Hologenix, LLC

CLINICAL INVESTIGATION PLAN

September 18, 2013

A Single Center Prospective Comparative study to evaluate the performance of a Upper Torso Garment Containing 100% Celliant Fibers that Emits Far Infrared (FIR) from Ceramic Particles contained within the Fibers in healthy Subjects

CIP Number: HC1-2

Hologenix LLC
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COMPANY CONFIDENTIAL INFORMATION:
Nothing herein is to be disclosed in any way without the prior written consent of Hologenix LLC.

INVESTIGATOR SIGNATURE PAGE

A Single Center Prospective Comparative study to evaluate the performance of a Upper Torso Garment Containing 100% Celliant Fibers that Emits Far Infrared (FIR) from Ceramic Particles contained within the Fibers in healthy Subjects

Sponsor: Seth Casden
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Hologenix LLC

Tel: 001-954-979-3845 / Fax: 001-954-979-7997

Designated Sponsor's Representative:

Print Name: _____
Seth Casden

Signature: _____ Date: _____

Principal Investigator: Name, position, qualification, address and contact numbers

Ian L. Gordon M.D.

I have read this Clinical Investigation Plan HC1-2 version 2, 18 September 2013 and understand its requirements. I agree to conduct the study as described herein and will not deviate from the Clinical Investigation Plan without prior written approval from the Sponsor or designee. Any Clinical Investigation Plan changes, other than administrative, must be made by written amendment to the protocol and will not be implemented until approved by the Institutional Review Board or Ethics Committee.

Print Name: _____

Signature: _____ Date: _____

PERSONNEL INVOLVED

Chief Investigator:	Dr Ian L. Gordon M.D.
Study Coordinator:	Kristopher Washington
Study Associate:	Trenton Horinek
Sponsor Project Manager:	Seth Casden
Clinical Research Organisation:	Maelor Group, Inc
Monitor:	James Wason Ph.D.
Statistician:	TBD
Data Management:	Maelor Group, Inc
QA / Auditor:	Maelor Group, Inc

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SYNOPSIS

A Single Center Prospective Comparative study to evaluate the performance of a Upper Torso Garment Containing 100% Celliant Fibers that Emits Far Infrared (FIR) from Ceramic Particles contained within the Fibers in healthy Subjects

Study Design

This is a Single Center Prospective Comparative study to evaluate the performance of a Upper Torso Garment Containing 100% Celliant Fibers that Emits Far Infrared (FIR) from Ceramic Particles contained within the Fibers in healthy Subjects to be conducted at one investigative site. A total of 200 healthy Study subjects will be evaluated that meet all the inclusion / exclusion criteria and will be selected to participate in the study.

The study will compare transcutaneous partial pressure of oxygen determined by using the PeriFlux System 500 and recording data continuously and reporting ever 30 minutes using the Perisoft Version 2.55 for both the active and control uppers body garment. This is a non-invasive technique.

The Western Institutional Review Board (WIRB) has approved the revised protocol (HC1-2) dated (6 September 2013) and consent form (Ca11). The approved Protocol should be reviewed with this Clinical investigation plan.

Study Objectives and Endpoints

The **Primary Objective** of this clinical investigation is -

The primary objectives is to evaluate changes in transcutaneous oxygen tension (tcPO2,), and the inferred change in local cutaneous blood flow, in healthy subjects wearing a control and a 100% Celliant® fiber upper torso garment.

<u>Performance Endpoints</u>

Comparison of individual measurements taken at 0,30,60 and 90 minutes with the active and

Safety Endpoints

All adverse events will be collected and recorded throughout the study

The **Secondary Objectives** of the clinical investigation is –

To evaluate changes in local skin temperature by infrared imaging (skin Temperature) and/ or adjacent skin temperature (thermo couples).

Secondary Endpoint

Comparison of results obtained by the subject with Celliant upper torso garment, with results obtained by temperature measurement.

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Study Population

A total of 200 subjects will be enrolled in the study at one site.

Subjects who give written informed Consent, meet all the inclusion / exclusion criteria and can adhere to the Visit schedule will be selected to participate in the study.

Follow-up Procedures

During the first visit the patient will be assessed on clinical suitability for inclusion in the study and the data collected. No other follow up or visits is required.

Study Duration

It is expected that the study will last for a total of 6 months. This timeframe includes 1 months for all the necessary approvals, (IRB), 3 to 4 months for patient recruitment, and a further one month for follow up after the final subject has been recruited.

Study Device

During the testing, each subject will wear two different garments. The upper torso garments will contain either100% Celliant fibers (active) or one containing no Celliant material only cotton, which will serve as a control.

The garment is a short sleeve tee shirt with a round next.

All devices will be returned to Hologenix after conclusion of the study.

Regulatory Status

The upper torso garment manufactured from 100% Celliant is not cleared by the FDA. The study device is considered to be non-significant risk by Hologenix and approved by WIRB. This is a performance evaluation, and the protocol has been submitted and approved by the Western Institutional review Board

The results of the Clinical Investigation will form part of the overall submission to support de novo and 510k application with the FDA.

INTRODUCTION AND BACKGROUND

Adequate blood supply is necessary for many physiologic processes. However, there are few valid, reproducible, non-invasive methods with which to assess it. One such measure is transcutaneous partial pressure of oxygen (tcPO2). This measurement is a non-invasive method of measuring oxygen tension at the skin surface; represents the amount of oxygen diffusing outward across the skin; and can be used as a surrogate for arterial perfusion. This method is reproducible with clinically acceptable intra-subject variability; is used for a variety of conditions, including peripheral vascular disease evaluation, predicting the outcome of patients requiring amputation and survival of skin grafts; and correlates well to angiography and increases in blood flow rates. However, tcPO2 is affected by many variables, including oxygen concentration in inspired air, lung function and hemoglobin saturation, as well as local factors, such as skin thickness, sympathetic tone, the presence of inflammation, capillary formation and skin oxygen consumption.

Several other modalities exist to assess tissue oxygenation and perfusion. Ultrasonic Doppler flowometry, pulse oximetry, the gas discharge visualization (GDV) and hyperspectral imaging.

The biometric signatures for the identification purposes are based on physiological and/or behavioral trait and help in the verification process. It is important to understand that all biometrics are based on probability measures. Biometrics is a mathematical model of a physical characteristic and, as in all mathematical models; there is always a probability of an error. However, biometrics is the most reliable way of verification and authentication. Physiological traits used in biometrics include iris, fingerprint (including nail), hand (including knuckle, palm, and vascular), face, lips, & earlobe. Behavioral traits are based on signature, keystroke, voice, and gait.

STUDY OBJECTIVES AND ENDPOINTS

The **Primary Objective** of this clinical investigation is –

The primary objectives is to evaluate changes in transcutaneous oxygen tension (tcPO2,), and the inferred change in local cutaneous blood flow, in healthy subjects wearing a control and a 100% Celliant® fiber upper torso garment.

Performance Endpoints

Comparison of individual measurements from the tcPO2 measuments taken with results obtained from the control device

Safety Endpoints

All adverse events will be collected and recorded throughout the study

The **Secondary Objectives** of the clinical investigation is –

To determine whether lay consumers, after receiving instruction in the uses of Celliant garments will receive a benefit.

To determine any sources of user error and the rate of user satisfaction.

DEVICE SAFETY

Testing has been conducted to show biocompatibility as required by ISO 10993, Sections 5 and 10. The biocompatibility testing consisted of Cytotoxicity, Sensitization and Irritation / Intracutaneous tests and has been conducted for all materials to come in contact with the human skin. The results confirmed all materials used have excellent biocompatibility.

Bench testing has been undertaken and has shown that the tcPO2 meets the requirements for precision, intermediate precision, repeatability, reproducibility, system accuracy, trueness, stability.

Unpublished:

Lavery, L. (2003). "Transcutaneous oxygen tension in patients with diabetes and vascular impairment."

This double blind, randomized, placebo controlled study evaluated changes in peripheral transcutaneous oxygen tension and perfusion. Twenty subjects were enrolled who had a history of diabetes and vascular impairment. Transcutaneous oxygen tension (Perimed Inc. North Royalton, Ohio, PF5040 transcutaneous module) and laser Doppler flowometry measurements (PF5010Laser Doppler Perfusion module) were the primary endpoints used to assess the efficacy of 100% Celliant stockings, 50% Celliant gloves vs. placebo socks and gloves. Measurements were made prior to wearing the garments and continuously over a one hour period. Data were analyzed at ten minute intervals. Measurements were taken of both the hand and foot with study subjects wearing Celliant versus standard fiber gloves and stockings.

Mean tcPO2 increased 8-12% in both Celliant conditions when compared to the placebo condition, which was statistically significant ($P < 0.05$).

McClue, G. M. (2005). "Peripheral blood flow in the dorsum of the left arm and the transmetatarsal region of the foot of a healthy subjects."

This single-blind study evaluated changes in peripheral blood flow in the dorsum of the left arm and the trans metatarsal region of the foot in thirteen (13) healthy subjects. Due to the vaso-active nature of the Celliant® material, the placebo condition was always offered first and served as a baseline. After a rest period of thirty (30) minutes,

subjects donned the Celliant® gloves and stockings. Transcutaneous oxygen tension (tcPO2) measurements were recorded over the course of 60-min for the placebo and the active condition. Mean tcPO2 values were increased in local tissue when the active condition was compared to the baseline condition.

Unpublished:

Gordon, I. L. (2009). "Effects of Shirt with 42% Celliant Fiber on TCPO2 Levels and Grip Strength in Healthy Subjects."

This study was a single center, prospective, double blind, and randomized trial. Twenty-four (24) healthy subjects were enrolled, 16 men and 8 women, with an average age of 30.3 years. The subjects wore standard polyester shirts for 90 minutes indoors in a constant temperature and indoor light environment and were asked to sit quietly in a chair. After a short rest, the procedure was continued for another 90 minutes with the subjects wearing 42% Celliant/58% polyester shirts. Mean tcPO2 values were statistically greater at t=10-min, t=30-min and t=90-min when compared to the Control condition.

Published:

York, R. M. and I. L. Gordon (2009). "Effect of optically modified polyethylene terephthalate fiber socks on chronic foot pain." *BMC Complement Altern Med* **9**: 10.

BACKGROUND: Increasing experimental and clinical evidence suggests thatillumination of the skin with relatively low intensity light may lead to therapeutic results such as reduced pain or improved wound healing. The goal of this study was to evaluate prospectively whether socks made from polyethylene terephthalate (PET) incorporating optically active particles (Celliant) ameliorates chronic foot pain resulting from diabetic neuropathy or other disorders. Such optically modified fiber is thought to modify the illumination of the skin in the visible and infrared portions of the spectrum, and consequently reduce pain. METHODS: A double-blind, randomized trial with 55 subjects (38 men, 17 women) enrolled (average age 59.7 +/- 11.9 years), 26 with diabetic neuropathy and 29 with other pain etiologies. Subjects twice completed the Visual Analogue Scale (VAS), Brief Pain Inventory (BPI), McGill Pain Questionnaire (MPQ), and SF-36 a week apart (W(1+2)) before receiving either control or Celliant socks. The same questionnaires were answered again one and two weeks (W(3+4)) later. The questionnaires provided nine scores for analyzing pain reduction: one VAS score, two BPI scores, five MPQ scores, and the bodily pain score on the SF-36.

Mean W(1+2) and W(3+4) scores were compared to measure pain reduction. RESULTS: More pain reduction was reported by Celliant subjects for 8 of the 9 pain questions employed, with a significant (p = 0.043) difference between controls and Celliant for McGill question III. In neuropathic subjects, Celliant caused more pain reduction in 6 of the 9 questions, but not significantly. In non-neuropathic subjects 8 of 9 questions showed more pain reduction with the Celliant socks. CONCLUSION: Socks with optically modified PET (Celliant) appear to have a beneficial impact on chronic foot pain. The mechanism could be related to the effects seen with illumination of tissues with visible and infrared light. PCMID: 2680395. ***doi:10.1186/1472-6882-9-10***

STUDY DESIGN

This is a single center, prospective, comparative study to evaluate the performance of a upper torso garment containing 100% celliant fibers that emits far infared (FIR) from ceramic particles contained within the fibers in healthy subjects. The participating center will be:

1617 Broadway Avenue.
2nd Floor
Santa Monica, CA
90404

A total of 200 subjects will be recruited. It is expected that the site will take 3 to 4 months to recruit their subjects.

Subjects who give written informed Consent, meet all the inclusion / exclusion criteria and can adhere to the Visit schedule will be selected to participate in the study.

Inclusion Criteria

- Subjects greater than or equal to18 years of age
- Men and women between the ages of 18 and 60 years
- Able to understand and consent to the study
- Able to follow directions of the Study Coordinators and/or the Principal Investigator
- Able to complete the study
- Male or female subjects of any ethnic origin such that the balance across ages and among population groups is reflective of the site population

Exclusion Criteria

- Active smokers
- No history of cardiovascular disease
- No history of peripheral vascular disease
- Engaged in recreational drug use for the six months prior to the start of the study
- Eaten within two (2) hours of the study
- Consumed caffeine within four (4) hours prior to the study
- Consumed alcohol with forty-eight (48) hours prior to the study
- Subjects with any unstable medical or psychiatric problem
- Subjects who are pregnant or nursing mothers
- Subjects who are currently taking part in another clinical study or have taken part in a drug or device study, in the past month.

Potential Benefits

There are no direct benefits for the subjects taking part in this clinical investigation, but participation will help to evaluate the new test device.

If the device is marketed, there will be benefits to the relevant population as a whole.

Potential Risks

The potential risks to the subjects taking part in this clinical investigation with the new device are possible irritation to the skin caused by the attachment of the tcPO2 electrode to the skin, which is applied to the upper shoulder for 180 minutes while the tcPO2 measurement is being read. The risk is not from the product being tested but the measurement of the tcPO2.

Informed Consent

Written Informed Consent must be obtained from each potential subject prior to conducting any study assessments. The Investigator or authorized designee, must explain to each subject, the nature of the study and provide the subject with an IRB approved copy of the subject Consent Form to read. The subject should be informed that participation in the study is voluntary and by not consenting, it will not affect his/her right to the most appropriate medical or surgical treatment, or affect the doctor / patient relationship. The patient must have adequate time (at least 24 hours) to consider their participation in the study and be able to discuss with others and ask the Investigator any questions. If the subject agrees to participate, they must sign and

date a copy of the IRB approved Subject Consent Form. A copy of the signed and dated form will be given to the subject and the original signed copy will be kept by the Investigator and will be placed in the Subject Site Binder.

It is understood that informed consent is a matter entirely between the investigator and the subject. The Sponsor will only confirm that it has been provided.

Subjects are free to withdraw Consent at any time, irrespective of their initial consent. Subjects who withdraw Consent will be replaced.
Each subject must also give permission for the Sponsor's representatives to review their site records for the purpose of source document verification.

Withdrawal

Each subject will be encouraged to complete the full course of the study as outlined in the Clinical Investigation Plan. However, it is understood that the subjects are free to withdraw Consent at any time and irrespective of the reasons.

The Investigator may withdraw a subject form the study at any time for the following reasons:

a) An adverse event which the investigator feels is justification for early study termination, or
b) The patient's clinical condition worsens at any time during the trial.
In all cases, the reason for withdrawal must be documented in the CRF. When a patient withdraws early from the study, regardless of the reason, all required evaluations should be performed at the final visit.

During the course of the study, the study subject's details will be kept anonymous (specific study identification codes will be used for each study subject). Study subject data will only be made available to authorized staff of the study Sponsor, it's authorized representatives and regulatory authorities.

Early Study Termination

Investigators should understand that the study as a whole, or an individual investigator's role in the study, may be discontinued at any time by the Sponsor.

STUDY PROCEDURES

An overview of the study requirements has been presented. Below these requirements are presented in detail.

All Visits

Subjects will be instructed the night before their appointments not to eat within 2 hours of the study or consume coffee within 4 hours of the study.

VISIT 1 (Only visit)

Clinical Assessment

Upon arrival at the appointed time, the study staff will confirm the subject's eligibility and medical fitness for participation in the study. The following data will be collected on HC1-2 Form 1.

Blood Pressure 100-180 / 60-100 mm/Hg
Heart rate 60-100 bpm at rest.
Demographics height and weight
Oxygen saturation

Not recorded
Signs or symptoms of acute illness (Y/N)
Relevant Medical History
Relevant Smoking and Drug History
Use of caffeine and Alcohol
Eating within 2 hours

Set Up

The tcPO2 meter will be calibrated using a standard calibration procedure.

Prior to measuring subjects with be assigned according to the randomization schedule and a study number assigned. All data will be recorded using this number.

1. During the test each subject will wear 2 different upper torso garments one containing celliant and the other a replica containing no celliant. The order has been determine by the randomization schedule.

2. **Measurement of transcutaneous oxygen (tcPO2) & Pulse Oxymetry (SpO2).** Subjects are seated in a comfortable chair. Room temperature is maintained at a constant temperature and humidity over the duration of the study and recorded. Blood pressure, heart rate, gender and age are recorded prior to the start of the study. Skin temperature will be measured by an IR thermometer. A standard, portable pulse oxymeter is placed on the index finger of the non-dominant hand (Crucial Medical System, model CMS50DL). Blood pressure and heart rate are also assessed before and after the ninety(90) minute trial. Baseline measurements of tcPO2 are recorded continuously for 15 minutes prior to donning the active (Celliant®) garments to insulate against cross over effect. During this time, the subject wears regular street clothes. After the baseline period, subjects don a test garment and subsequent measurements of tcPO2 are recorded for ninety (90) minutes using a PeriFlux System 5000 (Perimed, Inc., Kings Park, NY, USA) and modified Clarke Electrodes (Radiometer America, Inc., Ohio, USA). Data are sampled for 5 minutes and recorded ever 30 minute using Perisoft Version 2.55 (Perimed America, Inc., North Royalton, Ohio, USA). The data is recorded in the data section of the subjects record. The continuous data is electronically stored until the study is completed. The mean and standard deviation will be recorded.

   Calibration. Any effect on sympathetic tone is controlled by heating the skin under the tcPO2 electrode to 45oC to maximize cutaneous vasodilation and the heated electrodes are allowed to equilibrate on the skin for ten (10) minutes (until stable values are achieved).

   Self-adhesive fixation rings are affixed and the probes attached thereto. A buffer (KCl) solution is applied to each fixation ring; the probe, a modified Clarke Electrode with a heating element and thermostat, is also utilized. Each module is calibrated to an exact partial pressure of oxygen (PO2) by recording barometric pressure, room temperature and relative humidity.

3. All data will be collected on HC1-2 form 2 as shown. Data will be collected and measured at 30, 60, 90 minutes from the start for each garment. The software will be used to provide the mean and standard deviation for a period of 5

minutes. Data with a standard deviation of great than 2.0 will not be used. Any data point rejected will be re-measured by the study monitor and recorded. During the re-measurement the center point may be moved by up to 5 minutes to allow more controlled reading.

4. At the end of the study the subjects will be released and compensated and all forms checked.

ADVERSE EVENTS

Definitions

An Adverse Event (AE) – is any untoward medical occurrence in a subject irrespective of its relationship to any of the devices under investigation.

A Serious Adverse Event (SAE) – is an adverse event that –

- Led to death
- Led to a serious deterioration in the health of a subject that –
    - Resulted in a life-threatening illness or injury
    - Resulted in a permanent impairment of a body structure or a body function
    - Required in-patient hospitalization or prolongation of existing hospitalization
    - Resulted in medical or surgical intervention to prevent a permanent impairment of a body structure or a body function
- Led to foetal distress, foetal death or a congenital abnormality or birth defect

An Adverse Device Effect (ADE) – is any untoward and unintended response to a medical device.

This definition includes any event arising from insufficiencies or inadequacies in the Instructions for Use or the deployment of the device. It also includes any event that is the result of user error.

A Serious Adverse Device Effect (ADE) – is an adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event, or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less opportune.

Severity Definitions – the following definitions will be used to determine the severity rating for all SAEs

- Mild – awareness of signs or symptoms, that does not interfere with the subject's usual activity, or is transient which resolves without treatment and with no sequelae
- Moderate – a sign or symptom which interferes with the subject's usual activity
- Severe – incapacity with inability to do work or usual activities

Collection and Reporting of Adverse Events

Any adverse event (clinical or significant laboratory abnormality) which occurs in association with the use of the Celliant garment product will be evaluated by the study investigator and reported. Special note will be made of skin reactions and possible allergy to the test materials. Adverse events not attributable to Celliant garment usage (e.g., lightheadedness due to fasting before the appointment) will be assumed to be not related to the study device.

Any concurrent illness which develops during the course of the study must be recorded on the CRF describing dates and times of onset and termination, the severity of the illness, and any action taken or treatment administered. A concurrent illness is defined as an adverse medical or pathological condition of known etiology that is unrelated to the study or the study medication.

It is the responsibility of the Investigator at the site to ensure that **all** adverse events (AEs, SAEs, ADEs and SADEs) occurring during the course of the study are recorded on the Adverse Event Form. Details recorded should include the following information:

- Study site identifier
- A description of the event
- The dates of the onset and resolution
- Any action taken
- The outcome
- The relationship to the device
- Whether or not the adverse event is serious
- Whether the adverse events arises from insufficiencies in the IFU
- Whether the adverse event arises from user error

Any adverse event that occurs during the course of the study should be treated by established standards of care that will protect the life and health of the subjects.

Adverse events can be observed directly by the site Investigator or staff, or can be spontaneously reported by the subject. In addition each subject should be questioned about adverse events at each study visit. In all cases it is the responsibility of the Investigator to collect the information and record as outlined above. All adverse events should be followed up for the duration of the study.

It is the responsibility of the Investigator to ensure that all adverse events which fall in to the categories of ADEs, SADEs and SAEs are reported to the Sponsor or designee on a Serious Adverse Events Form by email or FAX, as soon as possible after becoming aware of the event but no later than 24 hours. Details to be included on the SAE Form are as above.

Within the following 5 working days, the investigator must provide further information on the serious adverse event in the form of a written narrative. This should include a copy of the completed Serious Adverse Event Form, and any other diagnostic information that will assist the understanding of the event. Significant new information on ongoing serious adverse events should be provided promptly to the study sponsor.

The Investigator will keep copies of all SAE forms at then investigative site.
Details of ADEs, SADEs and SAEs should be forwarded to:

Seth Casden
1112 Montana Avenue, Suite 13
Santa Monica, CA 90403
Seth.casden@celliant.com
310-586-6828

and

James Wason Ph.D.
Maelor-Group, Inc
7 Village Woods Dr.
Amherst, NH 03031
jwason@maelor-group.com
603-672-4678

Hologenix LLC and / or their appointed designee will immediately conduct an evaluation of any Serious Adverse Event involving the investigational device, including review by the study investigator and an independent physician, if deemed necessary. If Hologenix LLC and / or the independent monitor and / or the investigators determine

that the event or event rate presents an unreasonable risk to a patient, they will terminate all investigations, or parts of investigations presenting that risk as soon as possible. Termination shall occur not later than five working days after Hologenix LLC makes this determination and not later than fifteen days after Hologenix LLC or its appointed designee first receives notice of the event(s).

It is the responsibility of the Investigator to comply with the safety reporting requirements of the appropriate IRB, and the responsibility of the manufacturer / sponsor to comply with any safety reporting requirements of the FDA if required. Copies of all correspondence with the IRB and the FDA must be filed in the Investigator Site File.

It is the responsibility of the Sponsor or appointed designee to inform all other participating sites in writing, of any Serious Adverse Events involving the investigational device, that have been reported to the Sponsor.

STUDY PRODUCT

Device Description

During the testing, each subject will wear two different garments. The upper torso garments will contain either 100% Celliant fibers (active) or one containing no Celliant material only polyester, which will serve as a control.

The upper torso garment is a short sleeve tee shirt with a round neck.

Packaging and Labeling

The active (100% Celliant) and the Placebo control garments are identical except a small difference in natural color. They have the same feel and texture. Neither the Subjects nor the Investigator could distinguish among the active and control garments.

Device Storage

All test materials will be stored securely at room temperature (18 to 30 ˚C).

Device Accountability

The investigative site will inventory all test materials supplied, and maintain a log of material usage throughout the study. All unused materials will be returned to the study Sponsor upon completion of the study.

Device Training

Not Required

DATA ANALYSIS AND MANAGEMENT

All data collected on the Case Report Forms will be 100% verified against the Patient's Medical Records by the monitoring staff. The data from the CRFs will be entered in to a validated Database. Comparison of data will be performed and any resulting discrepancies adjudicated against the CRFs. After comparison is complete the data will be subjected to quality control checks and used to raise data queries. All data queries will be resolved at site with the assistance of the monitoring staff.

On resolution of all data queries, the database will be closed and study data will be prepared for statistical analysis. All adverse events will be subject to quality control checks.

Any data existing for subjects who withdraw voluntarily or are withdrawn from the study, will be used in the study analysis, unless the subject states this is contrary to their wishes. The inclusion of partial data will be documented in the final report.

All data relating to study specifics will be summarized using descriptive statistics. Frequency tables will be prepared for nominal and ordinal data. Where meaningful, the results will be presented graphically. Summary statistics for the description of course and change parameters of location and dispersion such as mean, median, range, quartile, standard deviation and coefficient of variation will be calculated.

The overall incidence of each adverse event will be tabulated. A critical analysis of the data, including the adverse events, will be performed.

STATISTICAL ANALYSIS

Sample Size

Data will be obtained on a minimum of 161 subjects at this only sites. It is anticipated a total subject population of 200 will be needed to complete this study.

Statistical Analysis

This study was a single blind, placebo controlled, within subject controlled study design. A repeated measures ANOVA was employed to test the equality of the means between the control garment and the active (100% Celliant) garment.

Further analysis may be conducted as needed or to determined by the Chief Investigator and / or Sponsor.

DATA REPORTING

A final report on the results of the study will be complied by Hologenix LLC and approved and signed off by the Investigator. A copy will be made available to the Investigator.

Copies of the final report may be provided to the FDA if required and the relevant Research Ethics Committees.

PUBLICATION OF RESULTS

Hologenix LLC commits to communicating or otherwise making available for public disclosure the results of the study regardless of the outcome. Public disclosure includes publication of a paper in a scientific journal, abstract submission with a poster or oral presentation at a scientific meeting, or by other means.

At the end of the study, one or more manuscripts for publication will be prepared in collaboration between Investigator(s) and Hologenix LLC. Hologenix LLC will not suppress or veto publications, however Hologenix LLC reserves the right to postpone publication and / or communication for a short time to protect intellectual property.

However, before publication the Sponsor must review any manuscript or abstract. This review is necessary to prevent premature disclosure of trade secrets or otherwise patent-protected material and is in no way intended to restrict publication of facts or opinions formulated by the investigators. Alterations in the manuscripts will only be made in agreement with the investigators.

REGULATORY, ADMINISTRATIVE AND CONTRACTUAL INFORMATION

Sponsor's Responsibilities

The Sponsor is responsible for providing Investigators with the information and training they need to conduct the clinical study properly and in accordance with the Clinical Investigational Plan. The Sponsor must ensure proper monitoring of the Clinical Study, that IRB approval is obtained and remains current, and that the IRB are informed of significant new information about the clinical study as required.

This information should include the following:

- A current signed copy of the Clinical Investigational Plan and protocol and any amendments
- A signed copy of the signed Clinical Investigation Agreement
- All information pertaining to IRB review and approval of this clinical study including a copy of the IRB, Certificate of Approval Letter and a blank copy of the approved Subject Information and Consent Form.
- All information pertaining to FDA notification of this clinical study including a copy of the FDA response.
- Copies of current signed and dated Curriculum Vitae's of the Investigator and all relevant site personnel

CIP / Protocol Amendments

Any change or addition to this Clinical Investigation Plan requires a written amendment which must be approved by the Sponsor before the change or addition can be considered effective. Where IRB approval is required, the Investigator must submit the appropriate documentation to the main REC, and obtain written approval for the amendment before it can be implemented at the investigative site(s). A copy of the written approval must be provided to the Sponsor. Amendments will be circulated promptly to all investigators by the Sponsor.

CIP / Protocol Deviations

A Deviation is a failure to comply with the requirements specified within this Clinical Investigational Plan without adequate justification. Examples of deviations may include enrolment of a study patient who does not meet all of the inclusion / exclusion

criteria specified in the Clinical Investigation Plan or missed study visits without documentation.

All deviations must be documented on the appropriate forms and reported to the Sponsor. All deviations will be reviewed and assessed for their impact on patient safety by Hologenix LLC.

The investigators shall conduct this clinical study in accordance with this Clinical Investigation Plan and any conditions of approval / notification imposed by the IRB. Failure to comply with and / or inability to meet these regulations may jeopardise further participation of the Investigator or Investigative Site in this and future clinical studies.

Investigator Brochure

Not used

Monitoring Procedures and Source Documents

A clinical monitor will be appointed by the Sponsor for each investigative site. The monitor is responsible for assessing the Investigator's compliance with the Clinical Investigation Plan and for performing Source Document Verification. The monitor is also responsible for reporting to the Sponsor on the progress of the Clinical Investigation.

Source documents include all information, original records of clinical findings, observations, or other activities in a clinical investigation necessary for the reconstruction and evaluation of the trial e.g patient's hospital records, clinical charts, laboratory reports, subject diaries or evaluation checklists, device accountability records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate and complete, and at medico-technical departments involved in the clinical investigation,

At the Initiation Visit the monitor will review the Clinical Investigation Plan, Case Report Forms and all associated study documentation and procedures with the Investigator and study personnel. During the course of the study, the monitor will maintain regular contact with the investigative site and conduct on-site monitoring visits and source data verification on a regular basis to ensure compliance with this clinical Investigation Plan. The number and frequency of the visits will be determined

by the rate of patient recruitment and complexity of the study. During monitoring visits the monitor will require access to patient medical records in order to carry out source document verification to ensure all data recorded in the study records is accurate and complete, and the data can be submitted to the sponsor in a timely manner and to verify that the investigative site facilities continue to be adequate. Throughout the study the monitor must check that all adverse events have been collected, recorded and reported as required and discuss the implication of all serious adverse events with the site Investigator.

The Investigator must set aside a reasonable amount of his / her time for these visits and the time of the relevant site personnel.

Quality Assurance Auditing and Inspection

During the course of this Clinical Investigation, the Sponsor will appoint Quality Assurance personnel to provide audit of the administration and conduct of the study, both at the study sites and at the Sponsor's co-ordination centre. These procedures are in accordance with Good Clinical Practice (GCP) to ensure that complete, accurate and timely data are collected, that the Clinical Investigational Plan requirements are followed and that all complications and adverse events are reported in a timely manner. The FDA may also conduct audits / inspections.

The Investigator and the relevant site personnel must set aside a reasonable amount of his / her time for study related monitors, audits and inspection by the Sponsor, REC, government regulatory bodies, and institution compliance and quality assurance groups, and provide adequate access to all study related documents (e.g. source documents, regulatory documents, data collection instruments, study data etc).

Data Recording and Reporting

All subjects recruited to the study will be identified by a unique site and subject identification number in order data collected on them will be anonymysed. The investigator will maintain a confidential subject identification code list of all subjects enrolled in the study (by name and subject number). The list will be maintained at the site.

The sites will adhere to all appropriate national and local regulations to protect health information and maintain patient confidentiality.

All data generated during the course of this Clinical Investigation will be recorded on standardised Case Report Forms. CRFs should be completed as soon after the patient visit as possible and only the Principle Investigator or the study coordinator at each site may sign and date the designated pages of the CRF.

CRF pages should be completed according to the following guidelines:

- All forms are to be completed in black or blue pen.
- All evaluations and procedures indicated in the Clinical Investigation Plan must be performed.
- Erasures on the Case Report Form are not to be made. Any errors are should be crossed through with one line and the correct data entered above the erroneous information. All changes must be Initialed and dated.
- The unique site number and subject number must be filled in on each page at the time that page is completed.
- All dates are to be recorded as follows:
  dd/mmm/yyyy For example - 01/APR/2002
- All times are to be recorded in 24 hour clock format; for example:
  12 Noon = 12:00; 12 Midnight = 00:00
- All questions on the Case Report Forms must be completed. If a subject does not complete the study or completes the study before using all Case Report Form pages, unused pages are to be crossed through, and 'patient no longer in study' is to be written; the page is then to be signed and dated
- Additional follow up data will be recorded in appropriate study documentation.
- Any assessments not carried out must be completed as ND (not done). Where this constitutes a Clinical Investigation Plan deviation / violation this must be documented.

Maintenance, Retention and Archiving of Study Records

Investigators are to maintain all source documents required by regulation, including diagnostic test reports, laboratory results, completed case report forms, supporting medical records and informed consents. The source documents will be referenced during regular monitoring visits to verify the information documented on the case report forms.

The investigator will retain records for a period of five years following the date a marketing application is approved for the study device for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for this indication, until five years after the investigation is discontinued.

Arrangements for archiving of all study documentation will be discussed between the Sponsor, investigator and the CRO.

Investigator and Site Personnel Training

All key site personnel must undergo GCP training in advance of the Initiation Visit unless they have done so already. Such training will be documented.

In addition, training on the investigational device will be provided in advance of recruitment of the first patient by the Sponsor. A record of all device training will be maintained.

Study Termination

The study will be terminated upon completion of follow-up of the last patient recruited. Any decision to either terminate the study early or to increase the patient numbers or follow-up periods will be by mutual agreement between Sponsor, the Investigators and approval by the IRB.

Investigator Responsibilities

The Investigator is responsible for ensuring that this clinical study is conducted according to the Clinical Investigation Plan, the Clinical Investigation Agreement, all conditions of appropriate IRB approval, and applicable national regulations.

Written confirmation of IRB approval, and any relevant local approvals must be provided to Hologenix LLC prior to the enrolment of any subject in the clinical study.

The Investigator is responsible for ensuring that written Informed Consent is obtained from all subjects prior to any diagnostic tests or treatments that are outside the standard course of treatment that would be followed if this patient were not being considered for enrolment in this clinical study. The Investigator is responsible for informing subjects that Hologenix LLC authorized designee [the study monitor of Maelor Group, Inc.] or authorized representatives of the FDA may have access to their medical records for the purpose of the study. Subjects must be informed that they are free to refuse to participate in this clinical study without any impact on their medical treatment and that if they choose to participate, they may withdraw at any time without prejudice to future care. The IRB approved Informed Consent must be signed prior to study participation.

While awaiting for approvals, the Investigator may discuss with a study subject their interest in participating in the clinical study, but shall not request the written informed consent nor allow any patient to participate in the clinical study before all relevant approvals are received.

Upon completion of the clinical study or the Investigator's participation in the clinical study, or at the Sponsor's request, the Investigator must return to Hologenix LLC, any remaining devices.

It is the responsibility of the Investigator to maintain complete, accurate and current study records. Each Investigator will be provided with an Investigator Site File, Case Report Forms and other associated study specific documentation by the Sponsor. Such records will be maintained during the course of the clinical study and for five years following the date on which the study is terminated or completed. Investigator records shall include the following:

- A current copy of the Clinical Investigational Plan and Protocol and any amendments
- A copy of the signed Clinical Investigation Agreement
- All information pertaining to IRB review and approval of this clinical study including a copy of the IRB Certicate of Approval and a blank copy of the approved Patient Information and Consent Form on hospital headed paper.
- Copies of current signed and dated Curriculum Vitae's of the Investigator and all relevant site personnel
- Signed Informed Consent Forms and copies of all completed Case Report Forms and supporting documents (laboratory reports, reports of diagnostic tests, medical records etc.)
- Records of all reports and information pertaining to unanticipated device events
- Accountability records of receipt, use and disposition of all investigational devices and other study materials.

ETHICAL CONSIDERATIONS

The Clinical Investigation will be performed in accordance with the following standards and guidelines:

- Declaration of Helsinki on Biomedical Research involving Human Subjects (52nd World Medical Association General Assembly Edinburgh Revision, October 2000)

- International Conference on Harmonisation Good Clinical Practice guidelines (ICH GCP)

- European Standard of BS EN ISO 14155 Parts 1 & 2 – "Clinical Investigations of Medical Devices for Human Subjects"

- ISO 14971:2000, Medical devices – Application of risk management to medical devices

Before the study can begin the Investigator must have written evidence of Favourable Opinion for the Clinical Investigation Plan and associated relevant documentation from the appropriate Research Ethics Committee and must have supplied the following for review:

- Clinical Investigation Plan
- Patient Information Sheet and Consent Form
- Investigator's Curriculum Vitae

Once approval has been granted, the Investigator is responsible for ensuring that he / she complies with the terms of the approval, namely with adverse event reporting, notification of amendments, interim and final reports on the progress of the study.

Written responses from the relevant IRB and any other local approvals must also be obtained prior to starting the study.

Informed Consent

Written Informed Consent must be obtained from each potential patient prior to conducting any study assessments. The Investigator or authorized designee, must explain to each subject, the nature of the study and provide the subject with an IRB approved copy of the Patient Information Sheet / Consent Form to read. The subject should be informed that participation in the study is voluntary and by not consenting, it will not affect his/her right to the most appropriate medical or surgical treatment, or affect the doctor / patient relationship. The patient must have adequate time (at least 24 hours) to consider their participation in the study and be able to discuss with others and ask the Investigator any questions. If the patient agrees to participate, they must sign and date a copy of the IRB approved Patient Information Sheet and Consent Form. A copy of the signed and dated form will be given to the subject and the original signed copy will be kept by the Investigator and placed in the Patient's medical Records. A further copy will be placed in the Investigator Site File.

It is understood that informed consent is a matter entirely between the investigator and the subject. The Sponsor will only confirm that it has been provided; no copy will be taken for use by the company.

Subjects are free to withdraw Consent at any time, irrespective of their initial consent. Subjects who withdraw Consent will be replaced.

Each subject must also give permission for the Sponsor's representatives to review their hospital records for the purpose of source document verification.

During the course of the study, the study subject's details will be kept anonymous (specific study identification codes will be used for each study subject). Study subject data will only be made available to authorized staff of the study Sponsor, it's authorized representatives and regulatory authorities

Disclosure and Confidentiality

By conducting the study, the Investigator agrees that all information provided by the Sponsor will be maintained by the Investigator and the site personnel in strict confidence. It is understood that the confidential information provided to the Investigator will not be disclosed to others without authorization from the Sponsor.

REFERENCES

1.

APPENDICES

The Patient Information Sheet
The Patient Consent Form
Declaration of Helsinki