PROTOCOL TITLE:

Central venous catheterization in obese patients with Compass device.

Brief title: Compass Device Trial

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1.0 Objectives*

1.1 This is a single-arm observational trial of a new FDA-approved device (Compass Vascular Access device, Centurion Medical Products, Williamston MI; formerly Mirador Boimedical). This device is a compact, sterile, single-use extravascular blood pressure transducer with a continuous digital pressure display. This pressure measurement provides an aid in the confirmation of appropriate venous access. The device has FDA 510(k) clearance as substantially equivalent to existing devices on the market. Evidence of this clearance is included with this application.

1.2 The investigators plan to enroll 40 consenting patients with BMI ≥35 who require central venous catheterization for clinical reasons independent of the existence of this study. For purposes of the study, the investigators will record data germane to the procedure as well as operator satisfaction. Analysis of these data will be used to evaluate the appropriateness of the device for this procedure in the obese population, where device ergonomics may be more of a factor than in previous studies.

1.3 This study is not investigating the safety of the device, because the primary outcome is operator satisfaction. None of the observed outcomes relate directly to device safety, and the study is not powered to detect rare adverse events.

1.4 This study is also not investigating the effectiveness of the device. The investigators are not gathering any data that would permit evaluation of the device's accuracy or precision, which are the salient factors for effectiveness of a measurement device.

1.5 Deidentified study data may be shared with the sponsor, but the investigators do not plan to submit study data to the FDA.

2.0 Background*

Central venous catheterization (CVC) is a common perioperative procedure that is associated with a number of potential mechanical complications. It involves three steps: first a needle is introduced to the target vein, followed by a guidewire, and finally the catheter itself. The needle is relatively fine, and the guidewire slightly larger, but the catheter is relatively large, with corresponding increases in the severity of complications associated with arterial puncture. Inadvertent arterial cannulation is the most common mechanical complication of CVC placement and is associated with significant morbidity and mortality.(1) Complications of arterial puncture or cannulation may lead to uncontrolled hemorrhage, airway compromise related to neck hematoma, cerebrovascular accident, hemothorax, mediastinal bleeding, cardiac tamponade, aortic dissection, and death.

The use of ultrasound guidance for CVC has mitigated the risk for arterial cannulation but not eliminated it. Ultrasound guidance has decreased the rate of arterial puncture to rates as low as 0.5%.(1) Nonetheless, arterial cannulation can still occur during CVC placement with ultrasound guidance for a variety of reasons primarily

related to either incorrect identification of the target vein or the inability to accurately determine the location of the tip of the access needle.(2)

Due to the limitations of two-dimensional surface ultrasound and the goal of further mitigating the risk of arterial access during CVC insertion, various methods have been employed to confirm that only the target vein has been accessed. One method is echocardiographic confirmation of guidewire placement in the superior vena cava and/or the right heart; however, aside from select operative procedures, use of echocardiography in the perioperative period or in the intensive care unit (ICU) is limited, costly, and may not be contemporaneous with CVC placement. A second method is the use of column manometry to transduce the intravascular pressure. However, performance of manometry may be cumbersome and may generate a false negative finding (fluid column appears venous) even when the CVC is intra-arterial due to obstruction of the proximal transduction site or a low cardiac output state.

An FDA-approved electronic extravascular blood pressure monitor (Compass® Vascular Access device, Centurion Medical Products, Williamston, Mi.) has been recently developed which provides an aid in the confirmation of appropriate CVC access. The device is a compact, sterile, single-use pressure transducer that has a continuous digital pressure (mmHg) display. The device connects in a luer-lock fashion to all standard syringes and needles and has a separate self-sealing channel for CVC guidewire insertion and withdrawal. The device is intercalated between the syringe proper and the needle used to access the target vessel. The device permits confirmation of guidewire insertion into the target vein via its pressure display. There are two previous reports on the use of this device in the perioperative and ICU settings.(3,4) In the report by Togashi et al(3), 298 CVC placements were performed with the device and five inadvertent arterial punctures occurred even though ultrasound guidance was utilized. All five of these inadvertent arterial punctures were correctly identified prior to cannulation because of the use of the device.(3) The device did not produce any adverse events. Furthermore, Togashi et al performed a cost-benefit analysis comparing the claim costs associated with a single mechanical CVC injury (per American Society of Anesthesiology Closed Claims Database(5): $95,000 / event) versus device costs and found that the use of the novel device generated a net savings of $116 for each CVC insertion.(3) The Togashi group (3) noted that some operators would prefer a smaller device, but most were satisfied with it as tested. The planned case series is intended to evaluate use of the device in the obese population (BMI $\geq$ 35 kg/m^2), where device ergonomics may be more of a factor.

References:

1. Fragou M, Gravvanis A, Dimitriou V, Papalois A, Kouraklis G, Karabinis A, Saranteas T, Poularas J, Papanikolaou J, Davlouros P, Labropoulos N, Karakitsos D. Real-time ultrasound-guided subclavian vein cannulation versus the landmark method in critical care patients: a prospective randomized study. Crit Care Med 2011;39:1607-12.
2. Reusz G, Csomos A. The role of ultrasound guidance for vascular access. Curr Opin Anaesthesiol 2015;28:710-6.
3. Togashi K, Nandate K, Hoaglan C, Sherman B, Bowdle A. A multicenter evaluation of a compact, sterile, single-use pressure transducer for central venous catheter placement. Anesth Analg 2013;116:1018-23.

4. Visweswaran GK, Lightfoot J, Gilchrist IC. Novel use of a disposable digital pressure transducer to increase the safety of pericardiocentesis. Catheter Cardio Inte 2013;81:E68-E71.
5. Domino KB, Bowdle TA, Posner KL, Spitellie PH, Lee LA, Cheney FW. Injuries and liability related to central vascular catheters: a closed claims analysis. Anesthesiology 2004;100:1411-8.

3.0 Inclusion and Exclusion Criteria*

3.1 The study population consists of obese (≥35 kg/m^2) adult (≥18 yrs) patients presenting at the UNM Hospital main/adult operating rooms who require central venous catheter (CVC) placement for their perioperative care. The investigators will exclude pregnant women, adults unable to consent, and prisoners.

3.2 Members of the commonly recognized vulnerable populations will not be enrolled: pregnant women, prisoners, neonates of uncertain viability or that are nonviable, and minors.

4.0 Study-Wide Number of Subjects*

4.1 The planned completed sample size is 40 patients. The investigators request HRRC permission to enroll **up to 45 patients** in order to accommodate any whose CVC procedures may be cancelled between consenting and commencement of the actual procedure, but will only complete data collection for 40 patients.

5.0 Study-Wide Recruitment Methods*

This is a single-site study; local recruitment methods are described in section 22 below.

6.0 Multi-Site Research*

6.1 This is a single-site study.

7.0 Study Timelines*

7.1 Describe:

- A given individual will participate in the study for approximately 15 minutes, representing the time required for the CVC placement.
- The investigators anticipate that the study sample can be enrolled in approximately six months to one year.
- The investigators estimate that all analyses will be completed in one year after completion of enrollment.

8.0 Study Endpoints*

8.1 This is an observational study. The main data point of interest is operator satisfaction. The number of inadvertent arterial punctures

identified by the device (if any) will also be recorded. The data collection form is included with this HRRC application.

8.2 The investigators have not identified any safety endpoints.

9.0 Procedures Involved*

9.1 This is an observational study to be completed on 40 patients meeting the inclusion/exclusion criteria. Subjects presenting for CVC placement at the UNMH operating suites will be prepared as usual and consent obtained. The Compass pressure measurement device will be included in the CVC placement apparatus as per the manufacturer's directions. Data will be recorded on the placement procedure as well as routine patient demographic data. Identifiers will not be recorded.

9.2 A photograph of the device (with attached syringe and needle) is below.

9.3 The only research procedure is the inclusion of the device in the CVC placement apparatus, for patients who would already be having CVC placement regardless of the existence of this study. The research does not modify routine practice surrounding CVC placement (patient selection and preparation, operating personnel, catheter equipment, the procedure itself, or medications used) in any way. These considerations should mitigate risks.

9.4

- As noted above, enrollment of subjects from a population already presenting for CVC placement regardless of the existence of this study mitigates study risks. The investigators are similarly not modifying routine CVC practice except to specify the use of the studied device.
- The project does not specify the use of any drugs. The device being studied is the Compass for CVC pressure transducer device (Centurion Medical Products, Williamston MI).
- The data collection form is included with this application.

9.5 Data to be collected include routine demographic data (age, sex, height, weight, BMI, ASA status), data surrounding the CVC placement procedure (insertion location, use of ultrasound guidance, venous pressure before/after guidewire placement, operator satisfaction), and incidence of inadvertent arterial puncture.

10.0 Data and Specimen Banking*

10.1 Data will be recorded on paper forms with identifiers in order to permit resolution of any incomplete/unclear data entries. Data will be deidentified upon transfer to an electronic spreadsheet for analysis. The identifiable data forms will be retained until publication of results in order to permit any supplemental analyses requested by peer reviewers. The deidentified data may be retained indefinitely for potential future use, such as in serving as the underlying dataset for power analysis of a future study.

10.2 Deidentified data may be reviewed by the study sponsor. Release of deidentified data may be requested by contacting the PI and/or sponsor. Both the PI and study sponsor must approve release. Release will only be made to personnel who are qualified researchers pursuing legitimate research projects, in the opinion of the PI and/or sponsor. Identifiable data will not be released except as required by law.

11.0 Data Management* and Confidentiality

11.1 Data will be summarized by reporting mean (SD) of continuous variables such as BMI and age, percentages for categorical data such as patient sex, and raw count for inadvertent arterial punctures.

11.2 As this is an observational study, a power analysis is not useful.

11.3 All investigators are CITI- and HIPAA-certified. Completed data collection forms will be maintained in locked cabinets in Anesthesiology department offices, which are a patient-restricted area. As noted in section 10 above, the deidentified data will be retained indefinitely. Only investigators will have access to study data, but they will transmit an electronic copy of deidentified study data to the sponsor upon request. Qualified researchers may request an electronic copy of the deidentified data as listed in section 10 above. Identifiable data will not be released except as required by law.

12.0 Provisions to Monitor the Data to Ensure the Safety of Subjects*

The investigators believe that this is a Minimal Risk study. The only research-related procedure is the inclusion of a small FDA-approved device in the apparatus used to perform CVC placement, in accordance with its labeling.

13.0 Withdrawal of Subjects*

13.1 The investigators have not identified any circumstances in which participants would be withdrawn without their consent.

13.2 The investigators do not anticipate situations in which advance plans for orderly termination of research participation would be required.

13.3 The investigators do not anticipate any requests for withdrawal from the study.

14.0 Risks to Subjects*

14.1 Previous studies on this sterile, single-use device have identified no adverse events arising due to its use. The only issue identified to date is the size of the device; a few operators (reported in reference 3 listed above) would prefer that it be smaller. It is therefore possible, but has not ever been demonstrated, that the device's presence may impede CVC placement in some way. This risk is completely reversible, because the device can simply be removed from the needle apparatus if it is in the way. As in any study, there are risks of confidentiality breach. This study does not gather data that are especially sensitive, so the consequences of any confidentiality breach are minor. All risks are mitigated to the extent possible by restricting enrollment to a population that would have received CVC placement regardless of the existence of this study.

14.2 The presence of the device in the needle apparatus may present some unforeseeable risk, but as noted above, no such risks have been reported, and the device can simply be removed so that the CVC placement can proceed as usual.

14.3 The investigators have not identified any risks to the embryo or fetus should a subject be pregnant at the time of the study.

14.4 The investigators have not identified any risks to others who are not subjects.

15.0 Potential Benefits to Subjects*

15.1 While rare, inadvertent arterial puncture is possible during CVC placement. The studied device does not eliminate this risk, but rather permits early identification of arterial placement through pressure measurement; pulsatile pressure indicates arterial placement. Identification of arterial puncture at this point, before introduction of the guidewire or catheter, greatly reduces the consequences of arterial puncture. In a previous study on this device (reference 3 above), arterial puncture was identified in 1.7% of subjects, and all were recognized before guidewire insertion (and thus clearly before catheter insertion; no guidewires or catheters were inserted in arteries). Subjects in this study may similarly

receive the benefit of early identification of inadvertent arterial puncture, if any of these punctures do occur.

16.0 Vulnerable Populations*

16.1 This project does not involve the commonly-recognized vulnerable populations.

17.0 Community-Based Participatory Research*

This study does not constitute community-based participatory research.

18.0 Sharing of Results with Subjects*

18.1 This study does not involve testing or other results that may affect future treatment decisions for subjects, so there are none to share with subjects. Final study results will also not be shared with patients, because others' experience has no direct effect on the patient.

19.0 Setting

19.1 Research activities will occur at the UNMH operating suites and in the Anesthesiology department offices.

- Subjects will be identified from among the patient population at the UNMH operating suites. CVC placement for recruited patients will occur as planned at the UNMH main operative setting.

20.0 Resources Available

20.1 All investigators who will perform the CVC placements are licensed physicians authorized to practice and perform this procedure at UNMH. Investigator Tim Petersen PhD is a staff member in the Department of Anesthesiology with experience in study design and data analysis.

20.2 Describe other resources available to conduct the research: For example, as appropriate:

- A conservative estimate of the number of patients presenting to the UNMH main OR suites who require CVC placement is 10-20 per week. Of these, approximately 1/3 have BMI $\geq$35.
- Investigators will conduct study activities in conjunction with their routine clinical and non-clinical duties.
- The operating suites at UNMH are equipped with the personnel, facilities, and other resources needed to place CVCs and respond to any eventuality arising from the placement of a CVC.
- Upon HRRC approval, the approved version of the protocol will be distributed to all participating investigators. The

investigators do not anticipate any need for protocol modifications after HRRC approval.

21.0 Prior Approvals

21.1 Beyond the routine departmental review process and HRRC review, no other approvals are necessary for this project.

22.0 Recruitment Methods

22.1 After HRRC approval, enrollment will occur among at least 40 and up to 45 patients meeting the inclusion/exclusion criteria.

22.2 Subjects will be drawn from adult patients requiring CVC placement at the UNMH main operating rooms.

22.3 Investigators will identify subjects from among their routine patients.

22.4 No patient recruitment materials will be used.

22.5 Subjects will not be paid.

22.6 Investigators have drafted a proposed information handout for participating physicians who will place CVCs with the Compass device in this study. The handout notes that an investigator will obtain patient consent, and outlines both the target population and the study procedures. It also encourages participating physicians to contact the PI with any remaining questions.

23.0 Local Number of Subjects

23.1 As noted above, up to 45 patients will be included in this study, with a target completed sample size of 40.

24.0 Provisions to Protect the Privacy Interests of Subjects

24.1 All research-related activity will occur in the context of medical care, which already occurs in a suitable private location. Similarly, investigators are already authorized to initiate contact with potential subjects as part of clinical care.

25.0 Compensation for Research-Related Injury

25.1 The investigators believe that this is a Minimal Risk study. As such, there is not a plan for compensation for research-related injury.

26.0 Economic Burden to Subjects

26.1 Participation will not modify patient costs in any way.

27.0 Consent Process

27.1. Consent will be obtained by an HRRC-approved investigator prior to the commencement of research procedures. All investigators are CITI- and HIPAA-certified.

27.1.1. The consent process will occur in the UNMH operating suites.

27.1.2. Coercion and undue influence will be avoided by not paying participants, and by assuring prospective enrollees that their participation is entirely voluntary: they can still receive CVC placement without participating.

27.1.3. Additional lead time for prospective subjects to consider participation is not available in this study because CVC placement is usually performed shortly after the decision that one is needed. Similarly, there is published research that examines the effect of additional consideration time on patients' views of the consent process and their rights in anesthesia clinical trials. This research has shown that consent on the day of surgery for trials of treatments with similar risks/benefits does **not** compromise patient rights or welfare. The study authors (Murphy et al., "Consent for Anesthesia Clinical Trials on the Day of Surgery," *Anesthesiology* 2016; 124:1246-55) found that anesthesia patients approached for research consent on the day of surgery were **satisfied with the consent process**, felt that the protocol was **well explained and comprehended**, and agreed that **the setting was appropriate**. Conversely, these patients strongly disagreed that they were anxious at the time of consent, felt any obligation to participate, or regretted participating. Importantly, **these results were not changed by the use of a preadmission telephone call** to describe the research protocol and provide greatly extended time for patients to consider their participation. If patients felt that day-of-surgery consent represented a violation of their rights or an imposition on their welfare, these results would have been very different.

27.1.4. As this study involves a one-time clinical procedure, the investigators believe that a one-time consent procedure is appropriate, and the study thus does not require provisions for ensuring ongoing consent.

Subjects not fluent in English

27.1.5. As this study involves a relatively small sample, the investigators anticipate that few subjects will speak Spanish exclusively. If any eligible patients are Spanish speakers, the investigators will use the routine UNMH oral translation procedures to obtain consent, document it with the Spanish short form consent included with this application, and provide subjects with a copy of the English consent document as well.

Cognitively Impaired Adults/Adults Unable to Consent/Use of a Legally Authorized Representative

27.1.6. Inability to consent is an exclusion criterion.

Subjects who are not yet adults (infants, children, teenagers)

27.1.7. Only adults will be enrolled.

28.0 Process to Document Consent in Writing

28.1 Consent will be documented on an HRRC-approved consent form; a proposed form is included with this application.

29.0 Drugs or Devices

29.1 The devices to be studied will be stored in the Cardiac Anesthesia office, which is a separate area within the patient-restricted Department of Anesthesiology administrative offices. These offices are adjacent to the UNMH operating suites, so obtaining a device for a relevant patient will not present significant delay to any procedures. In this way, the devices will be maintained separately from regular operating room supplies and equipment, so they will not be mistakenly used on non-subject patients.

29.2 Device trade name: Compass for CVC

29.3 Device common name: Extravascular blood pressure transducer

29.4 Manufacturer: Centurion Medical Products, Williamston MI (formerly Mirador Biomedical)

29.5 The device received FDA 510(k) clearance (K133624) without a requirement for clinical testing, and there is not an IDE for this study (see section 29.7 below).

29.6 The use of the device in this setting does not present a potential for serious risk to the health, safety, or welfare of a subject.

29.7 This study is **IDE-exempt** in accordance with 21 CFR 812.2(c) and the FDA's "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors: Frequently Asked Questions about Medical Devices" available at http://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM127067.pdf (see section 12C on page 8 of that document), because the device will be used in accordance with the indications in its approved labeling in this study. The study does not modify the labeling, indications, instructions for use, or any other aspect of device administration. The study reviews operator satisfaction when using the device as directed in one subset of the intended population.