Document Description: ModPG3 Neo-Infant ISO 81060-2 Study Protocol	Document Number: 60106449 **Version: K**
Hill-Rom	Page 1 of 29
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Author: [redacted]

Version	Sec, Pg, Para Changed	Description of Change	Reason for Change	Date Version Created	Version Created By (initials)
A	All	Initial Release	Initial Release	[redacted]	
B	Approvers List All	Updated Approvers List Updated the document to the new protocol format.	[redacted]		
C	Pg. 9 V. Study Population A. 2 Age Pg. 9-10 C. Subject selection Criteria; Pg. 11 Determine appropriate cuff size; pg. 12 Pre-Screen; Pg17-18 Inclusion/Exclusion criteria; Pg. 21-22 Demographic Sheet Section III. A. 1	Corrected 2nd bullet:29 days old to 1 year old to less than 3 years. Updated cuff placement to side closest to arterial line. Removed lateral difference and use of radial/brachial art lines Reference to Reusable cuff changed to Disposable	Align with ISO Standard requirements Corrected Terminology	[redacted]	
D	Pg. 1- Req. Approvers Pg. 2 Clinical Site added	Updated Approvers List and document version Added second Clinical Site for Infant.	[redacted] Only Neo site identified-now have Infant site	[redacted]	
E	1.)Pg. 2- Req. Approvers 2.)Pg.8 I.E. 3.) Pg 14 VIII F Data Collection	1.)Updated Approvers List and document version 2.)Added Publication and Disclosure section 3.)Added steps 6-9	[redacted] 2.) MOH recommendations	[redacted]	

	4.) Pg 16. XA and pg 18. XH	4.) Added Section A. Training of Investigator & Site Staff and Section XH Discontinuation of the Study per MOH recommendations.	3.) MOH recommendations 4.) MOH recommendations		
F	1.) Pg 2 Sponsor contact 2.) Pg 8 I.D. 3.) Pg 18 X.F and G 4.) Pg 20-27 Appendix A-D	[redacted] 2.) Added the 7th bullet 3.) F: updated AE section for clarity on reporting. G: moved IRB reporting timeframe to Safety Plan 4.) Added 'Sample' to appendix	1. Admin changes 2. MOH recommendations 3. MOH recommendations 4. Admin changes	[redacted]	
G	1.) Pg 12 V.C.2 2.)Pg 13 VIIIB 3).Pg 15. IX and IX. A. Data Analysis	1.) Removed 4th from the last bullet in the exclusion section. 2.) Added information on how to measure subjects' arm to decide which cuff the subject will fit in. 3.) Added information to data analysis and stats plan	1.) This is an internal activity as opposed to site level activity. 2.) Clarity on arm measurement per ISO standard. 3.) Clarity to the data analysis and stats plan.	[redacted]	
H	1.)Pg 2 req. approves 2.)Pg 13 V.C.2 3.)Pg 22 Appendix A 4.)Pg 25 Appendix C	1.) Updated Approvers List and document version 2.) Added bullet on sedation exclusion requirements. 3.) Added bullet on sedation exclusion requirements. 4.) Added bullet on sedation exclusion requirements.	[redacted] 2.-4.) Clarity on patients that are sedated in the ICU and their ability to participate to align with RAS	[redacted]	
J	1.) Required approvers 2.) Section II - #2 3.) Section VIII (E) #2 4.) Section VIII (E) #3 5.) Appendix D	[redacted] 2.) Added 2 new pieces of equipment to approved equipment list	1.) Team Change 2.) Necessary to conduct the testing properly	[redacted]	

		3.) added setup step to collect hospital monitor baseline measurement. [redacted] 5.) Worksheet template was previously updated and did not require an amendment	3.) To allow for baseline hospital measurement 4.) Y connector is unable to display data to both devices. 5.) Worksheet template was previously updated and did not require an amendment		
K	VII D. Pre-Screening Hospital Arterial Determination	The word "Pre-Screening" removed	Wording removed to clarify this activity can be done post-consent 1. This change also removes "pre-screening" in the exclusion criteria for: 2. Does the subject have a Standard of Care systolic or diastolic difference > 12 mmHg between the Hospital's Intra-arterial blood pressure measurement and NIBP/Automated device blood pressure measurement? 3.Sample Worksheet Demographic Information Page 2 updated to Hospital Equipment Determination to reflect change.	[redacted]	

[redacted]

Required Approvers		
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Protocol Number: 60106449

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Clinical Sites: [redacted]

Proprietary Information

[redacted]

Contents

I. General Information

A. Purpose

The purpose of this study is to determine performance of [redacted] per the American National Standard ANSI/AAMI/ISO 81060-2:2018/Amd 1:2020: Non-invasive sphygmomanometers - Part 2: Clinical investigation of automated measurement type. The Welch Allyn blood pressure cuffs to be used in this study are all currently CE-marked under EU MDR. The Connex Vital Signs Monitor with ModPG3 is an investigational device.

This clinical study shall follow section 6 “Clinical investigation with reference invasive blood pressure monitoring equipment” in the ISO 81060-2:2018+A1:2020 standard. The subject populations covered by this study shall be neonate subjects defined as 0 to 28 days of age, and infant subjects defined as 29 days of age to under 3 years of age.

For each of the [redacted] the justification for the sample size is based on the requirements outlined in the American National Standard ANSI/AAMI/ISO 81060-2:2018/Amd 1:2020 Non-invasive sphygmomanometers - Part 2: Clinical validation of automated measurement type. The database shall contain no fewer than 18 neonatal and infant subjects with a minimum of 180-paired observations and no more than 100 subjects.

B. Intended Use, Indications for use, Intended Purpose

1. ModPG3 Investigational Device (Connex Vital Signs Monitor modified to include ModPG3)

- Intended Use: ModPG3 is a noninvasive blood pressure measurement system that measures a signal from which systolic, diastolic, and mean can be derived through the use of a blood pressure cuff.
- Indications for Use: ModPG3 will provide interfaces to allow the host to implement manual, long-term automated and short-term automated modes per ISO 80601-2-30. ModPG3 also provides patient modes that support neonate, infant, pediatric, and adult patients as defined in ISO 81060-2.

- Intended Purpose: ModPG3 will provide interfaces to allow the host to implement manual, long-term automated and short-term automated modes per ISO 80601-2-30. ModPG3 also provides patient modes that support neonate, infant, pediatric, and adult patients as defined in ISO 81060-2.

2. Specific limitations pertaining to this study

This study is a clinical investigation conducted per ISO 81060-2:2018+A1:2020. The scope of this study is limited to subjects that are under 3 years of age. This limits the use of the ModPG3 test device to its neonate mode.

C. Determination of Nonsignificant Risk Investigation

The risks associated with the ModPG3 investigational device were assessed and documented in the ModPG3 Hazard Analysis, [redacted] The risks associated with the protocol and investigational test set up were assessed and mitigated in the [redacted] Per [redacted] these devices, algorithms, and modules, have undergone the required risk analysis that designates the product as safe and effective for investigational use. All hazards and risks are accounted for in this protocol. The Hazard Analysis also supports the determination that this study is not a significant risk (NSR) study per 21 CFR 812.3(m).

The Connex Vital Signs Monitor (CVSM) will be used in conjunction with Hillrom tubing and cuffs as the test setup. The representative risk documentation related to this test and setup is shown below. The associated risk documentation contains the listing of all the risk management deliverables identified as well as the location of the objective evidence type, and results used:

- CVSM**:** CVSM RMFI [redacted]
- ModPG3: MODPG3 Hazard Analysis; [redacted]
- ModPG3 Neonate Prototype Hazard Analysis: [redacted]
- BP Cuffs: BP Cuff RMFI: [redacted]
- BP Cuff RAS: [redacted]

This study is a Non-Significant Risk (NSR) Investigation because the study devices do not present a potential for serious risk to the health, safety, or welfare of the subject. The study devices are not implants, do not support, or sustain human life, and are not substantially important in diagnosing, curing, mitigating or treating disease or in preventing impairment to human health.

This testing does not represent a potential for serious risk to the health, safety, or welfare of a subject. This assessment is based on the Code of Federal Regulations, Section 21, Part 812, Subpart A, as the testing:

- Is noninvasive.
- Does not require an invasive sampling procedure that presents significant risk.
- The devices are not used in sustaining or supporting human life.
- Does not by design or intention introduce energy into a subject.

- During this testing, no reliance will be made on data collected via the ModPG3 investigational device for the purpose of making a medical diagnosis.
- Risks are minimized by using procedures which are consistent with sound research design and already being performed on the subject in the clinical environment.

Furthermore, testing will be performed with intended users in their respective intended use environments and the data collected will not be used for clinical diagnostics or patient management. The device will also be labeled as an investigational device and not for clinical use.

D. Compliance Statement

This study will be conducted in compliance with the following regulations, standards, and guidance, as incorporated into Standard Operating Procedure (SOP) 20139: CGP—Good Clinical Practice:

- I.S. EN ISO 14155:2020 Clinical investigation of medical devices for human subjects – Good clinical practice
- 21 CFR 50 Protection of Human Subjects
- 21 CFR 54 Financial Disclosure by Clinical Investigators
- 21 CFR 56 Institutional Review Boards
- 21 CFR 812 Investigational Device Exemptions
- Medical Device Regulation (EU) 2017/745
- MDCG 2020-10/1 Safety Reporting in clinical investigations of medical devices under the Regulation (EU) 2017/745
- ICH E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1)

Institutional Review Board/Independent Ethics Committee (IRB/IEC) approval must be obtained from each institution's IRB/IEC of record. Institutions that do not have an IRB/IEC of record may use an independent IRB.

Health Insurance Portability and Accountability Act (HIPAA) authorization will be required as health information will be obtained from the human subjects.

E. Publication and Disclosure

[redacted]

In accordance with the Declaration of Helsinki, a description of the clinical investigation shall be registered in a publicly accessible database before the start of recruitment activities and the content shall be updated throughout the conduct of the clinical investigation.

[redacted]

II. Study Objectives

A. Primary Objective

The primary objective of this study protocol is to collect data with the Welch Allyn Mod PG3 Neonate Step BP algorithm and neonatal blood pressure cuffs. The data collected shall be used to calculate the performance metrics needed to determine compliance to the American National Standard ANSI/AAMI/ISO 81060-2:2018/Amd 1:2020 Non-invasive sphygmomanometers - Part 2: Clinical investigation of automated measurement type. Per the Standard test requirement, non-invasive blood pressure measurements will be compared to intra-arterial references to determine whether the blood pressure algorithms meet the clinically acceptable level of accuracy.

III. Study Design

A. Equipment

The equipment used in this study falls into 2 categories. The first category is equipment used with the ModPG3 investigational device, and the other category is equipment needed by the clinicians to take invasive reference readings per ISO 81060-2:2018+A1:2020.

Note: Additional equipment that is not listed here may be necessary to complete testing. The equipment used during testing will be documented on the corresponding equipment accountability log.

1. ModPG3 Investigational Device

- Connex Vital Sign Monitor with ModPG3
- Laptop
- Data Collection Software
- USB cable
- Power strip
- Welch Allyn FlexiPort Disposable Blood Pressure Cuffs

Model Number	Cuff Name	Cuff Range (cm)
NEO-1-1	Neo 1	3.3-5.6
NEO-2-1	Neo 2	4.2-7.1
NEO-3-1	Neo 3	5.4-9.1
NEO-4-1	Neo 4	6.9-11.7
NEO-5-1	Neo5	8.9-15

2. Approved Invasive Equipment List

- Surveyor S12/S19
- Hill-Rom ICU Medical data collection cable [redacted]
- Hill-Rom Edwards data collection cable [redacted]
- Hill-Rom [redacted]
- Fogg Medical [redacted] Interface Cable for ICU Medical Transpac IV transducer to Mortara S12

B. Design

1. Study Design

This study is a multi-person, non-randomized study. Data will be collected at clinical sites enrolled to participate in the study.

The study shall include a minimum of 18 subjects who are under 3 years of age and a minimum of 180 paired determinations.

A more detailed breakdown of subject requirements is provided in section V.

2. Sample Size Justification

ISO 81060-2:2018+A1:2020 defines a minimum sample size of 18 subjects and 180 paired determinations. Those limits are captured in this protocol to ensure compliance with the requirements of the standard.

3. Acceptance Criteria

To determine acceptance of the results of this study the ModPG3 investigational device shall have a mean error within or equal to +/- 5.0 mmHg and an experimental standard deviation no greater than 8.0 mmHg as defined in section 6.2.6 of the ISO 81060-2:2018+A1:2020 standard.

IV. Informed Consent

Documentation of Informed Consent is required for all subjects participating in this study per 21 CFR 50.27 (a) and ICH E6 (R2) 4.8.

A copy of the Informed Consent document will be available to all participants for review and if agreed upon the study subject or legally authorized representative (LAR) will sign the IRB approved informed consent. The patient subject or LAR will be given a copy of the signed consent to keep for their records. They will be informed by the study staff that their participation is voluntary. They may withdraw their participation at any time for any reason without loss of benefits to which they would be entitled.

The Principal Investigator (PI), or an authorized representative, will be responsible for reviewing the informed consent document with the study subjects and LAR, answering all questions, and obtaining a signed informed consent for all participants.

V. Study Population

A. Study Subject Demographics

For this study, a full set of subjects as prescribed by ISO 81060-2:2018/Amd 1:2020 is required. The demographics required are captured in a series of requirements defined in section 6.1.3.2 of the standard based on weight and age. The following sections of this document detail the requirements for each of those categories.

1. Weight

- At least 3 patients shall be less than 1,000 g in weight.
- At least 3 patients shall be 1,000 g to 2,000 g in weight.
- At least 3 patients shall be greater than 2,000 g in weight.

2. Age

- At least 3 patients shall be greater than or equal to 29 days old and less than 1 year old.
- At least 3 patients shall be greater than or equal to 1 year old and less than 3 years old.
- The remaining patients may be from any of the above age or weight groups in order to complete the sample size of 18. (A patient can be in more than one category simultaneously.)

B. Expected Time Requirements

Commitment time for each subject is expected to be approximately- two hours for the consent and data collection steps to be completed.

C. Subject Selection Criteria

1. Inclusion Criteria

- Meets the neonatal or infant (less than 3 years of age) subject population.
- The neonate and infant subjects will already have an indwelling intra-arterial line.
- Subject's legally authorized representative must consent for the subject to participate.
- Subject's legally authorized representative must be able to read, write, speak in English and/or Italian.
- Subject must have an arm circumference in the range of 3.3-15.0 cm.
- Subject must be able to have blood pressures taken on the upper extremity closest to the arterial line
- The subject has one upper arm that is free of indwelling catheters or IV lines, shunts, oximetry sensors, dressings, etc. for attachment of a NIBP cuff.

2. Exclusion Criteria

- Lack of Informed consent.
- Subjects with deformities or abnormalities that may prevent proper application of the device under test.
- Subject is evaluated by the investigator or clinician and found to be medically unsuitable for participation in this study.
- Subjects with known heart dysrhythmias or arrhythmias during the measurement period.
- Subjects with compromised circulation or peripheral vascular disease.
- Subjects who have had surgery or have shunts or implants in the upper extremity being tested.
- Those who have a heart rate that is irregular for any reason other than normal fluctuations in the R-to-R interval associated with respiration.

- Hospital System NIBP: those who have a systolic and/or diastolic blood pressures difference > 12 mmHg between the hospital intra-arterial measurement and the hospital blood pressure cuff/automated vital signs monitor are excluded. The device under test cannot be used for this reading.
- Subjects with clotting disorders or taking prescribed blood thinners.
- Subjects with a severe contact allergy to sensors or cuff material.
- Subjects with a history of skin fragility or breakdown, such as ecchymosis or lacerations, affecting the upper extremities that would affect the application of noninvasive blood pressure cuff.
- Subjects whose arm circumference does not fall within 3.3 and 15.0 cm.
- Arterial line is not properly damped.
- The subject has an unstable condition in which noninvasive BP cannot be obtained
- Subjects who have radial or brachial arterial lines.
- Subjects who require sedation solely for the purpose of this study and/or prolonged sedation from a prior procedure.

A source document - NIBP Eligibility Criteria will be completed for all subjects (see Appendix A) and data entered in the electronic Case Report Form (eCRF).

VI. Subject Confidentiality

All participant data will be kept fully confidential to the extent possible. All data collected will include the participant identification number to minimize participant identification.

A Participant Screening/Enrollment Log will be utilized to assign all participants with a participant identification number to be used to complete data forms.

VII. Subject Remuneration

The study sponsor will enter into a written Clinical Testing Agreement with each study site. Clinicians who participate by collecting data from their patients for the external study will be compensated on a per-patient basis at the Fair Market Value rate. The study site, its clinicians, and staff will not receive any additional payments for participating in this study.

VIII. Study Procedures

A. Informed Consent and HIPAA Authorization

The Principal Investigator or his / her designee conducts the informed consent process

1. Verify that the subject's legally authorized representative acknowledges ability to read or write in English/Italian.
2. Allow subject's legally authorized representative ample time to read the entire form and ask questions.
3. Give a thorough description of the study and the subject's involvement – especially explain that they may withdraw or be withdrawn from the study at any time.

4. After the subject's legally authorized representative has read the form ask if they understand everything.
5. Ask if they will allow the subject to take part in the study and if so explain that they may sign and date the form.
6. Once the subject's legally authorized representative has signed and dated the informed consent, the principal investigator or authorized designee will sign and date the form.
7. Give a copy of the informed consent to the subject's legally authorized representative.
8. No procedure may be performed before the informed consent is signed by the subject's legally authorized representative.

If an investigator uses a device without obtaining informed consent, the investigator shall report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.

B. Determine Appropriate Cuff Size

Measure the circumference of the upper arm and place the appropriate size reference blood pressure cuff on the bicep of the subject. The upper arm midpoint is first determined by marking the arm posteriorly at a point halfway between the acromion and olecranon, measured while the arm is flexed 90 degrees at the elbow with the palm facing up. The subject's upper arm circumference shall be determined by measuring at the midpoint of the upper arm while the elbow is relaxed, and the arm is dangling freely to the side. Record the remaining demographic information, including arm used, arm circumference, cuff fit (standard or tapered), and cuff size used as well as additional data to be collected on the Demographic Information Sheet (see Appendix C).

Each cuff supplied to the site by the Sponsor is labeled with its circumference size. Most subjects will fit into 2 size cuffs. Always apply the largest available cuff first. If the larger cuff is too long for the subject's arm and crosses over the antecubital fossa, then the smaller size cuff within the measurement range may be used to measure the blood pressure. If the smaller size cuff must be used (within the subject's arm measurement range) then it must be documented why the smaller of the 2 cuffs was used. Document the cuff size choice decision on Appendix C. For this study, the upper extremity closest to the arterial line is the only acceptable cuff placement site.

C. Arterial Line Verification, IBP, and NIBP Measurements

Trained delegated study staff [redacted] are to complete the following series for each subject who has been consented and is eligible to participate. It is expected that at least two qualified study staff will complete the following steps, one to perform the procedure and the other to monitor the subject as well as record the data.

D. Hospital Arterial Determination

1. Take any necessary steps to remove air bubbles and clots from the system prior to taking any measurements.
2. Follow guidelines to perform a fast flush of the arterial system to generate a square wave test.

[redacted]

3. Observe the number of oscillations and record on the subject's demographic form (Page 2, section 1)
4. Apply the hospital's cuff to the subject's upper extremity closest to the arterial line that is going to be used for testing the UUT (Unit under test). Make sure that the cuff being used is the appropriate size cuff for the subject's arm measurement size per Section B above. Radial or brachial arterial reference sites are excluded.
5. Attach cuff connector to the hospital's vital signs monitor. Once the cuff is applied, allow the subject to rest quietly for 5 minutes.
6. Once 5 minutes has passed, record the systolic, diastolic, and mean arterial pressure from the intra-arterial line.
7. Then take an initial non-invasive blood pressure using the hospital's NIBP device.
8. Record findings on the Subject Demographic Form (Page 2, sections 1 & 2).

E. Equipment Setup

1. Bring the data collection computer, Surveyor S12/S19, and the ModPG3 Investigational Device to the subject.
2. Take a baseline invasive blood pressure reading from the hospital monitor.
3. Using the correct data collection cable listed in Section 2 above, depending on the brand of the subject's arterial transducer, connect the subject's arterial line to the Surveyor S12/S19.
4. Power on the S12/S19 and zero the transducer.
5. Ensure that the Systolic and Diastolic values indicated by the Surveyor S12/S19 is within 1mmHg of the baseline hospital monitor measurement.
6. Power on the data collection laptop,
7. Connect the communications cables from the ModPG3 investigational device and the Surveyor S12/S19 to the PC.
8. Load the data collection software.

F. Data Collection

Welch Allyn will be supplying the participating sites with a laptop loaded with data acquisition software specific to the surveyor and the ModPG3 Investigational Device. The instructions below apply to collection of IBP (invasive blood pressure) and cuff blood pressure readings that will be transcribed to the NIBP Data Collection sheet and eCRFs. Instructions will be provided in a separate training document for use of the data acquisition software.

Follow these steps to collect and record data and discharge the subject from the study. All steps in section 6.2.3 of the standard are reflected here except for step a which is captured as step 1 of the pre-screening and step c because the data collection software runs cycles in a mode where there is no reading-to-reading memory, so there is nothing to clear.

Report all requisite data as noted on the Demographics Info Form. (See Appendix C). Comments may be included on an additional sheet if needed.

1. Apply the cuff determined in section VIII.B above to the patient's upper arm.

2. Using the data acquisition software provided, start a reading for the subject. The tool will automatically record the pre invasive blood pressure readings, then take the NIBP measurement with the device under test, and it will follow up with a post invasive blood pressure reading.
3. When complete, record the data in the subject NIBP data collection sheet (Appendix D).
4. Start a stopwatch and wait 3 minutes before starting the next cycle.
5. Repeat steps 2 to 4 until a maximum of 11 readings have been performed on the study subject.
6. The subjects nurse and study staff will monitor the subject's comfort level to determine participation throughout the study. The study staff will additionally monitor the cuff test site throughout the duration of the study and upon removal of the cuff.
7. The subjects legally authorized representative will be advised during the study that he/she may stop the participation at any time, free of negative repercussions.
8. All equipment will be removed from the subject. No further treatment will be required upon termination/completion of the study.
9. The observers will record any final notes. The subject will be released with no follow-up required.

[redacted]

Monitor Subject for any Potential Discomfort.

After the NIBP readings have been completed, remove the NIBP cuff from the subject and check the condition of the arm for signs of petechiae, bruising, etc. Record any adverse events on Sponsor-provided Adverse Event Form and Log.

G. Patient Participation Completion

When a subject's participation in the study has completed the subject needs to be disconnected from the [redacted] and ensure that the subject is returned to the normal connection configuration prior to the execution of the study.

IX. Data Analysis and Reporting

Further details of the planned statistical methods will be provided in the study statistical analysis plan (SAP). [redacted] Any changes to the statistical methods described in the protocol will be documented in the SAP.

A. Analysis Population

Two main analysis populations will be used for this study. The efficacy analyses will be based on the full analysis set (FAS) which will include all subjects meeting inclusion/exclusion criteria and have at least one valid paired blood pressure measurement. The following criteria will result in an entire subject being removed from the FAS:

- The invasive reference systolic blood pressure range is more than 20 mmHg (2,67 kPa) or if the reference diastolic blood pressure range is more than 12 mmHg (1,6 kPa) during or before a determination by the ModPG3 investigational device.

Safety analyses will be based on the safety analysis set (SS) which will be the set of all participants who were connected to the Mod3PG device, regardless of whether a valid blood pressure measurement was obtained.

The FAS shall be analyzed according to the formulas called out in section 6.2.6 of ISO 81060-2:2018/Amd 1:2020. The following provides a summary of the formulas and calculations for Systolic, Diastolic, and mean arterial pressure (MAP).

B. Criteria 1

Criteria 1 has two values that shall be calculated from the data collected in the study for both systolic and diastolic blood pressure independently. The first is $\bar{x}_n$ which is the mean value of the differences between the ModPG3 investigational device and the paired reference reading. The second is S_n which is the experimental standard deviation. The acceptance criteria for these values are defined in section III Study Design, subsection B (3).

1. $\bar{x}_n$ Calculation

$$\bar{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} (x_i)$$

$\bar{x}_n$ Is the mean value of the differences

x_i Is the error of the i[th] individual determination per section D.

n Is the total number of determinations.

i Is the index of the individual determination.

2. S_n Calculation

$$S_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} (x_i - \bar{x}_n)^2}$$

$\bar{x}_n$ Is the mean value of the differences as calculated above for criteria 1.

x_i Is the error of the i[th] individual determination per section D.

n Is the number of determinations

i Is the index for the individual determination

C. Reference Blood Pressure Determination

- If the invasive blood pressure signal is interrupted due to the inflation of the cuff a period of at least 30 seconds prior to the start of the inflation shall be used.
- If the invasive blood pressure signal is not interrupted due to the inflation of the cuff a period of at least 30 seconds that includes the period of the ModPG3 investigational device's determination shall be used.
- The mean arterial pressure (MAP) from the invasive blood pressure signal shall be calculated for each individual beat by using the area under the blood pressure curve divided by the duration of the heartbeat.
- Using the extracted arterial signal calculate the mean and experimental standard deviation of the systolic, diastolic and MAP pressures.
- The reference blood pressure is defined as a range of +/- 1 experimental standard around the mean value of the invasive blood pressure value.
- Isolated premature ventricular beast (VPBs) shall be addressed by removing the pressure pulse associated with the VPB and the following compensatory beat.

D. x_i Calculation

- If the determination of the ModPG3 investigational device lies within the range of the reference blood pressure determined per section C, the error shall be assigned as 0.

- If the determination of the ModPG3 investigational device lies outside the range of the reference blood pressure determined per section C, subtract the adjacent limit of the reference blood pressure from the determination of the ModPG3 investigational device.

X. Administration of the Study

A. Training of Investigator & Site Staff

The Study Monitor will ensure that the Investigator and study site personnel have understood all requirements of the protocol and his/her regulatory responsibilities as an Investigator. Training may be provided at an investigator's meeting, at the study site, and/or by instruction manuals and [redacted] In addition, the Study Monitor will be available for consultation with the Investigator and serve as the liaison between the study site and the Sponsor.

The Investigator is responsible for the conduct of all aspects of the study at the study site and verified by signature the integrity of all data transmitted to the responsible party. Whenever the term 'investigator' is noted in the protocol text, it may refer to either the Principal Investigator (PI) at the site, or an appropriately qualified, trained and delegated individual of the investigational site. Sub-investigators or other authorized study personnel are eligible to sign for the Investigator, except where the Investigator's signature is specifically required. No additional clinical training is needed for the use of the investigational device.

B. Monitor Site Visits

Once the clinical site begins to screen and enroll subjects that are willing to participate, the site will also be responsible for data collection. The sponsor will be responsible for monitoring the site and verifying that the site is following Welch Allyn's Standard Operating Procedures for study monitoring in accordance with Good Clinical Practice (GCP) recommendations and FDA regulatory requirements.

If the site is not meeting the minimum requirements to conduct the study or has administrative, procedural, or data quality deficiencies that require correction in order to comply with regulatory requirements, the protocol, or to meet the requirements of the sponsor, the site will be notified in writing of the deficiencies and permitted a reasonable opportunity to rectify deficient conditions. The inability of the site to rectify seriously deficient conditions in a timely manner or to maintain compliance with regulatory requirements may be the cause for termination of the study activities, closure of the investigational site, and notification of that decision to the relevant Institutional Review Board (IRB) and other regulatory authorities as appropriate.

The participating site will have an initial qualification visit by the sponsor, routine interim monitoring [redacted] during the study, and a study close-out meeting conducted by the sponsor. Additional monitoring meetings may be scheduled as needed.

Each monitoring meeting will utilize a standard checklist of elements to be reviewed at the site, tailored to the specific requirements of the study. Site monitoring visits will routinely review the participating site staff roster, study administrative and financial documents, required regulatory documentation, status of IRB approvals, changes or actions taken since any previous visit, participant recruitment status, documentation of informed consent for each participant, review of adverse events, investigational product storage conditions, outstanding data clarification, and a review of data elements against source documentation. Site visits follow standard Welch Allyn procedures, and a report will be prepared for study records.

C. Maintenance of Study Records

All study related files must be maintained in a secure storage area to which only authorized personnel have access. Welch Allyn must maintain all Clinical Investigation Files for 2 years following the life of the device or 7 years whichever is greater.

D. Risk/Safety Assessment

There are minimal risks to subjects, as described in Section I, C, Determination of Non-Significant Risk.

E. Anticipated Benefits to Subjects or Others

There are no direct benefits to subjects for taking part in this study. However, subjects may help Welch Allyn develop a new device to help benefit patients in the future.

F. Adverse Events

Adverse Events (AEs), including Serious Adverse Events (SAEs), will be documented and reported per EU MDR Article 80 and MDCG 2020-10/1 as applicable. Sites shall complete an AE form for all AEs,

SAEs, and UADEs and send to the applicable sponsor team members for review and appropriate reporting. Investigators will follow all unrelated AEs until resolution, stable, or the end of the study, whichever occurs first, and follow all adverse device effects (study device related and study procedure related) until resolution or stable, including following the subject after the end of the study if necessary.

G. Unanticipated Adverse Device Effects

An Unanticipated Adverse Device Effect (UADE) is any serious adverse effect on health or safety, or any life-threatening problem or death caused by, or associated with, a device, to a subject if:

1. That effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or
2. Any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

H. Discontinuation of the Study

If a clinically significant safety finding is identified during the clinical study, the Investigator or the IRB may determine if any change in patient management is needed. The Sponsor shall review AEs and assess risks during the conduct of a clinical investigation. The Sponsor shall terminate the clinical investigation if an unacceptable risk is confirmed. Decision to restart the study will be made jointly by Sponsor, the regulatory authority, the site-specific IRB, and the PI, following evaluation of the problems encountered.

The Investigator may terminate a patient's study participation at any time during the study if he/she judges it to be in the patient's best interest.

If a patient is withdrawn from the study, the study Monitor must be informed in the shortest possible time, regardless of the reason for withdrawal. In addition, a patient or the patient's legally authorized representative may discontinue his or her participation at any time during the study. If a patient's participation is discontinued, the reason(s) must be recorded in the source documents and in the eCRFs.

If a patient is prematurely removed from the study, all data prior to discontinuation should be recorded and all available data will be included in the statistical analyses.

APPENDIX A: Sample NIBP Eligibility Criteria

The following sheets are used to record information associated with a subject to determine eligibility to participate I the study.

Welch Allyn Protocol Title: ModPG3 Neo-Infant ISO 81060-2 Study Protocol	**Welch Allyn Protocol ID:** [redacted]	
Clinical Site:	**Principal Investigator:**	
Evaluation Date: (YYYY/MM/DD)	**Subject ID Number:**	
Inclusion Criteria (All questions should be checked **YES**.)	**YES**	**NO**
Does the subject meet the neonate/infant subject population per the Standard (a neonate or infant less than 3 years of age)?	☐	☐
Does the neonate/infant subject have an existing indwelling arterial catheter?	☐	☐
Does the subject have one upper arm that is free of indwelling catheters or IV lines, shunts, oximetry sensors, dressings, etc. for attachment of a NIBP cuff?	☐	☐
Does the subject's Parent or Legally Authorized Representative consent to the subject's participation in the study and is able to read, write, speak in English and/or Italian?	☐	☐
Does the subject have a regular sinus rhythm (no arrhythmias during the measurement period or known dysrhythmias)?	☐	☐
Does the subject have an arm circumference in the range of 3.3-15.0 cm?	☐	☐
Does the subject fit into one of the buckets for the subject distribution listed?	☐	☐
Is the subject able to have blood pressures taken on the upper extremity closest to the arterial line?	☐	☐
Exclusion Criteria (All answers should be checked **NO**.)	**YES**	**NO**
Does the subject have an unstable condition in which noninvasive BP cannot be obtained?	☐	☐
Is the subject medically unsuitable for the participation in the study?	☐	☐
Does the subject have deformities or abnormalities that may prevent proper application of the ModPG3 investigational device?	☐	☐
Does the subject have a severe contact allergy to sensors or cuff material	☐	☐
Does the subject have clotting disorders or is the subject taking prescribed blood thinners?	☐	☐
Has the subject had surgery or have shunts or implants in the upper extremity being tested?	☐	☐
Does the subject have compromised circulation or peripheral vascular disease?	☐	☐
Does the subject have an arm circumference that falls outside the 3.3 and 15.0 cm range requirements?	☐	☐

Does the subject have a history of skin fragility or breakdown, such as ecchymosis or lacerations, affecting the upper extremities that would affect the application of noninvasive blood pressure cuff?	☐	☐
Does the subject have a heart rate that is irregular for any reason other than normal fluctuations in the R-to-R interval associated with respiration?	☐	☐
Does the subject have a Standard of Care systolic or diastolic difference > 12 mmHg between the Hospital's Intra-arterial blood pressure measurement and NIBP/Automated device blood pressure measurement?	☐	☐
Does the subject have an arterial line that is not properly damped?	☐	☐
Does the subject have an existing radial or brachial arterial line?	☐	☐
Does the subjects require sedation solely for the purpose of this study and/or prolonged sedation from a prior procedure.	☐	☐

☐ The subject meets all inclusion criteria and does not meet any of the exclusion criteria.

☐ The subject does not meet all inclusion criteria and/or meets at least one of the exclusion criterions.

Study Staff Signature _____ Date_____

APPENDIX B: Sample Screening/Enrollment Log

The following sheet is used to log the screening of the subjects for eligibility to participate in the study.

Welch Allyn Protocol Title: ModPG3 Neo-Infant ISO 81060-2 Study Protocol	**Welch Allyn Protocol ID:** [redacted]
Clinical Site:	**Principal Investigator:**

Instructions: The Screening/Enrollment Log is the only link that should exist, linking the subject consents with the study data. It should be kept with the consents in a locked and secure environment.

Subject screening may consist of: (a) reviewing a subject's information to determine if s/he is eligible for entry into the study, and (b) discussing the study with the subject or the subject's legally authorized representative.

Please record all subjects screened and/or enrolled for this study. Mark each subject as either an enroller or an excluded subject. Identify each by code as to why subjects were excluded. Refer to the protocol for inclusion/exclusion criteria.

[redacted]

- Digit 1, 2, 3, 4, = [redacted]
- Digit 5, 6, 7, 8 = [redacted]

Date of Screening /Enrollment (YYYY/MM/DD)	Subject Initials	Enrolled	Excluded	Subject ID Number if Enrolled or NA	Reason Why Excluded	Data retired/ destroyed

Principal Investigator signature below confirms agreement of above information and that these individuals were either screened and did not meet the criteria to be enrolled in the study or that the individuals met the inclusion/exclusion criteria and have provided informed consent/assent, as required.

PI Signature

Date

APPENDIX C: Sample Demographic Sheet

The following sheet will be filled out for each subject. It captures the demographic information for the subject including what cuff is used and the arm circumference.

Demographic Information Continued - Page 1 of 2

Welch Allyn Protocol Title: ModPG3 Neo-Infant ISO 81060-2 Study Protocol	**Welch Allyn Protocol ID:** [redacted]
Clinical Site:	**Principal Investigator:**
Subject ID:	**Date:** **(YYYY/MM/DD)**

Test Device SN:_____

Subject Age:

☐ **Neonate (N)** (<29 days)

Gestational Age: _____ weeks _____ days

☐ **Infant (I)** (≥29 days to < 3 years old)

Age: _____ years _____ months _____ weeks _____ days

Subject Height: _____ cm **Subject Weight:** _____ gm

Subject Diagnosis: _____

Cardiac Surgery: _____ **Date:** _____

Subject Position (Supine Preferred): ☐ Supine ☐ Other:_____

Gender: ☐ Male ☐ Female

Race:

☐ White ☐ Black or African American ☐ American, Indian, or Alaska Native

☐ Asian ☐ Native Hawaiian or Other Pacific Islander ☐ Other: _____

Sedated: ☐ No ☐ Yes , agent used_____

Level of Sedation: (Circle one) Light Moderate Heavy

Arm measurement

Arm Used:_____**Length:** _____cm **Circumference:** _____cm

Neonate Soft Disposable Cuff Size Selected:

☐ **Cuff Size 1: 3.3-5.6** ☐ **Cuff Size 2: 4.2-7.1** ☐ **Cuff Size 3: 5.4-9.1**

☐ **Cuff Size 4: 6.9-11.7** ☐ **Cuff Size 5: 8.9-15**

If largest available cuff was not used, please state why: _____

Demographic Information Continued - Page 2 of 2

Welch Allyn Protocol Title: ModPG3 Neo-Infant ISO 81060-2 Study Protocol	**Welch Allyn Protocol ID:** [redacted]
Clinical Site:	**Principal Investigator:**
Subject ID:	**Date:** **(YYYY/MM/DD)**

Hospital Equipment Determination:

Square Wave Test Oscillations: _____ (1 to 2 oscillations are acceptable)

Baseline Vital Signs (Military Time): _____

Invasive Blood Pressure (IBP, sys/dia): _____ /_____ MAP: _____ HR: _____ RR: _____

Noninvasive Blood Pressure (NIBP, sys/dia): _____/_____

Difference between IBP and NIBP:

Systolic Difference _____mmHg* **Diastolic Difference** _____mmHg*
*If systolic or diastolic is > 12 mmHg remove the BP cuff and discharge the subject as the subject is not eligible to participate in the study.

Location of the Art line:

☐ UAC

☐ Right Subclavian ☐ Right Femoral ☐ Right Pedal

☐ Right Posterior Tibial

☐ Left Subclavian ☐ Left Femoral ☐ Left Pedal

☐ Left Posterior Tibial

Other: _____

Age of the Art line (Days): _____

Verify No Air Bubbles or blood in line (Clinician Initials)**:** _____
Arterial Line Zero & Calibrated (Military Time): _____
Study Staff Signature: _____ **Date:** _____
(YYYY/MM/DD)

APPENDIX D: Sample NIBP Data Collection Form

The following sheet will be filled out for each subject. It captures the readings for the individual subject.

Subject ID: _____ **Date:** _____ **Time Equipment taken to subject care area:** _____ (Hours, using military time)

Series	Pre-ART Start Time	Pre-Test Device Motion (0-5)	During Test Device Motion (0-5)	Post-Test Device Motion (0-5)	Post-ART End Time	Does the Subject ID on Screen Match the Input Sheet? (Y/N)	Reading	Status	File Name
1	:				:				
2	:				:				
3	:				:				
4	:				:				
5	:				:				
6	:				:				
7	:				:				
8	:				:				
9	:				:				
10	:				:				
11	:				:				

Time use military time (1:00 pm = 13:00), Sys (Systolic) Dia (Diastolic), HR (Heart Rate), Motion (see Motion Table)

Hospital Monitor Invasive Line Post Vital Signs: Time _____ HR _____ RR _____ BP _____Hospital Monitor Invasive Line Post Vital Signs:
me _____ HR _____ RR _____ BP _____

Time equipment removed from subject care area: _____ (Hours, using military time)

Staff Signature: _____ Date:_____ (YYYY/MM/DD)