Exponent®

The Effect of AppTrim on Appetite Suppression, Weight Loss, and Reduction in Percent Body Fat: Clinical Study Report

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Synopsis

Purpose: The study was designed to compare the effect of a proprietary obesity management product, AppTrim combined with a calorie-controlled diet and a 10,000-step exercise program versus a placebo combined with the same diet and exercise program on body weight and percent body fat.

Dates of Treatment: The first dose of randomized study treatment was administered on September 15, 2006 and the last dose was administered on July 6, 2007. The final study evaluation was completed on July 6, 2007.

Results: Using an intent-to-treat analysis, the group taking the AppTrim formula lost significantly more weight (an average of 1.6kg) than the group receiving placebo (0.1kg, p-value<0.05). The average percent weight loss was also significantly different (independent samples t-test p-value<0.05). The AppTrim group had significantly larger changes in BMI (average of 0.9) than the placebo group (average of 0.1, p-value<0.05). The AppTrim group lost an average of 1.0% body fat, while the placebo group lost only 0.1%, but these differences were not statistically different, due to the large variability in body fat measurements (independent samples t-test p-value>0.05). There were no other statistically significant differences in between the two treatment groups.

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List of Abbreviations

AUC	Area Under the Curve
BMI	Body Mass Index
BMR	Basal Metabolic Rate
BUN	Blood Urea Nitrogen
CBC	Complete Blood Count
CRF	Case Report Form
CS	Completed Subjects
GRAS	Generally Regarded as Safe
IRB	Institutional Review Board
ITT	Intent-to-Treat
LOCF	Last Observation Carried Forward
PI	Principal Investigator
SGOT	Serum Glutamic Oxaloacetic Transaminase
SGPT	Serum Glutamic Pyruvic Transaminase
VAS	Visual Analogue Scale
WHO	World Health Organization

1.0 Introduction

There are a large number of published clinical trials of methods to aid in weight control including pharmaceuticals, dietary supplements, and mechanical interventions. It is not established that traditional weight loss programs, using various diets and exercise, are effective in producing either short-term or long lasting weight reduction results without appetite suppression. However, many of the proposed treatments, particularly the pharmaceuticals, demonstrate potential for significant side effects, including deaths and serious heart valve disease. Moreover many people have difficulty remaining on a weight loss program that depends on diet and exercise alone since these programs induce hunger. Accordingly, there is a need for a safe and effective treatment method based on naturally occurring food ingredients.

The Medical Food product, AppTrim, an amino acid and protein formula combined with a calorie controlled diet and the 10,000 step exercise program is believed to reduce body weight and percent body fat compared to placebo. AppTrim induces appetite suppression and reduces carbohydrate craving, which would facilitate compliance with a calorie reduced diet and a 10,000 step exercise program, resulting in body weight loss and reduction of body fat percentage compared to placebo. The hypothesis that AppTrim will reduce body weight and a reduction of body fat percentage was tested in this 12-week double-blind placebo controlled study of parallel design.

AppTrim contains a formula of selected GRAS (generally regarded as safe) ingredients that are derived from the normal human food chain. The primary ingredients are key amino acids, the building blocks of protein. AppTrim is designed to increase neurotransmitter function associated with weight control by the conversion of a neurotransmitter precursor into a neurotransmitter. AppTrim is designed to increase the function of five neurotransmitters (serotonin, acetylcholine, epinephrine, norepinephrine, and histamine) using precursors that include choline, tyrosine, 5-hydroxytryptophan, and histidine. Choline produces acetylcholine. Tyrosine produces epinephrine and norepinephrine. 5-hydorxytryptophan produces serotonin. Histidine produces histamine.

AppTrim contains both caffeine and cocoa but no ephedra or ephedrine alkaloids. Caffeine has actions similar to those of theobromine in cocoa. Both agents function by inhibition of the neuronal adenosine brake. The concentration of caffeine in a single dose is similar to that in a cup of coffee.

In addition to the use of AppTrim, there are three other components of the trial: an individualized calorie prescription, a calorie-counting diet, and an exercise program. The calorie prescription provided to the active and placebo groups in this study was based on baseline basal metabolic rate. The calorie-counting program was implemented with diaries, calorie-counting tools, and meal plans with specific calorie-defined meals. Subjects were not required to divide calories into pre-defined meals but could divide calories into portions of their choosing to fit their 24-hour calorie prescription. All participants were instructed in a 10,000-step exercise program and received a pedometer to monitor and recorded daily exercise.

The endpoints of the study were appetite reduction, weight loss, and reduction of percent body fat. Since it was anticipated that the placebo group might experience a high dropout rate because reduced calorie diets with exercise induce hunger, the dropout rate was analyzed as an endpoint. The study was a double-blind placebo controlled parallel design.

2.0 Study Objectives

This study was designed to evaluate the ability of AppTrim to produce greater weight loss and reduction of percent body fat than placebo when given for a 12-week period along with a calorie restricted diet and a 10,000-step exercise program**.**

3.0 Investigators and Study Administrative Structure

The study was conducted at one center (the Medical University of South Carolina) in the United States. The principal investigator at the site was Dr. Kit N. Simpson (DrPH Professor and Director of Outcomes Research, Center for Health Economics, College of Health Professions) and the site coordinator was Carol A. Lambourne (MSc, Faculty Research Associate, Outcomes Research, Department of Health Administration & Policy). The research organization that worked with the site and conducted the analysis was Exponent, Inc. Exponent is certified to ISO 9001.

4.0 Ethics

4.1 Institutional Review Board

The site and investigator were not supplied study materials until after approval by the site IRB.

4.2 Ethical Conduct of the Study

The study was conducted according to the Declaration of Helsinki (1964) as amended in Tokyo (1975) and Venice (1983).

4.3 Subject Information and Consent

Prior to entry into this study, all subjects provided informed consent. A blank subject consent form is provided in Appendix D.

5.0 Investigational Plan

5.1 Overall Study Design and Plan

This was a double blind placebo controlled study of 66 subjects. One group of 33 subjects received the appetite suppressant, AppTrim, a calorie prescription, a calorie

controlled diet and a 10,000-step exercise program. A second group of 33 subjects received placebo, a calorie prescription, a calorie controlled diet and a 10,000-step exercise program. Each subject was given a calorie prescription based on his/her Basal Metabolic Rate (BMR), instructed to begin following a restricted calorie counting diet in conjunction with a 10,000-step exercise program, and began AppTrim or placebo.

Prior to receiving the study drug, subjects' height, weight, abdominal girth and percentage of body fat were measured. At enrollment, all subjects were asked to fill out a medical history questionnaire. A baseline blood survey was performed. Weight and percent body fat were measured at baseline, week 2, week 4, week 6, week 8 and week 12. Percentage of body fat was assessed using bioelectrical impedance. A blood survey was completed at week 12 in both groups.

The original study protocol indicated that a total of six subjects (three in each treatment group) would receive the reverse product in order to ensure the double-blind. However, the products were not labeled in such a manner as to permit this analysis; this is discussed further in Protocol Deviations.

5.2 Materials and Dosage Schedule

At the initial visit, subjects were provided with either AppTrim or placebo capsules of identical appearance, according to randomization assignment. The placebo was a mixture of amino acids that do not produce the neurotransmitters lysine, valine, aspartic acid or Leucine. The placebo was isocaloric to the AppTrim; placebo capsules used sodium chloride and silicon dioxide as excipients.

Also at the initial visit, subjects were provided with a pedometer, a calorie-counting book (Allan Borushek, The Calorie King Calorie, Fat & Carbohydrate Counter, Family Health Publications, 2006), and a binder providing additional information on the study diet and recipes. At each subsequent visit, subjects returned any remaining product and were re-issued additional product for the interval until the next visit.

5.3 Randomization

A randomization scheme was created using a random number generator. The subjects were entered sequentially. There were no replacements for dropouts. Data from all subjects were analyzed on an intent-to-treat basis. Records were kept of all dropouts and their data were analyzed as if they had experienced no change.

5.4 Compliance

5.4.1 Compliance with AppTrim

The number of capsules dispensed at each clinic visit was recorded and the subject returned any unused drug at the subsequent visit. Returned capsules were counted to determine the actual number of capsules taken by the subject. It was anticipated that the

compliance of the active group would be greater than the placebo group because of the effect of AppTrim on appetite from each dose. There was no adjustment of the data for compliance variables.

5.4.2 Compliance with Diet

A questionnaire was used to assess compliance with diet. This was assessed as a secondary endpoint. It was anticipated that the active group would be able to maintain dietary control because of the appetite suppression effects of AppTrim.

5.5 Selection of Study Population

Subjects were identified by solicitation of persons interested in taking a product that may promote weight loss and fat reduction. All solicitations were approved by the university IRB. Recruitment materials were posted on campus and on local hospital, community center, and grocery store bulletin boards. In addition, advertisements were placed in the campus newspaper.

5.5.1 Inclusion Criteria

Subjects were eligible for inclusion in the study if they met all of the following criteria:

1. Males and females at least 18 years of age and no older than 50 years of age.
2. Subjects with a Body Mass Index (BMI) of between 25 and 40.
3. Women who are either post-menopausal or who agree to use some form of medically approved birth control during the duration of the study.
4. Subjects who are a low risk for this intervention, documented by either a physical examination at Visit 1 or a letter from their personal physician indicating approval for participation in this study.

5.5.2 Exclusion Criteria

Subjects were excluded from the study if they met any of the following criteria:

1. Subjects currently taking phentermine, Meridia, or other anorexic agents.
2. Subjects who have previously taken AppTrim.
3. Subjects with cancer.
4. Subjects with serum creatinine greater than 2.5 mg/dL.
5. Subjects who have lost more then 10% of their body weight in the preceding 6 months.
6. Pregnant or lactating females. Women who are not postmenopausal or surgically sterile must use a medically accepted contraceptive regimen, and agree to continue such use throughout the duration of the study. Reliable forms of contraception include oral, implanted, or injected contraceptives; intrauterine devices in place for at least 3 months; or adequate barrier methods in conjunction with spermicide. Abstinence is also considered an acceptable contraceptive regimen.
7. Subjects with implanted pacemakers or other implanted electrical devices.

8. Subjects who cannot consume caffeine contained in the equivalent of a cup of coffee.
9. Subjects who have any other medical condition or laboratory abnormalities that, in the opinion of the investigator, would interfere with study participation or results.

5.6 Treatments Administered

Subjects were instructed to ingest study product mid-morning and mid-afternoon as a 2-capsule dose. Subjects were instructed to follow this schedule of product use each day throughout the 12-week study.

5.7 Study Procedures

A summary of study procedures is presented in Appendix A. Below is a detailed list of each study visit and its requirements.

5.7.1 Baseline Visit

The following data were collected at the baseline visit:

a. Physical examination or review of letter from personal physician indicating approval for study participation
b. Baseline characteristics: Height, Age, Sex
c. Questionnaire A (Participant Information)
d. Blood sample for Complete Blood Count (CBC), liver panel and kidney panel
e. Weight
f. Percent body fat and BMI measured by bioelectrical impedance
g. Abdominal girth, waist and hip measurements
h. Questionnaire-Visual Analog Scale (Q-VAS) at baseline, 5, 15, 30 and 60 minutes post ingestion of either placebo or active
i. Blood pressure, heart rate, temperature and respiratory frequency

In addition, subjects received their initial study drug and were instructed in the diet and exercise program.

5.7.2 Visit Two / Week Two

The following data were collected at visit 2:

a. Questionnaire B, week 2
b. Weight
c. Percent body fat and BMI measured by bioelectrical impedance
d. Abdominal girth, waist and hip measurements
e. Blood pressure, heart rate, temperature and respiratory frequency
f. Adverse events (assessed by spontaneous report)
g. Study sample bottle returned and exchanged for new study sample

5.7.3 Visit Three / Week Four

The following data were collected at visit 3:

a. Questionnaire C, week 4
b. Weight
c. Percent body fat and BMI measured by bioelectrical impedance
d. Abdominal girth, waist and hip measurements
e. Blood pressure, heart rate, temperature and respiratory frequency
h. Adverse events (assessed by spontaneous report)
f. Study sample bottle returned and exchanged for new study sample

5.7.4 Visit Four / Week Six

The following data were collected at visit four:

a. Questionnaire D, week 6
b. Weight
c. Percent body fat and BMI measured by bioelectrical impedance
d. Abdominal girth, waist and hip measurements
e. Blood pressure, heart rate, temperature and respiratory frequency
i. Adverse events (assessed by spontaneous report)
f. Study sample bottle returned and exchanged for new study sample

5.7.5 Visit Five / Week Eight

The following data were collected at visit five:

a. Questionnaire E, week 8
b. Weight
c. Percent body fat and BMI measured by bioelectrical impedance
d. Abdominal girth, waist and hip measurements
e. Blood pressure, heart rate, temperature and respiratory frequency
j. Adverse events (assessed by spontaneous report)
f. Study sample bottle returned and exchanged for new study sample

5.7.6 Visit Six / Week Twelve

The following data were collected at visit six (final study visit):

a. Questionnaire F, week 12
b. Blood survey for CBC, liver panel and kidney panel
c. Weight
d. Percent body fat and BMI measured by bioelectrical impedance
e. Abdominal girth, waist and hip measurements
f. Appetite Questionnaires Visit 12 (Q-VAS) at baseline, 5, 15, 30 and 60 minutes post ingestion of either placebo or active treatment
g. Blood pressure, heart rate, temperature and respiratory frequency
k. Adverse events (assessed by spontaneous report)
h. Study sample bottle returned

5.7.7 Study Measurements

All study measurements were obtained in the morning after an overnight fast (from 10 pm). The subject was instructed to urinate before obtaining measurements. Measurements were obtained while the subject was dressed in a paper hospital gown while wearing underwear but without shoes.

5.8 Efficacy and Safety Variables

5.8.1 Body Weight and Percent Body Fat

Body composition measurements were obtained using a Quantum II Body Composition Analyzer (RJL Systems, Detroit, Michigan). The equations used to convert bioelectrical impedance to percent body weight have been peer reviewed. The scale was calibrated to 0.1 kg. Body composition measurements included height, weight, and % body fat. BMI was calculated. Two successive measurements, separated by 30 seconds, were obtained. The average of the two measurements was used in the analysis.

5.8.2 Abdominal Girth, Hip, and Waist Measurements

Abdominal girth was measured midway between the lateral lower rib margin and the iliac crest. Abdominal girth was measured with a calibrated metallic tape measure that controlled for the degree of stretch.

5.8.3 Visual Analogue Scale Measurement of Appetite and Carbohydrate Craving

Appetite and sweets and carbohydrate craving were measured using a 10 cm visual analogue scale. There were four questions to assess appetite: 1) "How strong is your desire to eat?" 2) "How hungry do you feel?" 3) "How full do you feel?" and 4) "How much food do you think you can eat?" There were two questions to assess cravings for sweets and carbohydrates: 1) "How strong is your craving for sweets?" and 2) "How strong is your craving for breads and other carbohydrates?" The subject was asked to mark an X to represent the subjective sensation. The scale was measured in cm using a calibrated ruler. The distance on the line was used as the score, with higher scores representing greater satiety for question 3 and lower for questions 1, 2 and 4. Question 3 was reverse coded and then the four appetite questions were averaged to get an overall measure of appetite. The questionnaire is included in Appendix B.

At visit one, the scale was administered a baseline, 5, 15, 30 and 60 minutes after ingestion of either placebo or active. The subject was blinded to the nature of the capsule at the time the Q-VAS was administered. The procedure was repeated in the subjects at visit 12. A modified Q-VAS scale was measured at other visits to represent perceived appetite and satiety between visits.

5.8.4 Blood Chemistries

Blood chemistries were obtained and analyzed at the study site or sent to a commercial laboratory. CBC (red cell count, white cell count, and platelet count), liver function (Serum Glutamic Oxaloacetic Transaminase (SGOT) and Serum Glutamic Pyruvic Transaminase (SGPT)), and kidney function (Blood Urea Nitrogen (BUN) and creatinine) panels were performed.

5.8.5 Safety

Data on subject safety, including blood pressure, heart rate, temperature and respiratory frequency, were collected at each study visit. Adverse events were assessed by spontaneous report and recorded on the Case Report Form (CRF). All adverse events and serious adverse events were summarized in terms of frequency, severity and relatedness to the study medication using the World Health Organization (WHO) code. Subjects with adverse events were referred for medical care through the study physician.

5.9 Data Quality

Data quality was monitored during the study. All collected data were entered into Excel spreadsheets by different study personnel. Designated study personnel reviewed a randomly selected subset of the collected data using the original sources and compared values with those in the summary Excel spreadsheet. Identified discrepancies were corrected.

5.10 Statistical Evaluation

5.10.1 Data Analysis Plan

The study design and statistical analyses are similar to the methods outlined in Gadde et al. (Gadde et al., 2003; Gadde et al., 2001) describing the Obesity Clinical Trials Program at Duke University. These methods are state-of-the-art for weight loss trials and have been peer reviewed and published in a major medical journal.

Analyses were performed at the end of the study. There were no interim analyses and the codes were not broken until the completion of the data collection phase of the study. The codes were broken by the biostatistician and not by either the study site personnel or the sponsor.

Continuous variables were analyzed using t-tests and the non-parametric Mann-Whitney and Wilcoxon tests. Variances were tested for equivalence. When variances were unequal, corrections for unequal variance were used. Contingency tables were used to analyze the dichotomous variables.

All analyses were performed using SAS v 9.1. A p-value of less than 0.05 indicated statistical significance.

5.10.2 Populations Analyzed

Primary and secondary endpoints were analyzed on an intent-to-treat basis. All randomized subjects were included in the intent-to-treat analysis. There was no subject replacement after randomization.

In the intent-to-treat analysis, the last observation of each subject who did not complete the entire study was carried forward (LOCF) for all subsequent observations. This means that the final value for drop-out subjects was the last measured value for each variable prior to dropout. In an extreme case, this could mean that if a subject did not return for Visit 2, the initial value would be taken as the final value. The dropout rate was compared across treatment groups using a Chi-square analysis.

The primary analysis population was the intent-to-treat population. However, as a secondary analysis, data for those subjects who completed the full study period were also analyzed in a similar manner. Both completing subjects and the intent-to-treat replacement analysis were performed as described by Gadde et al. (Gadde et al., 2003).

5.10.3 Comparison of Baseline Characteristics

The baseline demographics and initial starting measurements of the active and placebo groups were statistically compared.

5.10.4 Efficacy Evaluation

5.10.4.1 Primary Endpoints

The bivariate change in subjects' weight, percent body fat, and abdominal girth data at baseline were analyzed as the primary endpoints. The primary endpoint was the difference between the initial entry weight and the final weight. Study endpoints include:

1. The average difference in body weight from start to finish in the active group,
2. The average difference in percent body fat from start to finish in the active group,
3. The average difference in BMI from start to finish in the active group,
4. The average difference in abdominal girth from start to finish in the active group,
5. The average difference in waist from start to finish in the active group,
6. The average difference in hip circumference from start to finish in the active group,
7. The average difference in body weight from start to finish in the placebo group,
8. The average difference in percent body fat from start to finish in the placebo group,
9. The average difference in BMI from start to finish in the placebo group,
10. The average difference in abdominal girth, from start to finish in the placebo group,
11. The average difference in waist from start to finish in the placebo group,

12. The average difference in hip circumference from start to finish in the placebo group,
13. The 12-week difference in body weight between the active and placebo groups,
14. The 12-week difference in percent body fat between the active and placebo groups,
15. The 12-week difference in BMI between the active and placebo groups,
16. The 12-week difference in abdominal girth between the active and placebo groups,
17. The 12-week difference in waist between the active and placebo groups, and
18. The 12-week difference in hip circumference between the active and placebo groups.

5.10.4.2 Secondary Endpoints

Secondary endpoint analyses were performed on the average percent change in weight, the number of subjects who lost weight, the number of subjects who reduced body fat, the number of subjects who reduced abdominal girth and the number of individuals who achieved weight losses of 5% and 10% (dichotomized variables). These dichotomized analyses were done using chi-square and Fisher's exact tests.

Additional secondary endpoints include appetite suppression and change in carbohydrate craving. Appetite suppression and change in carbohydrate craving were analyzed using methods described by Kaplan (Kaplan et al., 2002) and others. For the Q-VAS, the area under the curve (AUC) was computed using the trapezoidal method. In addition, an average appetite suppression index was computed using an average of the four appetite questions. The individual time points, AUC and appetite index were analyzed with t-tests and non-parametric tests. The change in variables was calculated as: measure at time 1 – measure at time 6. Changes in measurements were compared with t-tests and non-parametric tests.

5.10.5 Safety Evaluation

Data on safety endpoints (blood pressure, heart rate, temperature, and respiratory rate, CBC results, and spontaneously-reported adverse events) were reviewed. During the study, these data were used as appropriate to refer subjects for medical care.

6.0 Study Subjects

6.1 Disposition of Subjects

All 66 subjects included in the analysis, participated in the baseline visit, while 52 completed all study visits according to the study protocol (see Table A for more details). No subjects who missed a visit returned for subsequent visits; that is, once a subject missed a study visit, they did not complete any further visits.

6.2 Protocol Deviations

The original protocol submitted and approved by the clinical site's institutional review board required that six subjects' study drug (three in each treatment group) be reverse allocated and excluded from the analysis. The required labeling was not performed by the study sponsor, and thus all subjects received the study drug to which it appears they were assigned and are included in this analysis. The practical implication of this protocol deviation was to increase the sample size; it had no negative effect on the integrity of the results.

7.0 Efficacy Evaluation

7.1 Data Sets Analyzed

The data set used for the primary analysis is the intent to treat (ITT) population, which consists of all subjects who participated in the baseline visit and received one or more doses of active treatment or placebo. The ITT population consisted of 33 subjects who received active treatment and 33 subjects who received placebo.

A secondary data set was the population of completed subjects (CS), which consists of all subjects who participated in all mandated study visits. Inclusion in this data set does not ensure full compliance with either the study drug protocol or the diet; these were assessed separately. The CS population consisted of 27 subjects who received active treatment and 25 subjects who received placebo.

The end-of-study drop-out rate was 18% in the treatment group and 24% in the placebo group. These rates were not statistically different (Chi-square p-value>0.05). Table A lists the numbers of subjects participating in each study visit. There were no subjects who missed one visit and subsequently returned for a later visit.

Table A: Numbers of subjects in each treatment group participating in each study visit (percentage of dropouts in parentheses)

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
Treatment	33 (0%)	32 (3%)	32 (3%)	29 (12%)	28 (15%)	27 (18%)
Placebo	33 (0%)	31 (6%)	28 (15%)	28 (15%)	27 (18%)	25 (24%)
Total	66	63	60	57	55	52

7.2 Demographic and Other Baseline Characteristics

7.2.1 Demographic Characteristics

There were a total of 60 women and 6 men in the ITT study population. Among those randomized to active treatment, there were 29 women and 4 men, while among those randomized to placebo, there were 31 women and 2 men. There were no significant differences in gender between the study groups (Fisher's exact test).

Demographic characteristics of the study population are presented in Tables B and C.

The mean age in the ITT population was 34.5 years (standard deviation 8.1 years). Among those randomized to active treatment, the mean age was 34.1 ± 8.9 compared to 34.9 ± 7.3 among those randomized to placebo. The mean age was not statistically different between the two groups.

Table B: ITT Population demographic statistics

	Placebo (N=33)		Treatment (N=33)		Comparison
Gender	31 (94%) women	2 (6%) men	29 (88%) women	4 (12%) men	p>0.05
Age (years)	Mean=34.9	Std. Dev.=7.3	Mean = 34.1	Std. Dev.=8.9	p>0.05
Height (cm)	Mean=164.5	Std. Dev.=7.7	Mean = 168.0	Std. Dev.=9.4	p>0.05

In the CS population, there were a total of 48 women and 4 men in the study population. Among those randomized to active treatment, there were 24 women and 3 men, while among those randomized to placebo, there were 24 women and 1 man. There were no significant differences in gender between the study groups (Fisher's exact test).

The mean age in the CS population was 34.7 years (standard deviation 8.4 years). Among those randomized to active treatment, the mean age was 33.9 ± 9.0 compared to 35.5 ± 7.8 among those randomized to placebo. The mean age was not statistically different between the two groups.

Table C: CS Population demographic statistics

	Placebo (N=25)		Treatment (N=27)		Comparison
Gender	24 (96%) women	1 (4%) men	24 (89%) women	3 (11%) men	p>0.05
Age (years)	Mean=35.5	Std. Dev.=7.8	Mean = 33.9	Std. Dev.=9.0	p>0.05
Height (cm)	Mean=163.8	Std. Dev.=7.3	Mean = 168.0	Std. Dev.=9.6	p>0.05

7.2.2 Baseline Clinical Characteristics

Baseline clinical characteristics are presented in Tables D (ITT) and F (CS). Baseline Appetite Questionnaire results are presented in Tables E (ITT) and G (CS).

7.2.2.1 ITT Population

In the ITT population, the baseline mean weight in the treatment group was 91.9 ± 16.0 kg and 86.0 ± 12.3 kg in the placebo group. These differences were not statistically

significant using either a t-test or a non-parametric test. The baseline BMI was 32.8 ± 4.6 among subjects receiving active treatment and 31.8 ± 4.1 among those receiving placebo. The baseline percentage body fat was 40.9 ± 6.7 among subjects receiving active treatment and 41.0 ± 5.9 among those receiving placebo. The baseline abdominal girth was 41.1 ± 4.7 inches among subjects receiving active treatment and 40.1 ± 3.5 inches among those receiving placebo. The baseline hip circumference was 45.9 ± 3.4 inches among subjects receiving active treatment and 45.5 ± 2.8 inches among those receiving placebo. The baseline waist measurement was 38.0 ± 4.3 inches among subjects receiving active treatment and 37.2 ± 3.5 inches among those receiving placebo. None of these differences were statistically significant using either t-tests or non-parametric tests.

Treatment subjects reported drinking 1.2 ± 1.3 cups of caffeinated coffee, 1.1 ± 1.3 cups of caffeinated sodas, 0.4 ± 0.7 cups of caffeinated tea, and 0.06 ± 0.2 cups of caffeinated power drinks per day; whereas placebo subjects reported drinking an average of 0.7 ± 0.9 cups of caffeinated coffee, 1.5 ± 1.7 cups of caffeinated sodas, 0.8 ± 1.5 cups of caffeinated tea, and 0.01 ± 0.04 cups of caffeinated power drinks per day. None of these differences were statistically different across groups using either a t-test or a non-parametric test. See Table D for details.

Treatment subjects reported participating in 1.9 ± 2.2 hours of organized exercise per week and rated their activity level at 5.6 ± 1.8 on a scale of 1 to 10 where 10 is very active and 1 is no activity at all. Placebo subjects reported participating in 1.2 ± 1.7 hours of organized exercise per week and rated their activity level at 5.9 ± 1.9 on a scale of 1 to 10 where 10 is very active and 1 is no activity at all. These differences were also not statistically significant by either parametric or non-parametric tests.

Table D: ITT Population Baseline Statistics

	Placebo (N=33)		Treatment (N=33)		Comparison
	Mean	Std. Dev.	Mean	Std. Dev.	t-test p-value
Weight (kgs)	86.0	12.3	91.9	16.0	p>0.05
BMI	31.8	4.1	32.8	4.6	p>0.05
Body fat (%)	41.0	5.9	40.9	6.7	p>0.05
Abdominal girth (inches)	40.1	3.5	41.1	4.7	p>0.05
Waist (inches)	37.2	3.5	38.0	4.3	p>0.05
Hip (inches)	45.5	2.8	45.9	3.4	p>0.05
Coffee (cups per day)	0.7	0.9	1.2	1.3	p>0.05
Soda (cups per day)	1.5	1.7	1.1	1.3	p>0.05
Tea (cups per day)	0.8	1.5	0.4	0.7	p>0.05
Caffeinated power drinks (cups per day)	0.01	0.04	0.06	0.2	p>0.05
Activity level	5.9	1.9	5.6	1.8	p>0.05
Exercise (hours per day)	1.2	1.7	1.9	2.2	p>0.05

Full results from the baseline Appetite Questionnaire are presented in Table E. There were no significant differences in the groups at baseline using t-test or Mann-Whitney tests. The mean sum for the four key appetite questions was 4.9 ± 2.5 for the active treatment subjects and 4.5 ± 2.4 for the placebo subjects; these were not statistically different.

Table E: Baseline Appetite Questionnaire Statistics, ITT Population (scale of 0 to 10, with 0 representing very weak, very little, or rarely, and 10 representing very much, very strong or very often)

	Placebo (N=33)		Treatment (N=33)		Comparison
How	Mean	Std. Dev.	Mean	Std. Dev.	t-test p-value
Strong is your desire to eat?	5.9	1.7	6.0	2.0	p>0.05
Hungry are you between meals?	4.5	1.8	4.6	1.7	p>0.05
Satisfied after meals?	7.4	2.3	7.4	2.2	p>0.05
Much food can you eat?	6.0	1.8	6.5	1.8	p>0.05
Strong is your craving for sweets?	5.1	2.9	6.3	2.8	p>0.05
Strong is your craving for carbs?	5.7	2.5	6.9	2.2	p>0.05
Often do you snack?	4.9	2.4	4.9	2.0	p>0.05

7.2.2.2 CS Population

In the CS population, the only significant difference in the mean baseline variables was the average number of cups of coffee per day, which was higher in the treatment group (independent t-test and Mann-Whitney test); however, this difference was not significant when the p-value was adjusted (using a Bonferonni adjustment) for the 13 baseline comparisons done (adjusted p-value=0.02x13=0.26).

Table F: CS Population Baseline Statistics

	Placebo (N=25)		Treatment (N=27)		Comparison
	Mean	Std. Dev.	Mean	Std. Dev.	p-value
Age (years)	35.5	7.8	33.9	9.0	p>0.05
Weight (kgs)	85.6	12.8	90.2	15.2	p>0.05
BMI	31.9	4.2	32.3	4.2	p>0.05
Body fat (%)	41.2	5.6	40.7	6.7	p>0.05
Abdominal girth (inches)	40.2	3.6	41.2	4.1	p>0.05

	Placebo (N=25)		Treatment (N=27)		Comparison
	Mean	Std. Dev.	Mean	Std. Dev.	p-value
Waist (inches)	37.3	3.5	37.7	4.4	p>0.05
Hip (inches)	45.4	2.9	45.4	2.9	p>0.05
Coffee (cups per day)	0.6	0.8	1.3	1.4	p<0.05
Soda (cups per day)	1.5	1.8	1.3	1.3	p>0.05
Tea (cups per day)	0.7	1.2	0.4	0.7	p>0.05
Caffeinated power drinks (cups per day)	0.01	0.04	0.07	0.3	p>0.05
Exercise (hours per day)	1.2	1.8	2.0	2.3	p>0.05
Activity level	5.7	1.9	5.4	1.6	p>0.05

Full results from the baseline Appetite Questionnaire are presented in Table G. There were no significant differences between the treatment groups to any of the questionnaire responses. The mean sum for the four key appetite questions was 4.9 ± 2.7 for the active treatment subjects and 4.6 ± 2.3 for the placebo subjects; the mean reported appetite was not significantly different between the treatment and placebo groups.

Table G: Baseline Appetite Questionnaire Statistics, CS Population (scale of 0 to 10, with 0 representing very weak, very little, or rarely, and 10 representing very much, very strong or very often)

	Placebo (N=33)		Treatment (N=33)		Comparison
How	Mean	Std. Dev.	Mean	Std. Dev.	t-test p-value
Strong is your desire to eat?	5.9	1.7	6.0	2.0	p>0.05
Hungry are you between meals?	4.5	1.8	4.6	1.7	p>0.05
Satisfied after meals?	7.4	2.3	7.4	2.2	p>0.05
Much food can you eat?	6.0	1.8	6.5	1.8	p>0.05
Strong is your craving for sweets?	5.1	2.9	6.3	2.8	p>0.05
Strong is your craving for carbs?	5.7	2.4	6.9	2.2	p>0.05
Often do you snack?	4.9	2.4	4.9	2.0	p>0.05

7.3 End of Study Clinical Assessments

End of study primary endpoint evaluations are presented in Tables H (ITT) and K (CS). End of study secondary endpoint evaluations for the ITT population are presented in Tables I and J.

7.3.1 ITT Population

Compliance

Overall, 8 (24%) of the treatment group and 13 (39%) of the placebo group complied with the study protocol and returned their bottles of pills at every visit. Compliance decreased over the study period: on the second visit, 26 (79%) of the treatment group and 23 (70%) of the placebo group returned their bottle of pills; on the third visit, 27 (81%) of the treatment group and 22 (67%) of the placebo group returned their bottle of pills; on the fourth visit, 23 (70%) of the treatment group and 21 (64%) of the placebo group returned their bottle of pills; on the fifth visit, 21 (64%) of the treatment group and 20 (61%) of the placebo group returned their bottle of pills; on the last visit, 14 (42%) of the treatment group and 17 (52%) of the placebo group returned their bottle of pills. There were no significant differences in compliance at any time point (Chi-square tests) or in the average number of visits with returned bottles (t-test).

Of those who returned unused pills at one or more time points, the treatment group returned an average of 7.5 pills, and the placebo group returned an average of 11.5 pills. There was a significant difference in this average number of pills returned, with the placebo group returning more pills on average (t-test p-value<0.05). Given that at each visit, up to 20% of subjects did not return their pill bottles for an assessment of compliance, this small but statistically significant difference in the number of pills returned is likely not clinically meaningful.

Primary Endpoints

In the ITT population, the end of study BMI was 31.9 ± 4.5 among subjects receiving active treatment and 31.7 ± 4.4 among those receiving placebo. The mean changes from baseline were 0.9 ± 1.9 in the treatment group and 0.1 ± 1.0 in the placebo group. The change from baseline in the treatment group was significant (paired t-test p-value<0.05), but the change from baseline in the placebo group was not (paired t-test p-value>0.05). The changes from baseline were significantly different between the groups (independent samples t-test p-value<0.05).

The end of study weight was 90.3 ± 15.8 among subjects receiving active treatment and 86.0 ± 12.8 among those receiving placebo. The mean weight loss in the treatment group was 1.6 kg, which was statistically significant (paired t-test p-value<0.01). In contrast, the placebo group lost an average of 0.1 kg, which was not statistically significant (paired t-test p-value>0.05). The average weight loss was significantly different between the groups (independent samples t-test p-value<0.05).

The treatment group lost an average of 1.0% body fat, while the placebo group lost only 0.1%. These differences were not statistically different, however, due to the large variability in body fat measurements (independent samples t-test p-value>0.05).

The results from non-parametric tests (Mann-Whitney and Wilcoxon tests) were the same as for the parametric tests. All other changes were not significantly different between treatment and placebo groups (see Table H).

Table H: ITT Population End of Study Primary Endpoint Statistics

	Placebo (N=33)		Treatment (N=33)		Comparison
	Mean	Std. Dev.	Mean	Std. Dev.	p-value
Weight (kgs)	86.0	12.8	90.3	15.8	p>0.05
BMI	31.7	4.4	31.9	4.5	p>0.05
Body fat (%)	40.8	5.7	39.9	6.8	p>0.05
Abdominal girth (inches)	39.7	3.7	40.6	3.9	p>0.05
Waist circumference (inches)	36.8	4.2	37.4	4.7	p>0.05
Hip circumference (inches)	44.8	3.3	45.2	3.3	p>0.05
Weight loss (kgs)	0.06	3.1	1.6	2.9	p<0.05
BMI loss	0.08	1.0	0.9	1.9	p<0.05
Body fat loss (%)	0.1	4.7	1.0	3.1	p>0.05
Abdominal girth loss (inches)	0.3	1.8	0.5	2.9	p>0.05
Waist circumference loss (inches)	0.4	2.0	0.6	1.7	p>0.05
Hip circumference loss (inches)	0.7	1.2	0.6	1.1	p>0.05

Secondary Endpoints

The ITT treatment group lost an average of 1.8 ± 3.0 % of their body weight, whereas the placebo group lost an average of 0.08 ± 3.7 %. The average percent weight loss was significantly different between the groups (independent samples t-test p-value<0.05). In terms of percentages achieving various goals: 64% of the treatment group and 42% of the placebo group lost weight; 61% of the treatment group and 48% of the placebo group lost body fat; 70% of the treatment group and 42% of the placebo group reduced their BMI; 64% of the treatment group and 45% of the placebo group lost abdominal girth; 12% of both the treatment and placebo groups lost 5% or more of their body weight; and 3% of the treatment group and 0% of the placebo group lost 10% or more of their body weight. Of these differences, only the percentages of subjects who reduced their BMI were statistically significant (Chi-square p-value<0.05).

Full results from the Appetite Questionnaire (baseline and visit 6) are presented in Tables I and J. There were no significant differences between the treatment groups in any of the appetite measures at the end of the study. Both treatment and placebo subjects had significant decreases in the desire to eat (p-value<0.01 and <0.001), decreases in satisfaction after meals (p-value<0.001 and <0.001), the amount of food they could eat (p-value<0.05 and <0.001), and cravings for both sweets (p-value<0.001 and <0.001) and

carbs (p-value<0.001 and <0.001). Also, both treatment groups reported decreases in snacking (p-value<0.05 and 0.001). The treatment groups were not significantly different in their changes from baseline to end of study in these measures. The mean sum for the four key appetite questions was 4.9 ± 2.5 for the active treatment subjects and 4.5 ± 2.4 for the placebo subjects at baseline and 4.0 ± 4.5 for the active treatment subjects and 4.8 ± 4.3 for the placebo subjects at the end of the study. The treatment groups did not report significantly different appetites at baseline or at the end of study, and the change in appetites over the course of the study was not significantly different in the treatment groups.

There were no significant differences in any AUC measurement between the treatment groups at baseline or at the end of the study and there were no significant changes from baseline to the end of the study in either group (all parametric and non-parametric p-values>0.05).

Table I: End of Study Appetite Questionnaire Statistics, ITT Population (scale of 0 to 10, with 0 representing very weak, very little, or rarely, and 10 representing very much, very strong or very often)

	Placebo (N=33)		Treatment (N=33)		Comparison
How	Mean	Std. Dev.	Mean	Std. Dev.	t-test p-value
Strong is your desire to eat?	4.7	2.4	4.6	2.8	p>0.05
Hungry are you between meals?	4.5	2.5	4.2	2.6	p>0.05
Satisfied after meals?	4.8	2.5	5.1	2.9	p>0.05
Much food can you eat?	4.9	2.0	4.6	2.3	p>0.05
Strong is your craving for sweets?	3.4	2.5	3.7	2.4	p>0.05
Strong is your craving for carbs?	4.2	2.7	4.6	2.6	p>0.05
Often do you snack?	3.9	2.3	3.8	2.2	p>0.05

Table J: ITT Population Appetite Survey AUC at baseline and End of Study

	Baseline				End of Study			
	Placebo (N=33)		Treatment (N=33)		Placebo (N=33)		Treatment (N=33)	
AUC	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.	Mean	Std. Dev.
Strong is your desire to eat?	259.5	110.8	262.9	125.8	233.8	124.2	239.5	147.6
Hungry are you between meals?	258.6	107.3	256.6	123.6	228.1	123.6	237.0	150.2
Satisfied after meals?	212.7	75.3	233.7	123.7	229.3	117.5	247.5	144.0
Much food can you eat?	242.5	87.0	258.7	118.4	221.9	106.6	236.4	130.2
Strong is your craving for sweets?	134.1	89.8	163.3	125.1	137.1	113.7	173.5	134.0
Strong is your craving for carbs?	188.2	120.5	238.7	139.2	170.1	137.2	210.9	151.1

7.3.2 CS Population

Primary Endpoints

In the CS population, the end of study BMI was 31.3 ± 4.1 among subjects receiving active treatment and 31.8 ± 4.6 among those receiving placebo. The mean changes from baseline were 1.0 ± 2.0 in the treatment group and 0.1 ± 1.2 in the placebo group. The change from baseline in the placebo group is not significant (paired t-test p-value>0.05), but the change from baseline in the treatment group is significant (paired t-test p-value<0.05). The between-group difference was not significantly different.

The end of study mean weight was 88.6 ± 14.9 among subjects receiving active treatment and 85.5 ± 13.3 among those receiving placebo. The mean changes from baseline were 1.6 ± 2.8 in the treatment group and 0.1 ± 3.5 in the placebo group. The change from baseline in the placebo group is not significant (paired t-test p-value>0.05), but the change from baseline in the treatment group is significant (paired t-test p-value<0.01). The between-group difference was not significantly different.

All other changes were not significantly different between treatment and placebo groups (see Table K).

Table K: CS Population End of Study Statistics

	Placebo (N=25)		Treatment (N=27)		Comparison
	Mean	Std. Dev.	Mean	Std. Dev.	p-value
Weight (kgs)	85.5	13.3	88.6	14.9	p>0.05
BMI	31.8	4.6	31.3	4.1	p>0.05
Body fat (%)	41.0	5.7	39.9	6.7	p>0.05
Abdominal girth (inches)	39.9	3.8	40.4	3.9	p>0.05
Waist circumference (inches)	36.8	4.4	37.1	4.7	p>0.05
Hip circumference (inches)	44.6	3.4	44.7	2.8	p>0.05
Weight loss (kgs)	0.1	3.5	1.6	2.8	p>0.05
BMI loss	0.1	1.2	1.0	2.0	p>0.05
Body fat loss (%)	0.2	5.3	0.9	2.7	p>0.05
Abdominal girth loss (inches)	0.3	2.0	0.8	2.0	p>0.05
Waist circumference loss (inches)	0.5	2.2	0.6	1.7	p>0.05
Hip circumference loss (inches)	0.7	1.3	0.7	1.1	p>0.05

Secondary Endpoints

The CS treatment group lost an average of 1.7 ± 3.0 % of their body weight, whereas the placebo group lost an average of 0.09 ± 4.2 %. The average percent weight loss was not significantly different between the groups (independent samples t-test p-value>0.05). In terms of percentages achieving various goals: 67% of the treatment group and 48% of the placebo group lost weight; 63% of the treatment group and 52% of the placebo group lost body fat; 70% of the treatment group and 48% of the placebo group reduced their BMI; 67% of the treatment group and 52% of the placebo group lost abdominal girth; 11% of the treatment and 16% of the placebo groups lost 5% or more of their body weight; and 4% of the treatment group and 0% of the placebo group lost 10% or more of their body weight. None of these differences was statistically significant (Chi-square p-value>0.05).

There were no significant differences between the treatment groups in any of the appetite measures at the end of the study. Both treatment and placebo subjects had significant decreases in the desire to eat, satisfaction after meals, the amount of food they could eat, and cravings for both sweets and carbs. Also, both treatment groups reported significant decreases in snacking. However, the treatment groups were not significantly different in their changes from baseline to end of study in these measures. The mean sum for the four key appetite questions was 4.9 ± 2.7 for the active treatment subjects and 4.6 ± 2.3 for the placebo subjects at baseline and 4.0 ± 4.5 for the active treatment subjects and 4.8 ± 4.3

for the placebo subjects at the end of the study. The treatment groups did not report significantly different appetites at baseline or at the end of study, and the change in appetites over the course of the study was not significantly different in the treatment groups.

There were no significant differences in any AUC measurement between the treatment groups at baseline or at the end of the study and there were no significant changes from baseline to the end of the study in either group (all parametric and non-parametric p-values>0.05).

8.0 Safety Evaluation

Adverse events were reported by seven subjects in the treatment group. The most common complaint (reported by one subject twice and another subject four times) was constipation. Nausea was reported by two subjects on one visit each. Other events reported were frequent urination, gas and feeling "jumpy." The subject who reported feeling jumpy dropped out of the study after the fourth visit, all others reporting adverse events remained in the study until the end.

Eight subjects in the placebo group reported adverse events including face acne, sleep disturbance, morning dizziness, thirst, inability to taste food, odd aftertaste, jumpiness, gas, evening hunger, nocturnal sweet binges and morning upset stomach. The subject who reported jumpiness dropped out of the study after the fifth visit, all other subjects who reported adverse events completed the study.

9.0 References

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Appendix A. Schedule of Study Assessments

Schedule of Study Assessments

Visit / Week	Physical examination	Baseline Characteristics (Age, Sex, Height)	Questionnaire	Blood panel (CBC, liver, kidney panel)	Efficacy Assessments (weight, BMI, abdominal girth, waist, hip measurements)	Safety Assessments (BP, HR, respiratory frequency, temperature)	Return / reissue product
1 / 0	X	X	X (A)	X	X	X	X (issue only)
2 / 2			X (B)		X	X	X
3 / 4			X (C)		X	X	X
4 / 6			X (D)		X	X	X
5 / 8			X (E)		X	X	X
6 / 12			X (F)	X	X	X	X (return only)

Appendix B. Case Report Forms

Date_____ ID Number_____

Research Study

AppTrim Research Study
Questionnaire A ~ Participant Information

Please print the following information:

First and Last Name _____

Address _____

City, State, Zip Code _____

Phone _____ Email _____

Age ___ Date of Birth ___/___/_____ Male ____ Female ___

Are you pregnant? ___ Yes ___ No

Height ___/____ Weight _____lbs Waist _____ inches

Abdominal Girth _____ inches Hip Circumference_____ inches

Percent Body Fat _____ BMI _____

Are you diabetic?
_____ Yes _____ No

Do you have a medically diagnosed thyroid problem or other glandular condition?
_____ Yes _____ No

Are you currently taking any weight loss medications?
_____ Yes _____ No If "yes" name of medication _____

Have you taken any weight loss medications in the last 60 days?
_____ Yes _____ No If "yes" name of medication _____

Have you ever taken ***AppTrim*** before?
_____ Yes _____ No

Are you currently taking any anti-depressant medications?

_____ Yes _____ No

How many cups of caffeinated beverages do you drink each day? (1 cup = 8 ozs)

_____cups of caffeinated coffee _____cups of caffeinated sodas

_____cups of caffeinated tea _____cups of caffeinated power drinks

Date_____ ID Number_____

Do you have an implanted pacemaker or any other implanted electrical device?

_____ Yes _____ No

If female, are you pre-menopausal?

_____ Yes _____ No

If you are pre-menopausal, what form of birth control do you use?

_____

If pre-menopausal, will you agree to use an acceptable form of birth control during the study duration?

_____ Yes _____ No

How much organized exercise do you participate in each week?

_____Hours

Type of work do you do?

_____

Rate you activity level on a scale of 1 to 10 where 10 is very active and 1 is no activity at all.

_____

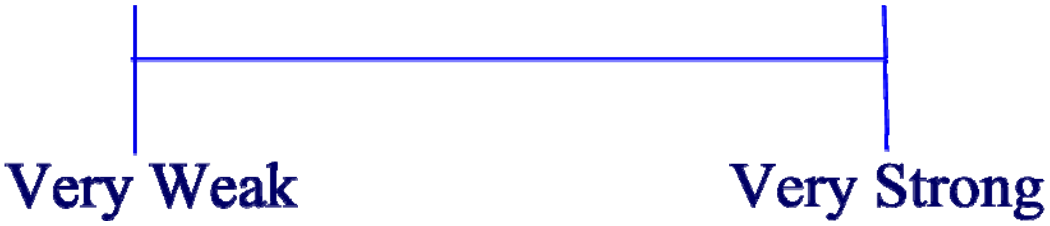
Date _____ Subject ID Number _____

Signature _____

Date_____ ID Number_____

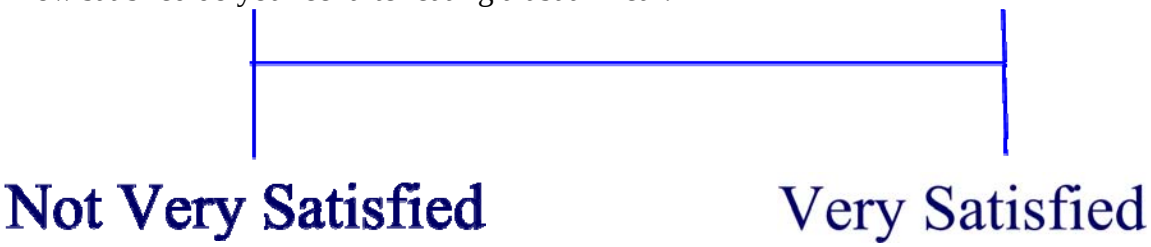
Appetite Questionnaire Visit 1 Baseline

How strong is your desire to eat during the day?

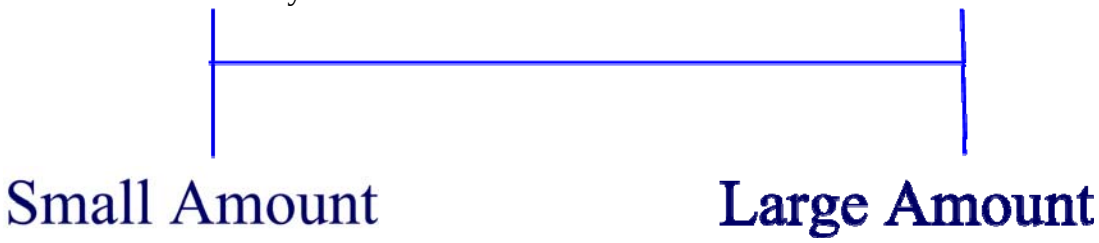


How hungry do you feel between meals?

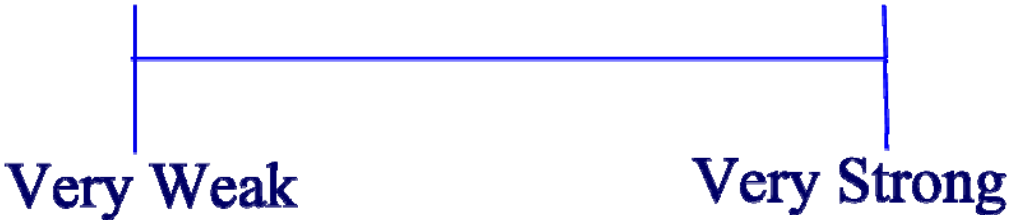
How satisfied do you feel after eating a usual meal?



How much food can you eat at a usual meal?

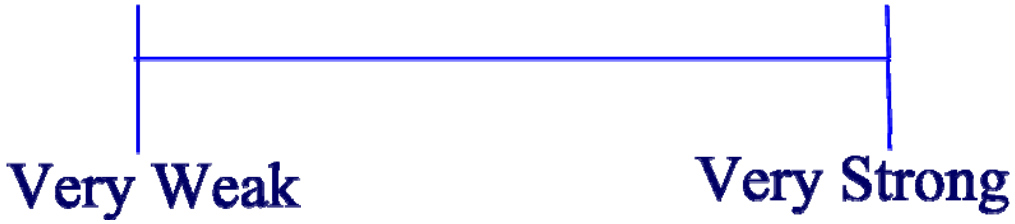


How strong is your craving for sweets?

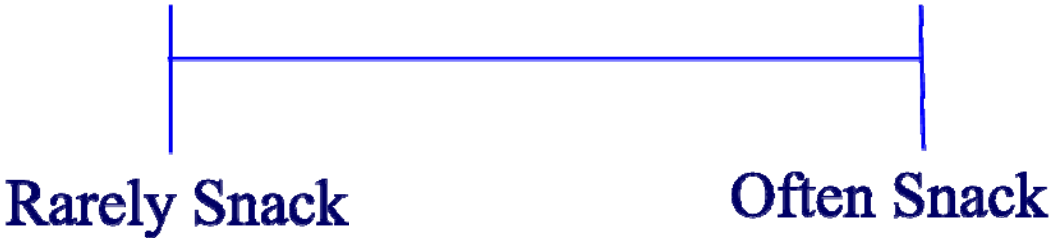


Date_____ ID Number_____

How strong is your craving for breads and other carbohydrates?



How much do you snack between meals?

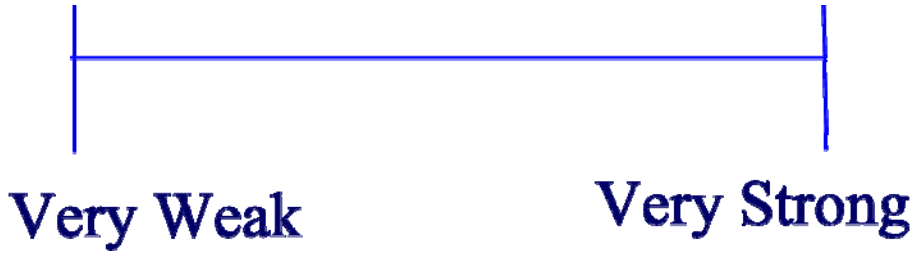


Date_____ ID Number_____

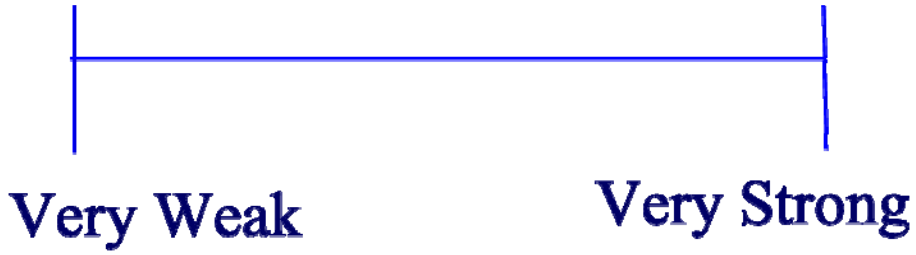
Appetite Questionnaire Visit 1 5 minutes

How strong is your desire to eat?

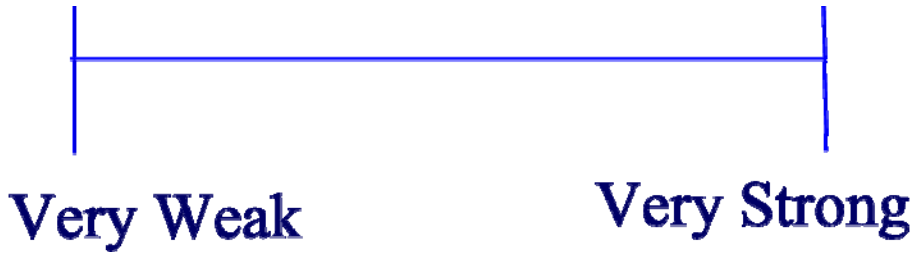
How hungry do you feel?



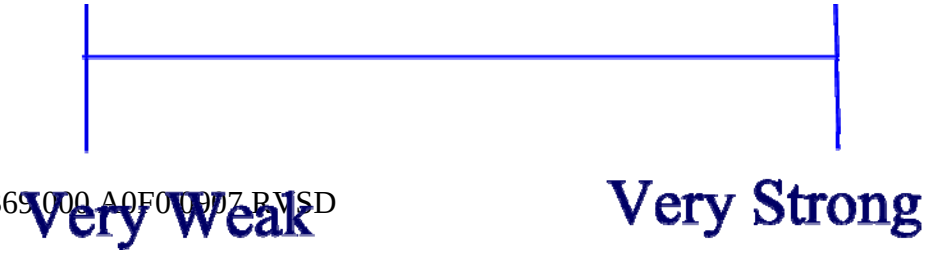
How full do you feel?



How much food do you feel you can eat?

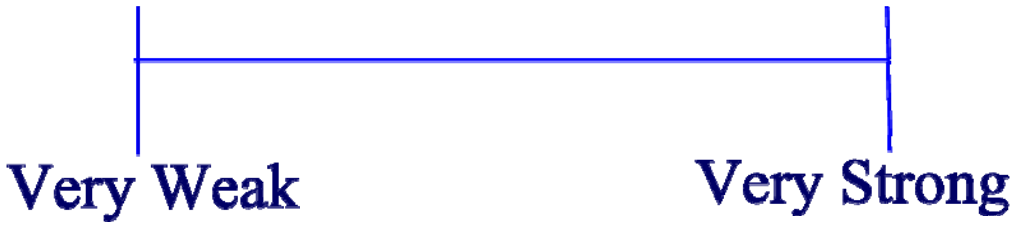


How strong is your craving for sweets?



Date_____ ID Number_____

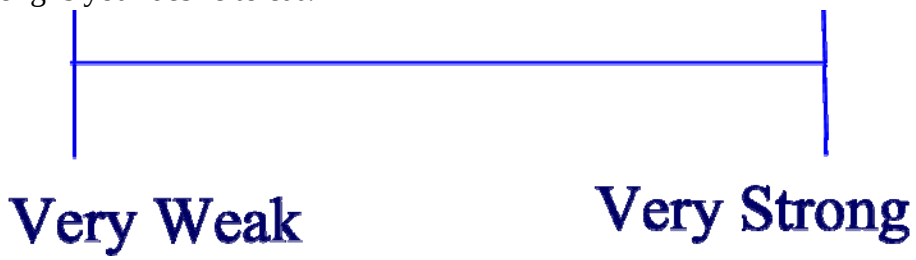
How strong is your craving for breads and other carbohydrates?



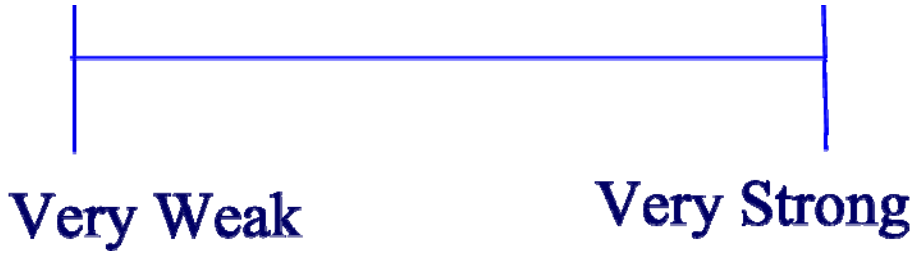
Date_____ ID Number_____

Appetite Questionnaire Visit 1 15 minutes

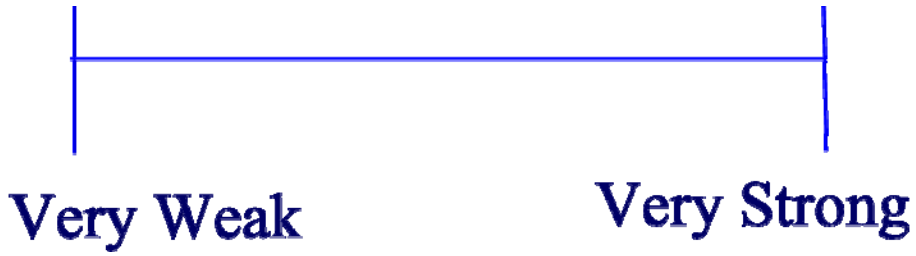
How strong is your desire to eat?



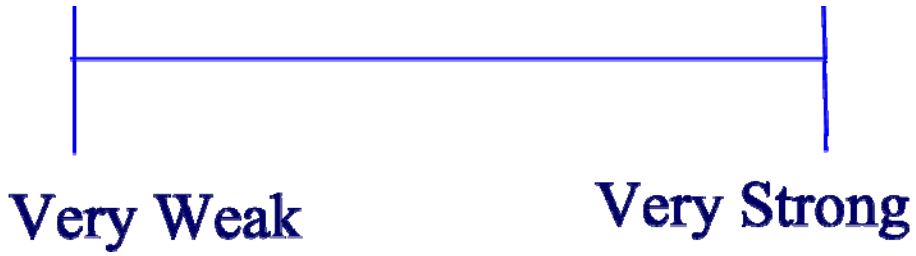
How hungry do you feel?



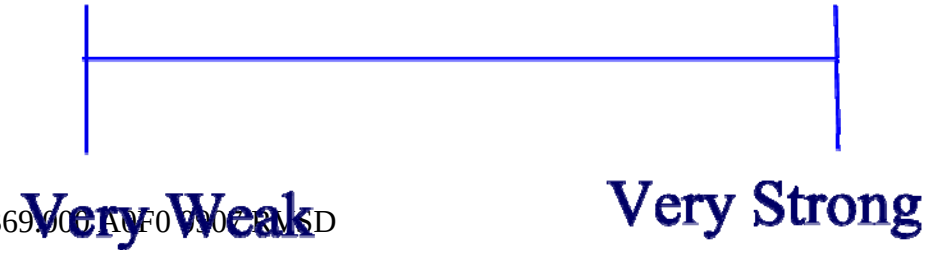
How full do you feel?



How much food do you feel you can eat?

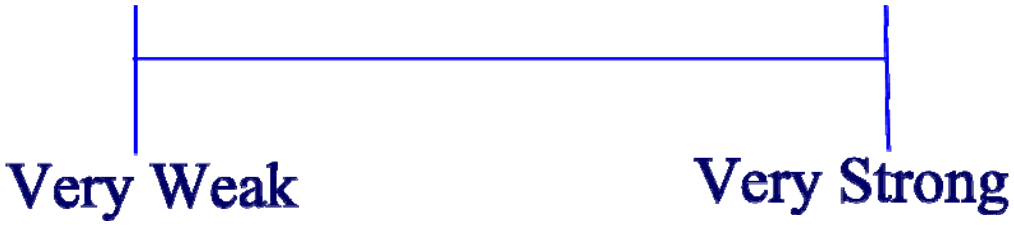


How strong is your craving for sweets?



Date_____ ID Number_____

How strong is your craving for breads and other carbohydrates?



Date_____ ID Number_____

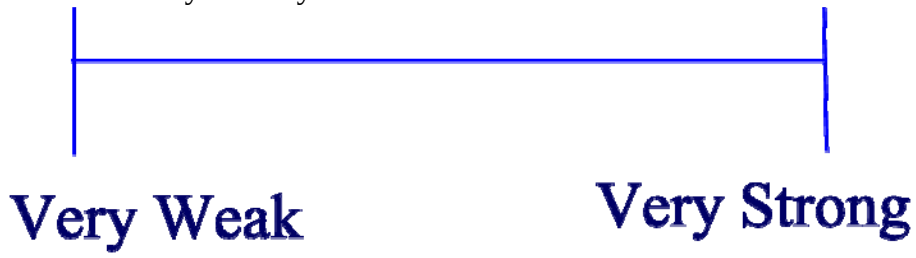
Appetite Questionnaire Visit 1 30 minutes

How strong is your desire to eat?

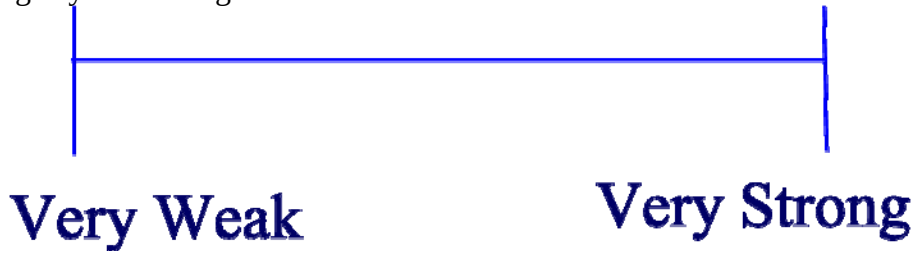
How hungry do you feel?

How full do you feel?

How much food do you feel you can eat?

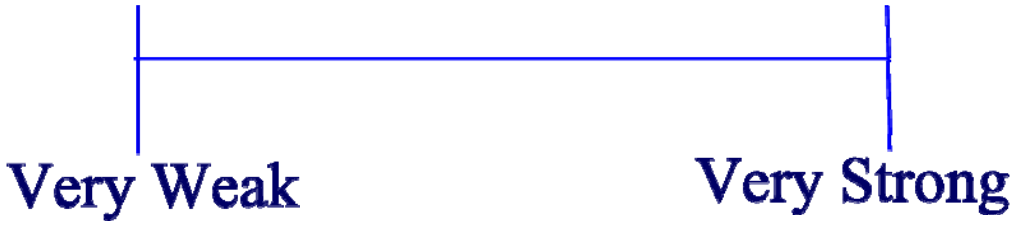


How strong is your craving for sweets?



Date_____ ID Number_____

How strong is your craving for breads and other carbohydrates?



Date_____ ID Number_____

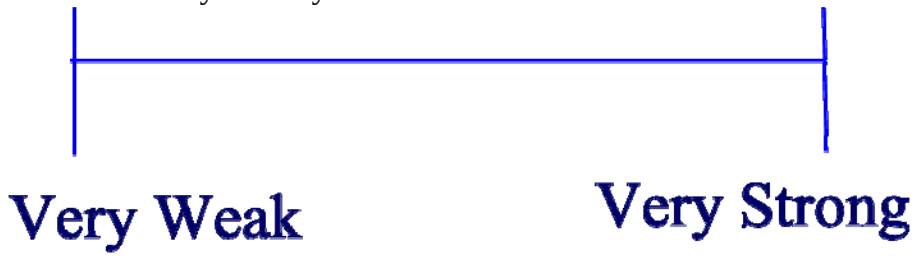
Appetite Questionnaire Visit 1 60 minutes

How strong is your desire to eat?

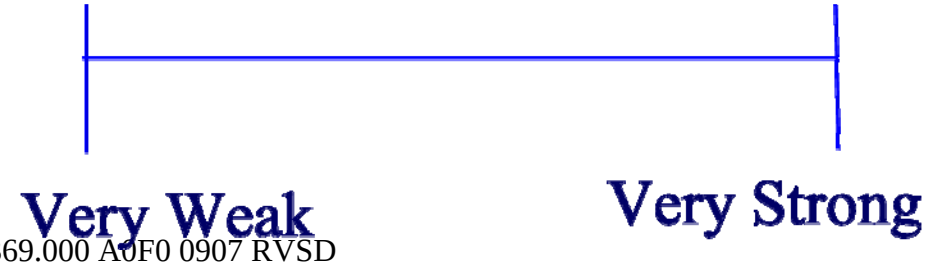
How hungry do you feel?

How full do you feel?

How much food do you feel you can eat?

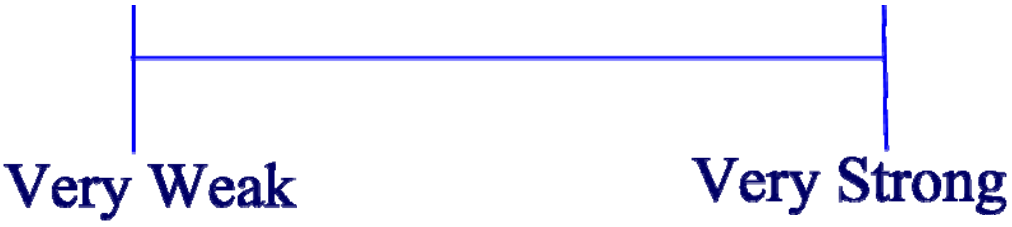


How strong is your craving for sweets?



Date_____ ID Number_____

How strong is your craving for breads and other carbohydrates?



Date_____ ID Number_____

Questionnaire B ~ Week 2

Please print the following information:

First and Last Name _____

Age _____ Date of Birth ___/___/_____ Male ____ Female ___

Weight _____lbs Hip Circumference_____ inches

Abdominal Girth _____ inches Waist _____ inches

Percent Body Fat _____ BMI _____

Did you have any side effects in the last two weeks? _____ Yes _____ No

What were the side effects_____

_____

Did you experience a change in hunger (rate on a scale of 1 to 10 where 10 was complete hunger suppression, 5 is no change and 1 severe increase in hunger)_____?

How long after ingestion of the capsules did you note appetite suppression_____(minutes)? Use zero minutes for no appetite suppression.

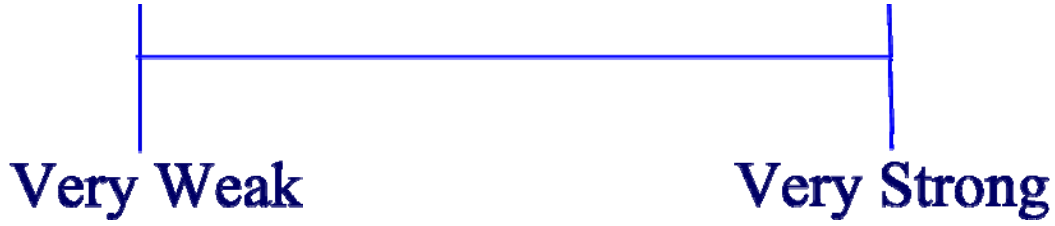
How long did the appetite suppression last_____(hours)? Use zero hours for no appetite suppression.

How many cups of caffeinated beverages did you drink each day in the past two weeks? (1 cup = 8 ozs)

_____cups of caffeinated coffee _____cups of caffeinated sodas

_____cups of caffeinated tea _____cups of caffeinated power drinks

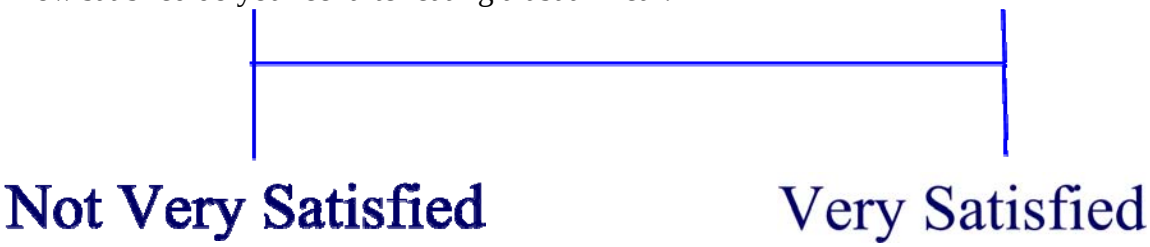
How strong is your desire to eat during the day?



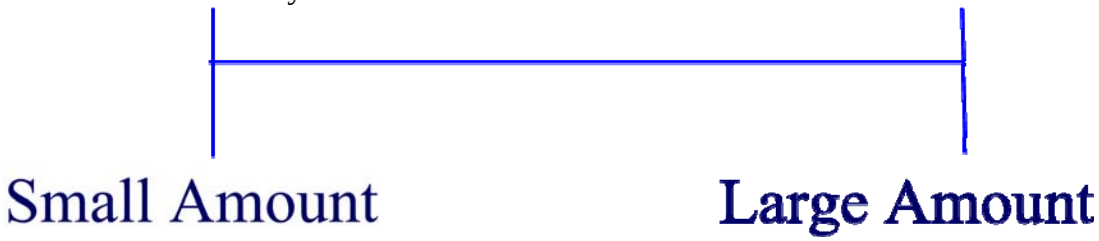
Date_____ ID Number_____

How hungry do you feel between meals?

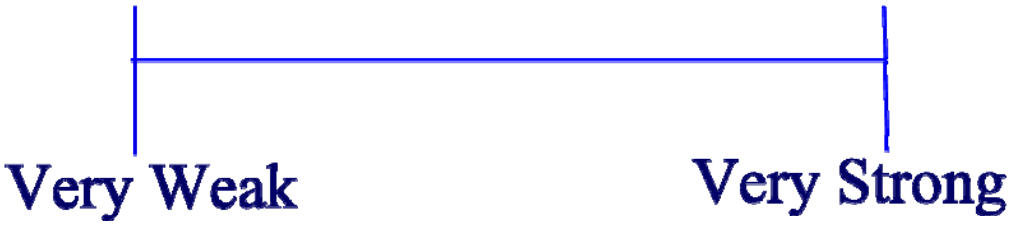
How satisfied do you feel after eating a usual meal?



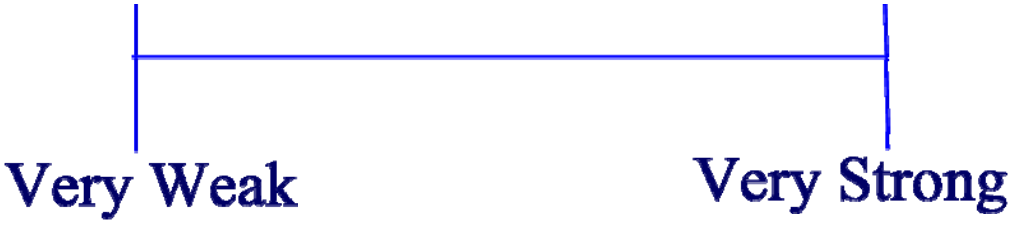
How much food can you eat at a usual meal?



How strong is your craving for sweets?



How strong is your craving for breads and other carbohydrates?



How much do you snack between meals?

Date_____ ID Number_____

Questionnaire C ~ Week 4

Please print the following information:

First and Last Name _____

Age _____ Date of Birth ___/___/_____ Male ____ Female ___

Weight _____lbs Hip Circumference_____ inches

Abdominal Girth _____ inches Waist _____ inches

Percent Body Fat _____ BMI _____

Did you have any side effects in the last two weeks? _____ Yes _____ No

What were the side effects_____

_____

Did you experience a change in hunger (rate on a scale of 1 to 10 where 10 was complete hunger suppression, 5 is no change and 1 severe increase in hunger) _____?

How long after ingestion of the capsules did you note appetite suppression_____ (minutes)? Use zero minutes for no appetite suppression.

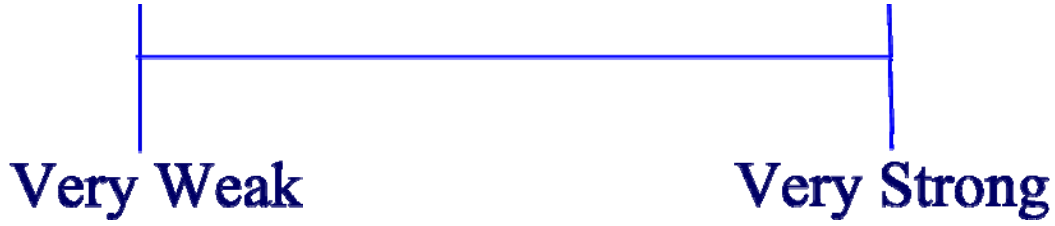
How long did the appetite suppression last_____ (hours)? Use zero hours for no appetite suppression.

How many cups of caffeinated beverages did you drink each day in the past two weeks? (1 cup = 8 ounces)

_____cups of caffeinated coffee _____cups of caffeinated sodas

_____cups of caffeinated tea _____cups of caffeinated power drinks

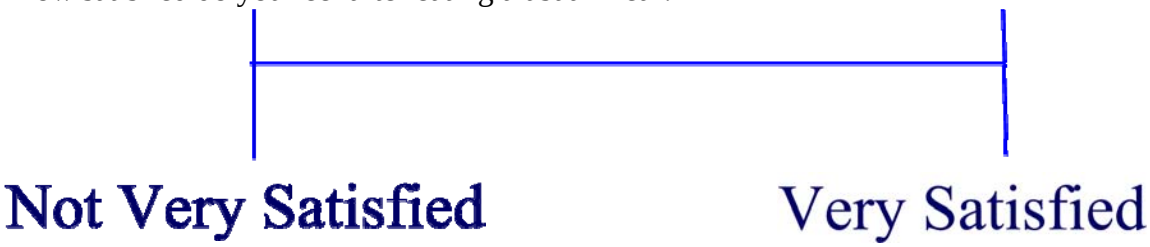
How strong is your desire to eat during the day?



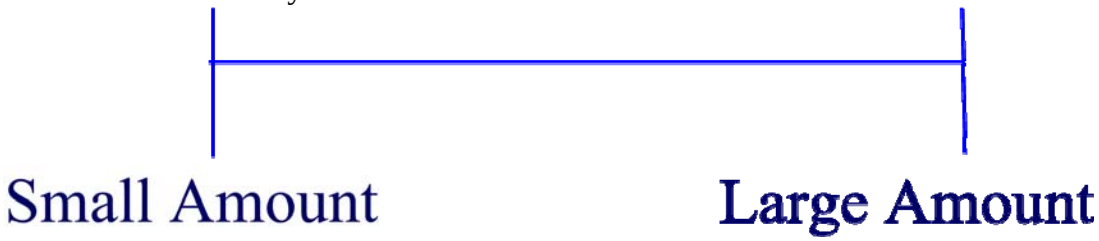
Date_____ ID Number_____

How hungry do you feel between meals?

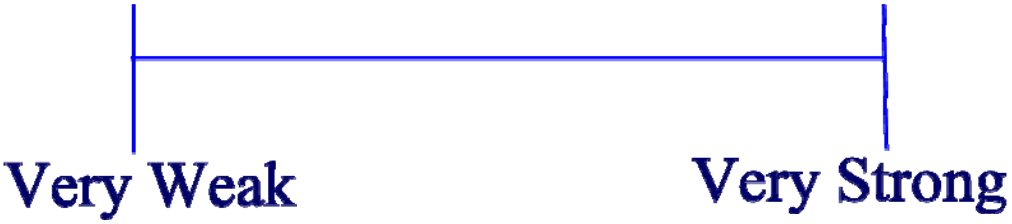
How satisfied do you feel after eating a usual meal?



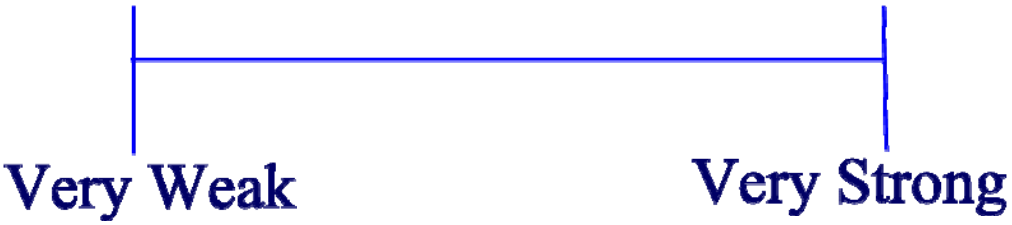
How much food can you eat at a usual meal?



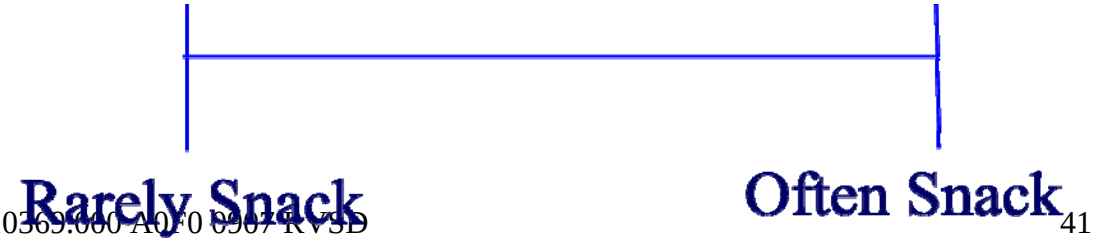
How strong is your craving for sweets?



How strong is your craving for breads and other carbohydrates?



How much do you snack between meals?



Date_____ ID Number_____

Questionnaire D ~ Week 6

Please print the following information:

First and Last Name _____

Age _____ Date of Birth ___/___/_____ Male ____ Female ___

Weight _____lbs Hip Circumference_____ inches

Abdominal Girth _____ inches Waist _____ inches

Percent Body Fat _____ BMI _____

Did you have any side effects in the last two weeks? _____ Yes _____ No

What were the side effects_____

_____

Did you experience a change in hunger (rate on a scale of 1 to 10 where 10 was complete hunger suppression, 5 is no change and 1 severe increase in hunger)_____?

How long after ingestion of the capsules did you note appetite suppression_____(minutes)? Use zero minutes for no appetite suppression.

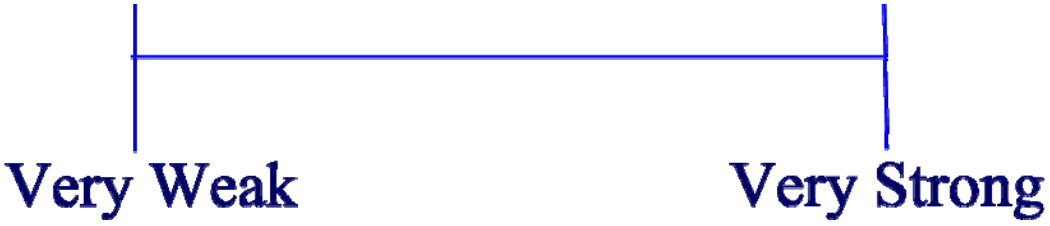
How long did the appetite suppression last_____(hours)? Use zero hours for no appetite suppression.

How many cups of caffeinated beverages did you drink each day in the past two weeks? (1 cup = 8 ounces)

_____cups of caffeinated coffee _____cups of caffeinated sodas

_____cups of caffeinated tea _____cups of caffeinated power drinks

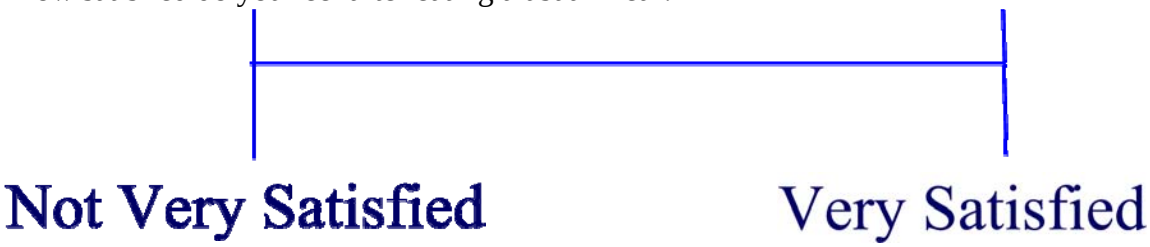
How strong is your desire to eat during the day?



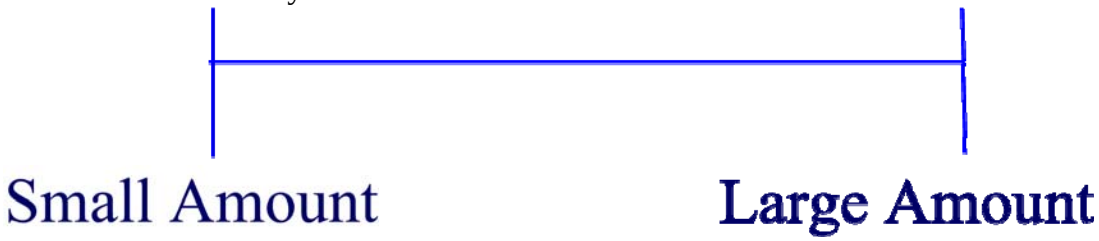
Date_____ ID Number_____

How hungry do you feel between meals?

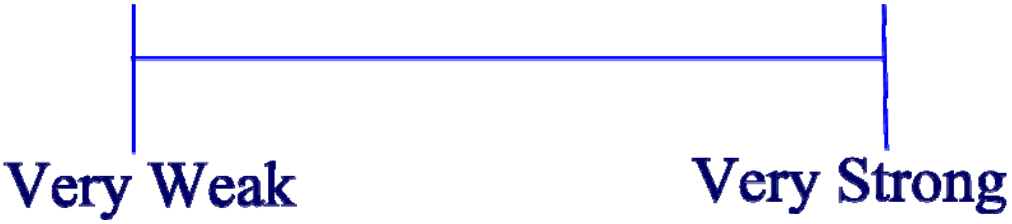
How satisfied do you feel after eating a usual meal?



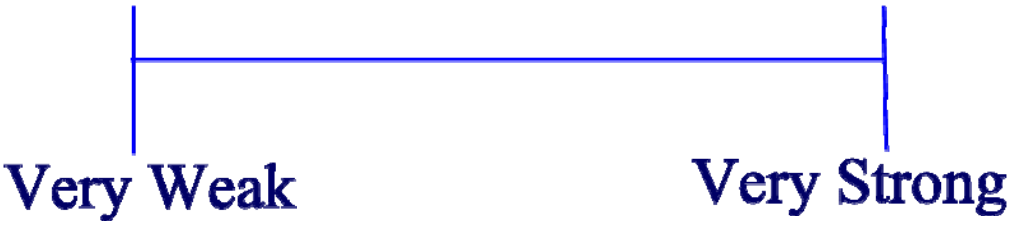
How much food can you eat at a usual meal?



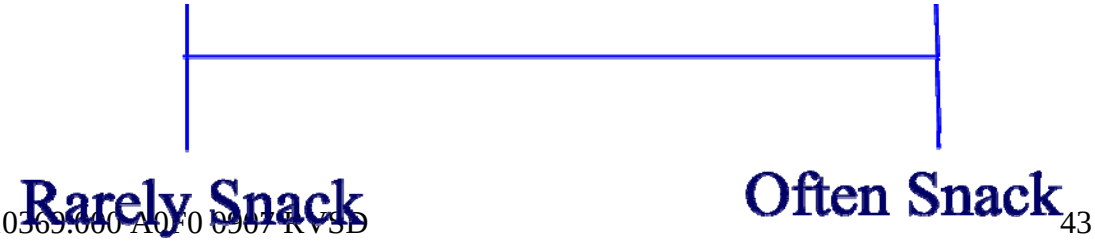
How strong is your craving for sweets?



How strong is your craving for breads and other carbohydrates?



How much do you snack between meals?



Date_____ ID Number_____

Questionnaire E ~ Week 8

Please print the following information:

First and Last Name _____

Age _____ Date of Birth ___/___/_____ Male ____ Female ___

Weight _____lbs Hip Circumference_____ inches

Abdominal Girth _____ inches Waist _____ inches

Percent Body Fat _____ BMI _____

Did you have any side effects in the last two weeks? _____ Yes _____ No

What were the side effects_____

_____

Did you experience a change in hunger (rate on a scale of 1 to 10 where 10 was complete hunger suppression, 5 is no change and 1 severe increase in hunger)_____?

How long after ingestion of the capsules did you note appetite suppression_____(minutes)? Use zero minutes for no appetite suppression.

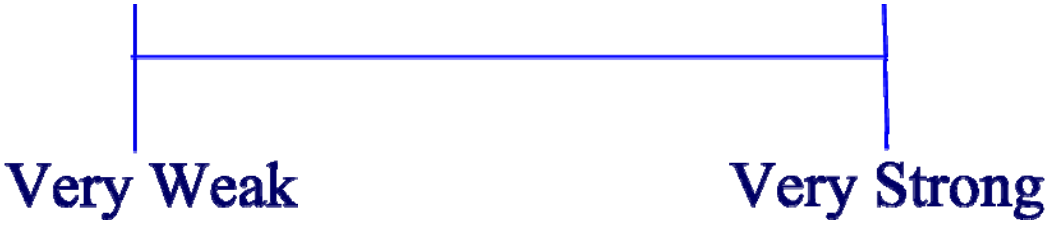
How long did the appetite suppression last_____(hours)? Use zero hours for no appetite suppression.

How many cups of caffeinated beverages did you drink each day in the past two weeks? (1 cup = 8 ounces)

_____cups of caffeinated coffee _____cups of caffeinated sodas

_____cups of caffeinated tea _____cups of caffeinated power drinks

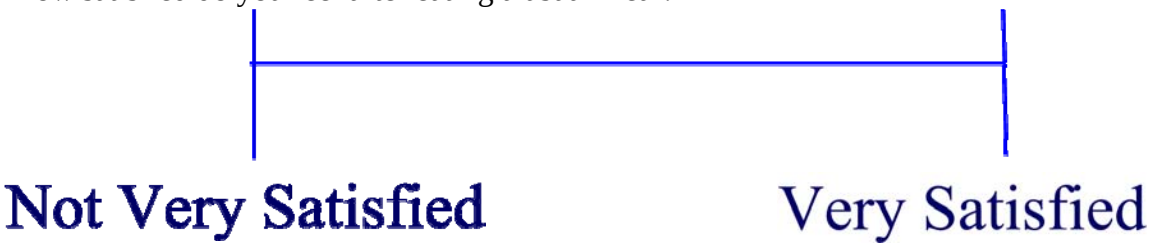
How strong is your desire to eat during the day?



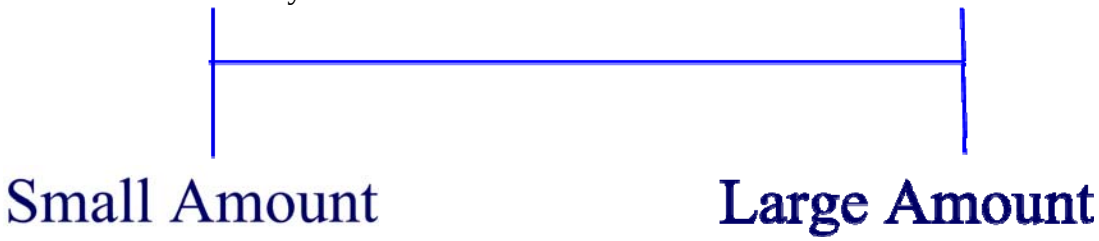
Date_____ ID Number_____

How hungry do you feel between meals?

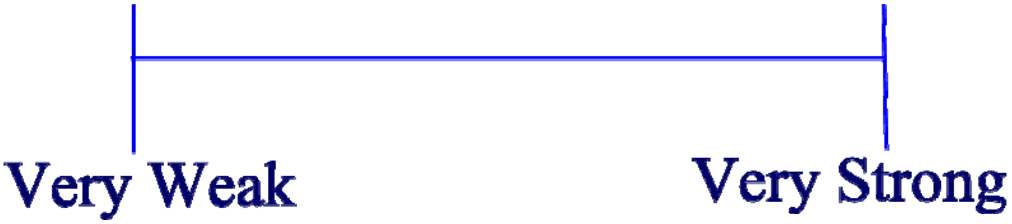
How satisfied do you feel after eating a usual meal?



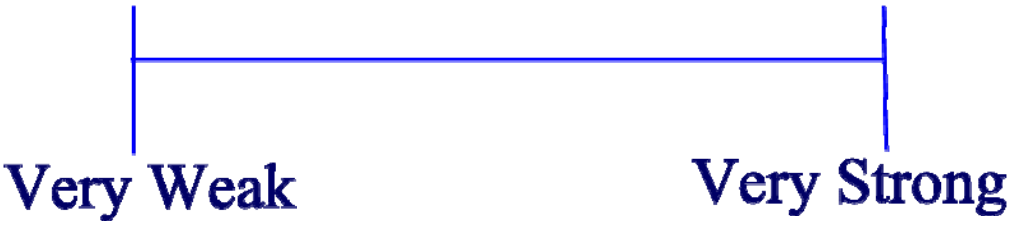
How much food can you eat at a usual meal?



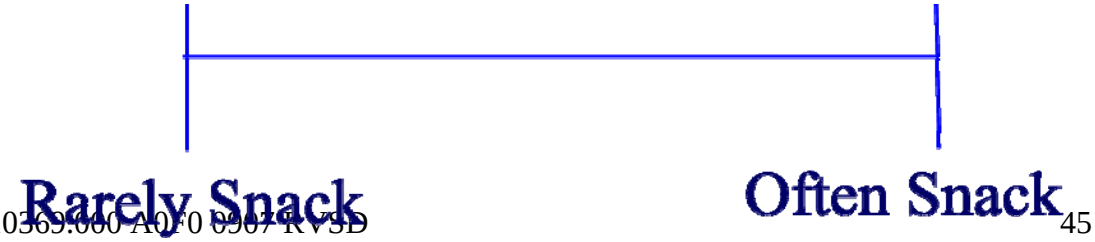
How strong is your craving for sweets?



How strong is your craving for breads and other carbohydrates?



How much do you snack between meals?



Date_____ ID Number_____

Questionnaire F ~ Week 12

Please print the following information:

First and Last Name _____

Age _____ Date of Birth ___/___/_____ Male ____ Female ___

Weight _____lbs Hip Circumference_____ inches

Abdominal Girth _____ inches Waist _____ inches

Percent Body Fat _____ BMI _____

Did you have any side effects in the last two weeks? _____ Yes _____ No

What were the side effects_____

_____

Did you experience a change in hunger (rate on a scale of 1 to 10 where 10 was complete hunger suppression, 5 is no change and 1 severe increase in hunger)_____?

How long after ingestion of the capsules did you note appetite suppression_____(minutes)? Use zero minutes for no appetite suppression.

How long did the appetite suppression last_____(hours)? Use zero hours for no appetite suppression.

How many cups of caffeinated beverages did you drink each day in the past two weeks? (1 cup = 8 ounces)

_____cups of caffeinated coffee _____cups of caffeinated sodas

_____cups of caffeinated tea _____cups of caffeinated power drinks

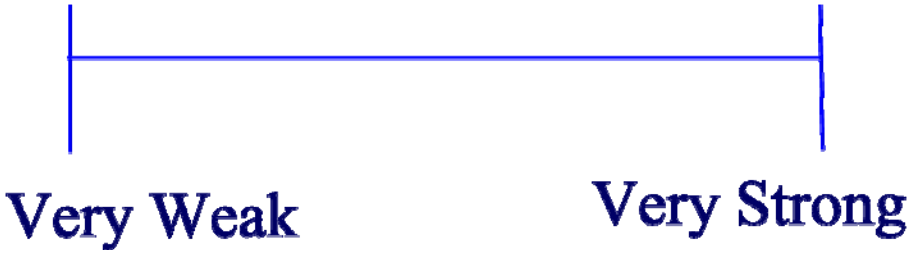
Date_____ ID Number_____

Date_____ ID Number_____

Appetite Questionnaire Visit 12 Baseline

How strong is your desire to eat?

How hungry do you feel?



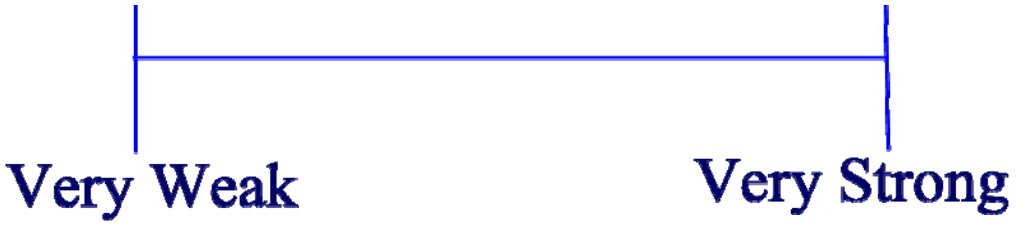
How full do you feel?

How much food do you feel you can eat?

How strong is your craving for sweets?

Date_____ ID Number_____

How strong is your craving for breads and other carbohydrates?

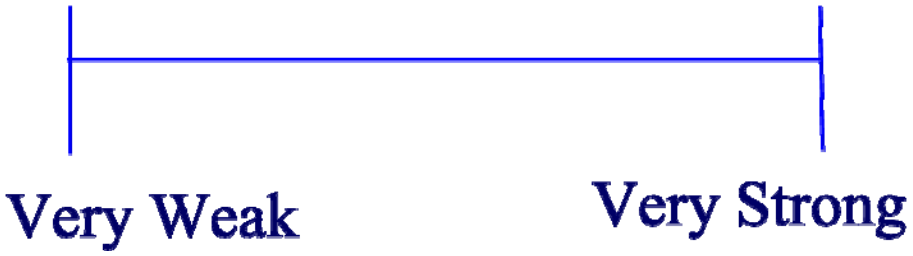


How much do you snack between meals?

Date_____ ID Number_____

Appetite Questionnaire Visit 12 5 minutes

How strong is your desire to eat?



How hungry do you feel?

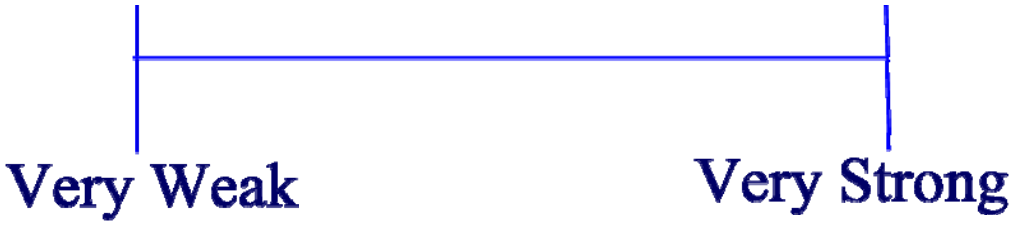
How full do you feel?

How much food do you feel you can eat?

How strong is your craving for sweets?

Date_____ ID Number_____

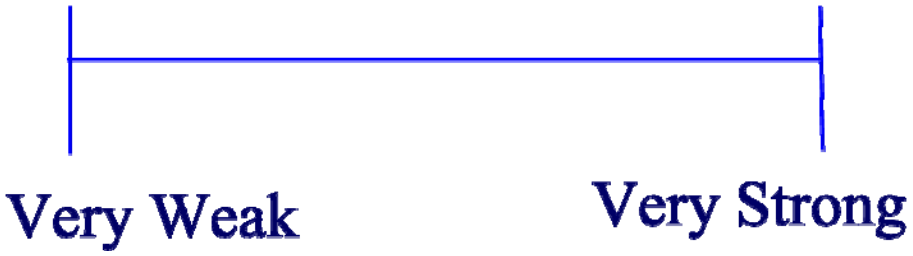
How strong is your craving for breads and other carbohydrates?



Date_____ ID Number_____

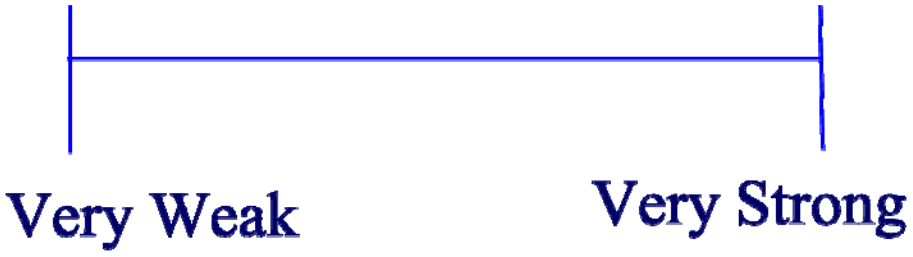
Appetite Questionnaire Visit 12 15 minutes

How strong is your desire to eat?

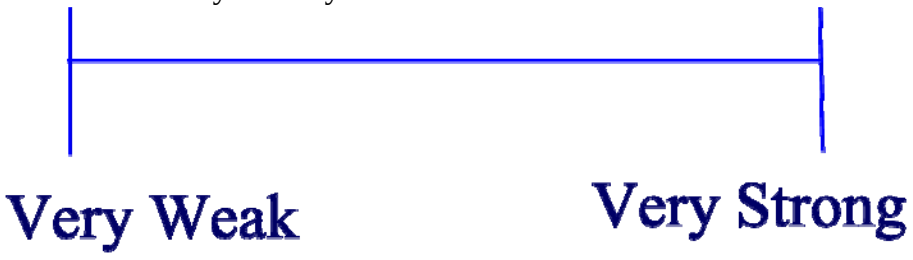


How hungry do you feel?

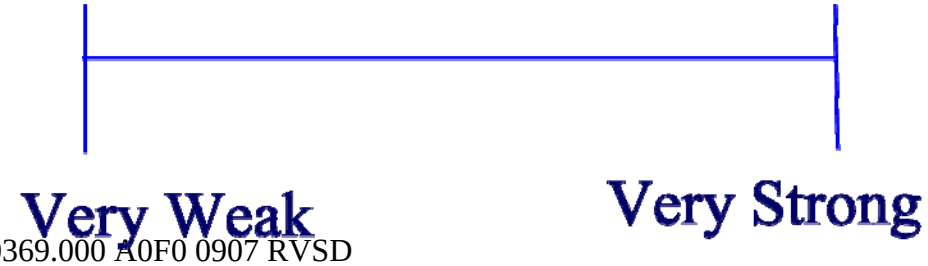
How full do you feel?



How much food do you feel you can eat?

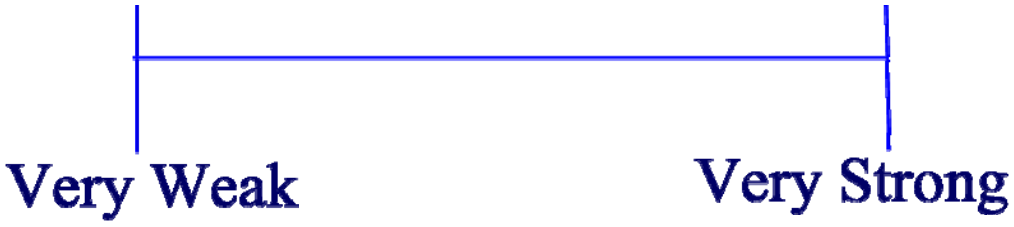


How strong is your craving for sweets?



Date_____ ID Number_____

How strong is your craving for breads and other carbohydrates?



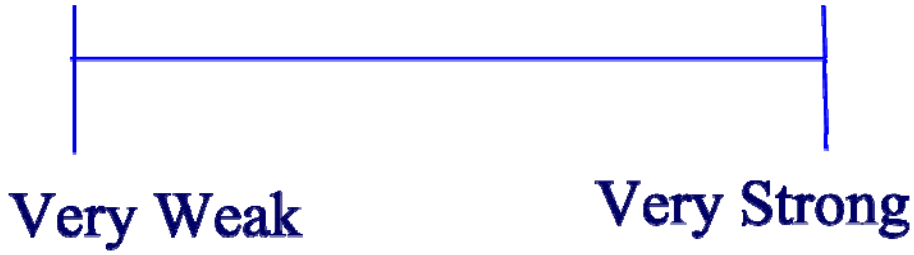
Date_____ ID Number_____

Appetite Questionnaire Visit 12 30 minutes

How strong is your desire to eat?

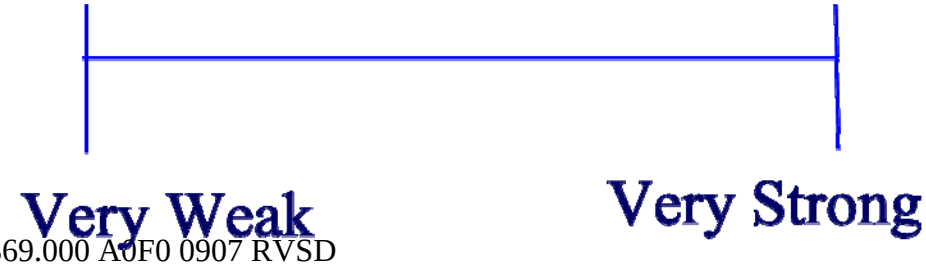
How hungry do you feel?

How full do you feel?



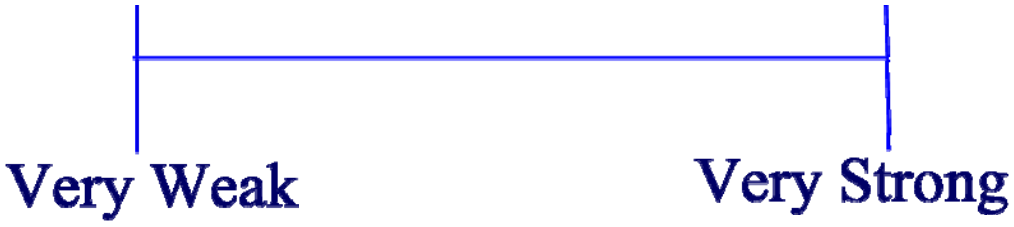
How much food do you feel you can eat?

How strong is your craving for sweets?



Date_____ ID Number_____

How strong is your craving for breads and other carbohydrates?



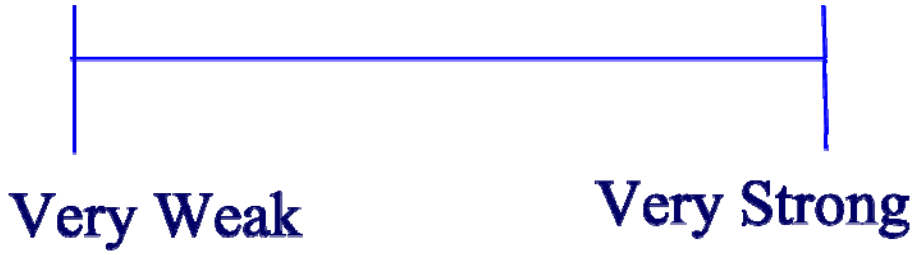
Date_____ ID Number_____

Appetite Questionnaire Visit 12 60 minutes

How strong is your desire to eat?

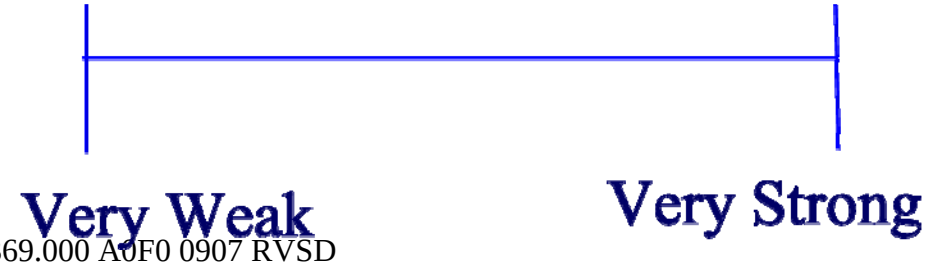
How hungry do you feel?

How full do you feel?



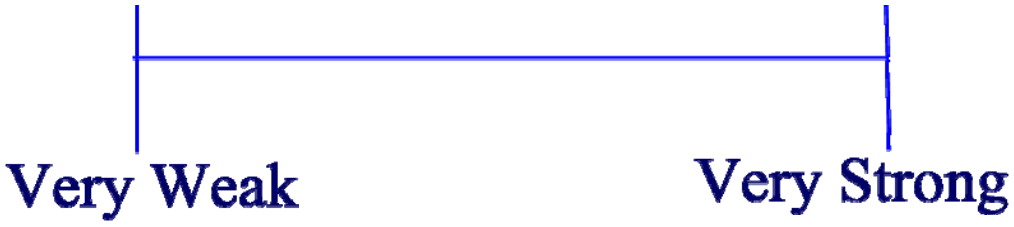
How much food do you feel you can eat?

How strong is your craving for sweets?



Date_____ ID Number_____

How strong is your craving for breads and other carbohydrates?



Appendix C. Instructions Provided to Subjects

Schedule to Follow

First Day:

Arrive at the study center with your stomach empty (at least one-hour after eating).

For the remainder of 12-week study you are encouraged to follow the reduced calorie guidelines provided and the 10,000 step exercise program.

If you experience appetite suppression, you may reduce your calorie consumption even further than the diet suggests.

For the remainder of the 12-week study, take the product as follows:

About mid morning, take two capsules with a glass of water.

About mid afternoon, take two capsules with a glass of water.

You are allowed to ingest caffeine-containing beverages if you wish.

Diet Guidelines

The diet that will be used in this study is a reduced calorie balanced protein and complex carbohydrate diet. Refined sugars and starches are restricted on this diet.

Take 2 capsules of ***AppTrim*** mid morning and mid afternoon. If your appetite is curbed and you do not feel hungry at mealtimes, decrease the amount of food ingested

You are permitted coffee, tea and sugar free soft drinks

AppTrim **may work as an appetite suppressant. If you are less hungry at each meal, any portion can be reduced or eliminated. You do not have to finish the amount of food listed above.**

Appendix D. Subject Consent Form

Medical University of South Carolina
CONSENT TO BE A RESEARCH SUBJECT
The Effect of AppTrim
on Weight Loss and Reduction of Body Fat Percent

A. PURPOSE AND BACKGROUND

The following information will describe the study and your role as a participant. The study doctor or principal investigator will answer any questions you may have about this form and about the study. Please read carefully and do not hesitate to ask anything about the information provided below.

Current methods for weight reduction are inadequate for many patients. The purpose of this study is to evaluate the effect of a new amino acid formulation on appetite, weight loss and body fat percent. This study is designed to evaluate the safety and effectiveness of the AppTrim's ability to suppress appetite, produce early satiety and activate energy consuming chemical reactions within the body so that fats are being utilized for fuel and produce greater weight loss than placebo. AppTrim is an amino acid and protein formulation that is currently available in the U.S. in the Medical Food category and dispensed to patients through the treating physician. The active ingredients in AppTrim are amino acids (L-Tyrosine, L-Glutamic acid, L-Histadine, L-Serine), choline bitartrate, green tea, whey protein, cocoa extract, griffonia seed, and grape seed extract. There is no ephedra or Ma Huang (other nutritional ingredients that have been a possible source of concern recently) in the product. There is caffeine in the product. Each dose of 2 capsules contains the amount of caffeine found in one cup of coffee (75 mg).

A total of 66 individuals will be enrolled in this study. This study is being directed by Dr. Kit Simpson of the Medical University of South Carolina. The sponsor of the study, Targeted Foods LLC, is paying for Dr. Simpson’s time to conduct this study.

B. PROCEDURES

If you agree to participate in this study, at the first study visit you will be randomly assigned to receive either the active product, AppTrim or a placebo, a formulation containing other amino acids (including lysine, valine, aspartic acid and leucine). This study is double-blind which means that neither you nor the clinic staff will know who is receiving active product (AppTrim) and who is receiving placebo. One group of subjects will receive AppTrim. A second control group will receive placebo. You have a 50% chance (like flipping a coin) of being in the placebo group. At the end of the eight-week period, you will be given an additional one-month supply of the product. You will be able to continue to have access to the product if you find it helps to maintain your weight loss.

During the first visit, you will undergo an examination including measurements of height, body weight, abdominal girth, and percent body fat. You will also be asked to complete a questionnaire and have a blood sample of about four teaspoons (20 milliliters) taken.

This blood sample will then be used for a complete blood count and to assess liver and kidney function. The AppTrim diet guidelines will then be explained. You will continue to follow the specified diet for 12 weeks. You will be weighed and have your body composition measured with bioimpedance, a non-invasive technique (that is, does not involve any needles) for determine percent body fat, at bi-weekly at the clinic. You will also be asked about any side effects you may have noticed during the past weeks, and have another four teaspoon (20 milliliter) blood sample taken at the twelve week visit (a total of about eight teaspoons of blood will be taken during the study). There are no invasive procedures in this study except for two blood samples that will be taken for routine blood analyses. You will fill out an additional questionnaire after weeks 2, 4, 6, 8 and 12. During your twelve-week participation in the study, you will be required to make four visits to the clinic. You will be asked not to take other appetite suppressants during the study.

C. DURATION

Participation in the study will have six visits over a period of 12 weeks.

D. RISKS/DISCOMFORTS

1. AppTrim: If you are in the group that receives AppTrim, there are no known side effects of this food based formulation. The ingredients are natural food components and are part of the normal diet. The product contains the amount of caffeine found in one cup of coffee (single dose of 2 capsules). You will be informed of any significant new findings, which develop during the course of this study that may relate to your willingness to continue your participation. You may consume as much coffee as you wish beyond the two one-half cup doses per day of caffeine. This amount of daily caffeine has no known side effects.
2. Randomization: You will be assigned to a treatment program by chance. The treatment you receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments.
3. Placebo: If you are in the group that receives placebo, your condition will go without active treatment for appetite suppression for 12 weeks.
4. Venipuncture: The risks of drawing blood include temporary discomfort from the needle stick, bruising and infection. Fainting could occur.
5. Bioimpedance devices to measure percent body fat have no risk, however it is recommended that individuals with implanted electrical devices, such as pacemakers should avoid contact with such devices.

E. BENEFITS

AppTrim may promote the release of fat from adipose tissue into the bloodstream as well as promote chemical reactions within the body that consume energy. It may also affect appetite and early satiety. You may or may not experience increased weight loss, appetite reduction, and a decrease in body fat percent while participating in this study.

F. COST

The cost of all study product, tests, examinations, and medical care required as part of this study are to be provided to you at no cost.

G. COMPENSATION

In return for your time, effort and travel expenses, you will be paid $200 for participation in this study. If you do not complete the study, you will receive $20 for each study visit you complete.

H. ALTERNATIVES

Alternative treatments are available and will be discussed with you by the investigator. If you choose not to participate in the study, you may obtain other weight management treatments including, dietary supplements from established retail sources or prescription drugs from a physician..

I. NEW INFORMATION

If there are significant new findings during the course of the study, you will be notified.

J. STUDENT PARAGRAPH

Your participation or discontinuance will not constitute an element of your academic performance nor will it be a part of your academic record at this Institution.

K. EMPLOYEE PARTICIPATION

Your participation or discontinuance will not constitute an element of your job performance or evaluation nor will it be a part of your personnel record at this Institution.

L. CONFIDENTIALITY

Every reasonable effort will be made to keep your medical records confidential. Your medical records may be inspected by employees of the Food and Drug Administration (FDA), the Federal Trade Commission (FTC), the study staff, and staff of Targeted Medical Foods LLC, the manufacturer of the product. The principal investigator in charge of this study may release the information obtained as a result of your participation in this study to these agencies.

You understand that medical records that reveal your identity will remain confidential except that they will be provided as noted above or as may be required by law. Published results of this study will not identify you by name.

M. PARTICIPATION INFORMATION

Your participation in this study is voluntary. You may refuse to participate or you may discontinue participation at any time during the study without penalty or loss of benefits to which you are otherwise entitled. Your participation may be terminated by the principal investigator or the clinic without regard to your consent for any reason. Any time your participation is terminated or if you withdraw voluntarily from the study, you will be asked questions about your participation in the study. Participation in this study should not be considered a substitute for treatment by your primary physician or specialist.

Results of this research will be used for the purposes described in this study. This information may be published, but you will not be identified Information that is obtained concerning this research that can be identified with you will remain confidential to the extent possible within State and Federal law. The investigators associated with this study, the sponsor, and the MUSC Institutional Review Board for Human Research will have access to identifying information. All records in South Carolina are subject to subpoena by a court of law.

In the event that you are injured as a result of participation in this study, you should immediately go to the emergency room of the Medical University Hospital, or in case of an emergency go to the nearest hospital, and tell the physician on call that you are in a research study. They will call your study doctor who will make arrangements for your treatment. If the study sponsor does not pay for your treatment, the Medical University Hospital and the physicians who render treatment to you will bill your insurance company. If your insurance company denies coverage or insurance is not available, you will be responsible for payment for all services rendered to you.

Your participation in this study is voluntary. You may refuse to take part in or stop taking part in this study at any time. You should call the investigator in charge of this study if you decide to do this. Your decision not to take part in the study will not affect your current or future medical care or any benefits to which you are entitled.

The investigators and/or the sponsor may stop your participation in this study at any time if they decide it is in your best interest. They may also do this if you do not follow the investigator's instructions.

Volunteers Statement

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. If I have any more questions about my participation in this study or study related injury, I may contact . I may contact the Medical University of SC Hospital Medical Director (843) 792-9537 concerning medical treatment.

If I have any questions about my rights as a research subject in this study I may contact the Medical University of SC Institutional Review Board for Human Research at (843) 792-4148.

I agree to participate in this study. I have been given a copy of this form for my own records.

I have read and understand this informed consent. I have fully discussed and understand the purpose and procedures of this study that have been explained to me. I have been invited to ask any questions that I have about the study, and all my inquiries have been answered. I acknowledge that I will be given a copy of this consent form. I will also receive a copy of the California Experimental Subject's Bill of Rights.

Having thoroughly read and understood all of the above information, I voluntarily agree to participate in this research study. I understand that I have not given up any of my legal rights by signing this informed consent.

If you wish to participate, you should sign below.

_____	_____	_____	_____
Signature of Person Obtaining Consent	Date	Signature of Participant	Date
_____	_____	_____	_____
Signature of Legal Guardian (if applicable)	Date	Signature of Witness	Date

HUMAN SUBJECT'S BILL OF RIGHTS

Any person who is requested to consent to participate as a subject in a research study involving a medical experiment, or who is requested to consent on behalf of another, has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be used.

3. Be given a description of any attendant discomforts and risks reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs, or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or other procedures involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time, and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of a signed and dated written consent form when one is required.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

Signature of Subject_____ Date_____

Witness_____ Date_____