Nu-Life Solutions
Miniaturized Wearable Medical Technology · Nu-ν^3

Unique Protocol ID: Nu-V3 Phase I
NCT Number: (not yet assigned)

Brief Title: Nu-V3 Non-Invasive Nerve Stimulation Device Trial for Pain, Anxiety, Depression, Sleeplessness
Official Title: A Phase I Prospective, Single-Arm, Open-Label, Multi-Center Study Using the Nu-V3 Cranial Nerve Stimulation Treatment Device in Patients With Pain, Anxiety, Depression, and/or Sleeplessness

INVESTIGATIONAL DEVICE: **Nu-V3**
SPONSOR: Nu-Life Solutions

Phase I & II Statistical Analysis Plan*

**All initial graphs and table data are simulated and will be updated at time of study submission

VERSION DATE: 03/APR/2018

Summary of Clinical Information

The primary pivotal study provided to support the De Novo request is the "Nu-V3 Protocol No. 1"- phases I & II. Details of the study design and selected clinical results are provided below.

Purpose: The objective of this research study was to collect data which demonstrates the ability of the Nu-V3 device to offer relief from one or more of the following symptoms: pain, depression, anxiety, and/or sleeplessness. The objective is to demonstrate the effectiveness of Nu-V3 for any or all of the four symptoms listed.

Design: The Nu-V3 Clinical Study was a prospective, single-arm, open-label, multi-center, global study using the Nu-V3 cranial nerve stimulation treatment device in patients with uncontrolled pain, anxiety, depression, and/or sleeplessness. For the Phase I study, a total of _____ patients at _____centers in the United States were registered for study participation. A total of _____ patients at _____centers in the United States, Japan, India, Germany, United Kingdom, Austria, Switzerland, _____, were registered to the Phase II study.

Phase I study consisted of 50-100 individuals who signed the informed consent form, met the inclusion and exclusion criteria, and were enrolled in the study at multiple sites. Enrolled participants are treated with the Nu-V3 device for 8 weeks, then observed for an additional 2 weeks. Interim analysis of reported data were conducted at 4, 8, and 12 weeks during this time. Post study, participants were given the chance to continue with an optional maintenance treatment with the Nu-V3 device per a 2-week on, 2-week off schedule, for an additional 12 weeks, with an 8-week observation.

Phase II of the study consisted of 100-200 individuals who signed the informed consent form, met the inclusion and exclusion criteria, and were enrolled in the study at multiple sites. Enrolled participants are treated with the Nu-V3 device for 8 weeks, then observed for an additional 2 weeks. Interim analysis of reported data were conducted at 4, 8, and 12 weeks during this time. Post study, participants were given the chance to continue with an optional maintenance treatment with the Nu-V3 device per a 2-week on, 2-week off schedule, for an additional 12 weeks, with an 8-week observation.

Subjects enrolled onto the Nu-V3 Clinical Trial underwent the following regimen:

- At the baseline visit, patients will be asked to complete study questionnaires regarding all of the following symptoms: pain, depression, anxiety, and/or sleeplessness, as well as their activity level, active medications, and demographics information.
- At each subsequent visit, patients will be asked to complete study questionnaires regarding all the following symptoms: pain, depression, anxiety, and/or sleeplessness, as well as their activity level.
- The sessions will begin with the Nu-V3 device being placed on the ear and three small pads (non-invasive) being placed on the ear. Each Nu-V3 device lasts for up to 14 days with a change in the pads approximately 7 days into the treatment.
- Each session takes approximately 15-20 minutes. The placement of the device takes approximately 5 minutes and the remaining time is spent verifying assessment form completion and checking for any immediate effects from the device.
- The Nu-V3 device is mobile and is worn externally on the ear 24 hours a day during treatment, fitting comfortably behind the ear. An electrical signal is sent to the external

ear through coated wire leads attached to the device and adhesive pads which attach to three sites on the ear.

- Participants should be able to perform their typical day-to-day activities while wearing the device. They may shower while wearing the Nu-V3 device, provided that they do not get the device wet and use the small disposable ear covers that are provided for them.
- Patients should not change their existing forms of treatment or medications without discussion with the investigator.
- Nu-Life reserves the right to capture video, photographs and written testimonials from patients with written permission. In the event subjects elect to participate in any or all of these activities, they will be asked to sign a waiver giving exclusive rights to the video, photographs and written testimonials captured to Nu-Life. Their participation in this study is not dependent upon their willingness to participate in video, photographs or written testimonials.

Study Treatment Assessments Table

*Evaluations are completed weekly, every 7 days ±3 days

Evaluation*	Study Treatment									
	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9-11	Week 12
Informed Consent	x									
Inclusion and Exclusion[1]	x									
Patient Registration[1]	x									
Medications Form[1]	x			x				x		x
Patient Onboarding and Orientation[2]	x									
In office assessment	x	x	x	x	x	x	x	x		x
New Device Placed	x		x		x		x			
Pad Replaced		x		x		x		x		
Treatment Forms[1]	x	x	x	x	x	x	x	x		
No Device									x	x
ePRO Questionnaires[3]	x	x	x	x	x	x	x	x	x	x
Patients' Global Impression of Change ePRO form (PGIC)[3]		x	x	x	x	x	x	x		x
Providers' Global Impression of Change ePRO form (PGIC)		x	x	x	x	x	x	x		x
Family Global Impression of Change ePRO form (PGIC)		x	x	x	x	x	x	x		x
Optional Patient Media Testimony	x			x				x		x

1. Inclusion/Exclusion, Registration, Medications, Treatment forms to be completed by site coordinator via online module.
2. Patient Onboarding and Orientation includes introductory demographics form, Nu-V3 patient training video
3. ePRO questionnaires completed on patient's mobile device: DQ-9 (baseline), PTB-7, PEG, GAD-7, PHQ-9, PROMIS 4a, PGIC
4. If patient consents to media testimony, site will collect via study collection process every 4 weeks.

Study Endpoints and Data Analysis: The study endpoints data were collected from each participant's study questionnaires. The data were collected electronically via the patient's own device, and were uploaded to an electronic data capture system. The data were used to demonstrate that the Nu-V3 device provides participants with relief of the symptoms of pain, depression, anxiety and/or sleeplessness. The data analysis includes comparative data for each participant's questionnaire prior to beginning treatment with the Nu-V3 device, the participant's weekly questionnaires during treatment and the questionnaire completed at the end of the treatment with the Nu-V3 device.

Primary Endpoints: Primary endpoints consisted of the following:

1. Safety: The primary safety endpoint was the occurrence of reported unanticipated problems involving risk to subjects or others ("UPIRTSOs"). These UPIRTSOs are defined as those problems which alter the risks to subjects or others. This includes any study suspensions or holds. The primary safety endpoint analyses were based on a risk-benefit conclusion.

2. Effectiveness: The primary effectiveness endpoints were overall reduction in median reported symptoms of pain, anxiety, depression, and/or sleeplessness via numeric rating scales at 8 weeks. This primary effectiveness is measured by median reported symptom reductions in pain, anxiety, depression, and/or sleeplessness via the following validated tools: Pain intensity and interference- PEG Scale, Anxiety- Generalized Anxiety Disorder 7-item (GAD-7) scale, Depression- Patient Health Questionnaire (PHQ-9), Sleeplessness- PROMIS short form 4a, and overall improvement of quality of life (QOL) - Patient's Global Impression of Change (PGIC).

   The patient's perceived treatment benefit and device comfort information, will be captured via the non-validated tool, Perceived Treatment Benefit Form (PTB-7). This effectiveness tool will measure median levels of reported perceived treatment benefit and device comfort.

   The hypothesis-driven criterion of effectiveness was to show that there was a statistically significant reduction in the median reported pain, anxiety, depression, and/or sleeplessness levels of patients using the Nu-V3 device. The second criterion was intended to show that there was a statistically significant improvement in reported quality of life and perceived treatment benefit secondary to overall reported symptom reduction of pain, anxiety, depression, and/or sleeplessness.

   Secondary Endpoints: Secondary endpoints consisted of the following:

1. Effectiveness: The secondary effectiveness endpoint was overall reduction in median reported symptoms of pain, anxiety, depression, and/or sleeplessness via numeric rating scales at 4, 8, and 12 weeks. This was measured via the following validated tools: Pain intensity and interference- PEG Scale, Anxiety- Generalized Anxiety Disorder 7-item (GAD-7) scale, Depression- Patient Health Questionnaire (PHQ-9), Sleeplessness- PROMIS short form 4a, and overall improvement of quality of life- Patient's Global Impression of Change (PGIC).

   The hypothesis-driven criterion was to show that there was a statistically significant reduction in the median reported pain, anxiety, depression, and/or sleeplessness levels of patients using the Nu-V3 device at weeks 4, 8, and 12. The second criterion was intended to show that there was a statistically significant improvement in reported quality of life and perceived treatment benefit secondary to overall reported symptom reduction of pain, anxiety, depression, and/or sleeplessness at weeks 4, 8, and 12.

2. Sub-analyses**:** The sub-analyses endpoints consisted of the mean number of weeks that pain, anxiety, depression, and sleeplessness response was achieved and sustained, without utilization of another device, during the 8-week intervention. In addition, study sub-analyses included the mean number of weeks to initial benefit from Nu-V3 device use, and the mean medication dosage reduction of short acting pain, anxiolytics, and/or insomnia. The device's

comfort-of-use, and patient's perceived treatment benefit were also captured for sub-analyses.

Eligibility Criteria Summary: The study population consisted of both male and female patients, at least 18 years of age.

Key inclusion criteria included the following:

- Participant presents with one or more of the following symptoms: pain, anxiety, depression, and/or sleeplessness
- Participant can commit to follow all protocol study time-points

Key exclusion criteria included the following:

- Participants with a Pacemaker
- Participants with irregular heart rate or a heart rate lower than 60 beats per minute (bradycardia)
- Have had a transplant within the last 2 years
- Have had a heart attack or cardiac bypass surgery within the last 12 months
- History of substance abuse, including prescription drugs, within the last 12 months
- Patients with complaints of dizziness or lightheadedness within the last 3 months
- Women who are pregnant
- Participants with Diabetic Retinopathy
- Current Ear infection
- SBP < 100 and/or DBP < 60
- History of uncontrolled bipolar disorder within the last 12 months
- History of uncontrolled seizures within the last 12 months
- History of Aneurysms
- History of syncope within the last 12 months
- Participants that have had a TIA or stroke within the last 12 months
- Participants with health problems deemed at risk for the study by the Principal Investigator
- Participants with any changes to Pain/Anxiety/Depression/Sleeplessness medications within last 60 days (participants that do not meet this medication change washout period may be delayed until 60-day period is met)
- Participants that are currently under adjudication process for disability support, VA or other

Accountability: Patients were exited from the study upon completing the final protocol-required questionnaires. In some cases, patients prematurely exited or withdrew from the study for the following reasons, including but not limited to:

- Not eligible for treatment (including patients who may have signed informed consent and been enrolled).
- Patient experienced a SAE or UPIRTSO.
- Voluntary withdrawal- the patient voluntarily chose not to participate further in the study.

- Lost to follow-up (LTFU) – the patient was more than 10 days late to a study visit and three documented attempts to contact the patient were unsuccessful. A patient who missed a study visit but attended subsequent visit (if required) was no longer considered lost to follow-up. A missed visit was considered a protocol deviation and the deviation was documented and reported.
- Physician decision – in the physician's opinion, it was not in the best interest of the patient to continue study participation.

The tables below summarize patients who exited the study early, as well as those who completed all study participation as per protocol.

Table 1: Study Exit Summary- Early Exit (<8 weeks)			
	Phase I	**Phase II**	**Total Enrolled**
Voluntary Withdrawal			
Lost to Follow-Up			
Physician's Decision			
SAE / UPIRTSO			
Other			
Overall "exited" Patients			

Table 2: Study Exit Summary (≥ 8 weeks)			
	Phase I	**Phase II**	**Total Enrolled**
Completion of Study as Planned			
Voluntary Withdrawal			
Lost to Follow-Up			
Physician's Decision			
SAE / UPIRTSO			
Other			
Overall "exited" Patients			

Insert Study Exit Analysis Here

Section 1.0: Participant Flow

ClinicalTrials.gov
A service of the National Institutes of Health

Edited: 19 August 2014

Participant Flow Data Preparation Checklist

Overview: A tabular summary of the participants' progression through each stage of a study by group. Use this checklist with the Participant Flow Template[Δ] and Results Data Element Definitions.

	Information to have available for Participant Flow	Term
☐	• Conceptual overview of the study design, including the type (e.g., single-group, cross-over, parallel) and any distinct stages (e.g., double-blind then open-label) • Tip: Have a CONSORT flow diagram available	Background
☐	• A description of any study events that occurred before participants were assigned to a study group (e.g., run-in phase, number of screen failures)	[Δ]Pre-assignment Details
☐	• Number of groups that accurately describes the study design from participant assignment to completion. Each group will be reported as a table column. • Tip: The number of groups is typically equal to the number of unique paths (participant experiences) in a CONSORT flow diagram, from beginning to end.	Arms/Groups
☐	• For each group, a detailed explanation of the participants and/or interventions ○ Title—A descriptive label for the group (header for the table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1"). ○ Description—A detailed explanation of the interventions administered or the groups observed during each stage of the study. Include details about the intervention and the frequency and time period of administration or observation.	*[Δ]Arm/Group Title [Δ]Arm/Group Description
☐	• Number of distinct stages or intervals of activity in the study	Periods
☐	• If there is more than one stage (Period), each Period will need a unique Title (the default for one Period is "Overall Study"). ○ A Period Title should be a descriptive label. For example, "Double-blind (0 to 24 weeks)" and "Open-label (24 to 48 weeks)" are more descriptive than "Period 1" and "Period 2."	*[Δ]Period Title
☐	• For each Period, the number of participants in each group that: ○ Started—Generally, the participants assigned (or randomized) to each group ▪ Additional Milestone (optional)—Any important event(s) during study ○ Completed—As defined for the study • Tip: If the number of participants starting the first Period is different from the total enrolled in the study, explain why in Pre-assignment Details	*[Δ]Started *[Δ]Completed
☐	• For each Period, the number of participants in each group that dropped out and the reasons they dropped out	[Δ]Reason(s) Not Completed

*Required
[Δ]Template Field

Figure 1.1- Participant Flow Checklist

NU-V3 CONSORT 2010 FLOW DIAGRAM

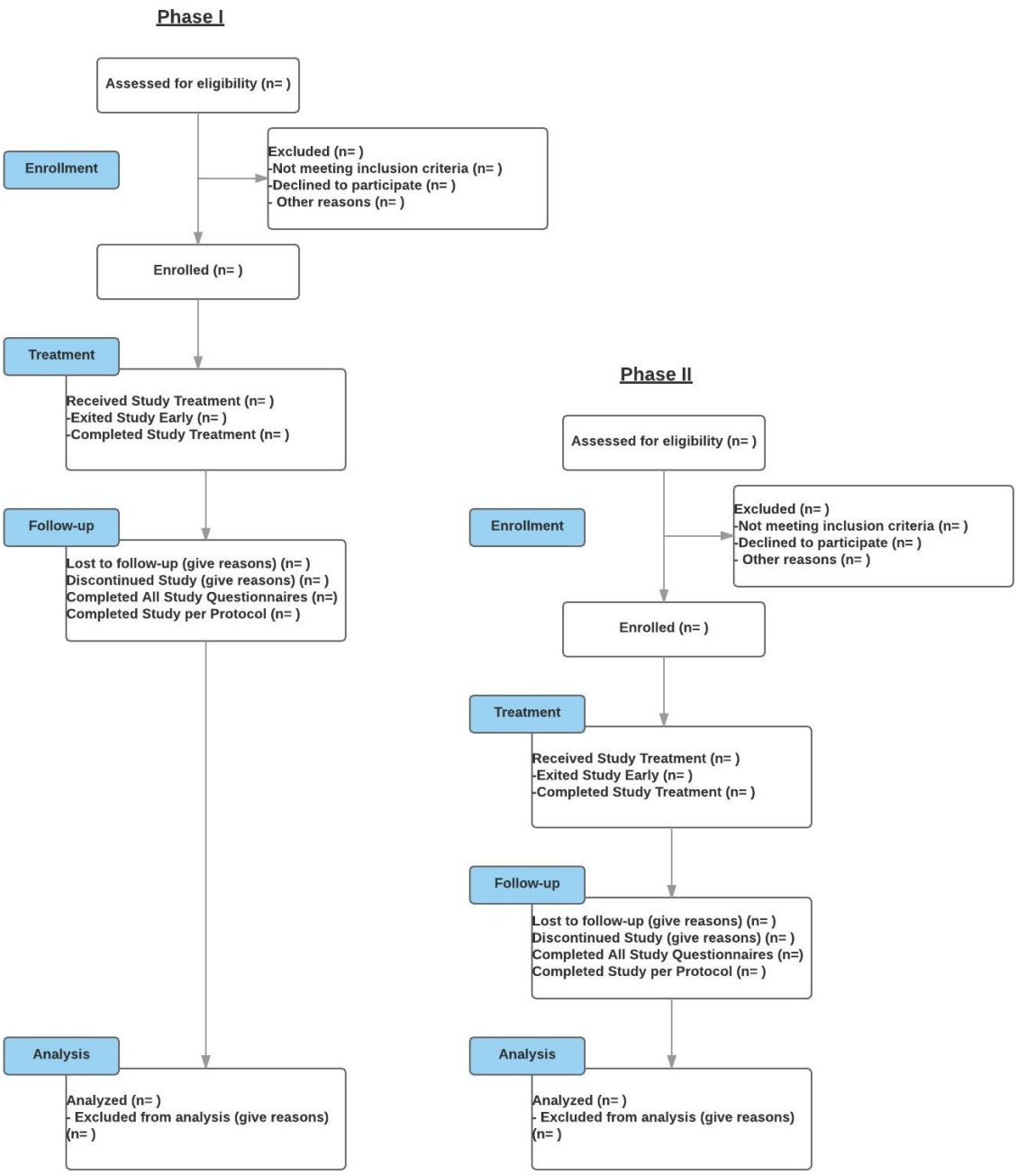


Figure 1.2- Participant Flow Diagram

Participant Flow Template		*Nu-Life Solutions*
Recruitment Details		
[*] Pre-assignment Details		
Period		
Phase I		Initial Clinical Study 50 - 100 participants
***Arm/Group Title**		
***Arm/Group Description**		
		Number of Participants
***Started**		
[*] Milestone Title		
[*] Milestone Title		
[*] Milestone Title		
***Completed**		
Not Completed		(automatically calculated)
Reason Not Completed		
[*] Voluntary Withdrawal		
[*] Lost to Follow-Up (LTFU)		
[*] Physician's Decision		
[*] SAE/ UPIRTSO		
[*] Protocol Violation		
[*] Other		
Phase II		Expanded Clinical Study 100-200 participants
***Arm/Group Title**		
***Arm/Group Description**		
		Number of Participants
***Started**		
[*] Milestone Title		
[*] Milestone Title		
[*] Milestone Title		
***Completed**		
Not Completed		(automatically calculated)
Reason Not Completed		
[*] Voluntary Withdrawal		
[*] Lost to Follow-Up (LTFU)		
[*] Physician's Decision		
[*] SAE/ UPIRTSO		
[*] Protocol Violation		
[*] Other		

***required** **[*] conditionally required**

Figure 1.3- Participant Flow Template

Insert Data Collection Summary Here

Section 2.0: Baseline Characteristics

Demographics: The total population consisisted of _____ patients. Information on the enrolled patients (n=) patients is provided in the following tables.

ClinicalTrials.gov

A service of the National Institutes of Health

Edited: 19 August 2014

Baseline Characteristics Data Preparation Checklist

Overview: A tabular summary of all characteristics measured at baseline for each group and overall. The table is similar to "Table 1" in a journal article. Use this checklist with the Results Data Element Definitions and the Simple Results Templates[Δ] for Age; Gender; Race, Ethnicity, Region; and Study Specific Measures.

	Information to have available for Baseline Characteristics	Term
☐	• Have a list of all baseline characteristics and the corresponding summary-level data (similar to Table 1 in a journal article). Age and Gender must be provided.	Background
☐	• The number of separate groups for which summary data will be provided. • Tip: Generally equal to the number of groups/intervention strategies to which participants were assigned (randomized) at the beginning of the study	Arm/Groups
☐	• For each group: ○ Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1"). ○ Description—A detailed explanation of the participants included in the group and the interventions received. This may include a description of how groups of participants were recombined for analysis purposes.	*[Δ]Arm/Group Title [Δ]Arm/Group Description
☐	• Number of participants, in each group and in the entire study population (total), from whom data were collected and summarized. Participants should only be represented in one group and in the total (i.e., do not double-count).	*[Δ]Overall Number Baseline Participants
☐	• An explanation of the criteria used to determine which participants were included in the analysis	[Δ]Baseline Analysis Population Description
	Information to have available for each Baseline Measure	**Term**
☐	• Title—Describe specifically what was measured and will be reported as data • Description—Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (i.e., not specialists in your field, but general readers of the medical literature). ○ If the measure was based on a scale, explain any numerical categories or provide the range and direction of possible scores (0=no pain; 10=worst possible pain) to allow a reader to properly interpret any reported values.	*[Δ]Baseline Measure Title [Δ]Baseline Measure Description
☐	• The method used to summarize baseline data: ○ Central tendency—E.g., mean, median, geometric mean ○ Number—E.g., count (of participants)	*[Δ]Measure Type
☐	• For a measure of central tendency, specify a measure that represents "the spread" of the summary data (e.g., standard deviation). ○ Tip: This is not applicable for a Number (e.g., count of participants)	*[Δ]Measure of Dispersion
☐	• Numerical values for the summary-level data in each group and overall (total)	*Baseline Data
☐	• The specific unit associated with the numerical data (e.g., mg/dL, participants)	*[Δ]Unit of Measure

*Required
[Δ]Template Field

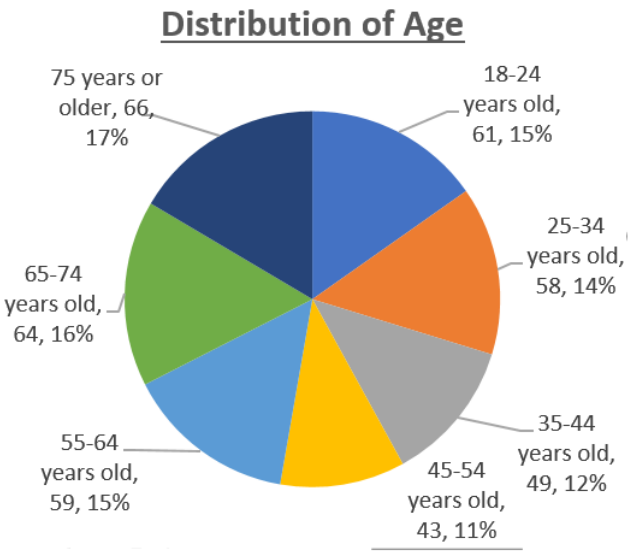
Figure 2.1- Baseline Characteristics Checklist

Baseline Characteristics Template	*Age**		*Nu-Life Solutions*			
Group Title		Phase I		Phase II		**Totals**
Group Description						
Overall Number of Baseline Participants						
(*) Baseline Analysis Population Description						
Age, Categorical						
18-24 years old						
25-34 years old						
35-44 years old						
45-54 years old						
55-64 years old						
65-74 years old						
75 years or older						
***Unit of Measure**	**Participants**					
Age, Customized						
***Measure Type**	***Measure of Dispersion**					
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean** **Geometric LSM** **Number** **Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Inter-Quartile Range** **Full Range**						
[*] Row/Category Title							
***Unit of Measure**							

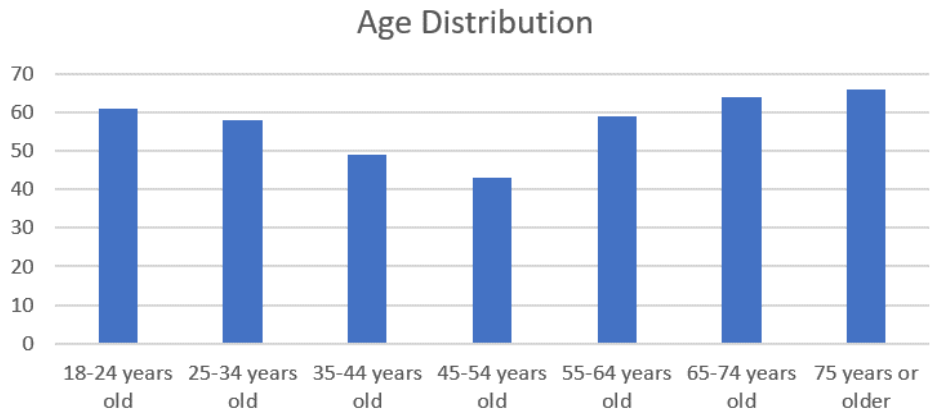
*Required [*] Conditionally required

Table 2.2- Baseline Characteristics Template- Age

Insert Graphs for Age Distribution Here (examples)



φ Figure 2.3 Distribution of Age Pie Graph



φ Figure 2.4 Distribution of Age Bar Graph

Insert Age Dispersion Statistical Analysis

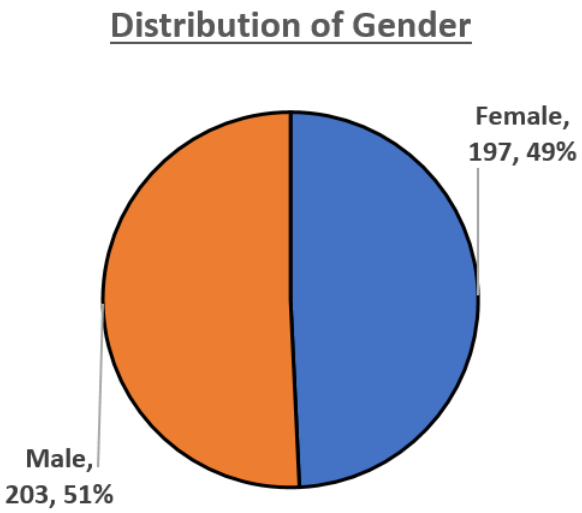
Baseline Characteristics Template	*Sex/Gender at Birth* (choose one)*	*Nu-Life Solutions*

Group Title		Phase I		Phase II		**Totals**	
Group Description							
Overall Number of Baseline Participants							
(*) Baseline Analysis Population Description							
Sex/Gender at Birth: Male, Female, Other, Choose not to answer							
Male							
Female							
Other							
Choose not to answer							
***Unit of Measure**	**Participants**						
Sex/Gender, Customized							
***Measure Type**	***Measure of Dispersion**						
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean** **Geometric LSM** **Number** **Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Inter-Quartile Range** **Full Range**						
[*] Row/Category Title							
[*] Row/Category Title							
[*] Row/Category Title							
***Unit of Measure**							

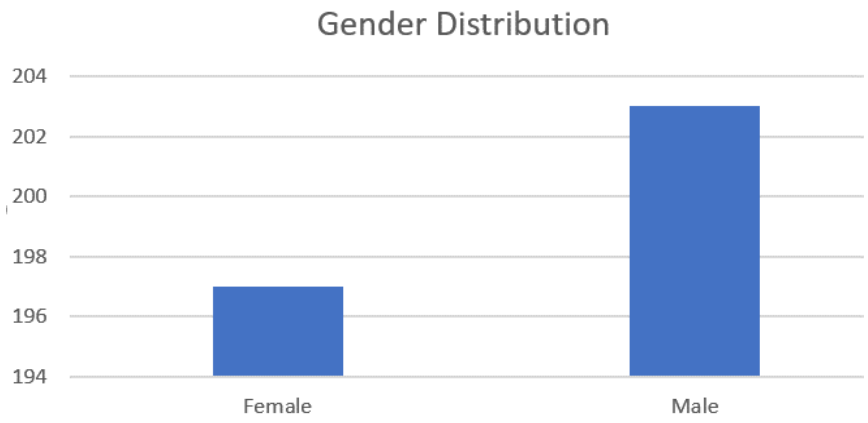
*Required [*] Conditionally required

Figure 2.5- Baseline Characteristics Template- Sex / Gender

Insert Graphs for Sex / Gender Here (examples)



φ Figure 2.6 Distribution of Gender Pie Graph



φ Figure 2.7 Distribution of Gender Bar Graph

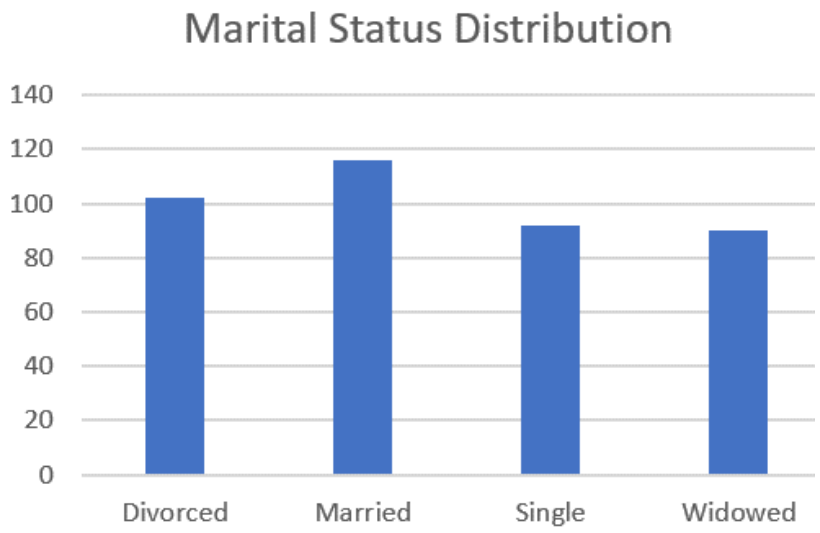
Insert Gender Dispersion Statistical Analysis

Baseline Characteristics Template	*Marital Status* (use at least one)*		*Nu-Life Solutions*			
Group Title	Phase I		Phase II		**Totals**	
Group Description						
Overall Number of Baseline Participants						
(*) Baseline Analysis Population Description						
Marital Status: Single, Married, Divorced, Widowed						
Single						
Married						
Divorced						
Widowed						
***Unit of Measure**	**Participants**					
Marital Status, Customized						
***Measure Type**	***Measure of Dispersion**					
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean** **Geometric LSM** **Number** **Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Inter-Quartile Range** **Full Range**						
[*] Row/Category Title							
[*] Row/Category Title							
[*] Row/Category Title							
***Unit of Measure**							

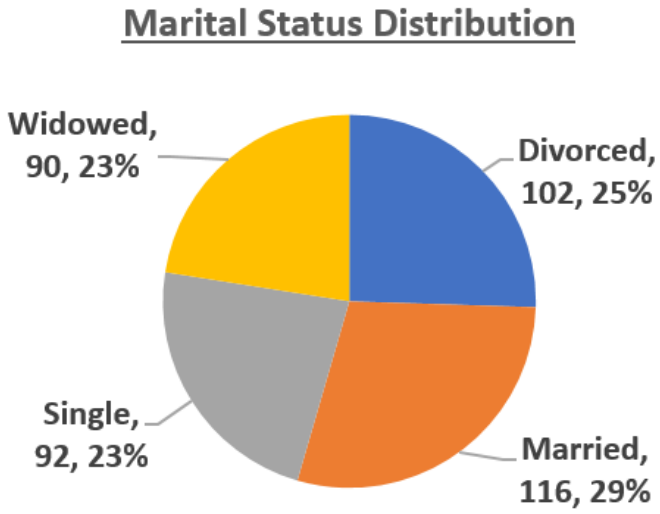
*Required [*] Conditionally required

Figure 2.8- Baseline Characteristics Template- Marital Status

Insert Graphs for Marital Status Here (examples)



φ Figure 2.9 Distribution of Marital Status Bar Graph



φ Figure 2.10 Distribution of Marital Status Pie Graph

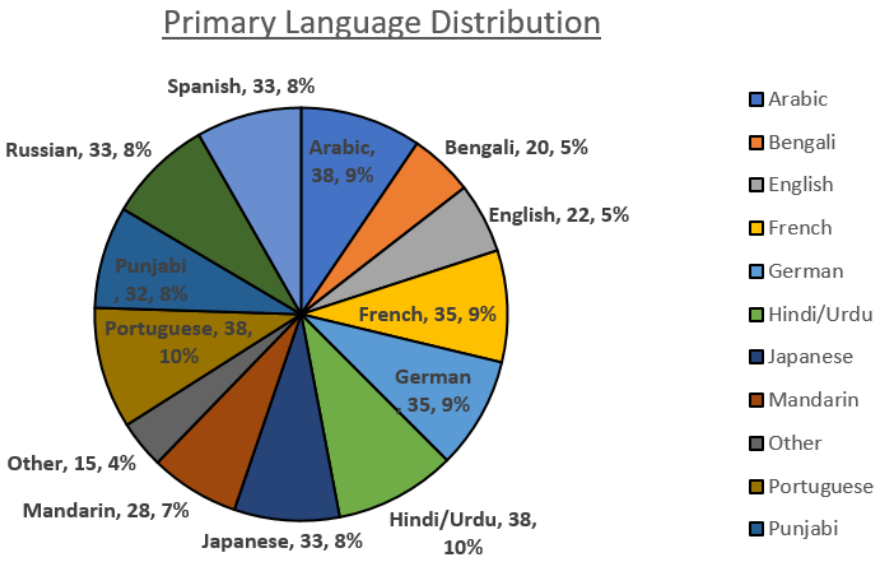
Insert Marital Status Dispersion Statistical Analysis

Baseline Characteristics Template	*Primary Language* (use at least one)*		*Nu-Life Solutions*			
Group Title	Phase I		Phase II		**Totals**	
Group Description						
Overall Number of Baseline Participants						
(*) Baseline Analysis Population Description						
Primary Language: Arabic, Bengali, English, French, German, Hindi/Urdu, Japanese, Mandarin, Portuguese, Punjabi, Russian, Spanish, Other						
Arabic						
Bengali						
English						
French						
German						
Hindi/Urdu						
Japanese						
Mandarin						
Portuguese						
Punjabi						
Russian						
Spanish						
Other						
***Unit of Measure**	**Participants**					
Primary Language, Customized						
***Measure Type**	***Measure of Dispersion**					
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean** **Geometric LSM** **Number** **Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Inter-Quartile Range** **Full Range**					
[*] Row/Category Title						
[*] Row/Category Title						
***Unit of Measure**						

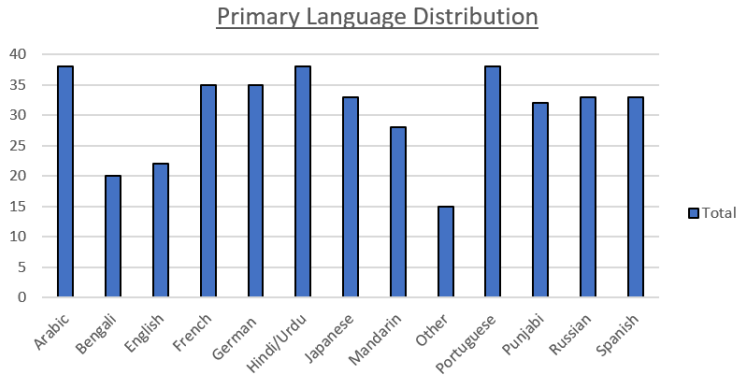
*Required [*] Conditionally required

Figure 2.11- Baseline Characteristics Template- Primary Language

Insert Graphs for Primary Language Here (examples)



φ Figure 2.12 Distribution of Primary Language Pie Graph



φ Figure 2.13 Distribution of Primary Language Bar Graph

Insert Primary Language Dispersion Statistical Analysis Here

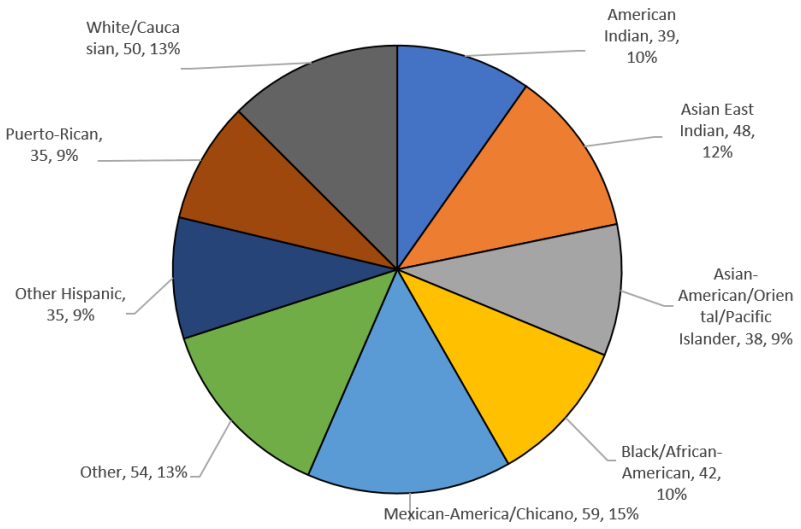
Baseline Characteristics Template	*Race/Ethnicity* (use at least one)*	*Nu-Life Solutions*

Group Title		Phase I		Phase II		**Totals**		
Group Description								
Overall Number of Baseline Participants								
(*) Baseline Analysis Population Description								
Race/Ethnicity: American Indian, Asian-American/Oriental/Pacific Islander, Asian East Indian, Black/African-American, Mexican-America/Chicano, Puerto-Rican, Other Hispanic, White/Caucasian, Other								
American Indian								
Asian-American/Oriental/Pacific Islander								
Asian East Indian								
Black/African-American								
Mexican-America/Chicano								
Puerto-Rican								
Other Hispanic								
White/Caucasian								
Other								
***Unit of Measure**	**Participants**							
Race/Ethnicity, Customized								
***Measure Type**	***Measure of Dispersion**							
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean** **Geometric LSM** **Number** **Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Inter-Quartile Range** **Full Range**							
[*] Row/Category Title								
[*] Row/Category Title								
***Unit of Measure**								

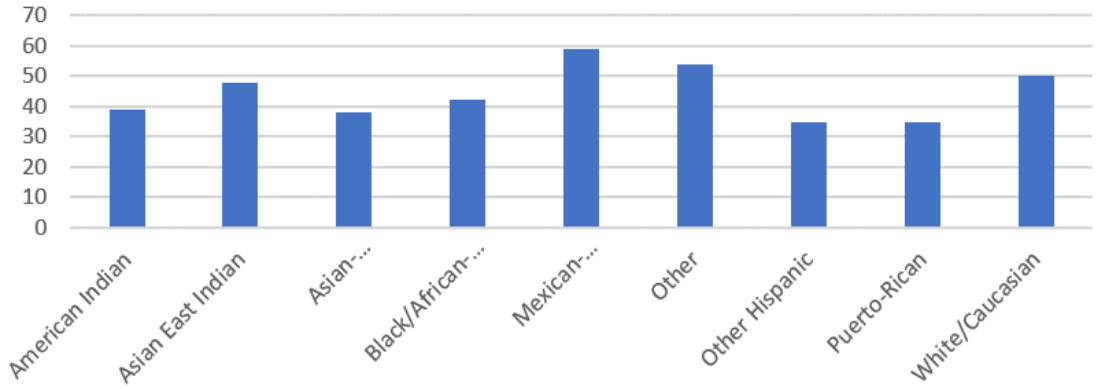
*Required [*] Conditionally required

Figure 2.14- Baseline Characteristics Template- Race, Ethnicity

Insert Graphs for Race/Ethnicity Here (examples)



φ Figure 2.15 Distribution of Race/Ethnicity Pie Graph



φ Figure 2.16 Distribution of Race/Ethnicity Bar Graph

Insert Race/Ethnicity Dispersion Statistical Analysis Here

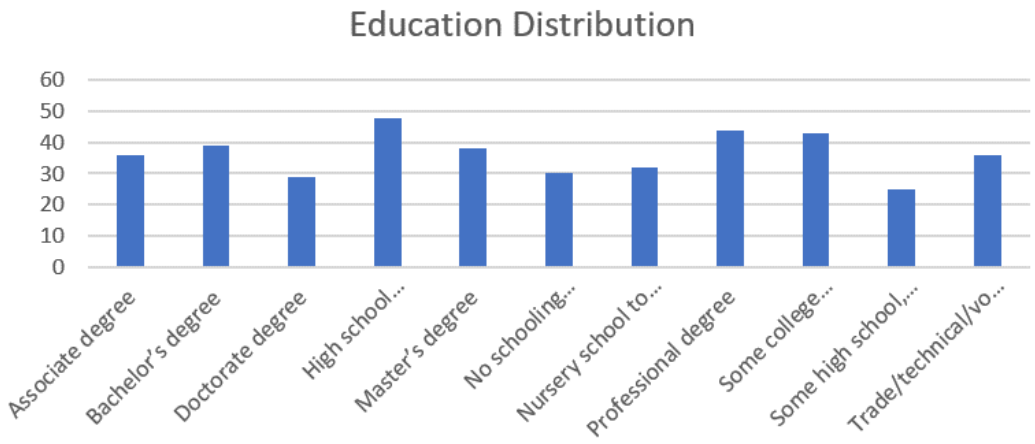
Baseline Characteristics Template	*Education History* (use at least one)*	*Nu-Life Solutions*

Group Title		Phase I		Phase II		**Totals**		
Group Description								
Overall Number of Baseline Participants								
(*) Baseline Analysis Population Description								
Education History: No schooling completed, Nursery school to 8th grade, Some high school- no diploma, High school graduate- diploma or the equivalent, Some college credit-no degree, Trade/technical/vocational training, Associate degree, Bachelor's degree, Master's degree, Professional degree, Doctorate degree								
No schooling completed								
Nursery school to 8th grade								
Some high school, no diploma								
High school graduate, diploma or the equivalent								
Some college credit, no degree								
Trade/technical/vocational training								
Associate degree								
Bachelor's degree								
Master's degree								
Professional degree								
***Unit of Measure**	**Participants**							
Education History, Customized								
***Measure Type**	***Measure of Dispersion**							
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean** **Geometric LSM** **Number** **Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Inter-Quartile Range** **Full Range**							
[*] Row/Category Title								
[*] Row/Category Title								
***Unit of Measure**								

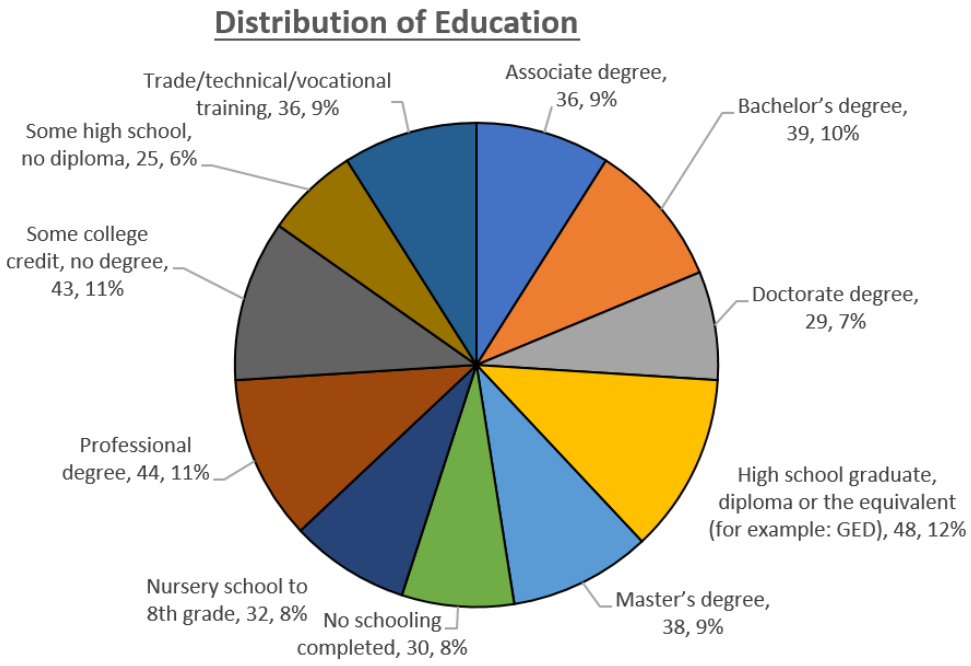
*Required [*] Conditionally required

Figure 2.17- Baseline Characteristics Template- Educational History

Insert Graphs for Educational History Measures Here (examples)



φ Figure 2.18 Distribution of Education Bar Graph



φ Figure 2.19 Distribution of Education Pie Graph

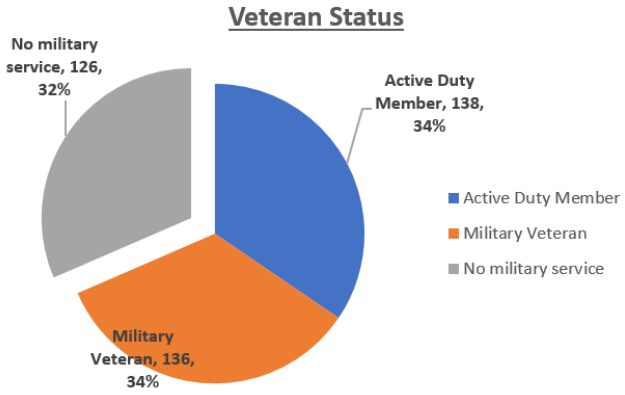
Insert Education Dispersion Statistical Analysis Here

Baseline Characteristics Template	*Service Status* (use at least one)*	*Nu-Life Solutions*	
Group Title	Phase I	Phase II	**Totals**
Group Description			
Overall Number of Baseline Participants			
(*) Baseline Analysis Population Description			
Veteran Status: Military Veteran, Active Duty Member, Never Served in the Armed Forces			
Yes, I am a military veteran			
Yes, I am an active duty member			
No, I have never served in the armed forces			
***Unit of Measure** **Participants**			
First Responder Status: Current or former First Responder, Not a First Responder			
Yes, I am a current or former First Responder			
No, I have never been a First Responder			
***Unit of Measure** **Participants**			
Service Status, Customized			
***Measure Type**	***Measure of Dispersion**		
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean** **Geometric LSM** **Number** **Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Inter-Quartile Range** **Full Range**		
[*] Row/Category Title			
[*] Row/Category Title			
***Unit of Measure**			

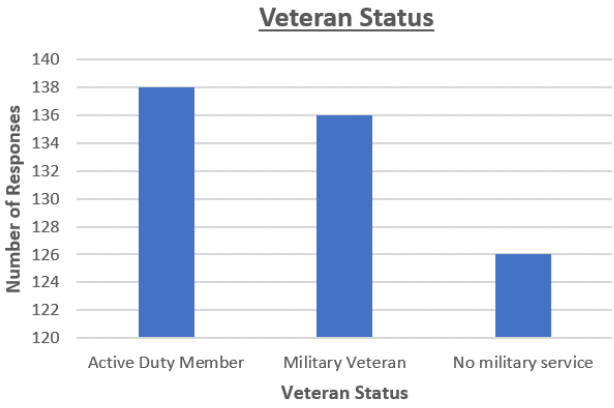
*Required [*] Conditionally required

Figure 2.20- Baseline Characteristics Template- Service Status

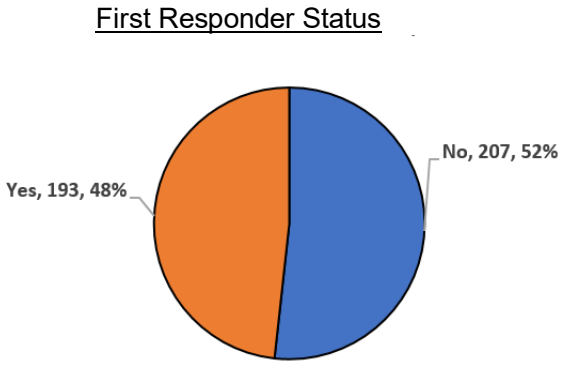
Insert Graphs for Service Status Measures Here (examples)



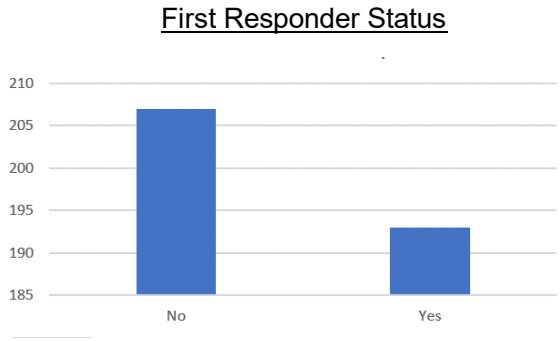
φ Figure 2.21 Distribution of Veteran Status Pie Graph



φ Figure 2.22 Distribution of Veteran Status Bar Graph



φ Figure 2.21 Distribution of First Responder Status Pie Graph



φ Figure 2.22 Distribution of First Responder Status Bar Graph

Insert Service Status Dispersion Statistical Analysis Here

Baseline Characteristics Template	*Study Specific Measure*	*Nu-Life Solutions*	
Group Title	Phase I	Phase II	**Totals**
Group Description			
Overall Number of Baseline Participants			
(*) Baseline Analysis Population Description			
[*] Study Specific Measure Title			
Baseline Measure Title			
***Measure Type**	***Measure of Dispersion**		
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean** **Geometric LSM** **Number** **Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Inter-Quartile Range** **Full Range**		
[*] Row/Category Title			
[*] Row/Category Title			
***Unit of Measure**			

*Required [*] Conditionally required

Figure 2.23- Baseline Characteristics Template- Study Specific Measures

Insert Graphs for Study Specific Measures Here (examples)

Insert Study Specific Measures Dispersion Statistical Analysis

Section 3.0: Outcome Measures and Statistical Analyses

Pain

Outcome Measure Data Preparation Checklist

Overview: A tabular summary of outcome measure results by comparison group. You must report tables for each pre-specified primary and secondary outcome and any appropriate statistical analyses. The outcomes that were pre-specified in the Protocol Section of the record will be available to use and edit during results data entry. You may also include other pre-specified and *post hoc* outcomes. Use this checklist with the Outcome Measure Simple Results Template[Δ] and Results Data Element Definitions.

	Information to have available for each Outcome Measure	Term
☐	• Label the measure as Primary, Secondary, Other Pre-specified, or Post hoc.	*[Δ]Outcome Measure Type
☐	• Title—Describe specifically what was measured and will be reported as data ○ For example, "Change from baseline in systolic blood pressure at 6 months" specifically describes what was measured and how the outcome data will be reported; "Principle Vital Signs" does not. • Description—Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (i.e., not specialists in your field, but general readers of the medical literature). ○ For example, a description of how the measure was taken, relevant definitions (e.g., explain "response"), any methods of assessment, and/or calculations that were performed to summarize the data ○ If the measure was based on a scale, explain any numerical categories or provide the range and direction of possible scores (0=no pain; 10=worst possible pain) to allow a reader to properly interpret any reported values.	*[Δ]Outcome Measure Title [Δ]Outcome Measure Description
☐	• The time point(s) or duration over which a participant was assessed for the measure, and for which data are being reported ○ For a time-to-event measure—A definition of the stopping rule and the longest duration over which a participant was observed (e.g., from randomization until death, up to 3 years)	*[Δ]Outcome Measure Time Frame
☐	• The number of separate groups for which summary data will be provided • Tip: Generally equal to the number of intervention strategies or groups compared	Arm/Groups
☐	• For each group: ○ Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1"). ○ Description—A detailed explanation of the participants included in the group and the interventions received. This may include a description of how groups of participants were recombined for analysis purposes.	*[Δ]Arm/Group Title [Δ]Arm/Group Description
☐	• Number of participants, in each group, from whom data were collected and summarized. ○ If the unit of analysis is not participants, also provide the name of the unit (e.g., eyes, lesions) and the number of units [Type/Number Units Analyzed].	*[Δ]Number of Participants Analyzed

*Required
[Δ]Template Field

	Information to have available for each Outcome Measure	Term
☐	• An explanation of the criteria used to determine which participants were included in the analysis.	ΔAnalysis Population Description
☐	• The method used to summarize outcome data: ○ Central tendency—E.g., mean, median, geometric mean ○ Number—E.g., count, percentage or proportion	*ΔMeasure Type
☐	• For a measure of central tendency, specify a measure that represents "the spread" of the summary data (e.g., standard deviation) or an estimate of precision (e.g., confidence interval). ○ Tip: Either Not applicable or Confidence interval may be appropriate for a Number (e.g., count or percentage of participants).	*ΔMeasure of Dispersion/Precision
☐	• Numerical values for the summary-level data in each group	*Outcome Data
☐	• The specific unit associated with the numerical data (e.g., mg/dL) ○ If a proportion or percentage, indicate what it is "of" (e.g., "percentage of participants")	*ΔUnit of Measure

*Required
ΔTemplate Field

Figure 3.1- Outcome Measures Checklist- Pain

Outcome Measure Template	***Pain***	***Nu-Life Solutions***
* Outcome Measure Type	(Select One) Primary Secondary Other Pre-specified Post-Hoc	
* Outcome Measure Title		
[*] Outcome Measure Description		
* Outcome Measure Time Frame		

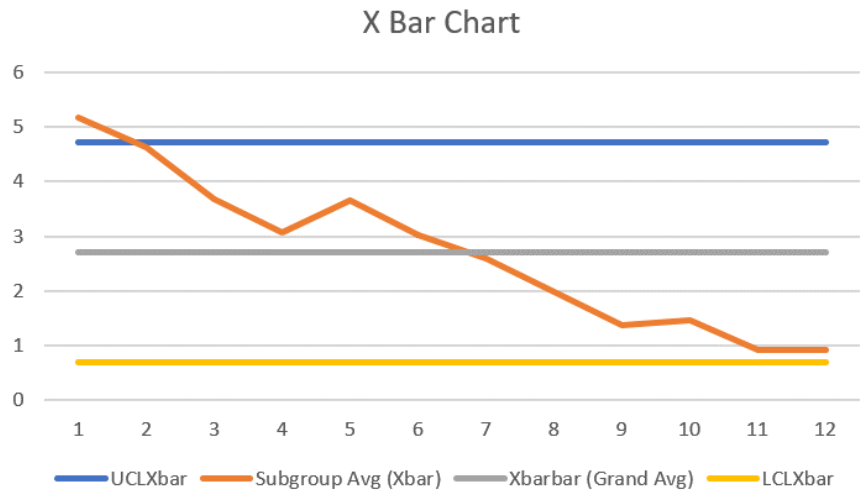
* Arm / Group Title	Phase I	Phase II	**Total**
* Arm / Group Description	Initial 50-100 pts	100-200 pts	150-300 patients
* Overall Number of Participants Analyzed			
[*] Analysis Population Description			

*Measure Type	*Measure of Dispersion / Precision						
(Select One) Count of Participants Mean Median Least Squares Mean (LSM) Geometric Mean Geometric LSM Number Count of Units	(Select One) Not Applicable Standard Deviation Standard Error Inter-Quartile Range Full Range _____% Confidence Interval Geometric Coefficient of Variation						
[*] Row/Category Title							
[*] Row/Category Title							
*Unit of Measure							

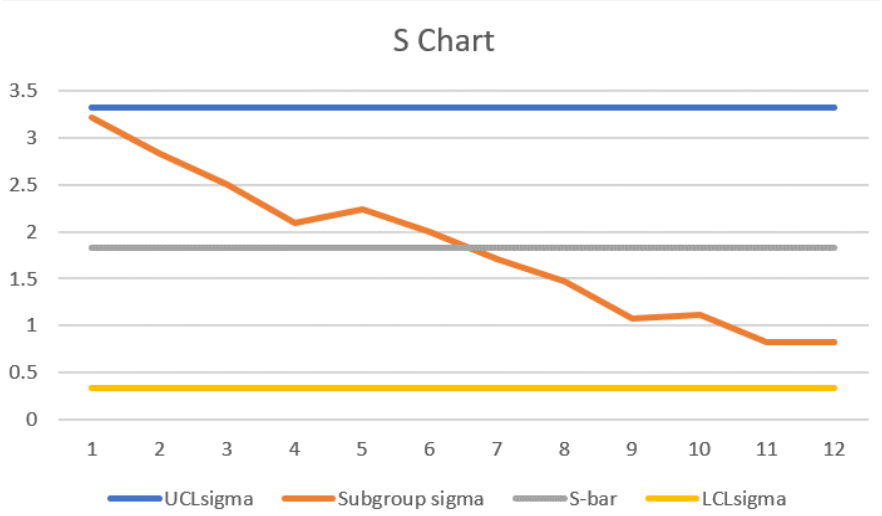
*Required [*] Conditionally required

Figure 3.2- Outcome Measures Template- Pain

Pain Analysis Graphs



φ Figure 3.3- Outcome Measures Analysis- Xbar Chart Pain



φ Figure 3.4- Outcome Measures Analysis- S Chart Pain

Statistical Analysis Here

Outcome Measure - Statistical Analysis (optional)

Overview: The statistical analysis section is a table associated with an Outcome Measure. It summarizes the results of any scientifically appropriate tests of statistical significance or other parameters estimated from the Outcome Measure data. If a statistical analysis is provided, it must include either a P-Value[*] or an Estimation Parameter[*]. You may include as many statistical analyses as is necessary to accommodate all data calculations. Use this checklist with the Results Data Element Definitions.

	Information to have available for each Statistical Analysis	Term
☐	• The Outcome Measure group(s) used in the analysis ○ Explain any of the following, if applicable: ▪ Null hypothesis for the comparison ▪ Power calculation	*Comparison Group Selection Comparison Comments
☐	• Was the analysis a test of non-inferiority or equivalence? [Yes or No] ○ If Yes, provide the defined non-inferiority margin.	*Non-inferiority or Equivalence Analysis? [*]Non-inferiority/Equivalence Comments
	And have one or both of the following:	
☐	• Computed p-value and the statistical method used (e.g., ANOVA, t-test) ○ Additional explanatory comments to interpret the value, if needed: ▪ Adjustments for multiple comparisons or covariates ▪ Degrees of freedom ▪ *A priori* threshold for statistical significance (e.g., < 0.05)	[*]P-Value and Method P-Value Comments
☐	• Value of any parameter derived from the outcome measure data (e.g., hazard ratio, mean difference, correlation coefficient) ○ Any of the following, if available: ▪ Confidence Interval ▪ Standard deviation or standard error ○ Additional explanatory comments to interpret the value, if needed: ▪ Directionality of comparison. For subtraction (i.e., A – B or B – A) or a ratio (i.e., A/B or B/A)	[*]Estimation Parameter and Value Confidence Interval Parameter Dispersion Estimation Comments

*Required
[*] Conditionally required

Figure 3.5- Statistical Analysis Checklist- Pain

Insert Summary of Results Here

Anxiety

Outcome Measure Data Preparation Checklist

Overview: A tabular summary of outcome measure results by comparison group. You must report tables for each pre-specified primary and secondary outcome and any appropriate statistical analyses. The outcomes that were pre-specified in the Protocol Section of the record will be available to use and edit during results data entry. You may also include other pre-specified and *post hoc* outcomes. Use this checklist with the Outcome Measure Simple Results Template[Δ] and Results Data Element Definitions.

	Information to have available for each Outcome Measure	Term
☐	• Label the measure as Primary, Secondary, Other Pre-specified, or Post hoc.	*[Δ]Outcome Measure Type

☐	• Title—Describe specifically what was measured and will be reported as data
	  ○ For example, "Change from baseline in systolic blood pressure at 6 months" specifically describes what was measured and how the outcome data will be reported; "Principle Vital Signs" does not.
	• Description—Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (i.e., not specialists in your field, but general readers of the medical literature).
	  ○ For example, a description of how the measure was taken, relevant definitions (e.g., explain "response"), any methods of assessment, and/or calculations that were performed to summarize the data
	  ○ If the measure was based on a scale, explain any numerical categories or provide the range and direction of possible scores (0=no pain; 10=worst possible pain) to allow a reader to properly interpret any reported values.
		*[Δ]Outcome Measure Title
		[Δ]Outcome Measure Description

☐	• The time point(s) or duration over which a participant was assessed for the measure, and for which data are being reported ○ For a time-to-event measure—A definition of the stopping rule and the longest duration over which a participant was observed (e.g., from randomization until death, up to 3 years)	*[Δ]Outcome Measure Time Frame
☐	• The number of separate groups for which summary data will be provided • Tip: Generally equal to the number of intervention strategies or groups compared	Arm/Groups

☐	• For each group:
	  ○ Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1").
	  ○ Description—A detailed explanation of the participants included in the group and the interventions received. This may include a description of how groups of participants were recombined for analysis purposes.
		*[Δ]Arm/Group Title
		[Δ]Arm/Group Description

☐	• Number of participants, in each group, from whom data were collected and summarized. ○ If the unit of analysis is not participants, also provide the name of the unit (e.g., eyes, lesions) and the number of units [Type/Number Units Analyzed].	*[Δ]Number of Participants Analyzed

**Required*
[Δ]*Template Field*

	Information to have available for each Outcome Measure	Term
☐	• An explanation of the criteria used to determine which participants were included in the analysis.	ΔAnalysis Population Description
☐	• The method used to summarize outcome data: ○ Central tendency—E.g., mean, median, geometric mean ○ Number—E.g., count, percentage or proportion	*ΔMeasure Type
☐	• For a measure of central tendency, specify a measure that represents "the spread" of the summary data (e.g., standard deviation) or an estimate of precision (e.g., confidence interval). ○ Tip: Either Not applicable or Confidence interval may be appropriate for a Number (e.g., count or percentage of participants).	*ΔMeasure of Dispersion/Precision
☐	• Numerical values for the summary-level data in each group	*Outcome Data
☐	• The specific unit associated with the numerical data (e.g., mg/dL) ○ If a proportion or percentage, indicate what it is "of" (e.g., "percentage of participants")	*ΔUnit of Measure

*Required
ΔTemplate Field

Figure 3.6- Outcome Measures Checklist- Anxiety

Outcome Measure Template	***Anxiety***	***Nu-Life Solutions***
* Outcome Measure Type	(Select One) Primary Secondary Other Pre-specified Post-Hoc	
* Outcome Measure Title		
[*] Outcome Measure Description		
* Outcome Measure Time Frame		

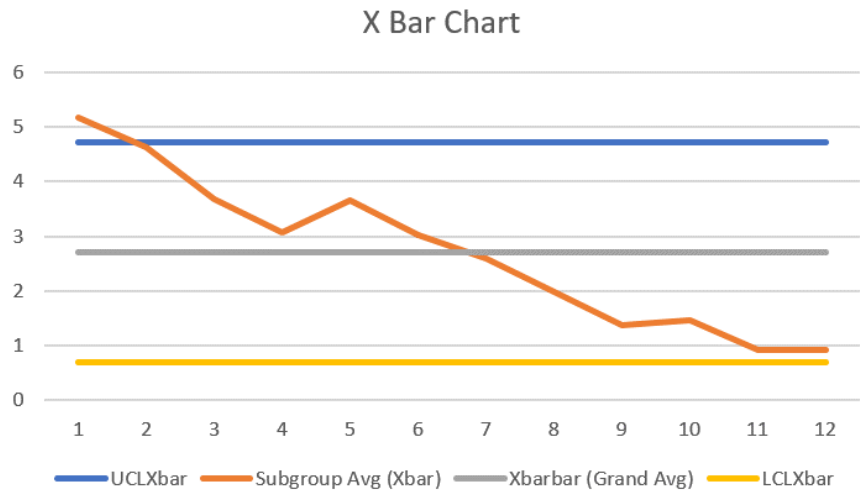
* Arm / Group Title	Phase I	Phase II	Total
* Arm / Group Description	Initial 50-100 pts	100-200 pts	150-300 patients
* Overall Number of Participants Analyzed			
[*] Analysis Population Description			

*Measure Type	*Measure of Dispersion / Precision						
(Select One) Count of Participants Mean Median Least Squares Mean (LSM) Geometric Mean Geometric LSM Number Count of Units	(Select One) Not Applicable Standard Deviation Standard Error Inter-Quartile Range Full Range _____% Confidence Interval Geometric Coefficient of Variation						
[*] Row/Category Title							
[*] Row/Category Title							
*Unit of Measure							

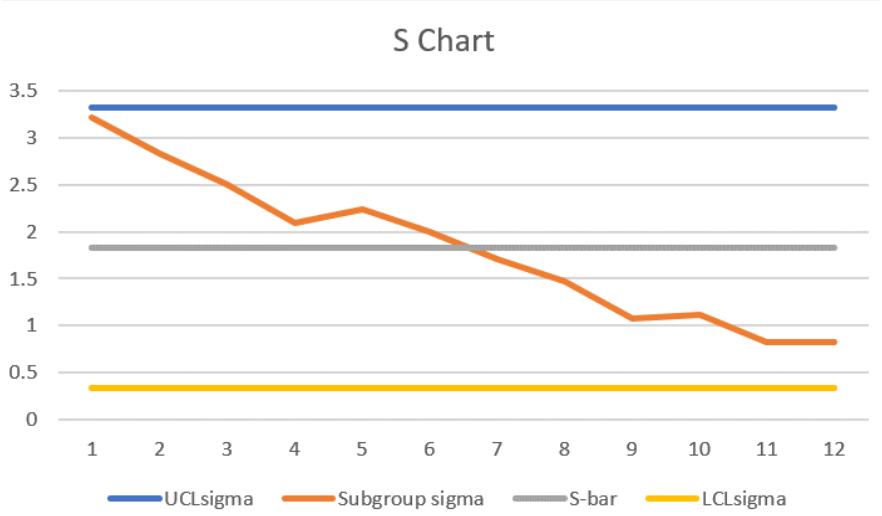
*Required [*] Conditionally required

Figure 3.7- Outcome Measures Template- Anxiety

Insert Anxiety Analysis Graphs Here



φ Figure 3.8- Outcome Measures Analysis- Xbar Chart Anxiety



φ Figure 3.9- Outcome Measures Analysis- S Chart Anxiety

Statistical Analysis Here

Outcome Measure - Statistical Analysis (optional)

Overview: The statistical analysis section is a table associated with an Outcome Measure. It summarizes the results of any scientifically appropriate tests of statistical significance or other parameters estimated from the Outcome Measure data. If a statistical analysis is provided, it must include either a P-Value[*] or an Estimation Parameter[*]. You may include as many statistical analyses as is necessary to accommodate all data calculations. Use this checklist with the Results Data Element Definitions.

	Information to have available for each Statistical Analysis	Term
☐	• The Outcome Measure group(s) used in the analysis ○ Explain any of the following, if applicable: ▪ Null hypothesis for the comparison ▪ Power calculation	*Comparison Group Selection Comparison Comments
☐	• Was the analysis a test of non-inferiority or equivalence? [Yes or No] ○ If Yes, provide the defined non-inferiority margin.	*Non-inferiority or Equivalence Analysis? [*]Non-inferiority/Equivalence Comments
	And have one or both of the following:	
☐	• Computed p-value and the statistical method used (e.g., ANOVA, t-test) ○ Additional explanatory comments to interpret the value, if needed: ▪ Adjustments for multiple comparisons or covariates ▪ Degrees of freedom ▪ *A priori* threshold for statistical significance (e.g., < 0.05)	[*]P-Value and Method P-Value Comments
☐	• Value of any parameter derived from the outcome measure data (e.g., hazard ratio, mean difference, correlation coefficient) ○ Any of the following, if available: ▪ Confidence Interval ▪ Standard deviation or standard error ○ Additional explanatory comments to interpret the value, if needed: ▪ Directionality of comparison. For subtraction (i.e., A – B or B – A) or a ratio (i.e., A/B or B/A)	[*]Estimation Parameter and Value Confidence Interval Parameter Dispersion Estimation Comments

*Required
[*] Conditionally required

Figure 3.10- Statistical Analysis Checklist- Anxiety

Insert Summary of Results Here

Depression

Outcome Measure Data Preparation Checklist

Overview: A tabular summary of outcome measure results by comparison group. You must report tables for each pre-specified primary and secondary outcome and any appropriate statistical analyses. The outcomes that were pre-specified in the Protocol Section of the record will be available to use and edit during results data entry. You may also include other pre-specified and *post hoc* outcomes. Use this checklist with the Outcome Measure Simple Results Template[Δ] and Results Data Element Definitions.

	Information to have available for each Outcome Measure	Term
☐	• Label the measure as Primary, Secondary, Other Pre-specified, or Post hoc.	*[Δ]Outcome Measure Type

☐	• Title—Describe specifically what was measured and will be reported as data
	  ○ For example, "Change from baseline in systolic blood pressure at 6 months" specifically describes what was measured and how the outcome data will be reported; "Principle Vital Signs" does not.
	• Description—Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (i.e., not specialists in your field, but general readers of the medical literature).
	  ○ For example, a description of how the measure was taken, relevant definitions (e.g., explain "response"), any methods of assessment, and/or calculations that were performed to summarize the data
	  ○ If the measure was based on a scale, explain any numerical categories or provide the range and direction of possible scores (0=no pain; 10=worst possible pain) to allow a reader to properly interpret any reported values.
		*[Δ]Outcome Measure Title
		[Δ]Outcome Measure Description

☐	• The time point(s) or duration over which a participant was assessed for the measure, and for which data are being reported ○ For a time-to-event measure—A definition of the stopping rule and the longest duration over which a participant was observed (e.g., from randomization until death, up to 3 years)	*[Δ]Outcome Measure Time Frame
☐	• The number of separate groups for which summary data will be provided • Tip: Generally equal to the number of intervention strategies or groups compared	Arm/Groups

☐	• For each group:
	  ○ Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1").
	  ○ Description—A detailed explanation of the participants included in the group and the interventions received. This may include a description of how groups of participants were recombined for analysis purposes.
		*[Δ]Arm/Group Title
		[Δ]Arm/Group Description

☐	• Number of participants, in each group, from whom data were collected and summarized. ○ If the unit of analysis is not participants, also provide the name of the unit (e.g., eyes, lesions) and the number of units [Type/Number Units Analyzed].	*[Δ]Number of Participants Analyzed

**Required*
[Δ]*Template Field*

	Information to have available for each Outcome Measure	Term
☐	• An explanation of the criteria used to determine which participants were included in the analysis.	ΔAnalysis Population Description
☐	• The method used to summarize outcome data: o Central tendency—E.g., mean, median, geometric mean o Number—E.g., count, percentage or proportion	*ΔMeasure Type
☐	• For a measure of central tendency, specify a measure that represents "the spread" of the summary data (e.g., standard deviation) or an estimate of precision (e.g., confidence interval). o Tip: Either Not applicable or Confidence interval may be appropriate for a Number (e.g., count or percentage of participants).	*ΔMeasure of Dispersion/Precision
☐	• Numerical values for the summary-level data in each group	*Outcome Data
☐	• The specific unit associated with the numerical data (e.g., mg/dL) o If a proportion or percentage, indicate what it is "of" (e.g., "percentage of participants")	*ΔUnit of Measure

*Required
ΔTemplate Field

Figure 3.11- Outcome Measures Checklist- Depression

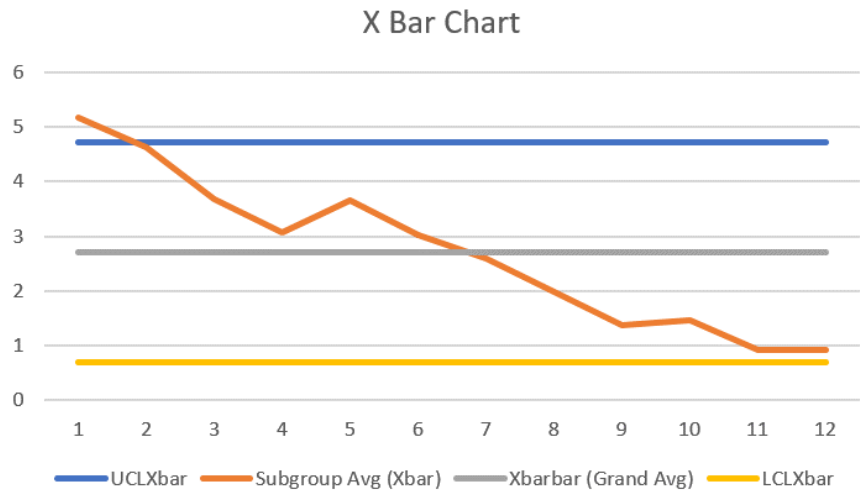
Outcome Measure Template	***Depression***	***Nu-Life Solutions***
* Outcome Measure Type	(Select One) Primary Secondary Other Pre-specified Post-Hoc	
* Outcome Measure Title		
[*] Outcome Measure Description		
* Outcome Measure Time Frame		

* Arm / Group Title		Phase I		Phase II		**Total**	
* Arm / Group Description		Initial 50-100 pts		100-200 pts		150-300 patients	
* Overall Number of Participants Analyzed							
[*] Analysis Population Description							
*Measure Type	*Measure of Dispersion / Precision						
(Select One) Count of Participants Mean Median Least Squares Mean (LSM) Geometric Mean Geometric LSM Number Count of Units	(Select One) Not Applicable Standard Deviation Standard Error Inter-Quartile Range Full Range _____% Confidence Interval Geometric Coefficient of Variation						
[*] Row/Category Title							
[*] Row/Category Title							
*Unit of Measure							

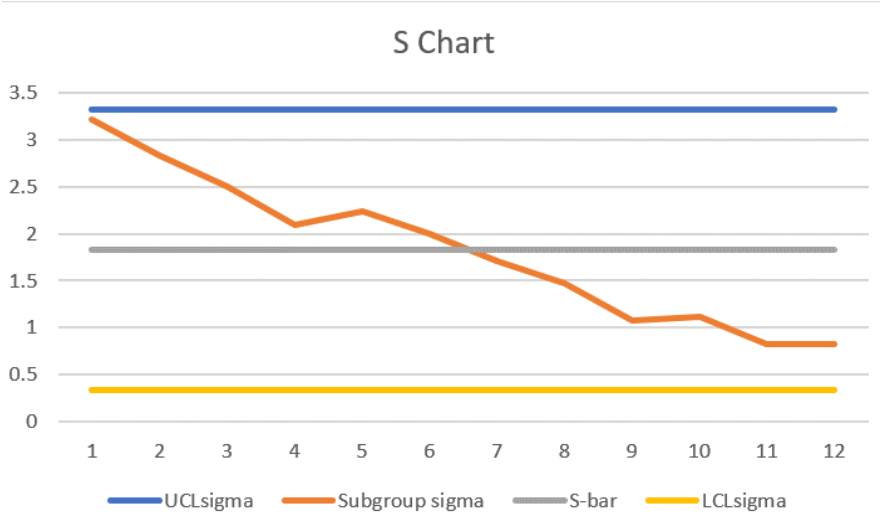
*Required [*] Conditionally required

Figure 3.12- Outcome Measures Template- Depression

Insert Depression Analysis Graphs Here



φ Figure 3.13- Outcome Measures Analysis- Xbar Chart Depression



φ Figure 3.14- Outcome Measures Analysis- S Chart Depression

Statistical Analysis Here

Outcome Measure - Statistical Analysis (optional)

Overview: The statistical analysis section is a table associated with an Outcome Measure. It summarizes the results of any scientifically appropriate tests of statistical significance or other parameters estimated from the Outcome Measure data. If a statistical analysis is provided, it must include either a P-Value[*] or an Estimation Parameter[*]. You may include as many statistical analyses as is necessary to accommodate all data calculations. Use this checklist with the Results Data Element Definitions.

	Information to have available for each Statistical Analysis	Term
☐	• The Outcome Measure group(s) used in the analysis ○ Explain any of the following, if applicable: ▪ Null hypothesis for the comparison ▪ Power calculation	*Comparison Group Selection Comparison Comments
☐	• Was the analysis a test of non-inferiority or equivalence? [Yes or No] ○ If Yes, provide the defined non-inferiority margin.	*Non-inferiority or Equivalence Analysis? [*]Non-inferiority/Equivalence Comments
	And have one or both of the following:	
☐	• Computed p-value and the statistical method used (e.g., ANOVA, t-test) ○ Additional explanatory comments to interpret the value, if needed: ▪ Adjustments for multiple comparisons or covariates ▪ Degrees of freedom ▪ *A priori* threshold for statistical significance (e.g., < 0.05)	[*]P-Value and Method P-Value Comments
☐	• Value of any parameter derived from the outcome measure data (e.g., hazard ratio, mean difference, correlation coefficient) ○ Any of the following, if available: ▪ Confidence Interval ▪ Standard deviation or standard error ○ Additional explanatory comments to interpret the value, if needed: ▪ Directionality of comparison. For subtraction (i.e., A – B or B – A) or a ratio (i.e., A/B or B/A)	[*]Estimation Parameter and Value Confidence Interval Parameter Dispersion Estimation Comments

*Required
[*] Conditionally required

Figure 3.15- Statistical Analysis Checklist- Depression

Insert Summary of Results Here

Sleeplessness

Outcome Measure Data Preparation Checklist

Overview: A tabular summary of outcome measure results by comparison group. You must report tables for each pre-specified primary and secondary outcome and any appropriate statistical analyses. The outcomes that were pre-specified in the Protocol Section of the record will be available to use and edit during results data entry. You may also include other pre-specified and *post hoc* outcomes. Use this checklist with the Outcome Measure Simple Results Template[Δ] and Results Data Element Definitions.

	Information to have available for each Outcome Measure	Term
☐	• Label the measure as Primary, Secondary, Other Pre-specified, or Post hoc.	*[Δ]Outcome Measure Type

☐	• Title—Describe specifically what was measured and will be reported as data
	  ○ For example, "Change from baseline in systolic blood pressure at 6 months" specifically describes what was measured and how the outcome data will be reported; "Principle Vital Signs" does not.
	• Description—Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (i.e., not specialists in your field, but general readers of the medical literature).
	  ○ For example, a description of how the measure was taken, relevant definitions (e.g., explain "response"), any methods of assessment, and/or calculations that were performed to summarize the data
	  ○ If the measure was based on a scale, explain any numerical categories or provide the range and direction of possible scores (0=no pain; 10=worst possible pain) to allow a reader to properly interpret any reported values.
		*[Δ]Outcome Measure Title
		[Δ]Outcome Measure Description

☐	• The time point(s) or duration over which a participant was assessed for the measure, and for which data are being reported ○ For a time-to-event measure—A definition of the stopping rule and the longest duration over which a participant was observed (e.g., from randomization until death, up to 3 years)	*[Δ]Outcome Measure Time Frame
☐	• The number of separate groups for which summary data will be provided • Tip: Generally equal to the number of intervention strategies or groups compared	Arm/Groups

☐	• For each group:
	  ○ Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1").
	  ○ Description—A detailed explanation of the participants included in the group and the interventions received. This may include a description of how groups of participants were recombined for analysis purposes.
		*[Δ]Arm/Group Title
		[Δ]Arm/Group Description

☐	• Number of participants, in each group, from whom data were collected and summarized. ○ If the unit of analysis is not participants, also provide the name of the unit (e.g., eyes, lesions) and the number of units [Type/Number Units Analyzed].	*[Δ]Number of Participants Analyzed

**Required*
[Δ]*Template Field*

	Information to have available for each Outcome Measure	Term
☐	• An explanation of the criteria used to determine which participants were included in the analysis.	ΔAnalysis Population Description
☐	• The method used to summarize outcome data: ○ Central tendency—E.g., mean, median, geometric mean ○ Number—E.g., count, percentage or proportion	*ΔMeasure Type
☐	• For a measure of central tendency, specify a measure that represents "the spread" of the summary data (e.g., standard deviation) or an estimate of precision (e.g., confidence interval). ○ Tip: Either Not applicable or Confidence interval may be appropriate for a Number (e.g., count or percentage of participants).	*ΔMeasure of Dispersion/Precision
☐	• Numerical values for the summary-level data in each group	*Outcome Data
☐	• The specific unit associated with the numerical data (e.g., mg/dL) ○ If a proportion or percentage, indicate what it is "of" (e.g., "percentage of participants")	*ΔUnit of Measure

*Required
ΔTemplate Field

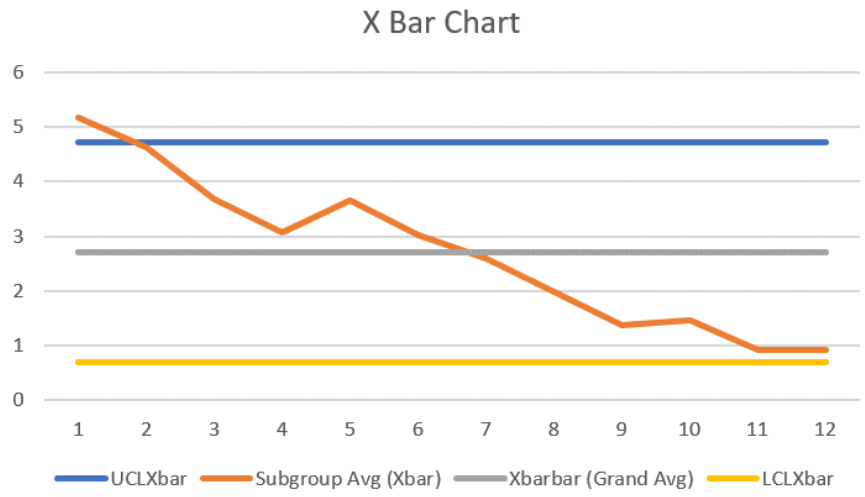
Figure 3.16- Outcome Measures Checklist- Sleeplessness

Outcome Measure Template	***Sleeplessness***		***Nu-Life Solutions***			
*** Outcome Measure Type**	**(Select One)**	**Primary**	**Secondary**	**Other Pre-specified**	**Post-Hoc**	
*** Outcome Measure Title**						
[*] Outcome Measure Description						
*** Outcome Measure Time Frame**						
*** Arm / Group Title**		Phase I		Phase II		**Total**
*** Arm / Group Description**		Initial 50-100 pts		100-200 pts		150-300 patients
*** Overall Number of Participants Analyzed**						
[*] Analysis Population Description						
***Measure Type**	***Measure of Dispersion / Precision**					
(Select One) **Count of Participants** **Mean** **Median** **Least Squares Mean (LSM)** **Geometric Mean Geometric LSM** **Number Count of Units**	**(Select One)** **Not Applicable** **Standard Deviation** **Standard Error** **Inter-Quartile Range** **Full Range** **_____% Confidence Interval** **Geometric Coefficient of Variation**					
[*] Row/Category Title						
[*] Row/Category Title						
***Unit of Measure**						

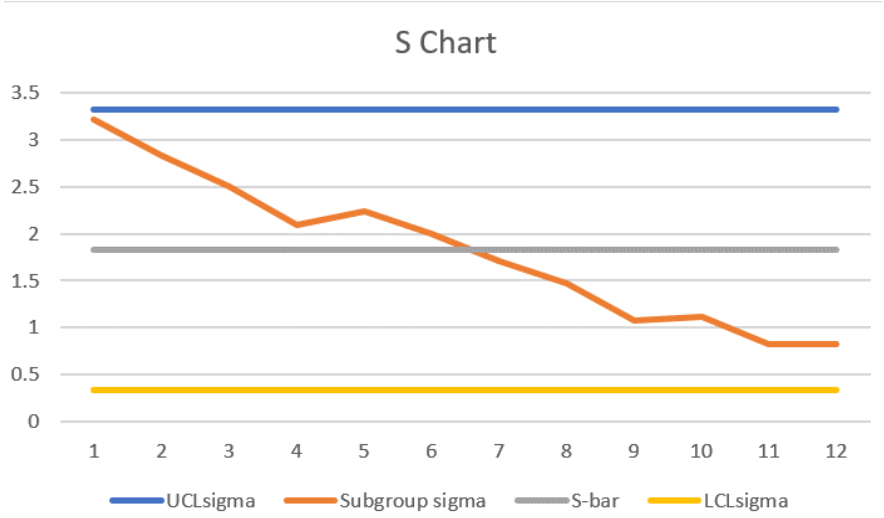
*Required [*] Conditionally required

Figure 3.17- Outcome Measures Template- Sleeplessness

Insert Sleeplessness Analysis Graphs Here



φ Figure 3.18- Outcome Measures Analysis- Xbar Chart Sleeplessness



φ Figure 3.19- Outcome Measures Analysis- S Chart Sleeplessness

Statistical Analysis Here

Outcome Measure - Statistical Analysis (optional)

Overview: The statistical analysis section is a table associated with an Outcome Measure. It summarizes the results of any scientifically appropriate tests of statistical significance or other parameters estimated from the Outcome Measure data. If a statistical analysis is provided, it must include either a P-Value[*] or an Estimation Parameter[*]. You may include as many statistical analyses as is necessary to accommodate all data calculations. Use this checklist with the Results Data Element Definitions.

	Information to have available for each Statistical Analysis	Term
☐	• The Outcome Measure group(s) used in the analysis ○ Explain any of the following, if applicable: ▪ Null hypothesis for the comparison ▪ Power calculation	*Comparison Group Selection Comparison Comments
☐	• Was the analysis a test of non-inferiority or equivalence? [Yes or No] ○ If Yes, provide the defined non-inferiority margin.	*Non-inferiority or Equivalence Analysis? [*]Non-inferiority/Equivalence Comments
	And have one or both of the following:	
☐	• Computed p-value and the statistical method used (e.g., ANOVA, t-test) ○ Additional explanatory comments to interpret the value, if needed: ▪ Adjustments for multiple comparisons or covariates ▪ Degrees of freedom ▪ *A priori* threshold for statistical significance (e.g., < 0.05)	[*]P-Value and Method P-Value Comments
☐	• Value of any parameter derived from the outcome measure data (e.g., hazard ratio, mean difference, correlation coefficient) ○ Any of the following, if available: ▪ Confidence Interval ▪ Standard deviation or standard error ○ Additional explanatory comments to interpret the value, if needed: ▪ Directionality of comparison. For subtraction (i.e., A – B or B – A) or a ratio (i.e., A/B or B/A)	[*]Estimation Parameter and Value Confidence Interval Parameter Dispersion Estimation Comments

*Required
[*] Conditionally required

Figure 3.20- Statistical Analysis Checklist- Sleeplessness

Insert Summary of Results Here

Quality of Life

Outcome Measure Data Preparation Checklist

Overview: A tabular summary of outcome measure results by comparison group. You must report tables for each pre-specified primary and secondary outcome and any appropriate statistical analyses. The outcomes that were pre-specified in the Protocol Section of the record will be available to use and edit during results data entry. You may also include other pre-specified and *post hoc* outcomes. Use this checklist with the Outcome Measure Simple Results Template[Δ] and Results Data Element Definitions.

	Information to have available for each Outcome Measure	Term
☐	• Label the measure as Primary, Secondary, Other Pre-specified, or Post hoc.	*[Δ]Outcome Measure Type

☐	• Title—Describe specifically what was measured and will be reported as data
	  ○ For example, "Change from baseline in systolic blood pressure at 6 months" specifically describes what was measured and how the outcome data will be reported; "Principle Vital Signs" does not.
	• Description—Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (i.e., not specialists in your field, but general readers of the medical literature).
	  ○ For example, a description of how the measure was taken, relevant definitions (e.g., explain "response"), any methods of assessment, and/or calculations that were performed to summarize the data
	  ○ If the measure was based on a scale, explain any numerical categories or provide the range and direction of possible scores (0=no pain; 10=worst possible pain) to allow a reader to properly interpret any reported values.
		*[Δ]Outcome Measure Title
		[Δ]Outcome Measure Description

☐	• The time point(s) or duration over which a participant was assessed for the measure, and for which data are being reported ○ For a time-to-event measure—A definition of the stopping rule and the longest duration over which a participant was observed (e.g., from randomization until death, up to 3 years)	*[Δ]Outcome Measure Time Frame
☐	• The number of separate groups for which summary data will be provided • Tip: Generally equal to the number of intervention strategies or groups compared	Arm/Groups

☐	• For each group:
	  ○ Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1").
	  ○ Description—A detailed explanation of the participants included in the group and the interventions received. This may include a description of how groups of participants were recombined for analysis purposes.
		*[Δ]Arm/Group Title
		[Δ]Arm/Group Description

☐	• Number of participants, in each group, from whom data were collected and summarized. ○ If the unit of analysis is not participants, also provide the name of the unit (e.g., eyes, lesions) and the number of units [Type/Number Units Analyzed].	*[Δ]Number of Participants Analyzed

**Required*
[Δ]*Template Field*

	Information to have available for each Outcome Measure	Term
☐	• An explanation of the criteria used to determine which participants were included in the analysis.	ΔAnalysis Population Description
☐	• The method used to summarize outcome data: ○ Central tendency—E.g., mean, median, geometric mean ○ Number—E.g., count, percentage or proportion	*ΔMeasure Type
☐	• For a measure of central tendency, specify a measure that represents "the spread" of the summary data (e.g., standard deviation) or an estimate of precision (e.g., confidence interval). ○ Tip: Either Not applicable or Confidence interval may be appropriate for a Number (e.g., count or percentage of participants).	*ΔMeasure of Dispersion/Precision
☐	• Numerical values for the summary-level data in each group	*Outcome Data
☐	• The specific unit associated with the numerical data (e.g., mg/dL) ○ If a proportion or percentage, indicate what it is "of" (e.g., "percentage of participants")	*ΔUnit of Measure

*Required
ΔTemplate Field

Figure 3.21- Outcome Measures Checklist- QOL

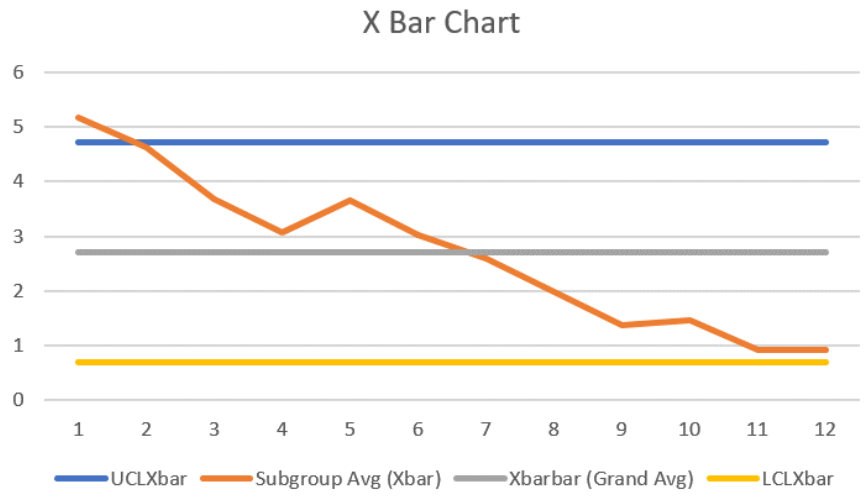
Outcome Measure Template	***Quality of Life- PGIC***	***Nu-Life Solutions***
* Outcome Measure Type	(Select One) Primary Secondary Other Pre-specified Post-Hoc	
* Outcome Measure Title		
[*] Outcome Measure Description		
* Outcome Measure Time Frame		

	* Arm / Group Title	Phase I	Phase II	Total
	* Arm / Group Description	Initial 50-100 pts	100-200 pts	150-300 patients
	* Overall Number of Participants Analyzed			
	[*] Analysis Population Description			
*Measure Type	*Measure of Dispersion / Precision			
(Select One) Count of Participants Mean Median Least Squares Mean (LSM) Geometric Mean Geometric LSM Number Count of Units	(Select One) Not Applicable Standard Deviation Standard Error Inter-Quartile Range Full Range _____% Confidence Interval Geometric Coefficient of Variation			
[*] Row/Category Title				
[*] Row/Category Title				
*Unit of Measure				

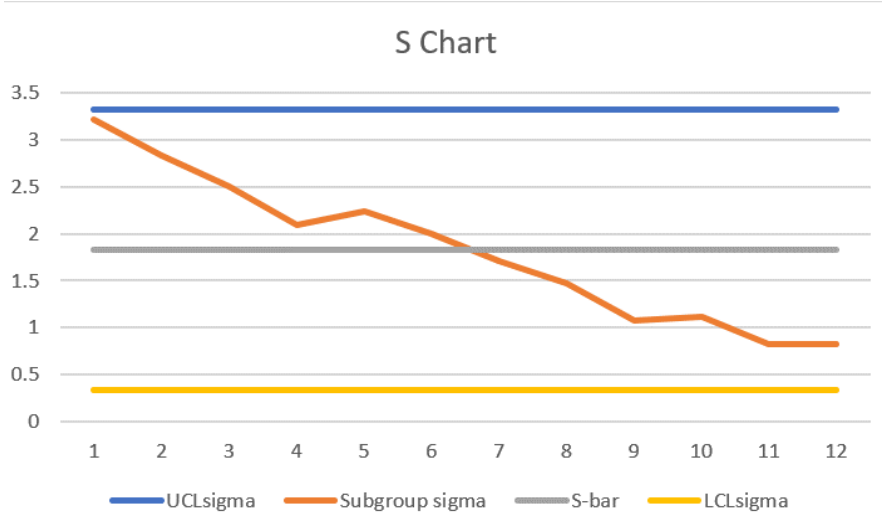
*Required [*] Conditionally required

Figure 3.22- Outcome Measures Template- Quality of Life

Insert Quality of Life Analysis Graphs Here



φ Figure 3.23- Outcome Measures Analysis- Xbar Chart QOL Level



φ Figure 3.24- Outcome Measures Analysis- S Chart QOL Level

Statistical Analysis Here

Outcome Measure - Statistical Analysis (optional)

Overview: The statistical analysis section is a table associated with an Outcome Measure. It summarizes the results of any scientifically appropriate tests of statistical significance or other parameters estimated from the Outcome Measure data. If a statistical analysis is provided, it must include either a P-Value[*] or an Estimation Parameter[*]. You may include as many statistical analyses as is necessary to accommodate all data calculations. Use this checklist with the Results Data Element Definitions.

	Information to have available for each Statistical Analysis	Term
☐	• The Outcome Measure group(s) used in the analysis ○ Explain any of the following, if applicable: ▪ Null hypothesis for the comparison ▪ Power calculation	*Comparison Group Selection Comparison Comments
☐	• Was the analysis a test of non-inferiority or equivalence? [Yes or No] ○ If Yes, provide the defined non-inferiority margin.	*Non-inferiority or Equivalence Analysis? [*]Non-inferiority/Equivalence Comments
	And have one or both of the following:	
☐	• Computed p-value and the statistical method used (e.g., ANOVA, t-test) ○ Additional explanatory comments to interpret the value, if needed: ▪ Adjustments for multiple comparisons or covariates ▪ Degrees of freedom ▪ *A priori* threshold for statistical significance (e.g., < 0.05)	[*]P-Value and Method P-Value Comments
☐	• Value of any parameter derived from the outcome measure data (e.g., hazard ratio, mean difference, correlation coefficient) ○ Any of the following, if available: ▪ Confidence Interval ▪ Standard deviation or standard error ○ Additional explanatory comments to interpret the value, if needed: ▪ Directionality of comparison. For subtraction (i.e., A – B or B – A) or a ratio (i.e., A/B or B/A)	[*]Estimation Parameter and Value Confidence Interval Parameter Dispersion Estimation Comments

*Required
[*] Conditionally required

Figure 3.25- Statistical Analysis Checklist- Quality of Life Level

Insert Summary of Results Here

Reduction of Total Daily Dosage: Indication- Relevant Medications Taken (Baseline, 30, 60, 90 Days)

Outcome Measure Data Preparation Checklist

Overview: A tabular summary of outcome measure results by comparison group. You must report tables for each pre-specified primary and secondary outcome and any appropriate statistical analyses. The outcomes that were pre-specified in the Protocol Section of the record will be available to use and edit during results data entry. You may also include other pre-specified and *post hoc* outcomes. Use this checklist with the Outcome Measure Simple Results Template[Δ] and Results Data Element Definitions.

	Information to have available for each Outcome Measure	Term
☐	• Label the measure as Primary, Secondary, Other Pre-specified, or Post hoc.	*[Δ]Outcome Measure Type

☐	• Title—Describe specifically what was measured and will be reported as data
	  ○ For example, "Change from baseline in systolic blood pressure at 6 months" specifically describes what was measured and how the outcome data will be reported; "Principle Vital Signs" does not.
	• Description—Any elaboration needed to understand the measure and the reported data. Information should be written for a public audience (i.e., not specialists in your field, but general readers of the medical literature).
	  ○ For example, a description of how the measure was taken, relevant definitions (e.g., explain "response"), any methods of assessment, and/or calculations that were performed to summarize the data
	  ○ If the measure was based on a scale, explain any numerical categories or provide the range and direction of possible scores (0=no pain; 10=worst possible pain) to allow a reader to properly interpret any reported values.
		*[Δ]Outcome Measure Title
		[Δ]Outcome Measure Description

☐	• The time point(s) or duration over which a participant was assessed for the measure, and for which data are being reported ○ For a time-to-event measure—A definition of the stopping rule and the longest duration over which a participant was observed (e.g., from randomization until death, up to 3 years)	*[Δ]Outcome Measure Time Frame
☐	• The number of separate groups for which summary data will be provided • Tip: Generally equal to the number of intervention strategies or groups compared	Arm/Groups

☐	• For each group:
	  ○ Title—A descriptive label for the group (header for table column). Use informative labels (e.g., "Placebo"), not generic labels (e.g., "Group 1").
	  ○ Description—A detailed explanation of the participants included in the group and the interventions received. This may include a description of how groups of participants were recombined for analysis purposes.
		*[Δ]Arm/Group Title
		[Δ]Arm/Group Description

☐	• Number of participants, in each group, from whom data were collected and summarized. ○ If the unit of analysis is not participants, also provide the name of the unit (e.g., eyes, lesions) and the number of units [Type/Number Units Analyzed].	*[Δ]Number of Participants Analyzed

**Required*
[Δ]*Template Field*

	Information to have available for each Outcome Measure	Term
☐	• An explanation of the criteria used to determine which participants were included in the analysis.	ΔAnalysis Population Description
☐	• The method used to summarize outcome data: ○ Central tendency—E.g., mean, median, geometric mean ○ Number—E.g., count, percentage or proportion	*ΔMeasure Type
☐	• For a measure of central tendency, specify a measure that represents "the spread" of the summary data (e.g., standard deviation) or an estimate of precision (e.g., confidence interval). ○ Tip: Either Not applicable or Confidence interval may be appropriate for a Number (e.g., count or percentage of participants).	*ΔMeasure of Dispersion/Precision
☐	• Numerical values for the summary-level data in each group	*Outcome Data
☐	• The specific unit associated with the numerical data (e.g., mg/dL) ○ If a proportion or percentage, indicate what it is "of" (e.g., "percentage of participants")	*ΔUnit of Measure

*Required
ΔTemplate Field

Figure 3.26- Outcome Measures Checklist- Relevant Medication Dosage Decrease

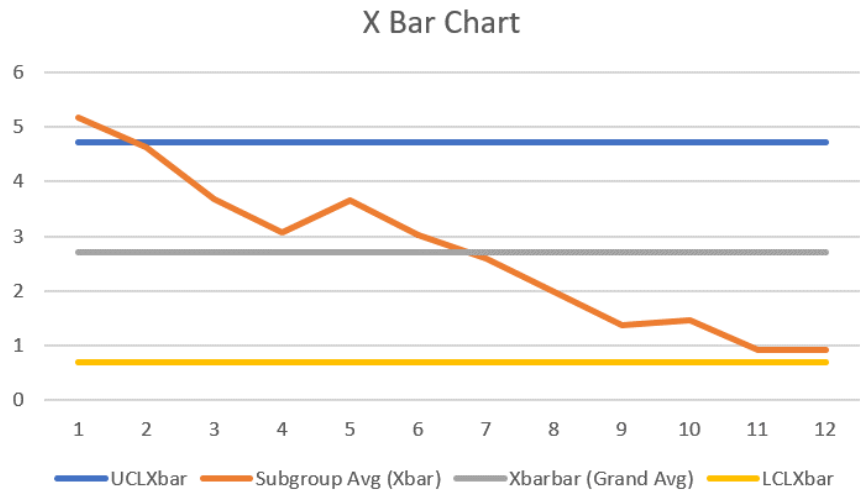
Outcome Measure Template	***Relevant Medications Dosage Decrease***	***Nu-Life Solutions***

* Outcome Measure Type	(Select One) Primary Secondary Other Pre-specified Post-Hoc							
* Outcome Measure Title								
[*] Outcome Measure Description								
* Outcome Measure Time Frame								
* Arm / Group Title		Phase I		Phase II		**Total**		
* Arm / Group Description		Initial 50-100 pts		100-200 pts		150-300 patients		
* Overall Number of Participants Analyzed								
[*] Analysis Population Description								
*Measure Type	*Measure of Dispersion / Precision							
(Select One) Count of Participants Mean Median Least Squares Mean (LSM) Geometric Mean Geometric LSM Number Count of Units	(Select One) Not Applicable Standard Deviation Standard Error Inter-Quartile Range Full Range _____% Confidence Interval Geometric Coefficient of Variation							
[*] Row/Category Title								
[*] Row/Category Title								
*Unit of Measure								

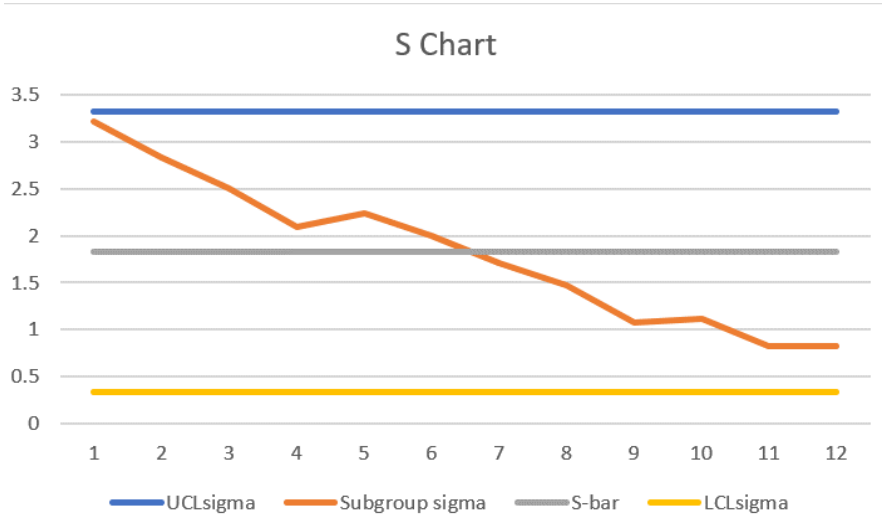
*Required [*] Conditionally required

Figure 3.27- Outcome Measures Template- Relevant Medication Dosage Decrease

Insert Relevant Medication Dosage Decrease Analysis Graphs Here



φ Figure 3.28- Outcome Measures Analysis- Xbar Chart Relevant Medication Dosage Decrease



φ Figure 3.29- Outcome Measures Analysis- S Chart Relevant Medication Dosage Decrease

Insert Relevant Medication Dosage Decrease Statistical Analysis Here

Outcome Measure - Statistical Analysis (optional)

Overview: The statistical analysis section is a table associated with an Outcome Measure. It summarizes the results of any scientifically appropriate tests of statistical significance or other parameters estimated from the Outcome Measure data. If a statistical analysis is provided, it must include either a P-Value[*] or an Estimation Parameter[*]. You may include as many statistical analyses as is necessary to accommodate all data calculations. Use this checklist with the Results Data Element Definitions.

	Information to have available for each Statistical Analysis	Term
☐	• The Outcome Measure group(s) used in the analysis ○ Explain any of the following, if applicable: ▪ Null hypothesis for the comparison ▪ Power calculation	*Comparison Group Selection Comparison Comments
☐	• Was the analysis a test of non-inferiority or equivalence? [Yes or No] ○ If Yes, provide the defined non-inferiority margin.	*Non-inferiority or Equivalence Analysis? [*]Non-inferiority/Equivalence Comments
	And have one or both of the following:	
☐	• Computed p-value and the statistical method used (e.g., ANOVA, t-test) ○ Additional explanatory comments to interpret the value, if needed: ▪ Adjustments for multiple comparisons or covariates ▪ Degrees of freedom ▪ *A priori* threshold for statistical significance (e.g., < 0.05)	[*]P-Value and Method P-Value Comments
☐	• Value of any parameter derived from the outcome measure data (e.g., hazard ratio, mean difference, correlation coefficient) ○ Any of the following, if available: ▪ Confidence Interval ▪ Standard deviation or standard error ○ Additional explanatory comments to interpret the value, if needed: ▪ Directionality of comparison. For subtraction (i.e., A – B or B – A) or a ratio (i.e., A/B or B/A)	[*]Estimation Parameter and Value Confidence Interval Parameter Dispersion Estimation Comments

*Required
[*] Conditionally required

Figure 3.30- Statistical Analysis Checklist- Relevant Medication Dosage Decrease

Insert Relevant Medication Dosage Decrease Summary of Results Here

Section 4.0: Safety

Labeling: The Nu-V3 labeling consists of Instructions for Use and packaging labels. The Instructions for Use include the indications for use; a description of the device, contraindications, warnings, precautions; a list of other devices that are compatible; a detailed summary of the clinical data collected in support of the device; a shelf life; and instructions for the safe use of the device. The labeling satisfies the requirements of 21 CFR 801.109.

Please see the Limitations section above for important warnings and precautions presented in the device labeling.

Risks to Health: Potential unanticipated problems require prompt reporting to Aspire IRB These problems potentially place subjects or others at greater risk of physical or psychological harm than was previously recognized, and warrant consideration of substantive changes in the protocol or informed consent process or other action in order to protect the safety, welfare, or rights of participants. Aspire IRB must be notified within 5 calendar days of the event. The completed IRB Unanticipated Problem form (Appendix 3) must be received by Aspire IRB within 10 calendar days of the event. Unanticipated problems are defined as those problems which alter the risks to subjects or others. This includes any study suspensions or holds. This form will be used to report any problem that is unforeseen or involves risk. One form will be used per event or problem.

Table 4.1: Unanticipated Problems Involving Risk to Patients or Others

	Phase I	Phase II	Total
UPIRTSO 1 (number)			
UPIRTSO 2 (number)			
UPIRTSO 3 (number)			
Overall UPIRTSOs Reported			

Table 4.2: Risk/ Mitigation Measures

Identified Risk	Mitigation Measures

Insert Safety Analysis Here

Section 5.0: Results

Results: The principal safety and effectiveness results from patients in the Nu-V3 study are provided below. The primary safety analysis was based on all patients registered and included all reported UPIRTSO events. The primary safety endpoint included imputation for missing clinical outcomes data using the logistic regression method. The imputation model included baseline characteristics including age, sex/gender, marital status, primary language spoken, race/ethnicity, education history, and veteran status.

Primary Safety Endpoint:

Insert Primary Safety Endpoint Statistical Analysis

Insert Primary Safety Endpoint Statistical Table

Primary Effectiveness Endpoint:

Insert Primary Effectiveness Endpoint Statistical Analysis

Insert Primary Effectiveness Endpoint Statistical Table- 8 weeks

Secondary Effectiveness Endpoint:

Insert Primary Effectiveness Endpoint Statistical Analysis

Insert Primary Effectiveness Endpoint Statistical Table: 4, 8, 12 weeks

Sub-Analyses:

Insert Sub-Analyses Statistical Analysis

Insert Sub-Analyses Statistical Tables

Special Controls:

Insert Special Control Section Here

Benefit/Risk Determination:

Insert Benefit/Risk Section Here

Section 5.0: Administrative Information

Administrative information consists of the study results point of contact and any agreement between the sponsor and principal investigator (PI) restricting the ability of the PI to discuss the results after the completion of the study.

Conclusion:

The de novo for Nu-V3 is _____ and the device is classified under the following:

Product Code:

Device Type:

Class:

Regulation: