A FEASIBILITY STUDY TO EVALUATE THE CLINICAL SAFETY OF ENVIZION™ NASOENTERAL FEEDING TUBE PLACEMENT USING THE ENVIZION ™ ENVUE™ SYSTEM IN PATIENTS

Protocol Number: NUTRI-002

Principal Investigator: Dr. Lewis Jacobson

Sponsor: ENvizion Medical Ltd.

Version Number: 1.3

July 11, 2018

NCT Number: NCT03505593

STATEMENT OF COMPLIANCE

Investigator Signature Page

Study Title:	A Feasibility Study to Evaluate the Clinical Safety of ENvizion™ Nasoenteral Feeding Tube Placement using the ENvizion™ ENVUE™ System in Patients (NUTRI-002)
Investigational Devices:	ENVUE System
	ENvizion™ NasoEnteral Tube
Protocol Version:	Version 1.3
Protocol Date:	July 11, 2018
Sponsor:	ENvizion Medical Ltd.

Prior to participation in the clinical study (Protocol Number: NUTRI-002), as the Principal Investigator, I understand that I must obtain written approval from my Institutional Review Board (IRB). This approval must include my name, and I must send a copy to ENvizion (the COMPANY) or designee along with the IRB-approved Informed Consent Form (ICF) prior to study enrollment at my study site.

As the Principal Investigator, I must also:

1. Conduct the study in accordance with the study protocol, the signed Clinical Investigation Agreement, HIPAA requirements, IRB requirements and applicable FDA regulations (21 CFR Part 812, 50, 54 and 56) and ensure all study personnel are appropriately trained.
2. Provide a copy of my curriculum vitae which includes my relevant professional experience including the dates, location, extent, and type of experience.
3. Supervise all testing of the investigational device in this study.
4. Ensure that the study has not commenced until IRB approval has been obtained.
5. Immediately inform the COMPANY in writing if I become debarred from conducting clinical studies by FDA, or any professional organization (e.g., loss of medical license).
6. Ensure that written informed consent is obtained from each patient prior to any study activities using the most recent IRB-approved Patient ICF.
7. Provide all required data and reports and agree to source document verification of study data with patients' medical records.
8. Allow the COMPANY personnel or its designees, as well as FDA representatives, to inspect and copy documents pertaining to this investigation.
9. Provide sufficient and accurate financial disclosure information and update information if any relevant changes occur during the investigation and for one year following the completion of the study.
10. If involved in research that was terminated, I will provide an explanation in writing of the circumstances that led to the termination of the research.

I have read and understand the contents of the Origin study protocol and agree to abide by the requirements set forth in this document.

Dr. Lewis Jacobson	St Vincent Indianapolis
Investigator Name	Investigative Site Name
_____	_____
Investigator Signature	Date

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

STUDY TITLE	A Feasibilty Study to Evaluate the Clinical Safety of ENvizion™ Nasoenteral Feeding Tube Placement using the ENvizion™ ENVUE System in Patients.
PROTOCOL NUMBER	NUTRI-002
DEVICE DESCRIPTION	The ENvizion™ ENVUE™ System is designed to aid qualified operators in the placement of the ENvizion™ NasoEnteral Tube™ of 10 Fr to 12 Fr into the stomach or small intestine of patients requiring enteral feeding. The ENVUE System is intended as an adjunct to current placement practices for assisting clinical practitioners who place feeding tubes in adult patients. The ENvizion™ NasoEnteral Tube has been specifically designed for use with the ENVUE™ System and is intended for placement in the stomach or small intestine. It is intended for use in adult patients who require intermittent or continuous feedings via the nasogastric or nasoenteric route.
STUDY OBJECTIVES	The objective of this study is to assess the safety of the ENVUE System as an adjunct to current practices for placement of nasoenteral feeding tubes.
STUDY DESIGN	The study is a prospective, single center, non-randomized clinical trial in patients that require placement of a nasoenteral feeding tube as a result of their current medical condition.
NUMBER OF SUBJECTS AND SITES	Up to fifty (50) subjects and at least forty (40) will complete the Procedure Visit (NasoEnteral Tube placement procedure, section 1.3) at a single center by at least five operators. This number (40-50 subjects) does not include screen failures. ENvizion nasoenteral feeding tubes will be placed in 5 run-in subjects prior to enrollment of the remaining subjects. All enrolled subjects (run-in subjects and trial subjects) will be included in the final analysis.
DURATION OF PARTICIPATION/STUDY	Each patient's individual participation will last approximately 20-48 hours. It is expected the entire study will take approximately two (2) months to complete.
STUDY ENDPOINTS	<u>Primary Endpoint</u>: Procedure success: Nasoenteral tube (NET) can be placed in the correct anatomical position without occurrence of guidance-related adverse events.

	Additional Assessments: Procedure Metric s: Number of placement attempts required Safety: Adverse Events
SAMPLE SIZE CONSIDERATIONS	There is no statistically based sample size for this study which is being conducted to obtain confirmatory evidence to support the safety of using the ENVUE System as an adjunct to current placement practices for nasoenteral feeding tubes. Forty (40) to Fifty (50) subjects (includes run-in subjects) completing the Procedure Visit (NasoEnteral Tube placement procedure) will provide evidence that the NET tube guidance system does not present new or different safety issues as compared to the predicate (confirmatory study). If less than 35 patients will complete the Follow-up Visit (confirmation of tube tip anatomical location), an enrollment of another 5 patients will be considered.
SCHEDULED VISITS	This study is an acute safety assessment of the ENVUE System covering the guidance functionality of the System. Screening The screening visit will occur at time zero and will assess eligibility for the study and obtain informed consent. Procedure The study procedure may occur within two days of screening. Informed consent will be affirmed and the patient will be considered enrolled. Final Follow Up The final follow-up visit will occur 20-48 hours following the procedure.
INCLUSION CRITERIA	• Patients must be ≥21 years of age • Patients must require placement of a nasoenteral feeding tube • Patients have an endotracheal tube, OR ○ Do not have an endotracheal tube but are sedated and/or classified as obtunded[1] at the time of placement • Patients or legal authorized representative must be able to understand and adhere to all protocol procedures and be willing and able to provide written informed consent[2]

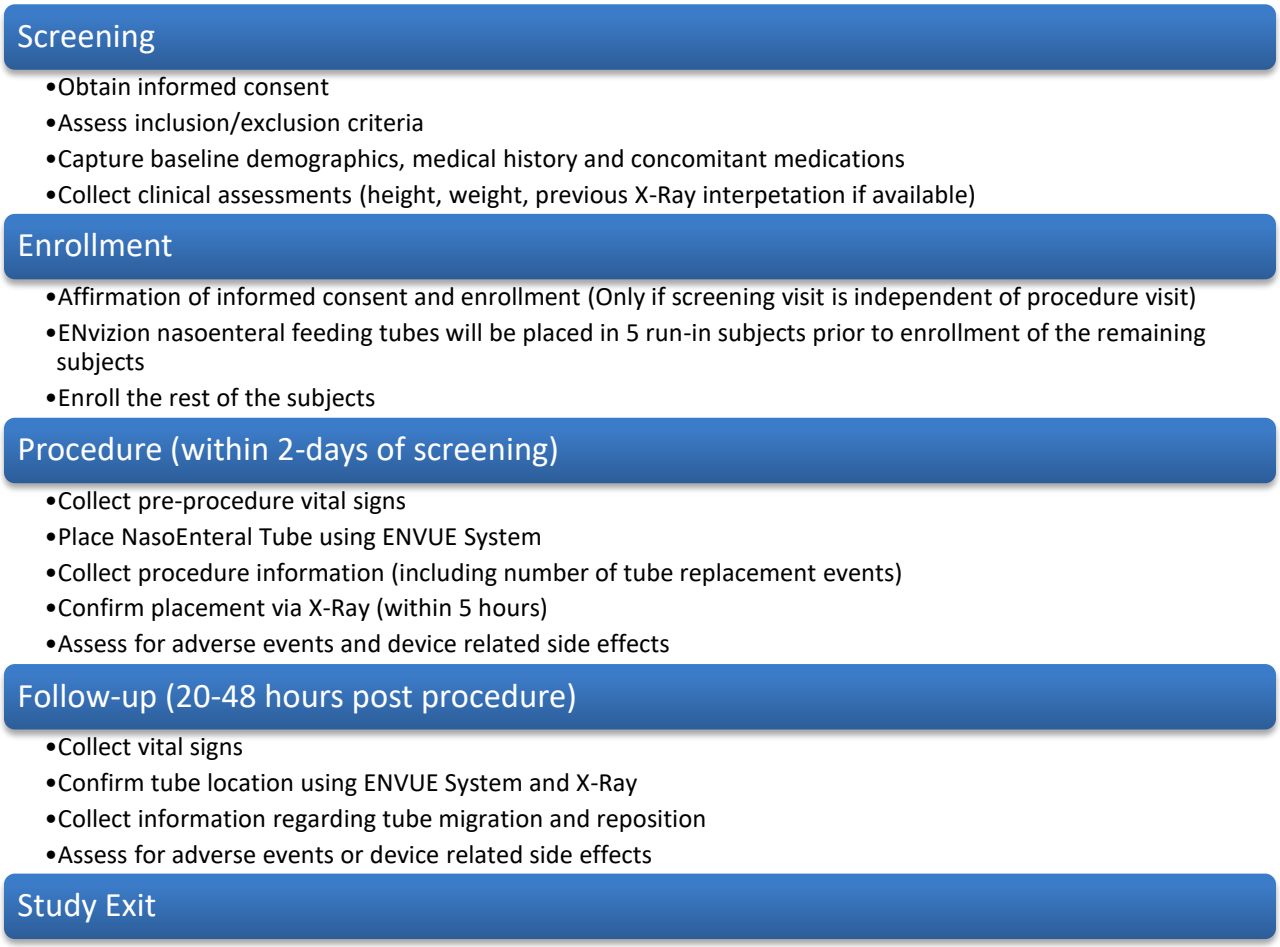
[1] Obtundation level evaluation is based on Glasgow-Coma scale with a score of between 9 and 12. Sedation level is based on Richmond Agitation-Sedation Scale (RASS) score of -2 or less.
[2] Consent may be provided by patient's legal authorized representative.

EXCLUSION CRITERIA	• Patients must not have a history of:
	  ○ Esophageal varices or ulcers
	  ○ Upper airway obstruction
	  ○ Upper GI stenosis or obstruction
	  ○ Trauma involving sinuses, nares face or neck that would prevent NG or oral tube insertion
	  ○ Deformities of the sinus cavities and/or skull base
	  ○ Esophageal cancer or neoplasm
	• Patients must not have a significant concomitant illness that would adversely affect their participation in the study
	• Female patients who are pregnant or lactating

STATISTICAL ANALYSIS	All data will be reported using summary statistics.
OTHER CONSIDERATIONS	No core lab will be charted for this study; thus, judgements regarding placement will be based on the investigator's assessment of X-Ray images. Assessments of relatedness of any noted adverse events to the study device will be adjudicated by a Clinical Events Committee (CEC). No DSMB will be chartered for this study based on the well-understood safety profile.
US REGULATORY STATUS	The ENVUE System is considered a non-significant risk investigational device in the United States.

1.2 SCHEMA

Figure 1: Study Flow Chart



1.3 SCHEDULE OF ACTIVITIES (SOA)

The study schedule for this evaluation is presented below in **Table 1.**

Table 1: Study Schedule

Procedures, Evaluations and Tests	**Study Visits**		
	Screening	**Procedure (Within 2 days of Screening Visit)**	**Follow-up (20-48 hours after Procedure Visit)**
Informed Consent	X	X[3]	
Inclusion/Exclusion Criteria	X		
Demographics	X		
Medical History (Acute and Past)	X		
Concomitant Medications[4]	X		
Examinations Targeted Physical Exam Vital Signs	X	 X	 X
ENvizion™ nasoenteral tube Placement		X	
Confirm Anatomical Location ENVUE System Abdominal and/ or thoracic X-ray[5]		 X[6]	 X X
Adverse Events		X	X

[3] Affirmation of informed consent is only required if procedure visit is independent of screening visit.
[4] Limited to sedatives/any medication with sedative effect, anticoagulants and prokinetic agents.
[5] Additional X-Rays may be taken if clinically indicated.
[6] Within five hours of placement.

2 STATISTICAL CONSIDERATIONS

2.1 STATISTICAL HYPOTHESES

There is no formal statistical hypothesis for the primary endpoint of this feasibility trial. The primary endpoint is defined as procedure success, e.g., NET tube can be placed in the correct anatomical position without occurrence of guidance-related adverse events.

2.2 SAMPLE SIZE DETERMINATION

This feasibility trial will include forty (40) to fifty (50) patients completing the Procedure Visit (NasoEnteral Tube placement) and at least five operators. ENvizion nasoenteral feeding tubes will be placed in 5 run-in subjects prior to enrollment of the remaining subjects. All enrolled subjects (run-in subjects and trial subjects) will be included in the final analysis. Patients or patients' LAR who chose not to participate after informed consent but prior to procedure, and patients who because of system malfunction or because of undiscovered or unreported physical reasons (e.g. deteriorating health, anatomical anomalies, mechanical obstruction, etc.) cannot complete the Procedure Visit (NasoEnteral Tube placement) will be considered Screen Failures, not be considered in the total patient count, but will be reported in the ITT dataset as defined below. If less than 35 patients will complete the Follow-up Visit (confirmation of tube tip anatomical location), an enrollment of another 5 patients will be considered.

2.3 POPULATIONS FOR ANALYSES

Populations that will be analyzed include the following:

- Intention-to-Treat (ITT) Analysis Dataset (i.e., all enrolled participants)
- Per-Protocol Analysis Dataset: defines enrolled patients for whom no protocol deviations were noted
- Full Cohort Dataset: includes the ITT population plus the Run-in patients

2.4 STATISTICAL ANALYSES

The procedure success will be calculated for all populations. Additional descriptive statistics will be presented as appropriate using means, standard deviations, medians and ranges for the continuous variables and as counts and percentages for categorical variables.

2.4.1 BASELINE DESCRIPTIVE STATISTICS

Baseline demographics will be tabulated and include descriptive statistics were applicable.

2.4.2 PLANNED INTERIM ANALYSES

Interim analyses will not be conducted in this trial.

2.4.3 SUB-GROUP ANALYSES

There are no planned sub-group analyses.