
  Subjects completed a self-assessment questionnaire regarding their perceptions of hair condition and life quality/emotional wellbeing.

Subjects were provided with a calendar of study visits, study instructions, and a daily diary. Subjects were instructed not to wash their hair within 48 hours prior to visit 2.

Subjects arrived at the clinic for visit 2 (day 3). Clinic personnel recorded concomitant medications and questioned subjects regarding changes in their health status since the previous visit. Adverse events were recorded as applicable.

Subjects participated in the following procedures as described for baseline:
- Hair dye procedures were performed.
- Macro photograph imaging procedures were performed.

Subjects had their hair washed over a sink containing cheesecloth, which was positioned to collect shedding hair. The number of hairs collected in the cheesecloth was counted and recorded.

Subjects were allowed to dry and style their hair according to their normal procedure.

Subjects were distributed a pre-counted unit of the test material (Active Supplement HT1000) and provided with the following verbal and written usage instructions:

- Take 3 capsules daily with food (either during or just after a meal). All 3 capsules may be taken at one time, or 1 capsule may be taken 3 times daily. Always take with food.

Subjects arrived at the clinic for visit 3 (day 45), having washed their hair with their regular shampoo and hair product within 24 hours prior to the visit. Clinic personnel recorded concomitant medications and questioned subjects regarding changes in their health status since the previous visit. Adverse events were recorded as applicable.

Daily diaries were collected, reviewed for compliance, and retained by the testing facility. New diaries were distributed to subjects. Test material units were collected, visually inspected and counted to verify compliance, and retained by the testing facility. New test material units were distributed to subjects. If necessary, subjects' tattoo markers were remarked as described for baseline.

Subjects participated in the following procedures:

- **Investigator Rating**
  An Investigator or trained grader rated hair loss/shedding/thinning, hair growth, impression of scalp hair coverage, and overall perception of treatment benefit using a 5-point Global Improvement Scale:

  0 = worsening
  1 = no change
  2 = mild improvement
  3 = moderate improvement
  4 = marked improvement

PROCEDURES AND METHODS (continued)

- **Subject Rating**
  Subjects rated the size of bald spot (if applicable), appearance of hair, growth of hair, slowing of hair loss/decreased shedding, and satisfaction with (a) hairline at the front of the head, (b) hair on the top of the head, and (c) hair overall as an overall improvement from baseline using a 5-point Global Improvement Scale:

  0 = worsening
  1 = no change
  2 = mild improvement
  3 = moderate improvement
  4 = marked improvement

- **Imaging Procedures**
  Standardized global photographs were taken as described for baseline.

Subjects were instructed not to wash their hair within 48 hours prior to visit 4.

Subjects arrived at the clinic for visit 4 (day 48). Clinic personnel recorded concomitant medications and questioned subjects regarding changes in their health status since the previous visit. Adverse events were recorded as applicable.

Subjects had their hair washed over a sink containing cheesecloth, which was positioned to collect shedding hair. The number of hairs collected in the cheesecloth was counted and recorded. Subjects were allowed to dry and style their hair according to their normal procedure.

Subjects arrived at the clinic for visit 5 (day 90). Clinic personnel recorded concomitant medications and questioned subjects regarding changes in their health status since the previous visit. Adverse events were recorded as applicable.

Daily diaries were collected, and reviewed for compliance. Test material units were collected, visually inspected and counted to verify compliance.

Subjects participated in the following procedures as described for baseline and visit 3:

- Investigator rating was performed;
- Subject rating was performed;
- Subjects completed a self-assessment questionnaire;
- Standardized global photographs were taken of each subject;
- Scalp shave and hair dying procedures were performed;
- Macro photograph procedures were performed.

Subjects arrived at the clinic for visit 6 (day 93). Clinic personnel recorded concomitant medications and questioned subjects regarding changes in their health status since the previous visit. Adverse events were recorded as applicable.

Daily diaries were collected, reviewed for compliance, and retained by the testing facility. Test material units were collected, visually inspected and counted to verify compliance, and retained by the testing facility.

Subjects participated in the following procedures as described for baseline:

- Macro photograph procedures were performed.

BIOSTATISTICS AND DATA MANAGEMENT
Statistical analyses of the study data and data management was conducted in accordance with the protocol and any modifications to this were noted in the Biostatistics Note to File. Refer to Appendix IV for complete biostatistics analyses procedures.

Note Regarding n-values:
Note that subject 021 was removed from the image analysis.

RESULTS
Investigator Rating
Use of the Sponsor's test material (Active Supplement HT1000) produced a statistically significant improvement (scores greater than 1 [no change]) for hair loss/shedding/thinning, hair growth, impression of scalp hair coverage, and overall perception of treatment benefit at day 45 and day 90. There was mild to moderate improvement at day 90 with mean scores of 2.08 for hair loss/shedding/thinning, 2.19 for hair growth, 2.27 for impression of scalp hair coverage, and 2.38 for overall perception of treatment benefits. Day 90 had better improvements in Investigator rating scores compared to day 45. In addition, there was a statistically significant improvement in Investigator rating scores for hair loss/shedding/thinning, hair growth, impression of scalp hair coverage, and overall perception of treatment benefit at day 90 when compared to day 45, suggesting continued improvement over time.

Subject Rating
Use of the Sponsor's test material (Active Supplement HT1000) produced a statistically significant improvement (scores greater than 1 [no change]) for slowing of hair loss/decreased shedding, growth of hair, size of bald spot (if applicable), appearance of hair, satisfaction with hairline at the front of the head, satisfaction with hair on the top of the head, and satisfaction with hair overall as an overall improvement from baseline at day 45 and day 90.

Shed Hair Counts
Use of the Sponsor's test material (Active Supplement HT1000) produced a 10.7% reduction in shed hair counts at day 48 when compared to baseline counts. By day 90, use of the Sponsor's test material (Active Supplement HT1000) produced reduced shedding in 65.4% of subjects.

Image Analysis
Use of the Sponsor's test material (Active Supplement HT1000) produced a 16.2% increase in vellus hair count after 3-months of product use when compared to baseline. The lack of statistical significance of this change could be due to the small sample size. The trend of this change, if continues, could potentially lead to a more beneficial overall result after longer period of product usage.

Self-Assessment Questionnaires
Results from the self-assessment questionnaire analysis indicated a majority of favorable responses at day 90 for the following inquiries:

- Today, do you avoid recreational activities because of your hair condition?
- Today, do you avoid social situations because of your hair condition?
- Did you find the test product was well tolerated (no discomfort) or adverse effects experienced)?
- Did you find the test product capsules easy to swallow?
- Did you find the test product convenient to take?
- How would you rate your results?
- What physical results have you experienced (less shedding of hair loss)?
- What physical results have you experienced (new hair growth)?
- Will you continue taking the test product?
- Would you recommend the test product to a friend?

Results from the self-assessment questionnaire analysis indicated a statistically significant improvement for the following inquiry at day 90 when compared to baseline:

- How do you feel about your hair condition today (embarrassed, worried or fearful/scared, frustrated or angry, it make me feel "less feminine", it makes me feel "less youthful", unhappy, and unconfident)?

Only 1 subject experienced moderate discomfort from the test product.

DISCUSSION AND CONCLUSIONS

Overall results from this clinical usage study indicate that the Sponsor's test material (Active Supplement HT1000) was effective in improving hair loss parameters as indicated by Investigator and subject ratings under the conditions of this test. The results from this clinical usage study indicate that the Sponsor's test material was effective in improving Investigator rating scores for hair loss/shedding/thinning, hair growth, impression of scalp hair coverage, and overall perception of treatment benefit after 45 and 90 days of use. In addition, the test material was effective in improving subject rating scores for size of bald spot (if applicable), appearance of hair, growth of hair, slowing of hair loss/decreased shedding, satisfaction with hairline at the front of the head, satisfaction with hair on the top of the head, and satisfaction with hair overall as an overall improvement from baseline after 45 and 90 days of use. Results from the self-assessment questionnaire indicate that a statistically significant proportion of subjects selected favorable responses for inquiries regarding hair condition and life quality/emotional wellbeing.

PHOTO RESULTS

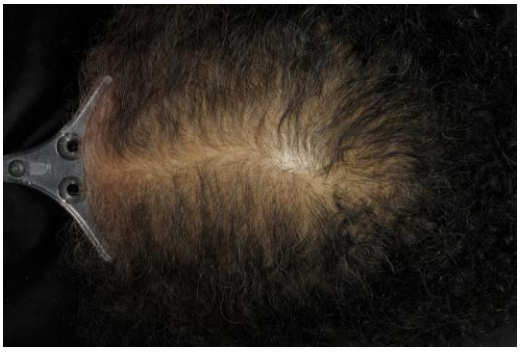
Photos below are samples of baseline (pre Hair Essentials) and 90 Day results.

Subject 4 (Day 0 and Day 90)

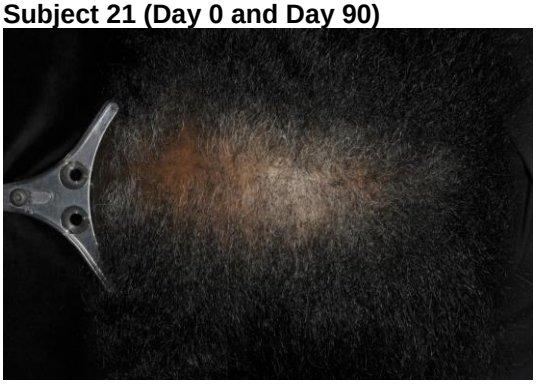

Subject 7 (Day 0 and Day 90)

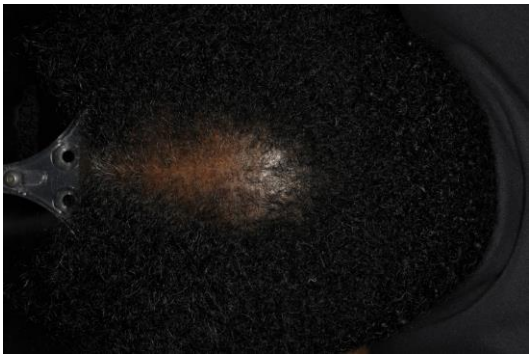

Subject 10 (Day 0 and Day 90)


Subject 11 (Day 0 and Day 90)

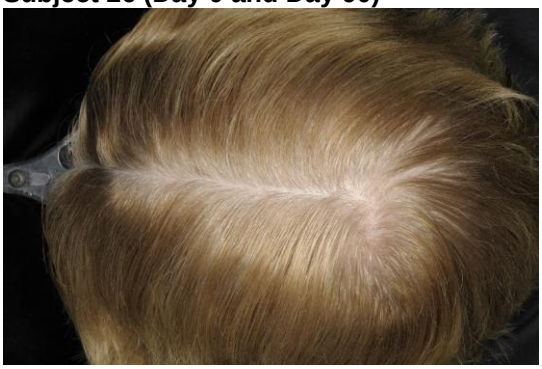


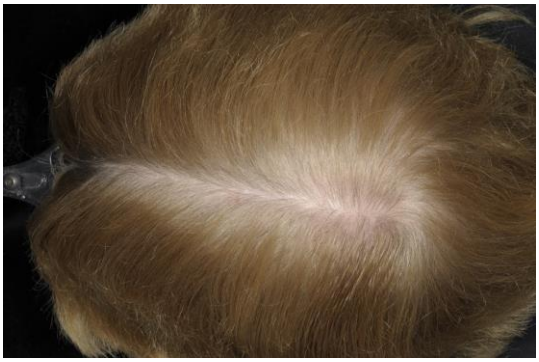
Subject 21 (Day 0 and Day 90)





Subject 26 (Day 0 and Day 90)





Subject 30 (Day 0 and Day 90)