AffloVest Comparative Study for Air Flow in the Lungs

Sponsor:	**International Biophysics Corporation** **2101 E. St. Elmo Rd Suite 275, Austin, TX 78744 USA** **512-814-0046** **Geoff Marcek, VP Engineering and Quality**
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Clinical Laboratory(ies):	**N/A**
Study Product:	**International Biophysics AffloVest** **Hill-Rom Monarch**
Protocol Number:	**2018-01** **Initial version date: 07/03/2018** **Amendment #: N/A** **Amended date: N/A**

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List of Abbreviations

IBC – International Biophysics Corporation

HFCWO – High Frequency Chest Wall Oscillation

FEV1 – Forced Expiratory Volume is the volume (L) of air measured in the first one (1) second of the FVC test

FVC – Forced Vital Capacity shows the volume (L) of air a person can forcefully and quickly exhale after taking a deep breath

PEF – Peak Expiratory Flow shows the maximum airflow (L/min) during a forced expiration beginning with the lungs fully inflated

TV – Tidal Volume describes the volume (L) representing the normal volume of air displaced between normal inhalation and exhalation when extra effort is not applied

FEF25 – 75% - The mean forced expiratory flow (L/s) over the interval from 25% to 75% remaining of the Forced Vital Capacity

STUDY SUMMARY

Title	*AffloVest Comparative Study for Air Flow in the Lungs*
Protocol Number	*2018-02*
Phase	*Device, Phase I*
Methodology	*The study will be broken into one (1) arm:* - *AffloVest® & Monarch™* *Within each arm, the order of products will be also randomized.* *Baseline spirometry (FEV1, FVC, PEF, FEF25-75% and TV) will be taken at the beginning, middle and end of each subject trial without any device on the subject.* *A product (AffloVest or Monarch vest) will be placed onto subject and turned ON to the highest frequency and intensity settings, then the subject will be given a certain period. The spirometry measurements will then be repeated. The product will be removed and the subject allowed a recovery period, then the other product will be placed on the subject, turned ON and spirometry measurements repeated. A short questionnaire will also be included.*
Study Duration	*Approximately one (1) month*
Study Center(s)	*Pulmonary Disease Specialists, PA (d/b/a PDS Research)* *1121 N. Central Avenue* *Kissimmee, FL 34741*
Objectives	*Investigate impact of high-frequency chest wall oscillation therapy on spirometry values (FEV1, FVC, PEF, FEF25-75% and TV) during use of different products and comparing to baseline values to determine any significant variation in air flow in the lungs.*
Number of subjects	*10*
Main Inclusion and Exclusion Criteria	*Inclusion: Healthy subject, ages 18 – 50* *Exclusion: Non-ambulatory, diagnosed neuromuscular disorder, currently using any type of oscillation vest therapy, diagnosed co-morbid condition (i.e. lung cancer, other lung disorder or disease), currently enrolled in a medical research study, non-English speaking, presence of the following active implantable devices: pacemakers, neurostimulators, infusion pumps, circulatory support devices, implantable cardioverter defibrillators (ICD's), cochlear implants, presence of head and/or neck injury that has not yet been stabilized, presence of active hemorrhage with hemodynamic instability*
Study product, Dose, Route, Regimen	*The International Biophysics AffloVest® and Hill-Rom Monarch™ will be included in the study.* *Each subject will be properly fitted with a product and then the product will be turned ON. The subject will wear the product for a brief time before taking spirometry readings. The subject will then switch to a different product after a recovery period and the procedure will be repeated. Each subject will then be asked to fill out a short questionnaire.*
Duration of subjects participation	*One (1) day, approximately two (2) hours per subject*

1 Introduction

This document is a clinical research protocol and the study will be conducted in accordance with this protocol. The study will be conducted in accordance with Good Clinical Practice Standards and all applicable regulatory requirements.

1.1 Background

High Frequency Chest Wall Oscillation (HFCWO) is a therapy that has been proven to be effective for many years[1] and is used for airway clearance for patients that have difficulty mobilizing secretions in the lungs. One method to accomplish HFCWO therapy utilizes air bladder compression of the torso to create oscillation in the lungs. Air bladder companies claim "The assumption is that the effectiveness of the treatment can be measured in the mouth airflow which is believed to be the indicator of the efficacy of the therapy"[2]. Air bladder devices claim that they create air shearing forces in the lungs by increasing air flow in the lungs by shaking and compressing the entire torso to supposedly generate airflow in the lungs to mobilize secretions. Moreover, air bladder companies have claimed that they create more air flow in the lungs then the newer oscillation technology[3]. The purpose of this study is to measure and compare airflow actually in the lungs while using two different motorized oscillation HFCWO technologies to determine the actual air flow in the lungs. Lung airflow will be measured using standard pulmonary spirometry clinical equipment. The results will be collected and analyzed.

1.2 Investigational/Study Product

The devices under study are all High-Frequency Chest Wall Oscillation (HFCWO) devices which are summarized in the following table. All these devices are Class II medical devices in the USA with 510(k) clearance from FDA.

Table 1 – Study Product

Manufacturer and Brand	510(k) Number	Indications for Use
International Biophysics Corporation AffloVest	K122480	"The International Biophysics Corporation AffloVest is intended for promoting airway clearance and improvement of bronchial drainage by enhancing mobilization of bronchial secretions where external manipulation of the thorax is the physician's choice of treatment"
Hill-Rom Monarch	K163378	The Monarch Airway Clearance System is intended to provide Airway Clearance Therapy and promote bronchial drainage where external manipulation of the thorax is the physician's choice of treatment. It is indicated for patients having difficulty with secretion clearance, or the presence of atelectasis caused by mucus plugging. The Monarch Airway Clearance System is intended to be used in the Home Care environment by patients,15 years and older.

The devices are similar in intended use, with similar modes of operation. Both products utilize mechanical oscillation of the chest wall to mobilize secretions.

Patients are prescribed these types product by a physician, along with the treatment regimen.

1.3 Preclinical Data

[1] Warwick et al 1991 Pediatric Pulmonology

[2] Analysis of High Frequency Chest Compression Devices and Modeling. A DISSERTATION SUBMITTED TO THE FACULTY OF THE GRADUATE SCHOOL OF THE UNIVERSITY OF MINNESOTA BY Yong Wan Lee IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE DEGREE OF DOCTOR OF PHILOSOPHY/ELETRICAL ENGINEERING Bruce F. Wollenberg, Thomas J. O'Dea December 2007

[3] Independent lab testing analyzed and compared average airflows at the mouth generated by high frequency chest wall oscillation (HFCWO) therapy in 10 subjects using home care garments Airflows measured at commonly prescribed medium pressures (50% of maximum) at multiple therapy frequencies (5, 10, 15, and 20 Hz). Test data and reports on file at Hill-Rom, Inc

Preclinical studies of the AffloVest product have been performed by IBC to demonstrate substantial equivalence of the device to other similar devices (predicates). The preclinical studies including electrical safety and EMC testing, testing for compliance with home-healthcare standards for electrically powered devices, human factors and usability testing, software validation and system verification testing.

Preclinical data has been gathered by the other products but is confidential to those manufacturers. A summary of the preclinical test data is included in the 510(k) summary for each device.

Preclinical data regarding these devices is not expected to have clinical significance nor relevance to this trial.

1.4 Clinical Data to Date

There is no clinical data to date regarding the spirometry measurements to be taken in this study.

There are no known potential risks to subjects using the AffloVest. The product has been marketed since 2014 with zero (0) adverse events reported in that timeframe.

IBC does not have any adverse event data on the competitor products, but these types of devices are widely regarded as safe.

The study provides no foreseeable benefits to the subjects.

1.5 Dose Rationale

These devices are typically prescribed to be used daily for 20 – 30 minutes one (1) or two (2) times daily at home.

The devices settings have been specified as the highest intensity and frequency for each device to ensure consistency across all devices. The approach taken will simulate spirometry values for patients during normal use of these products.

1.6 Risk/Benefits

This study poses no foreseeable risk to the subjects. The study provides no foreseeable benefits to the subject. These devices are generally considered safe with low incidence of adverse events in normal use. The study activities are not expected to impart greater than minimal risk to the subjects.

All data collected will remain confidential. Only the investigators involved with this study will have access to it. In order to maintain confidentiality, all records will be kept in locked filing cabinet(s) at the investigator site(s). If the results of the study are published, the data will be reported collectively without mention of any subject's identity, thereby ensuring subject anonymity.

2 Study Objectives

The purpose of this trial is to investigate the potential relationship between the use of common HFCWO devices to measure air flow in the lungs in healthy subjects using standard spirometry techniques.

3 Study Design

3.1 General Design

This pilot study has been designed as follows:

- One (1) arm
- This is a pilot investigational study, based on the study design there are no blinding or randomization measures taken. It is expected that the degree of bias shall be low based on the subjective endpoints under study. Each subject shall serve as their own control as

baseline spirometry measurements will be performed at the beginning and end of the visit.

- Each subject will participate for a period of approximately two (2) hours.
- There is no subject follow-up, all measurements will be performed within the initial subject visit. At the end of the visit, each subject shall be required to complete a brief survey regarding their experience.

3.2 Primary/Secondary Endpoints

The following primary and secondary endpoints are to be analyzed in the study:

Primary endpoints:

1. Difference in spirometry measurements (FEV1, FVC, PEF, FEF25-75% and TV) between the AffloVest device and Monarch devices.

Secondary endpoints:

1. Survey results using a Likert scale related to:
    a. Subject opinion on using each device on a daily basis
    b. Subject opinion on lifestyle fit for each device
    c. Subject opinion on lifestyle obtrusiveness of each device
    d. Subject opinion on mobility during use of each device
    e. Subject opinion on noise level of each device
    f. Subject opinion on compliance with treatment of each device

4 Subject Selection and Withdrawal

4.1 Inclusion Criteria

The following subjects shall be eligible for study enrollment:

1. Healthy subject, ages 18 – 50

4.2 Exclusion Criteria

The following subjects shall be ineligible for study enrollment:

1. Non-ambulatory
2. Diagnosed neuromuscular disorder
3. Currently using any type of oscillation vest therapy
4. Diagnosed co-morbid condition (i.e. lung cancer, other lung disorder or disease)
5. Currently enrolled in a medical research study
6. Non-English speaking
7. Presence of the following active implantable devices:
    a. Pacemakers
    b. Neurostimulators
    c. Infusion pumps
    d. Circulatory support devices
    e. Implantable cardioverter defibrillators (ICD's)
    f. Cochlear implants
8. Head and/or neck injury that has not yet been stabilized.
9. Active hemorrhage with hemodynamic instability

4.3 Subject Recruitment and Screening

Subjects will be recruited in accordance with the investigator standard operating procedure (SOP) for subject recruitment.

Based on the small number of subjects required and short study duration, it is expected that the following methods will be used for subject recruitment:

- Internet/company website
- Private practice database

Subjects will be screened by the investigator according to the standard operating procedure (SOP) in place at the investigator's site.

4.4 Early Withdrawal of Subjects

Subjects may choose to withdraw from the study at any time, for any reason without penalty or loss of benefit.

Due to the short duration of the subject participation in the study, there is only one (1) foreseeable scenario in which a subject could withdraw prior to completion of the study:

- A subject might withdraw from the subject if use of the device(s) is uncomfortable. Some patients could be claustrophobic and find the treatment uncomfortable.

For any subject that withdraws prior to completion of the study for this reason, the data will be omitted from the final analysis. The subject may be replaced with another subject to ensure that the full sample size is obtained.

Abrupt termination of study treatment is not expected to affect subject safety, therefore no transition procedures are required.

5 Investigational Product

5.1 Description

AffloVest Oscillation Vest - The product is a home-use device and appears as a wearable vest with accessories (i.e. battery, A/C power supply, etc.)

Hill-Rom Monarch – The product is a home-use device and appears as a wearable vest with accessories (i.e. battery, A/C power supply, etc.)

5.2 Treatment/Dosing Regimen

Each subject shall perform the following regimen:

1. Pre-baseline spirometry measurements (without device on patient)
2. Placement of either AffloVest or Monarch on subject, turn device ON, allow subject to acclimate to device for five (5) minutes
   a. Repeat spirometry measurements
3. Remove device from subject and allow subject to recover for fifteen (15) minutes
4. Interim-baseline spirometry measurements (without device on patient)
5. Placement of other product (either AffloVest or Monarch, whichever was not used previously) on subject, turn device ON, allow subject to acclimate to device for five (5) minutes
   a. Repeat spirometry measurements
6. Remove device from subject and allow subject to recover for fifteen (15) minutes
7. Post-baseline spirometry measurements (without device on patient)

5.3 Method for Assigning Subjects to Treatment/Dosing Groups

Subjects shall be assigned according to the following in order of study enrollment. This approach shall control for any effect from which device is used first by alternating the device order.

Subject Number	First Device	Second Device
1	AffloVest	Monarch
2	Monarch	AffloVest
3	AffloVest	Monarch
4	Monarch	AffloVest
5	AffloVest	Monarch
6	Monarch	AffloVest
7	AffloVest	Monarch
8	Monarch	AffloVest
9	AffloVest	Monarch
10	Monarch	AffloVest

5.4 Subject Compliance Monitoring

No compliance monitoring shall be required for this trial, it is expected that each subject shall participate for approximately 1 – 2 hours with no further follow-up required.

5.5 Prior and Concomitant Therapy

There are no restrictions regarding medication(s) and/or treatments before and/or after the trial.

5.6 Packaging, Receiving, Storage, Dispensing and Return

The devices will be shipped to the investigator in standard packaging and standard storage procedures shall be employed. The devices will be kept in a secured area.

At the completion of the study, all devices will be returned to the sponsor.

6 Study Procedures

The study procedure shall be broken down into several phases, as described below:

1. Phase 1 – Subject enrollment

    - Subjects shall be enrolled based on the plan presented previously in the protocol. Informed consent will be required from each subject.
    - General demographic data information (age, gender, race, ethnicity, height, weight, comorbidities) will be collected for each subject.

2. Phase 2 – Initial Spirometry measurements

    - After subject enrollment, the subject will be fitted with both an AffloVest product and Monarch vest
    - An initial spirometry baseline will be taken using standard spirometry equipment and according to standard spirometry procedures, without any device on the subject.
    - Depending on the subject enrollment number, the appropriate product will be placed onto the subject.
    - The device will be turned on to the maximum frequency and intensity settings.
    - The subject will be allowed five (5) minutes to acclimate to the device.
    - The spirometry measurements will then be repeated in the same manner as above
    - The device will be turned OFF and removed, and the subject will be allowed fifteen (15) minutes recovery
    - An interim spirometry baseline will be taken using standard spirometry equipment and according to standard spirometry procedures, without any device on the subject.
    - Depending on the subject enrollment number, the second appropriate product will be placed onto the subject.
    - The device will be turned on to the maximum frequency and intensity settings.
    - The subject will be allowed five (5) minutes to acclimate to the device.
    - The spirometry measurements will then be repeated in the same manner as above
    - The device will be turned OFF and removed, and the subject will be allowed fifteen (15) minutes recovery
    - A final spirometry baseline will be taken using standard spirometry equipment and according to standard spirometry procedures, without any device on the subject

3. Phase 3 – Survey

    - The subject will be provided a brief survey to complete

No interim analysis shall be completed.

7 Statistical Procedures

7.1 Sample Size Determination

This is a pilot investigational trial. No statistical analysis was performed in the generation of the sample size, however similar studies for these types of devices were reviewed to determine an adequate sample size.

7.2 Statistical Methods

The metrics for the study shall be calculated as follows:

- Subject baseline values: An average of the pre-baseline, interim-baseline and post-baseline measurements shall be taken for FEV1, FVC, PEF, FEF25-75% and TV for each subject
- Comparison of the subject baseline values will be made with their values while using each device. A Student's t-test will be used to look for statistically significant differences at the 95% confidence level

Any deviation(s) from the original statistical plan shall be communicated to the IRB and the protocol shall be revised, if required.

7.3 Subject Population(s) for Analysis

All eligible subjects shall be included in the analysis.

8 Safety and Adverse Events

8.1 Definitions

The study shall be monitored for Unanticipated Problems and for Adverse Events by the investigator and sponsor.

An Unanticipated Problem shall be defined as:

- Any issue arising during the study involving potential risk(s) to the subjects, which are not considered adverse events.
- Unanticipated Problems shall be reported to the IRB and sponsor within 7 calendar days, unless as described below:
    - Interim analysis, safety monitoring report, publication in literature or other information that indicates an increase in the frequency or magnitude of a given harm, uncovers a new risk, or provides more information about the benefits of the human research.
    - Change in FDA labeling or withdrawal of the device from the market
    - Protocol deviation that harmed participants or indicates participants might be at increased risk of harm. If the protocol deviation was made in order to eliminate an apparent immediate hazard to a participant, the investigator must submit the information to the IRB and sponsor within 24 hours.
    - Complaint of a participant that indicates participants or others might be at increased risk of harm or at risk of a new harm.
    - Finding of Non-Compliance or allegation of Non-Compliance.
    - Protocol deviations: Failure to follow the protocol due to the action or the inaction of the investigator or staff. Exception – If the protocol deviation was taken in order to eliminate an apparent immediate hazard to the participant, the investigator must report the information to the IRB and sponsor within 24 hours.
    - Breach of confidentiality – Must be reported to IRB and sponsor within 24 hours
    - Change to protocol taken without prior IRB review to eliminate an apparent immediate hazard to a participant, must be reported within 24 hours
    - Incarceration of a participant in a protocol not approved to enroll prisoners
    - Complaint of a participant that cannot be resolved by the research team

An Adverse Event shall be defined per 21 CFR Part 803. Any potential adverse event shall be reported to the IRB and sponsor within 7 calendar days, unless the Adverse Event could be considered reportable as a 5-day report, in which case the notification must be made within 24 hours.

- An event that reasonably suggests that a device has or may have caused or contributed to a death or serious injury
- An event that reasonably suggests that a device has malfunctioned and that the device or similar device would be likely to cause or contribute to a death or serious injury if the malfunction were to recur

- A serious injury/serious illness is one that (1) is life threatening, (2) results in permanent impairment of a body function or permanent damage to body structure, or (3) necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

8.2 Recording and Reporting of Adverse Events

All observed or volunteered adverse events, unanticipated problems involving risks to subjects, and serious or continuing noncompliance with the federal regulations or the requirements or determinations of the IRB will be reported. Investigators will pursue and obtain information adequate to determine the outcome of each adverse event and to assess whether it meets the criteria for classification as a serious adverse event requiring immediate notification to the sponsor, Investigational Review Board and FDA. Sufficient information will be obtained by the investigator to determine and assess the causality of adverse event. This study will be reviewed at set checkpoints, as specified in the research plan, by the principal investigators.

The sponsor has a duty to report adverse events to FDA per 21 CFR Part 803 and maintains SOP's detailing these requirements. Any adverse event reported to FDA by the sponsor related to a study subject will also be transmitted to the IRB.

8.4 Randomization Codes and Unblinding Procedures

There are no randomization and/or blinding procedures in this trial.

8.5 Stopping Rules

After any Unanticipated Problem and/or Adverse Event, a review shall be performed to determine whether the study should be terminated for individual subject(s), parts or all of the trial. This shall be determined by the investigator.

8.6 Medical Monitoring

No additional medical monitoring shall be performed throughout the duration of study.

8.7 Study-Related Injuries

Adverse events which are reported during execution of this study shall be handled and reported to relevant authorities in accordance with IBC's internal standard operating procedures.

IBC maintains suitable product liability insurance coverage in the event of any claims resulting from a study-related injury.

9 Data Handling and Record Keeping

9.1 Confidentiality

All data collected will remain confidential. Data will be stored securely under the subject's study identification number. All clinical data, images and surgical/procedural data will be de-identified prior to any in-house or public presentation of data or images. Coded data will only be released to those listed as study investigators or support staff. Paper data records will be stored in locked file cabinets in a locked office. All electronic research data will be stored on a researcher database that is password protected and encrypted. The principal investigator, sub-investigators, IRB, the Food and Drug Administration and any applicable regulatory agencies will have access to the study records upon request. If the results of this study are published, the data will be reported collectively without mention of any subject's identity, thereby ensuring subject anonymity.

Standard confidentiality safeguards will be applied, including keeping paper records in locked files, use of electronic security processes (passwords, etc.) for access to electronic data, and limiting access of records to only personnel directly involved in the study

9.2 Source Documents

The following documents shall be considered source documents:

- Subject spirometry measurement data
- Subject survey

9.4 Records Retention

The data and associated identifiers will be kept for up to 5 years in a locked facility accessible only to designated personnel, at which time the data will be destroyed per investigator policy.

10 Study Monitoring, Auditing, and Inspecting

The study will be monitored on an ongoing basis by the investigator. Due to the short nature of the study, no periodic study monitoring, auditing and/or inspecting is planned.

11 Ethical Considerations

The Principal Investigator will manage and administer the study and ensure that the established procedures and protocol for protection of human subjects and IRB requirements are followed in compliance with the Federalwide Assurance for the Protection of Human Subjects, NIH, FDA and OHRP requirements. The principal investigator is an experienced researcher and maintains well-established controls and policies for safeguarding subjects. International Biophysics Corporation also abides by written policies of clinical study ethics and patient protection.