Study Sponsor / Study Funded by: **Anesthesia Safety Products (ASP), LLC** 300 TradeCenter, Suite 5400 Woburn, MA 01801 781.933.6500	
Commercially Available **Device:**	**AirPurge™ AIR DETECTION AND REMOVAL SYSTEM FOR USE WITH INTRAVENOUS (I.V.) LINES**
Medical Monitor:	Achi Ludomirsky, M.D.

CONFIDENTIAL

PRINCIPAL INVESTIGATOR

_____
Print Name of Principal Investigator

X _____ _____
Signature Date

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A. List of Abbreviations:

AirPurge	AirPurge Air Detection and Removal System
CRF	Case Report Form
I.V.	Intravenous
Kg	Kilogram
ml	Milliliters
RH	Relative Humidity
MDR	Medical Device Reporting
SIV	Site Initiation Visit

B. Post-approval Multi-center Study Summary

Title	AirPurge™ Air Detection and Removal System Post-approval Multi-center Clinical Protocol
Protocol Number	CS001-2
Methodology	Prospective, observational, single arm / non-randomized post-approval study design
Study Duration	6-8 weeks
Clinical Sites	Multi-center; up to 5-8 Clinical Sites
Objectives	To measure the *amount of air removed from the intravenous (I.V.) line by the AirPurge System* in a clinical setting and to measure the f*requency and duration of the AirPurge purging mechanism activity* in a clinical setting with standardization of the procedure, I.V. fluid and I.V. line.
Number of Subjects	50 Study Subjects per Clinical Site; 200 to 300 Study Subjects in Total
Primary Inclusion Criteria / Procedure	Intravenous Fluid or Blood Delivery in Pediatric and Adult Patient Populations Undergoing arterial septal defect closure, ballooning of coarctation, craniotomy, craniosynostosis, patent ductus arteriosis, (pda) closure, pulmonary artery stent deployment, pulmonary valve balloon dilatation, spinal fusion, scoliosis or cardiac surgery involving cardiopulmonary bypass
Commercially Available Device and Planned Use	AirPurge™ Air Detection and Removal System used to remove air from intravenous line
Statistical Methodology	Final data analysis will be presented in text, tables, and graphical representations including mean, standard deviation and range outcomes and a time analysis of AirPurge purging activity during the procedure

1.0 INTRODUCTION

This document is a protocol for a human research post-approval study. This study is to be conducted in accordance with applicable Good Clinical Practice standards and individual Clinical Site research policies and procedures.

1.1 BACKGROUND

The AirPurge System is identified by the FDA as "an Intravascular Administration Set, Automated Air Removal System". It was classified as a Class II device under the *De Novo* process (K080644) and cleared for release for commercial marketing on March 4th, 2014.

The AirPurge System is designed to:

- Detect & remove air bubbles automatically with practically unhindered I.V. flow
- Remove air bubbles during infusion rates as high as 400 ml/minute
- Remove air bubbles as small as 25 micro-liters at high or low flow rates
- Remove air automatically during surgical procedures from intravenous solutions, blood, and blood products in I.V. setups that have single or multiple bags
- Eliminate the need for time-consuming manipulation during in-line air bubble removal (and the adjunct possibility of needle sticks).

1.2 COMMERCIALLY AVAILABLE DEVICE

The *commercially available* Class II AirPurge Air Detection and Removal System is comprised of the AirPurge Device (control unit) and disposable Cartridge. In this protocol they are referred to as the AirPurge System, the Device or the Cartridge. The Device functions by:

a) Detecting air in the intravenous (I.V.) line using software-controlled ultrasound sensing technology
b) Diverting the flow in the I.V. line to the Collection Bag using a two pinch valve configuration, when air is detected, and
c) Redirecting fluid back to the patient line after passage of the entrapped air.

The Device detects air in the I.V. line via two sensors (line-in and line to Collection Bag) and diverts flow into the Collection Bag. Flow to the patient is resumed when sensors indicate no air. Therefore, some of the I.V. fluid will be channeled to the Collection Bag during air removal. The volume of this I.V. fluid channeled to the Collection Bag is dependent on the I.V. flow rate and bubble configuration, (i.e., a discrete bubble or a string of connected bubbles).

Flow Rate	I.V. Fluid Volume Loss Per Purge
400 ml per minute	~7 ml
300 ml per hour	~0.1 ml

1.3 INTENDED USE & INDICATIONS FOR USE

The usage of the AirPurge System with Disposable Cartridge in conjunction with this post-approval clinical study will be in accordance with the Intended Use and Indications for Use from the AirPurge Operator's Manual reviewed by FDA under *De Novo* K080644 (approval date: 3.4.2014).

Intended Use: The AirPurge System is intended for the detection and automatic removal of air in intravenous lines during administration of blood, blood products and intravenous solutions.

Indications for Use: The AirPurge System is intended for the detection and automatic removal of air in intravenous lines during administration of blood, blood products, and intravenous solutions. It is indicated for use in the operating room and post anesthesia care areas. The AirPurge System is placed below I.V. bags using gravity feed or pressure, and may be used with or without fluid warmers.

1.4 PRECLINICAL DATA

De Novo K080644 which was approved by FDA on March 4, 2014 included the following preclinical supportive material: design FEMA, design functionality, sterilization and shelf life, biocompatibility, software verification and validation, electromagnetic compatibility / electrical safety, patient transport, cartridge internal clamp and overall device performance bench verification, validation and usability testing. The AirPurge System has been tested and found to be in compliance with IEC 60601-1-2 1994 medical device limits.

1.5 RISKS AND BENEFITS

1.5.1 RISK OF DEVICE

Use of the AirPurge System in this post-approval study represents no more than minimal to no additional risk beyond the routine use of intravenous (I.V.) fluid delivery since all Clinical Sites will be instructed to follow their standard of care visualization techniques for air bubble detection and removal *below* the AirPurge System and therefore there will be *no* modification in Clinical Sites' routine air bubble detection and removal procedures at the most distal end of the I.V. line closest to the patient; air filter usage if a standard of care will be placed *below* the AirPurge System. Clinical Sites will be trained on the proper use of the AirPurge including the importance of clearing the line *before* connection to the patient. Any boluses or critical medicine / contrast media delivery will be conducted *below* the AirPurge device. Risk mitigation will begin *prior to* study onset at each Clinical Site with a thorough review / Clinical Site personnel training on the recommended operating instructions provided in the AirPurge System Quick Operating Instructions and Operator's Manual including the Warnings and Caution sections from a risk related standpoint.

1.5.2 OTHER RISKS OF STUDY PARTICIPATION

No other risks of study participation have been identified since Clinical Sites will not be requested to modify their routine air bubble detection and removal procedures at the most distal end of the I.V. line closest to the patient.

1.5.3 POTENTIAL BENEFIT ANALYSIS

The AirPurge System provides automatic removal of air in intravenous (I.V.) lines during administration of intravenous solutions in the operating room and post anesthesia care areas. The major potential benefits include:

- Improved safety; reduced risk of venous air embolisms and associated complications (heart failure, stroke, extended recovery times, impaired cognition)
- Simple, hands free, auto purge, intuitive operation

- Labor and attention saving convenience resulting from auto-purge function
- Reduced risk of clinician needle sticks while de-airing I.V. bags and lines
- Compatible with other infusion technologies, standard fluids, and flow rates.

2.0 STUDY OBJECTIVES

2.1 PRIMARY STUDY OBJECTIVES

The primary objectives of this post-approval clinical study are:

1) to measure the *amount of air removed from the intravenous (I.V.) line by the AirPurge System* in a clinical setting with standardization of the surgical procedure, I.V. fluid and flow rate

2) to measure the *frequency and duration of the AirPurge purging mechanism activity* in a clinical setting with standardization of the procedure, I.V. fluid and I.V. line.

3.0 STUDY DESIGN

3.1 GENERAL DESIGN

The AirPurge Air Detection and Removal System Post-Approval Multi-Center Clinical Study is a prospective, observational, single arm / non-randomized post-approval study design. This multi-center post-approval clinical study is *not* a comparative study design *nor* is the clinical design intended to support the functional safety and efficacy of the *commercially available* AirPurge System for the purposes of obtaining FDA approval. Therefore, there is *no* investigational device and *no* prospective safety / efficacy success criteria or endpoints. The AirPurge System will be utilized for the current FDA approved intended use / indications for use. The overall goal of this post-approval study is information gathering in regards to the clinical value of the AirPurge System within the operating room setting utilizing a set of controlled I.V. set-up parameters including I.V. fluid, I.V. line including the usage of key I.V. pole accessory equipment and a standardized group of procedures.

The study endpoint is the discontinuation of AirPurge System usage during the procedure and therefore there are *no* post-procedure follow-up requirements minimizing the risk of lost-to follow-up study subjects. Study subjects will be recruited from the Clinical Sites' current patient population scheduled to undergo one of the inclusion criteria procedures. Subjects will be enrolled into the study in a sequential manner.

Data collection is limited to two time points:

The hard copy CS001-12LL Eligibility Checklist / Demographics case report form (CRF) will be completed *prior to* surgery. Operative Day data will be collected utilizing two data collection methodologies as follows:

1) CS001-13LL Operative Report: This hard copy case report form (CRF) will be completed by Clinical Site personnel and collect information on device performance from the clinician's perspective, intravenous line fluid delivery specifics, and relevant background concerning the procedure.

2) Data Monitor: The Data Monitor consists of hardware and software that are independent of and do *not* affect operation of the AirPurge device. The Data Monitor resides in the battery pack area of the AirPurge from which the batteries have been removed. The Data Monitor will collect objective data to measure 1) the *amount of air* removed from the intravenous line by the AirPurge, 2) the *frequency and duration of AirPurge mechanism activity* and 3) the *occurrence of any alarm conditions* in the AirPurge.

3.2 STUDY DURATION

Study duration is limited to the collection of preoperative eligibility criteria / baseline demographic information and procedure data. There are *no* post-procedure follow-up requirements for this post-approval study.

3.3 STUDY POPULATION

The study population for this post-approval clinical study will be comprised of up to 50 study subjects per Clinical Site with up to 5-8 participating Clinical Sites in total; 200-300 study subjects. Study Subjects will be drawn from Clinical Sites' pediatric and adult patient populations who are scheduled to undergo one of the following procedures: arterial septal defect closure, ballooning of coarctation, craniotomy, craniosynostosis, patent ductus arteriosis, (pda) closure, pulmonary artery stent deployment, pulmonary valve balloon dilatation, spinal fusion, scoliosis or cardiac surgery involving cardiopulmonary bypass.

4.0 SUBJECT SELECTION AND WITHDRAWAL

4.1 INCLUSION CRITERIA

Potential study subjects meeting *all* of the following criteria will be considered suitable study subjects.

Male or female, any race

Pediatric or adult patient

1.0 Study Subject's weight is at least 5kg.

2.0 Study Subject scheduled to undergo one of the following procedures: arterial septal defect closure, ballooning of coarctation, craniotomy, craniosynostosis, patent ductus arteriosis, (pda) closure, pulmonary artery stent deployment, pulmonary valve balloon dilatation, spinal fusion, scoliosis or cardiac surgery involving cardiopulmonary bypass

3.0 Study Subject or acceptable parent / guardian is able to provide written informed consent, if Clinical Site requires

4.2 EXCLUSION CRITERIA

Any study subject who does **not** meet *all* of the above inclusion criteria will be excluded from this clinical study. In addition, any study subject who meets one or more of the following exclusion criteria will also be excluded from study enrollment:

1.0 Study Subject's scheduled procedure involves the use of an infusion pump on the I.V. line that AirPurge will be attached to

2.0 Study Subject plans to participate or has participated in any other clinical trial within the 30 days prior to the start of the study.

3.0 Study Subject cannot be a homeless person, have an active drug/alcohol dependence or abuse history.

4.3 STUDY SUBJECT RECRUITMENT AND SCREENING

Study Subjects will be drawn from Clinical Sites' pediatric and adult patient populations who are scheduled to undergo one of the study procedures. Any study-specific recruitment materials will be reviewed by overseeing IRBs, if applicable. The *commercially available* FDA approved labeling materials may be utilized to explain the AirPurge device, based on Investigator preference.

4.4 EARLY WITHDRAWAL OF STUDY SUBJECTS

4.4.1 WHEN AND HOW TO WITHDRAW SUBJECTS

An Investigator may choose to discontinue a study subject from the study during the course of the procedure if in the opinion of the Investigator this action is in the best welfare of the study subject. If a study subject is withdrawn from the clinical study, this information will be recorded on the Operative Report including the reason for withdrawal. Subjects may also be withdrawn after the Eligibility Checklist / Demographics case report form has been completed based on Investigator judgment.

4.4.2 DATA COLLECTION FOR WITHDRAWN SUBJECTS

The Study Sponsor should be notified of any withdrawn study subjects and any completed CRFs submitted to the Study Sponsor with the reason for withdrawal.

4.4.3 STUDY SUBJECT DISCONTINUATION

Study subjects will be clearly informed during the Informed Consent process *(if applicable)* that they are free to withdraw from this post-approval study *after* they sign the Informed Consent Document and *before* their procedure. If this should occur, the Clinical Site should document the Study Subject's wish to discontinue their study participation by recording the date and reason for discontinuation *(if available)* on the study subject's Eligibility Checklist / Demographics form.

5.0 STUDY DEVICE

5.1 DESCRIPTION

The *commercially available* Class II AirPurge Air Detection and Removal System is comprised of the AirPurge Device (control unit) and disposable Cartridge. In this protocol they are referred to as the AirPurge System, the Device or the Cartridge.

The Study Sponsor will provide training on the recommended operation of the AirPurge System per ASP user training procedure; SOP-007, *prior to* the first study surgical procedure at each Clinical Site. Clinical Site personnel should read the "AirPurge™ System Quick Operating Instructions" and

"AirPurge™ System – Air Detection and Removal System with Intravenous (I.V.) lines Operator's Manual" thoroughly before use and have both readily available during device operation.

5.2 STANDARDIZED STUDY I.V. PARAMETERS / SET-UPS

The AirPurge System will be mounted to the "Active" I.V. line being used for maintenance and fluid replacement. The Intravenous Fluid and Flow Rate parameters will be standardized as follows for all study subjects:

I.V. Line: The AirPurge will be mounted to the free-flow, maintenance line
I.V. Fluid: Lactated Ringer's or Blood

Fluid warmers may or may not be used based on each Clinical Site's standard of care practices. The usage of a warmer and type of warmer will be recorded on the Operative Report.

Air filters may be used *below* the AirPurge based on each Clinical Site's standard of care practices. Clinical Sites should follow their routine procedures for air bubble detection and elimination *below* the AirPurge.

During this post-approval study, the following Equipment Set-Ups should ***not*** be used with the intravenous line connected to the AirPurge System: infusion pumps, inflatable pressure cuffs, pressurized infusers, rapid infusion systems or catheters. Any boluses or syringe injections should be delivered ***below*** the AirPurge.

If at any point during the procedure, it is in the best interest of the patient's welfare to modify this standard free-flow rate, the Investigator should proceed and record on the Operative Report, documenting the reason for modification. Deviation from the standardized flow will be categorized as a protocol deviation for analysis purposes.

5.3 PACKAGING

The reusable AirPurge Device(s) will be provided to each Clinical Site *prior to* the Site Initiation Visit and Clinical Site personnel training. An inventory of *single-use only* AirPurge Cartridges will be shipped *sterile* to Clinical Sites by Study Sponsor. Since the AirPurge is *not* investigational, *no* investigational device accountability process will be required. If any devices are damaged during shipment the Clinical Site will be instructed to notify the Study Sponsor.

5.4 CONTRAINDICATIONS

Do *not* use with fluids that are incompatible with standard I.V. lines.

5.5 WARNINGS

For a comprehensive description of *all* AirPurge System Warnings and Cautions refer to the "AirPurge™ System – Air Detection and Removal System with Intravenous (I.V.) lines Operator's Manual". Key study relevant Warnings are provided below:

a. The AirPurge System *cannot* purge air from I.V. extension line between AirPurge System and patient. The I.V. extension line must be cleared of air before connected to patient. Failure to clear

extension line could result in introduction of air to patient that could result in death or serious injury.
b. Fluid warmers, if used, must be installed above the AirPurge.
c. Mount the AirPurge lower than the infusion source, not higher than 4 feet (125 cm) and at or slightly below patient level. The I.V. pole should be vertical at all times
d. The AirPurge will *not* reliably purge air at flow rates greater than 400 ml/minute
e. Flow is diverted into the Collection Bag during air purging. Critical medication and contrast media should be injected *below* the AirPurge.

5.6 POWER

After plugging the AirPurge System into AC source, confirm all 3 battery lights are illuminated. Note: AC power (and *not* battery power) will be used for all study procedures.

5.7 MOUNTING THE DEVICE

Mount the AirPurge Device on the I.V. pole in a vertical position. Plug into AC outlet.

WARNING: The IV Pole must be kept vertical at all times. If the IV pole becomes non-vertical while the AirPurge System is in use, then:

-Check for air in the line connected directly to the study subject and take immediate and appropriate actions consistent with basic/standard I.V. practices.

-Check to see if any of the I.V. setup, tubing, equipment, has been damaged or disconnected; if yes, discontinue and restart the I.V. therapy set-up, as appropriate and consistent with basic/standard I.V. practices.

If the IV setup, tubing, and equipment, has not been damaged or disconnected, return the IV pole to a vertical position and check the functioning of the AirPurge System. If it is ON and not alarming then AirPurge System is removing all the air flowing into the AirPurge System.

5.8 INSTALLING THE CARTRIDGE

NOTE: Have "AirPurge™ System Quick Operating Instructions" available for a quick reference in the O.R. Handle according to your institution's procedures for sterile devices.
a. Remove single-use Cartridge from sterile pouch. Collection Bag connector must be tight; **Blue** and **Green** caps mounted in place.
b. Remove **Red** retaining clip; and discard. Open the Device Door. With **FRONT** of Cartridge facing you, push Cartridge onto pegs in the device. Close and latch the door.

5.9 SYSTEM START-UP / CLEARING THE LINES

CAUTION: Only use I.V. lines with Luer Lock connectors. When connecting the I.V. line to the top and bottom of Cartridge, do ***not*** over tighten Luer connections. Tighten connections ***only*** until slight resistance is felt.

a. Remove **Green** inlet cap on top of Cartridge and connect primary I.V. to connector of Cartridge marked **IN**. Remove **Blue** outlet cap on bottom of Cartridge and connect the extension set to the connector at bottom of the Cartridge marked **OUT**. Ensure there are ***no*** kinks in any tubing.

b. Turn the Device on. All front panel indicators (9) will illuminate for 3 seconds, then only the **ON** button and 3 battery lights (indicating AC power is present) will remain lit. If any other Indicator lights stay on or if there is an audible alarm, refer to Operator's Manual and follow instructions. Record information regarding all indicators / alarms on the Operative Report.
c. Start fluid flow for the primary I.V. lines. The Cartridge will fill with fluid; any air in line will be detected and diverted into the Collection Bag. When free of air, flow will then be diverted back to extension line. Once air free I.V. fluid clears the extension line, connect to the patient.

WARNING: The AirPurge System *cannot* purge air from I.V. extension line between AirPurge System and patient. The I.V. extension line must be cleared of air before connected to patient. Failure to clear extension line could result in introduction of air to patient that could result in death or serious injury.

5.10 REPLACING FULL COLLECTION BAG

a. Do ***not*** turn off the AirPurge. Open a new Cartridge package and remove Collection Bag by disconnecting Luer connector.
b. Ensure AirPurge is ***not*** purging (PURGING Indicator ***not*** lit) and pause flow into the AirPurge *(e.g. clamp line).*
c. Disconnect Luer connector to remove Full Collection Bag and attach New Collection Bag.
d. Resume flow.

5.11 REPLACING EMPTY I.V. BAG

a. Do ***not*** turn off the AirPurge. Replace I.V. bag as usual. *(The AirPurge will remove air admitted into primary I.V. line and divert liquid flow back to study subject line).*
b. If drip rate is too slow, increase the drip rate until "PURGING Light is off and flow is resumed to the study subject.

5.12 FLUID WARMERS

a. Any Fluid Warmer can be used based on the Clinical Site's preference and routine standard of care practices.
b. Follow Fluid Warmer manufacturer Instructions for Use (IFU).
c. Install Fluid Warmer **ABOVE** the AirPurge System. The AirPurge System can be connected to the Fluid Warmer with standard extension I.V. line sets.

5.13 INFUSION PUMPS

Infusion Pumps should *not* be used on the AirPurge line.

5.14 INDICATORS AND ALARMS

Refer to page 13 of the AirPurge Operator's Manual for further information on Indicators and Alarms. The incidence and timing of any Indicator Light or Alarm will be documented on the Operative Report.

Indicator	Alarm	Solution
TEMP	Yes	Discontinue Use. Turn Device Off and Open Door. Monitor Air Bubbles Manually & Contact ASP for Service.

TURN OFF-OPEN DOOR	Yes	Discontinue Use. Turn Device Off and Open Door. Monitor Air Bubbles Manually & Contact ASP for Service.
DOOR	Yes	Ensure Cartridge is Inserted Correctly, Red Retaining Clip Removed & Door Securely Latched. If Alarm Persists Discontinue Use and Contact ASP for Service.
↑↑VERT	Yes	Reposition Device on I.V. Pole using Clamp. When Positioned Correctly Device Resets Itself.
PURGING	PURGING Indicator Lights when device Purging. After 1 minute (Indicator begins Blinking + Alarm)	DO NOT TURN OFF Device. Check I.V. Line for Obstructions or I.V. bag Empty* Very Low Flow Rates can Cause Purge Times > 1 Minute; Wait for Alarm to Silence.

*If Alarm persists discontinue use. Turn device off and open door. Monitor air bubbles manually and contact ASP for service.

5.15 AIRPURGE SYSTEM DISPOSABLE CARTRIDGE STORAGE

Temperature	-20 to 60°C
Relative Humidity	10 to 93 %RH
Air Pressure	500 to 1060hPa (15-31Hg)
Elevation	0 to 9800 feet

5.16 CLEANING AND MAINTENANCE

a. Cartridges and Collection Bags are *for single use only*. Dispose in your medical waste.
b. Refer to Operator's Manual for AirPurge Device cleaning and disinfecting instructions.

5.17 DEVICE RETURNS

Any AirPurge Devices or Cartridges that do *not* function properly should be returned to the Study Sponsor for device complaint evaluation after Study Sponsor notification. Contact Customer Service for return instructions.

6.0 STUDY PROCEDURE

6.1 SCHEDULE OF EVENTS

Data collection for this post-approval study will occur as described in the below table. Data collection and required study visits are limited to the preoperative completion of the CS001-12LL Eligibility Checklist / Demographics and the Operative Day which involves both data collection from Clinical Site Personnel on the CS001-13LL Operative Report and objective measurements collected via the Data Monitor which is attached to the USB port on the AirPurge System. Refer to Schedule of Events provided in **Attachment 1** for additional details.

Data Collection	Visit Timeframe
CS001-12 Eligibility Checklist / Demographics	*Prior to* Procedure* **(Visit 1)**
CS001-13 Operative Report	Operative Day **(Visit 2)**
Data Monitor	Operative Day **(Visit 2)** *(Collected by Sponsor upon completion of Clinical Site's enrollment/ procedures**)*

*If study-specific Informed Consent Document (ICD) used, ICD must be signed *prior to* completion of CS001-12 Eligibility Checklist / Demographics
** Collection may occur at periodic intervals during study to verify Data Monitor operation

6.2 ELIGIBILITY CHECKLIST / DEMOGRAPHICS

Visit 1 will involve Clinical Site personnel collection of the following data fields:

Subject ID
Date / Time
Age
Gender
Race
Height
Weight
Surface Area
Scheduled Procedure Reason / Diagnosis for Procedure
Medication History

6.3 OPERATIVE REPORT

Visit 2 will involve Clinical Site personnel collection of the following data fields:

Subject ID #
Procedure Date
Procedure Start and End Time
AirPurge Start Time and End Time
Procedure (circle one): arterial septal defect closure, ballooning of coarctation, craniotomy, craniosynostosis, patent ductus arteriosis, (pda) closure, pulmonary artery stent deployment, pulmonary valve balloon dilatation, spinal fusion, scoliosis or cardiac surgery involving cardiopulmonary bypass
Procedure Complications
Use of Fluid Warmer
I.V. Fluid and Bag Volume
Additional I.V. Line Activity
Confirm AirPurge used on Free-flow maintenance line
AirPurge Waste Collection Bag
AirPurge Alarms
AirPurge Complaints

6.4 DATA MONITOR

Visit 2 will also involve the collection of the following objective measurements through the Data Monitor software:

-Total time (in milliseconds) that the AirPurge sensor detects incoming air in order to calculate total actual air volume captured

-How often purge mechanisms kicks in

-Frequency & Duration of Purging

-Total Time AirPurge device powered on, number of times device power turned on and off and number of Device Alarms Detected

7.0 STATISTICAL PLAN

This multi-center post-approval clinical study is *not* a comparative study design *nor* is the clinical design intended to support the functional safety and efficacy of the AirPurge System for the purposes of obtaining FDA approval. Therefore, there are *no* prospective safety / efficacy success criteria or endpoints. The overall goal of this post-approval study is information gathering in regards to the clinical value of the AirPurge System utilizing a set of controlled I.V. set-up parameters and group of procedures.

All available data will be entered into standard Excel spreadsheets for analysis purposes and data entry verified *prior to* the final analysis. Planned data analyses include:

1) **CS001-12LL Eligibility Checklist / Demographics:** Data will be analyzed using standard demographic variable presentation for age, race, gender, height, weight and surface area and to record any pre-existing conditions (medical / drug) that could impact intravenous fluid delivery during the procedure.
2) **CS001-13LL Operative Report:** Data collected will be used to evaluate the clinical activity in the clinical setting to provide key background regarding the overall procedure, I.V. fluid delivery parameters and the operation of the AirPurge. Data will be presented for individual study subjects, as applicable and for the overall study population as a whole.
3) **Data Monitor:** The Study Sponsor will analyze the objective measurement data collected from the Data Monitor software and correlate Data Monitor measurements with the clinical data collected from Clinical Site personnel and documented on the CS001-13LL Operative Report. Analytical measurements will include:
   - -Total volume of air captured (mean, range and SD) for individual study subjects and the overall study population as a whole)
   - -Duration of AirPurge purge mechanism activity (mean, range and SD) for individual study subjects and the overall study population as a whole)
   - -Frequency of AirPurge purge mechanism activity (mean, range and SD) for individual study subjects and the overall study population as a whole) to answer questions concerning the necessity of purging over the duration of a procedure (e.g. number of purging episodes; length of time between purging episodes)

-Summary of the incidence of AirPurge alarms and indicators will be prepared

-An analysis between the objective measurements collected with the Data Monitor and the clinical activity reported on the Operative Report to correlate what was occurring clinically during purging activity.

The final data analysis will be presented in text, tables, and graphical representations including a graphical time analysis of AirPurge usage over the duration of the procedure.

8.0 SAFETY ISSUES

8.1 AIRPURGE SYSTEM INDICATOR LIGHTS / ALARMS

Device performance in the clinical setting will be monitored as part of this post-approval study. The incidence and timing of AirPurge System Indicator Lights and Alarms during the procedure will be described on the CS001-13LL Operative Report with objective data collected via the Data Monitor. The incidence of procedure complications will also be recorded on the CS001-13LL Operative Report.

8.2 PROTOCOL DEVIATIONS, DEVICE COMPLAINTS AND REPORTABLE EVENTS

NOTE: The following safety data will be collected for Study Sponsor notification as described below. Clinical Site personnel will be responsible for notifying the Study Sponsor within 24 hours of any device complaints, potential medical device reporting (MDR) reportable events or significant protocol deviations. In addition, Clinical Sites conducting this post-approval study under Institutional Review Board (IRB) oversight will follow the guidelines outlined by their overseeing IRB for the reporting of the incidence of device complaints, medical device reporting (MDR) reportable events (including IRB notification and the completion of Form 3500A Medwatch Forms), as appropriate or significant protocol deviations.

Clinical Investigators / participating Clinical Sites should make every effort to comply with all aspects of this post-approval clinical protocol and *not* deviate in any way from the standardized protocol requirements. The Clinical Site will document any protocol deviations that may occur on the Operative Report and for Clinical Sites conducting the post-approval study under IRB oversight, the Principal Investigator will be responsible for submitting any *significant* protocol deviations to the IRB for review, based on individual IRB requirements. The Study Sponsor should be notified of any *significant* protocol deviations within 24 hours of occurrence.

8.3 DEFINITIONS

Complaint: Any written, electronic or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness, or performance of a device after it is released for distribution.

Medical Device Reporting (MDR) Reportable Event (or Reportable Event):

(1) An event that user facilities become aware of that reasonably suggests that a device has or may have caused or contributed to a death or serious injury; or

(2) An event that manufacturers or importers become aware of that reasonably suggests that one of their marketed devices:

(i) May have caused or contributed to a death or serious injury, or
(ii) Has malfunctioned and that the device or a similar device marketed by the manufacturer or importer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Serious Injury: An injury or illness that:

(1) Is life-threatening,
(2) Results in permanent impairment of a body function or permanent damage to a body structure, or
(3) Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.

8.4 MEDICAL MONITORING

It will be the responsibility of the Principal Investigator at each Clinical Site to closely monitor not only the overall study conduct at their Clinical Site but to oversee the safety outcomes from all study procedures. The Medical Monitor will be responsible for reviewing data from all Clinical Sites and providing guidance to the Investigator group, as necessary.

9.0 DATA HANDLING AND RECORD KEEPING

9.1 CONFIDENTIALITY

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Clinical Sites should follow the requirements of their institution, overseeing IRB and any and all applicable state and federal privacy regulations.

9.2 CASE REPORT FORMS (CRFS) AND SOURCE DOCUMENTS

The following standardized hard-copy case report forms (CRFs) will be utilized during this post-approval clinical study:

***CS001-12LL Eligibility Checklist / Demographics**
***CS001-13LL Operative Report**

The CS001-12LL Eligibility Checklist / Demographics will be completed by the Clinical Site *prior to* the surgical procedure. If the Clinical Site is utilizing a *study-specific* Informed Consent Document for this post-approval clinical study, the CS001-12LL Eligibility Checklist / Demographics should *not* be completed until after the Informed Consent Document has been signed. The CS001-13LL Operative Report will be completed by the Clinical Site during / shortly after the procedure.

Copies of the hard-copy forms will be maintained by the Clinical Sites and the *originals* of these forms will be sent to Anesthesia Safety Products. Clinical Site source documents (e.g. operative notes) may be used to assist in the completion of the study-specific hard copy case report forms.

All data requested on the CRF must be recorded. All missing data must be explained. If a space on the CRF is left blank because the procedure was not done or the question was not asked, write "N/D". If the item is not applicable to the individual case, write "N/A". All entries should be printed

legibly in *black* ink. If any entry error has been made, to correct such an error, draw a single straight line through the incorrect entry and enter the correct data above it. All such changes must be initialed and dated. DO NOT ERASE OR WHITE OUT ERRORS. For clarification of illegible or uncertain entries, print the clarification above the item, then initial and date it.

9.3 RECORDS/MATERIALS TO BE MAINTAINED

The Principal Investigator will maintain *copies* of the completed CS001-12LL Eligibility Checklist / Demographics and CS001-13LL Operative Report CRFs, all completed / signed Informed Consent Documents *(if applicable)*, all IRB correspondence *(if applicable)* and the Clinical Study Binder. The Clinical Site will send the *original* completed CS001-12LL Eligibility Checklist / Demographics and CS001-13LL Operative Report CRFs to Anesthesia Safety Products on a periodic basis throughout the duration of the post-approval study. The Clinical Site will return the Data Monitor to Anesthesia Safety Products upon completion of the *last* procedure. These records will be considered confidential and proprietary to Anesthesia Safety Products. Clinical Sites under the oversight of an IRB will follow their IRB's requirements for the length of record retention (typically a minimum of 2 years).

10.0 ADMINISTRATIVE INFORMATION

10.1 INVESTIGATOR SELECTION AND QUALIFICATIONS

Investigators will be selected based on their experience with intravenous line fluid delivery in the clinical setting, their qualifications for participation in a post-approval clinical study and their willingness to adhere to the Investigator responsibilities and requirements outlined in this post-approval clinical study protocol.

10.2 INFORMED CONSENT PROCESS *(OPTIONAL)*

The ASP AirPurge System is commercially available in the United States under *De Novo* K080644 and therefore informed consent is *not* required by a Clinical Site in order to participate in this post-approval clinical study. For Clinical Sites interested in obtaining informed consent, (either in conjunction with an Institutional Review Board (IRB) or not), Anesthesia Safety Products has prepared an Informed Consent Document template. If an Informed Consent is utilized, the document should be signed *prior to* the completion of the **CS001-12LL Eligibility Checklist / Demographics** case report form (CRF) and the study subject's procedure. In addition, Clinical Sites utilizing an IRB should follow all of their IRB's guidelines for obtaining informed consent and study conduct.

10.3 INSTITUTIONAL REVIEW BOARD (IRB) *(OPTIONAL)*

The ASP AirPurge System is commercially available in the United States under *De Novo* K080644 and therefore Institutional Review Board (IRB) is *not* required by a Clinical Site in order to participate in this post-approval clinical study. Clinical Sites who choose to conduct this post-approval clinical study under IRB oversight will be responsible for completing all necessary paperwork and following the guidelines set forth by their IRB including use of the IRB approved Informed Consent document and any specific Clinical Site reporting requirements.

10.4 PROTOCOL AMENDMENTS

In the event that a revision to this post-approval clinical protocol is made after study onset, information concerning protocol amendments will be provided to the Principal Investigator at each Clinical Site. A protocol history listing any protocol amendments, if they should occur, will be provided by the Study Sponsor for the Clinical Site's records. For Clinical Sites conducting the post-approval study under IRB oversight, the Principal Investigator will be responsible for submitting any protocol amendments to the IRB for review, based on individual IRB requirements.

10.5 SUBJECT IDENTIFICATION (ID) NUMBER

Each study subject in the clinical study will be identified by a unique subject ID number which will be recorded on the Eligibility Checklist / Demographics Report and Operative Report forms. The Study Sponsor will provide each Clinical Site with a subject ID number list.

11.0 TRAINING & MONITORING

The Study Sponsor will have three types of monitoring performed to ensure compliance with this clinical protocol and to provide each participating Clinical Site with adequate training concerning the operation of the AirPurge System and all clinical study responsibilities:

- data monitoring
- administrative monitoring /Clinical Site training
- safety monitoring

11.1 DATA MONITORING

The Study Sponsor will review all hard-copy study case report forms (CRFs) to verify completeness of documentation including missing and/or incomplete forms to ensure that the documentation is being completed properly and that all study case report forms are collected for analysis. Clinical Sites will be contacted in regards to missing forms and to clarify any unreadable data from the hard-copy forms, when necessary.

The Study Sponsor will oversee the objective measurement data collected from the Data Monitor to verify that the Data Monitor(s) performed as intended at each participating Clinical Site.

11.2 ADMINISTRATIVE MONITORING / CLINICAL SITE TRAINING

A site initiation visit (SIV) will be conducted at each Clinical Site *prior to* the enrollment of their first study subject to assure that Clinical Investigator(s) and Clinical Site personnel are adequately trained on the recommended operation of the AirPurge System and Data Monitor to be used in conjunction

with this clinical study. The clinical protocol will be reviewed in-depth with all relevant Clinical Site personnel during pre-enrollment conference calls to ensure all questions have been addressed and that overall study responsibilities have been clearly outlined and understood.

The Study Sponsor will remain in constant communications with each participating Clinical Site throughout the duration of the clinical study to monitor overall clinical study enrollment, case report form completion, informed consent and IRB reporting requirements (as applicable) and to provide any technique device troubleshooting support, as necessary.

11.3 SAFETY MONITORING

The Study Sponsor will review study outcomes to assure the continued safety of the device and that no study subjects are exposed to unwarranted risk.

12.0 PUBLICATION

Neither the complete nor any part of the results of the study carried out under this protocol, nor any of the information provided by the Study Sponsor for the purposes of performing the study, will be published or passed on to any third party without the consent of the Study Sponsor. Any Investigator involved with this study is obligated to provide the Study Sponsor with complete test results and all data derived from the study.

13.0 REFERENCES

1. Chau D, Tzanetos D, Zhang C et al. A dangerous side of in-line IV filters when used for vasoactive infusions in infants. *Offic Jour Anesthesia Patient Safety Foun* 2013;(Fall):1-7.
2. Giraldo M, Lopera LM, Arango M. Venous air embolism in neurosurgery. *Columbian Jour Anesthesiology* 2015;43(S1):40-44.
3. Gordy S, Rowell S. Vascular air embolism. *Intl Jour Critical Illness & Injury Science* 2013;3(1):73-76.
4. Minski M, Lele A, Fitzsmimmons L et al. Diagnosis and treatment of vascular air embolism. *Anesthesiology* 2007;106(1):177.
5. Muth C.M., Shank E.S. Gas embolism. *New England Jour Med* 2000;342(7):476-482.
6. Sowell M, Lovelady C, Brogdon B.G. et al. Infant death due to air embolism from peripheral venous infusion. *J Forensic Sci* 2007;52(1):183-188.
7. Wilkins RG, Unverdorben M. Accidental intravenous infusion of air. *Jour Infusion Nursing* 2012;35(6):404-408.

Attachment: 1

Schedule of Events

Activity	**Visit 1** Eligibility Checklist/ Demographics	**Visit 2** Operative Report	**Visit 2** Data Monitor
Study Team Procedures			
Informed Consent	X		
Age	X		
Gender	X		
Race / Ethnicity	X		
Height	X		
Weight	X		
Surface Area	X		
Scheduled Procedure	X		
Reason / Diagnosis for Procedure	X		
Medication History	X		
Operative Assessments			
Performed Procedure		X	
I.V. Line Set-up (including all accessories)		X	
I.V. Line Activity (fluid, confirm free-flow maintenance line, # bags)		X	
AirPurge Usage (including purging activity, alarms/indicators, #collection bags, remaining collection bag status)		X	
Procedure Complications		X	
Device Complaints		X	
Data Monitor Software Collected Data			
Duration / Frequency of Purge Mechanism Activity			X
Volume of Air Removed			X
Incidence / Timing of Alarms & Indicators			X