Document Description: ModPG3 Adult-Ped ISO 81060-2 Study Protocol	Document Number: 60115909 **Version J**
Hill-Rom	Page 1 of 30
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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]	[redacted]
B	All pages Pg 5 Pg 6-8 Pg9 Pg 11 Pg 12-14 Pg 24 CRF Pg 28 Demographic sheet	Included Sure and StepBP algorithms and updated signers General Info updated Cuff updates Per ISO. Changed work prototype to investigational device Design- Clarify 3rd observer added BP cuff note for clarity Updates to inclusion/exclusion criteria Updates to Limb size and update to steps CRF Updates Deleted inches and pounds to align with metric system	ISO standard updates	[redacted]	[redacted]
C	All	Updated the document to the new protocol format. Added clarifications to the document to make specifics about the protocol clearer.	Template update	[redacted]	[redacted]
D	1. Required Approvers 2.Pg 14, Section C1	1. [redacted] 2. Updated consent criteria to include	1. Team members changed 2. Inclusion criteria update to include large population that understands/speaks French language	[redacted]	[redacted]

	Pg 16, VIIIB Appendix C, #3	speaking French language.			
E	1.Required Approvers 2. Pg10 I.E. 3. Pg 16. C.2 Exclusion Criteria last bullet. Pg 29 Appendix C #16 4.VIII C Data Collection Pg 19 5.Pg 21. XA and pg 23. XH	1. [redacted] 2.Added Publication and Disclosure section 3.Exclusion Criteria and appendix C #16 updated to include Subject is pregnant and/or breastfeeding 4.Elaborated on steps 20 and 21-No further treatment needed post study participation 5.Added Section A. Training of Investigator & Site Staff and Section XH Discontinuation of the Study per MOH recommendations.	1. Team members changed 2. MOH recommendations 3. MOH recommendations 4.MOH recommendations 5. MOH recommendations	[redacted]	[redacted]
F	Pg 4. Sponsor Contact Pg.16 V.C. II. And Pg 28 Appendix C #10 Pg 16V.C. and Pg 28 Appendix C Pg 27 Appendix B	[redacted] Bullet: Subjects with clotting disorders or taking prescribed blood thinners. Added Right Arm as an inclusion criteria to take a blood pressure Added Gender to CRF	Team member updates Updated exclusion criteria requirement to remove "prescribed blood thinners" Align with ISO requirements Align with ISO requirements	[redacted]	[redacted]
G	Pg 17 VIII A #2.1 and 5	1. Revised statement to add laying comfortably with legs uncrossed and	1. For clarification on positioning of subjects	[redacted]	[redacted]

		added "operated by Observer 3"	and for clarification for Observer role		
	Pg 18-Pg 19 VIII C #1.2.1	2.Revised statement to add laying comfortably with legs uncrossed	2. For clarification on positioning of subjects		
	Pg 18 VIII C #2	3.Revised statement to add prior to reference reading	3. For clarification on when to take a pulse		
	Pg 18 VIII C #6	4.Revised statement to described how to measure the arms circumference	4. For clarification on how to measure the arm to determine the cuff to use		
	Pg 19 VIII C #9.2	5.Revised statement to define a subject with an irregular rhythm as a screening failure	5. For clarification on how to manage a subject with an irregular rhythm		
	Pg 19 VIII C #18	6.Revised statement to align target number of readings to the ISO	6. For clarification on number of reference readings to take to complete a subject enrollment per ISO		
	Pg 24,27, 28 Appendix A-C	7.Added 'Sample' to CRF	7. Admin change		
H	Pg 12 III A 2 Pg 28. CRF	Reverted Child Ref cuff range from 20-26 to 22-26	Admin change: transcription error between versions	[redacted]	[redacted]
J	Pg 4- Clinical Sites Pg 14 V.a.	Removed sites listed Added option to have internal recruitment	Admin changes Expand option for recruitment.	[redacted]	[redacted]

[redacted].

Required Approvers		
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Regulatory Representative	[redacted]	[redacted]
Risk Representative	[redacted]	[redacted]
Clinical Lead	[redacted]	[redacted]

ModPG3 Adult-Ped ISO 81060-2 Study

Welch Allyn Products: [redacted]

Protocol Number: 60115909

Principal Investigator: [redacted]

Sponsor Local Contacts: [redacted]

Sponsor: [redacted]

[redacted]

[redacted]

Contents

I. General Information

A. Purpose

Automated blood pressure cuff measurement is the standard in numerous medical settings today. Oscillometric devices using deflation algorithms estimate the amplitude of pressure changes as the cuff deflates from above the systolic pressure. The amplitude suddenly increases as the pulse breaks through the occlusion of the artery. As the cuff pressure decreases further, the pulsations increase in amplitude, reaching a maximum level (which approximates the mean pressure), and then diminishes. Studies show that, especially in critical cases (arrhythmia, vasoconstriction, hypertension, shock), oscillometric devices are more accurate and consistent than devices using other non-invasive measuring techniques.

This study is designed to provide supporting documentation for the ModPG3 module operating with SureBP and StepBP algorithms. Testing will be performed with a production equivalent CVSM modified to use ModPG3 (ModPG3 investigational device), running the SureBP and StepBP algorithms using the FlexiPort Reusable Blood Pressure Cuff on an adult and pediatric population. The process described below will be followed per algorithm in accordance with the same arm sequential method called out in ISO 81060-2:2018 + A1:2020.

The purpose of this study is to test the algorithms contained in the ModPG3 on Adult and Pediatric subjects to determine if they meet the requirements of ISO 81060-2:2018+A1:2020 Non-invasive sphygmomanometers – Part2: Clinical investigation of automated measurement type.

This clinical study shall follow section 5 “Clinical investigation with an auscultatory reference sphygmomanometer” from I.S. EN ISO ISO 81060-2:2018&A1:2020 Part 2: Clinical investigation of intermittent automated measurement type -Amendment 1 (ISO 81060-2:2018/Amd 1:2020). The subject populations covered by this study are adult subjects defined as greater than 12 years old, and pediatric subjects defined as 3 to 12 years of age.

ISO 81060-2:2018/Amd 1:2020 defines two methods that can be used to test devices according to this method. This study will use the same arm sequential method as defined in section 5.2.4.1 of the standard.

Testing of the ModPG3 on neonate and infant subjects under 3 years of age is not included in this study.

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

The scope of this study is limited to subjects that are 3 years and older. This limits the use of the ModPG3 investigational device to its adult/pediatric mode. A more detailed description of that mode is as follows:

- 2 user selectable algorithms (SureBP or StepBP)
- Patients 3 and up
- Total Limb Circumference Range 12 to 55 cm.
- Cuffs:

Model Number	Cuff Name	Cuff Range (cm)
REUSE-08	Small Child	12-16
REUSE-09	Child	15-21
REUSE-10	Small Adult	20-26
REUSE-11	Adult	25-34
REUSE-11L	Adult Long	25-34
REUSE-12	Large Adult	32-43
REUSE-12L	Large Adult Long	32-43
REUSE-13	Thigh	40-55

C. Determination of Nonsignificant Risk Investigation

The risks associated with the ModPG3 investigational device were assessed and documented in the ModPG3 Hazard Analysis, [redacted]. 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).

For detailed risk analysis and risks for the investigational device in the monitor system, see Connex Vital Signs Monitor (CVSM) Risk Assessment Summary (RAS), [redacted]. Potential hazards for the ModPG3 investigational device were identified in the ModPG3 Hazard Analysis [redacted] with risk acceptance occuring in the CVSM RAS.

Risks related to the Flexiport Cuffs used in this investigation are assessed in the BP Cuffs RAS [redacted]. The CVSM was previously FDA cleared under 510(k)-K171621. The FlexiPort Reusable Blood Pressure Cuff is an FDA cleared device (510(k)- K070060. There are no anticipated risks or adverse device effects to be further assessed. There are no contraindications for use in the proposed study / study population (See description of Study Population below)

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 or clinical determinations.
- 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) [redacted] 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
- 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.

The data generated by this study are the property of the Sponsor. This data may be used by the Sponsor, now and in the future, for presentation or publication at the Sponsor's discretion or for submission to regulatory agencies. In addition, the Sponsor reserves the right of prior review and approval of data from this study relative to the potential release of proprietary information to any publication or for any presentation.

II. Study Objectives

A. Primary Objective/Endpoint

The primary objective of this study is to collect a combination of non-invasive blood pressure readings using the ModPG3 investigational device and by trained clinicians using the auscultatory method. This data will be used to determine compliance of the ModPG3 with ISO 81060-2:2018/Amd 1:2020 on the adult and pediatric patient population.

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 second category is equipment needed by the clinicians to take auscultatory reference readings per ISO 81060-2:2018/Amd 1:2020.

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
- Blood Pressure Data Collection Software (not used for test report analysis)
- USB cable
- Power strip
- Welch Allyn FlexiPort Reusable Blood Pressure Cuffs

Model Number	Cuff Name	Cuff Range (cm)
REUSE-08	Small Child	12-16
REUSE-09	Child	15-21
REUSE-10	Small Adult	20-26

REUSE-11	Adult	25-34
REUSE-11L	Adult Long	25-34
REUSE-12	Large Adult	32-43
REUSE-12L	Large Adult Long	32-43
REUSE-13	Thigh	40-55

2. Auscultatory Equipment

- Reference Sphygmomanometer[1]
- Reference Cuffs[2]

Model Number	Cuff Name	Usable Cuff Range (cm)
5082-07	Newborn	10-14
5082-03	Infant	14-20
5082-42	Child	22-26
5082-43	Adult	29-37
5082-44	Large Adult	34-44
5082-45	Thigh	41-58

- Dual Auscultatory Stethoscope
- Tape measure
- Stopwatch

Note 1: The reference sphygmomanometer used in this study will comply with the requirements of ISO 81060-2:2018/Amd 1:2020, except that the maximum permissible error will be +/-1 mmHg per NIST traceable calibration verification.

Note 2: The newborn and infant two-piece cuffs are included in the study because of the need to cover the usable range of FlexiPort Reusable cuffs from size 8 (small child) to 13 (Thigh). The ISO 81060-2:2018/Amd 1:2020 provides limitations to the usable range for reference cuffs based on the size of the cuff's bladder. The small child cuff has a range of 12 to 16 cm and the child cuff has a range of 15 to 21 cm. The usable range of the newborn two-piece cuff is 10 to 14 cm and the infant cuffs is 14 to 20 cm. These cuffs are included to provide coverage for the entire 12 to 55 cm range of the device under test. All readings will be taken on subjects 3 years or older and the name of the cuffs newborn and infant does not mean that those subjects shall be included in the study.

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 will be conducted in 2 parts.

- Part 1 will test subjects using the ModPG3 Investigational device with the SureBP algorithm enabled.

- Part 2 will test subjects using the ModPG3 Investigational device with the StepBP algorithm enabled.

Each part of the study will be run in 2 phases.

- Phase 1 will enroll a minimum of 30 subjects that meet the inclusion criteria. At least 20 adult and at least 10 pediatric subjects will be included. At the completion of phase 1 the data will be reviewed by the sponsor and the sponsor will decide whether to continue with phase 2.
- Phase 2 will enroll a minimum of 55 more qualified subjects.

The resulting dataset when combining phase 1 and phase 2 (for each Part of the study), at a minimum, will contain the following.

- At least 85 subjects (Maximum 150)
- 35 pediatric subjects (3 – 12 years old)
- Remaining subjects will be adult subjects (over 12 years old)

A breakdown of all subject inclusion criteria is detailed in section V subsection C.

The study requires three observers. The first two observers take auscultatory readings that are averaged to use as reference blood pressures. The third observer operates the ModPG3 investigational device and records the readings for that device.

The two clinicians taking reference readings will be blinded to each other's readings and to the investigational device readings as required by section 5.2.2 of ISO 81060-2:2018/Amd 1:2020.

2. Sample Size Justification

This study is being conducted in accordance with ISO 81060-2:2018/Amd 1:2020. The justification for the sample size is defined in section 5.1.1 of Appendix A. The following is an excerpt justifying the sample size of 85 subjects.

> *The sample size of 85 was determined from the statistics for a normal distribution.*
>
> *A 98% confidence interval (α = 0,02) and a statistical power of 95% (β = 0,05) yield a sample size requirement of 85 subjects. This requirement originated from the early work of the AAMI blood pressure committee dating from 1987.*
>
> *Additionally, a sample size of 85 can be determined from the statistics for a t-distribution. A 95% confidence interval (α = 0,05) and a statistical power of 98% (β = 0,02) yield a sample size of 85 subjects.*

3. Acceptance Criteria

Each Part of the study (Part 1: SureBP Algorithm/Part 2: StepBP Algorithm) will be analyzed separately and accepted separately. For each part (Part 1/Part 2), the ModPG3 investigational device shall meet Criterion 1 and Criterion 2 as defined in section 5.2.4.1.2 of the ISO 81060-2:2018/Amd 1:2020 standard.

The limits for Criterion 1 are:

- $\bar{x}_n$ shall be within or equal to ± 5.0 mmHg (±0.67 kPa), where $\bar{x}_n$ is the mean value between the differences of the n individual paired determinations of the investigational device and the observers' readings for all subjects (calculated separately for systolic and diastolic blood pressure).
- S_n shall be no greater than 8.0 mmHg (1.07 kPa), where S_n is the standard deviation.

The limits for Criterion 2 are:

- S_m Shall meet the values listed in table 1 or table 2, where for each of m subjects S_m is the standard deviation of the averaged paired determinations per subject of the investigational device and the observers' readings.

Table 1 – Averaged subject data acceptance (criterion 2) in mmHg

$\bar{x}_n$	Maximum permissible standard deviation, S_m, as a function of, $\bar{x}_n$ mmHg									
	0.0	**0.1**	**0.2**	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**
±0	6.95	6.95	6.95	6.95	6.93	6.92	6.91	6.90	6.89	6.88
±1	6.87	6.86	6.84	6.82	6.80	6.78	6.76	6.73	6.71	6.68
±2	6.65	6.62	6.58	6.55	6.51	6.47	6.43	6.39	6.34	6.30
±3	6.25	6.20	6.14	6.09	6.03	5.97	5.89	5.83	5.77	5.70
±4	5.64	5.56	5.49	5.41	5.33	5.25	5.16	5.08	5.01	4.90
±5	4.79	–	–	–	–	–	–	–	–	–

Table 2 – Averaged subject data acceptance (criterion 2) in kPa

$\bar{x}_n$	Maximum permissible standard deviation, S_m, as a function of, $\bar{x}_n$ mmHg									
	0.000	**0.010**	**0.020**	**0.030**	**0.040**	**0.050**	**0.060**	**0.070**	**0.080**	**0.090**
±0.0	0.9266	0.9266	0.9266	0.9266	0.9266	0.9246	0.9233	0.9223	0.9213	0.9203
±0.1	0.9193	0.9183	0.9173	0.9163	0.9152	0.9138	0.9119	0.9099	0.9079	0.9059
±0.2	0.9039	0.9007	0.8989	0.8970	0.8946	0.8906	0.8878	0.8855	0.8826	0.8785
±0.3	0.8756	0.8723	0.8679	0.8641	0.8601	0.8562	0.8519	0.8471	0.8414	0.8374
±0.4	0.8333	0.8283	0.8226	0.8169	0.8119	0.8059	0.7999	0.7933	0.7853	0.7793
±0.5	0.7739	0.7669	0.7599	0.7531	0.7463	0.7388	0.7319	0.7237	0.7157	0.7077
±0.6	0.6999	0.6891	0.6802	0.6723	0.6670	0.6595	0.6488	0.6386	–	–

For details on how to calculate $\bar{x}_n$, S_n, and S_m see section IX.

IV. Informed Consent

Documentation of Informed Consent is requested 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/IEC 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 each part of this study (Part 1: SureBP Algorithm/Part 2: StepBP Algorithm) a full set of subjects as prescribed by ISO 81060-2:2018/Amd 1:2020 will be collected. [redacted] This may include, but not limited to, malls, zoos, doctors' offices, or retirement community centers. [redacted]. To reduce bias, no more than 15% of the total number of subjects may be recruited through the Baxter/Hillrom's friends and family policy. External data collection will be executed at clinicals sites who consent to participating in the study.The demographics required are captured in a series of requirements defined in section 5.1 of the standard and are broken up into the following categories: number, gender, age, limb size, and blood pressure distribution. The following sections of this document detail the requirements for each of those categories.

1. Number

- A minimum of 85 subjects shall be included in the study.
- At least three paired blood pressure values shall be taken for each subject.
- There shall be a minimum of 255 valid paired blood pressure values.

2. Gender Distribution

- At least 30% of the subjects shall be male.
- At least 30% of the subjects shall be female.

3. Age Distribution

- No children less than 3 years old shall be included in the study.
- 35 subjects between 3 and 12 years shall be included in the study.
- All remaining subjects shall be greater than 12 years old.

4. Limb Size Distribution

Limb circumference distribution has two requirements. The first is based on the total limb circumference range which is defined as a 12 to 55 cm as noted in the table below.

- At least 20% of the subjects shall have a limb circumference which lies within each quarter of the total limb circumference range.

Quarter	Limb Circumference Range (cm)
1	12 to under 22.75
2	22.75 to under 33.5
3	33.5 to under 44.25
4	44.25 to 55

- At least 10% of the subjects shall have a limb circumference that lies within the highest octile of the total limb circumference range.
- At least 10% of the subjects shall have a limb circumference that lies within the lowest octile of the total limb circumference range.

Octiles	Limb Circumference Range (cm)
Low	12 to 17.375
High	49.625 to 55

The second requirement is that all cuffs shall be tested on at least N_{cuff} subjects as calculated according to the following formula.

$$N_{cuff} = \frac{r_{cuff}}{2 \times r_{total}} \times N_{total}$$

- N_{total} is the total number of subjects in the study
- r_{cuff} is the size of the limb circumference range for the cuff

Model Number	Cuff Name	Cuff Range (cm)	r_{cuff} (cm)
REUSE-08	Small Child	12-16	4
REUSE-09	Child	15-21	6
REUSE-10	Small Adult	20-26	6
REUSE-11	Adult	25-34	9
REUSE-11L	Adult Long	25-34	9
REUSE-12	Large Adult	32-43	11
REUSE-12L	Large Adult Long	32-43	11
REUSE-13	Thigh	40-55	15

- r_{total} is the size of the total limb circumference range. (55-12 = 43 cm)

5. Blood Pressure Distribution

- At least 5% of the reference systolic readings shall be less than or equal to 100 mmHg.
- At least 5% of the reference systolic readings shall be greater than or equal to 160 mmHg.
- At least 20% of the reference systolic readings shall be greater than or equal to 140 mmHg.
- At least 5% of the reference diastolic readings shall be less than or equal to 60 mmHg.
- At least 5% of the reference diastolic readings shall be greater than or equal to 100 mmHg.
- At least 20% of the reference diastolic readings shall be greater than or equal to 85 mmHg.
-

B. Expected Time Requirements

Commitment time for each subject is expected to be approximately 1 hour for the consent and data collection steps to be completed.

C. Subject Selection Criteria

1. Inclusion Criteria

- Subjects must be able to provide an informed consent or have legally authorized representative consent to participate.
- Subject must be willing and able to comply with the study procedures.
- Subject must be ≥ 3 years of age
- Subjects that are between 7 and 17 years of age must provide assent to participate in the study.
- Subject or legally authorized representative must be able to read, write, speak in English, French or Italian.
- Subjects must have an arm circumference in the range of 12-55 cm and fit into the usable range for the reference cuffs.
- Subject must be able to have blood pressures measured on the Left or Right arm.

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.
- The subject is in acute distress, i.e., severe pain or, severe emotional distress or agitation that would inhibit him/her from participating in the study.
- The subject has any known contraindication to blood pressure measurement.
- Subjects with compromised circulation or peripheral vascular disease.
- Subjects with clotting disorders.
- Subjects that cannot tolerate sitting for up to 1 hour.
- Subject with a blood pressure demographic that has already been filled.
- Subjects with a severe contact allergy to 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 the unusable range for the reference cuffs.
- Subjects with no audible K5 sound.
- Subject is pregnant and/or breastfeeding.

VI. Subject Confidentiality

All participant data will be kept confidential as much as possible. Data collected will include the participant identification number to minimize participant identification.

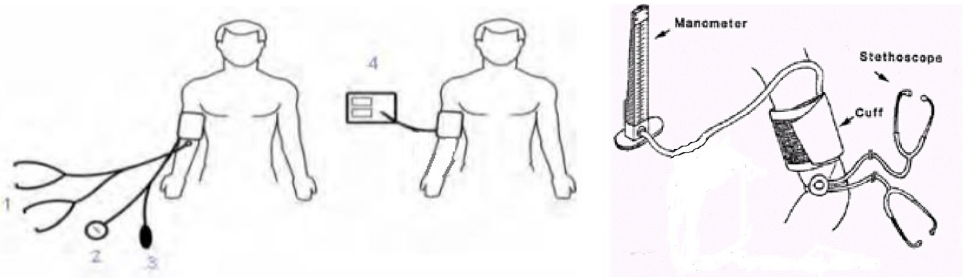
A Participant Screening/Enrollment Log will be utilized to assign all participants with a participant identification number to be used to complete data forms.

VII. Subject Remuneration

The study sponsor will enter into a written Clinical Trial Agreement (CTA) 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, or staff will not receive any additional payments for participating in this study.

VIII. Study Procedures

A. Equipment Setup



Equipment Key

1 Dual stethoscope
2 Reference sphygmomanometer display
3 Reference sphygmomanometer hand pump
4 Sphygmomanometer under test

Find a location and set up the equipment so that these requirements are met.

1. The location shall be quiet enough to ensure the clinicians ability to hear the subject's pulses when taking reference readings.
2. The location shall have a seat for the subject that allows the subject
   2.1. to be sitting with feet flat on floor or laying comfortably with legs uncrossed
   2.2. has their back, elbow, and forearm supported,
   2.3. places the cuff level with the left ventricle of the heart.
3. The location shall allow for the positioning of the reference sphygmomanometer in a way that allows both observers taking reference measurements to be able to read it and avoid errors due to positioning.
4. The location shall allow sufficient space to ensure Observer 1 and Observer 2 keep their readings hidden from each other.
5. The ModPG3 investigational device, operated by Observer 3, shall be positioned so that its readings are hidden from Observer 1 and Observer 2.

Once all equipment and space in the location is organized as listed above the equipment is considered set up.

B. Informed Consent and HIPAA Authorization

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

1. Verify that the subject acknowledges ability to read, write, speak in English, French or Italian.
2. Instruct the subject to ask questions at any time during the process, especially about things they do not understand.
3. Allow subject ample time to read the entire form and ask questions.
4. Give a thorough description of the study and the subject's involvement – especially explain that they may withdraw from the study at any time.
5. After the subject has read the form ask if they understand everything
6. Ask if they would like to take part in the study and if so explain that they may sign and date the form.
7. Once the subject has signed and dated the informed consent, the principal investigator or authorized designee will sign and date the form.
8. Give a copy of the informed consent to the subject.
9. No procedure may be performed before the informed consent is signed by the subject.

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

C. Data Collection

Equipment shall be set up and the subject shall be consented before beginning these steps.

1. Prepare the subject for the study.
    1.1. The subjects should be asked to empty their bladders prior to sitting down.
    1.2. The subject will be positioned such that the subject:
        1.2.1. Is to be sitting with feet flat on floor or laying comfortably with legs uncrossed
        1.2.2. has the back, elbow and forearm supported
        1.2.3. has the measurement site at the level of the left ventricle of the heart.
    1.3. Recommend that the subject be as relaxed as possible and that they avoid talking during the procedure.
    1.4. Before the first reading is taken, five minutes should elapse.
2. Palpate subject's pulse checking for a regular rhythm prior to each reference reading
3. Record subject initials, subject number, and demographic information.
4. Review the Subject Eligibility Form. If the subject meets the inclusion/exclusion criteria to the study, then accept into the study and continue.
5. Record device information for tracking. (Manufacturer, model #, serial or lot, hardware/software control info).
6. 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.

7. Attach the reference sphygmomanometer to the connector hose on the appropriate port on the blood pressure cuff.
8. Make sure the observers for the reference sphygmomanometer are positioned according to the instructions of the reference sphygmomanometer to avoid errors.
9. An initial baseline reference blood pressure determination from Observer 1 and Observer 2 using a dual stethoscope shall be performed.
    9.1. The last audible Korotkoff sound, fifth phase or K5, will be used. If K5 is not audible, the subject shall be excluded. Record the baseline reference blood pressure reading.
    9.2. If the observer detects a significant irregular rhythm, they should mark it on the input sheet and the subject would be a screening failure.
    9.3. Observers 1 and 2 will show their reading to observer 3. Observer 3 will confirm that the readings don't differ by more than 4 mmHg and that neither observer marked the reading as having an irregular rhythm. If the reading is good, Observer 3 will indicate it is good. If they differ by more than 4 mmHg, the Observer 3 will indicate that it needs to be repeated.
10. Once a successful reference reading is taken, apply the appropriate Device Under Test (DUT) cuff.
11. Connect the DUT to the connector hose on the appropriate port of the blood pressure cuff.
12. Power on the DUT. Wait at least 60 seconds and then take the initial baseline device-under-test blood pressure determination. During the 60-second delay, either Observer 1 or 2 shall measure the subject's pulse rate.
13. Observer 3 will record the data for the device-under-test when complete
14. Power off the DUT.
15. For each subsequent blood pressure determination, wait at least 60 seconds between the readings.
16. The observers will start with the reference sphygmomanometer and will alternate with the DUT. The final reading should be on the reference sphygmomanometer. During the 60-second wait prior to the DUT reading, Observer 1 or 2 shall measure the subject's pulse rate.
17. Record each blood pressure determination and the pulse rate.
18. The target for the study is to get five reference readings surrounding four DUT readings for each subject. Once that is achieved, the subject can be disconnected and released from the study. If reference readings need to be replaced, no more than ten reference readings shall be taken. If an eleventh reference reading is required, the subject shall be released from the study and excluded from the data analysis. Make note of this in the notes section of the datasheet.
19. The observer 1 or 2 will monitor the subject's comfort level and the cuff test site throughout the duration of the study and upon removal of the cuff.
20. The subject will be advised during the study that he/she may stop the test at any time, free of negative repercussions.
21. All equipment will be removed from the subject. No further treatment will be required upon termination/completion of the study.
22. The observers will record any final notes. The subject will be released with no follow-up required.

IX. Data Analysis and Reporting

Data shall be analyzed according to the formulas called out in section 5.2.4.1.2 of ISO 81060-2:2018/Amd 1:2020. The following provides a summary of the formulas and calculations.

A. Criterion 1

Criterion 1 has two values that shall be calculated from the data collected in the study for both systolic and diastolic 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 standard deviation of the errors. The acceptance criteria for this defined in section III Study Design, subsection B three.

1. $\bar{x}_n$ Calculation

$$\bar{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} \left(p_{SUT_i} - p_{REF-sq_i} \right)$$

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

$p_{SUT_i} - p_{REF-sq_i}$ Is the difference between the i[th] paired blood pressure value.

p_{SUT_i} Is the ModPG3 investigational device determination.

p_{REF-sq_i} Is the reference blood pressure for the i[th] value as calculated according to the following formula.

$$p_{REF-sq_i} = \frac{1}{4} \times \left(p_{REF_{i,1}} + p_{REF_{i,2}} + p_{REF_{i+1,1}} + p_{REF_{i+1,2}} \right)$$

$p_{REF_{i,1}}$ Is the blood pressure determined by Observer 1 for the i[th] reading.

$p_{REF_{i,2}}$ Is the blood pressure determined by Observer 2 for the i[th] reading.

In summary the p_{REF-sq_i} is the average of the observer readings surrounding the ModPG3 investigational device 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 criterion 1.

n Is the number of determinations

x_i Is $p_{SUT_i} - p_{REF-sq_i}$ where i is the i[th] paired blood pressure determination.

B. Criterion 2

Criterion 2 calculates a single value S_m for systolic and diastolic. S_m represents the standard deviation of the averaged paired determinations per subject. The acceptance criteria for this defined in section III Study Design, subsection B three.

1. S_m Calculation

$$S_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} \left(x_j - \bar{x}_n\right)^2}$$

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

m Is the number of subjects in the study.

j Is the index for the individual subject.

x_j Is the average error for the subjects as calculated by the following formula.

$$x_j = \frac{1}{d} \times \sum_{k=1}^{d} \left(p_{SUT_{j,k}} \times p_{REF-sq_{j,k}}\right)$$

d Is the number of determinations per subject.

k Is the index for the individual element.

$p_{SUT_{j,k}}$ Is the k[th] device reading for the individual subject.

$p_{REF-sq_{j,k}}$ Is the reference blood pressure calculated according to the following formula.

$$p_{REF-sq_{j,k}} = \frac{1}{4} \times \left(p_{REF_{j,k,1}} + p_{REF_{j,k,2}} + p_{REF_{j,k+1,1}} + p_{REF_{j,k+1,2}}\right)$$

$p_{REF_{j,k,1}}$ Is the blood pressure determined by observer 1 for the k[th] reading for the j[th] subject.

$p_{REF_{j,k,2}}$ Is the blood pressure determined by observer 2 for the k[th] reading for the j[th] subject.

In summary the $p_{REF-sq_{j,k}}$ is the average of the observer readings surrounding the ModPG3 investigational device determination.

C. Other Report Requirements

The report shall also include a plot of Arm circumference vs Reading Error for both systolic and diastolic where cuff borders are marked with vertical lines.

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. 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), Independent Ethics Committee (IEC), and other regulatory authorities as appropriate.

The participating site will have an initial qualification visit by the sponsor, routine interim monitoring in person or via WebEx and/or phone calls by the sponsor 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 two years following the life of the device or seven 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) will be documented and reported per FDA requirements. AEs will be recorded on the appropriate form per procedure. The appropriate follow-up and safety measures will be completed and documented.

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.

Welch Allyn must conduct an evaluation of any UADE and report the results of the evaluation to the FDA, IRB/IEC, and Investigator within 10 working days after receipt of notice. Where appropriate, Welch Allyn will review UADEs for potential impact on clinical test results.

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 on the CRFs.

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

APPENDIX A: Sample NIBP Cycle Results Data Sheet

The following sheets are to be used by the 3 observers to record data take for each subject

Clinical Site:					Principal Investigator:			
Date: ____ __ __ Y Y Y Y M M D D					Subject ID: _____			
Reading #	Reading Source:	Time (Military)	Pulse Rate	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)	Arm Used **R**-Right arm **L**- Left arm* preferred	Irregular pulse	Cuff Size: _____ Notes:
SAME ARM SEQUENTIAL METHOD/ DETERMINATION – Observer 1 _____								
BP1	Auscultatory						Y or N	
BP2	Auscultatory						Y or N	
BP3	Auscultatory						Y or N	
BP4	Auscultatory						Y or N	
BP5	Auscultatory						Y or N	
BP6	Auscultatory						Y or N	
BP7	Auscultatory						Y or N	
BP8	Auscultatory						Y or N	
BP9	Auscultatory						Y or N	
BP10	Auscultatory						Y or N	
BP11	Auscultatory						Y or N	
BP12	Auscultatory						Y or N	
BP13	Auscultatory						Y or N	
BP14	Auscultatory						Y or N	
BP15	Auscultatory						Y or N	

Observer (Sign): _____ Date: _____

Clinical Site:	Principal Investigator:
Date: _____ ____ ____ Y Y Y Y M M D D	Subject ID: _____

Reading #	Reading Source:	Time (Military)	Pulse Rate	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)	Arm Used **R**-Right arm **L**- Left arm* preferred	Irregular pulse	Cuff Size: _____ Notes:
SAME ARM SEQUENTIAL METHOD/ DETERMINATION – Observer 2 _____								
BP1	Auscultatory						Y or N	
BP2	Auscultatory						Y or N	
BP3	Auscultatory						Y or N	
BP4	Auscultatory						Y or N	
BP5	Auscultatory						Y or N	
BP6	Auscultatory						Y or N	
BP7	Auscultatory						Y or N	
BP8	Auscultatory						Y or N	
BP9	Auscultatory						Y or N	
BP10	Auscultatory						Y or N	
BP11	Auscultatory						Y or N	
BP12	Auscultatory						Y or N	
BP13	Auscultatory						Y or N	
BP14	Auscultatory						Y or N	
BP15	Auscultatory						Y or N	

Observer (Sign): _____ Date: _____

Document Description: ModPG3 Adult-Ped ISO 81060-2 Study Protocol	Document Number: 60115909 **Version: J**
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Clinical Site:	Principal Investigator:
Date: __ __ __ __ __ __ __ __ Y Y Y Y M M D D	Subject ID: _____

Reading #	Reading Source	Ref Within 4 mmHg	Time (Military)	Pulse Rate	Systolic Pressure (mmHg)	Diastolic Pressure (mmHg)	Arm Used **R**-Right arm **L**- Left arm* preferred	Cuff Size: _____ File:
SAME ARM SEQUENTIAL METHOD/ DETERMINATION – Device Observer _____								
BP1	DUT	☐						File #:
BP2	DUT	☐						File #:
BP3	DUT	☐						File #:
BP4	DUT	☐						File #:
BP5	DUT	☐						File #:
BP6	DUT	☐						File #:
BP7	DUT	☐						File #:
BP8	DUT	☐						File #:
BP9	DUT	☐						File #:
BP10	DUT	☐						File #:
BP11	DUT	☐						File #:
BP12	DUT	☐						File #:
BP13	DUT	☐						File #:
BP14	DUT	☐						File #:
BP15	DUT	☐						File #:

Observer (Sign): _____ Date: _____

APPENDIX B: 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.

[redacted]	Welch Allyn Protocol ID: DIR 60115909 Ver ___
Clinical Site:	Principal Investigator:
Subject ID:	Date:(YYYY/MM/DD):

Time of Consent (00:00 24 hr)

Observer Initials #1_____ #2_____ #3_____
Subject Age (years): _____ **Subject Gender:** Male/Female
Subject Height: _____ cm
Subject Weight: _____ kg
Time of Assessment (00:0024hr)

Race:

☐ White ☐ Black or African American ☐ American Indian or Alaska Native
☐ Asian ☐ Native Hawaiian or Other Pacific Islander ☐ Other: _____

BP Cuff Placement:
Limb Used ☐ **Left** ☐ **Right**
Arm measurement:
Length: _____ cm
Circumference: _____ cm

FlexiPort – Reusable Cuff (DUT) Size Selected:

☐ Cuff Size 8: 12-16cm ☐ Cuff Size 9: 15-21cm ☐ Cuff Size 10: 20-26 cm
☐ Cuff Size 11/11L: 25-34 cm ☐ Cuff Size 12/12L: 32-43 cm ☐ Cuff Size 13: 40-55 cm

Note: For 11L and 12L please circle that when used, otherwise 11 or 12 will be assumed.

2 Piece – Cuff Size Selected (Auscultatory):

☐ Newborn: 10-14 cm ☐ Infant: 14-20 cm ☐ Child: 22-26 cm
☐ Adult: 29 – 37 cm ☐ Large Adult: 34-44 cm ☐ Thigh: 41-58 cm

Note: If subject falls in a gap for the 2 Piece cuff they should be excluded from the study.

Cuff Lot #: _____

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

APPENDIX C: Sample Study Subject Eligibility Form

Welch Allyn Protocol [redacted]	**Welch Allyn Protocol Number: 60115909 Ver___**
Clinical Site:	**PI / Clinician:**
Date: __ __ __ __ __ __ __ __ Y Y Y Y M M D D	**Subject ID:** _____ _____ _____ _____ _____ _____ _____ _____

Assigned Subject ID Numbers will be consecutive. The Subject ID consists of an eight-digit alpha-numeric number.

- Digit 1 = investigative population (P = pediatric, A = adult)
- Digit 2, 3, 4, 5 = [redacted]
- Digit 6, 7, 8 = Numbers are assigned consecutively (e.g., 001, 002, 003).

Inclusion Criteria (In order to include the subject in the study, all criteria should be checked **YES.**)	**YES**	**NO**
1. The subject is greater than or equal to 3 years of age (pediatric) to geriatric adult.		
2. The subject and/or legal guardian completes consent / assent process as required.		
3. The subject or legal guardian providing consent can read, write, speak in English, French or Italian.		
4. The subject must have an arm circumference in the range of 12-55cm and fit into the usable range for the reference cuffs.		
5. The subject must be able to have blood pressures measured on the Left or right Arm.		
Exclusion Criteria (In order to include the subject in the study, all criteria should be checked **NO**.)	**YES**	**NO**
1. The subject or legal guardian refuses to allow the study subject to participate for any reason.		
2. The study subject is unable to sit still for a blood pressure for up to 1 hour.		
3. The subjects with deformities or abnormalities that may prevent proper application of the device under test.		
4. The subject is in acute distress, i.e., severe pain or, severe emotional distress or agitation that would inhibit him/her from participating in the study.		
5. The subject has any known contraindication to blood pressure measurement.		
6. The subject is not alert or unable to follow simple commands.		
7. The subject is evaluated by the investigator or clinician and found to be medically unsuitable for participation in this study		
8. The subject has known heart dysrhythmias		
9. The subject has compromised circulation or peripheral vascular disease		
10. The subject has known clotting disorders.		
11. The subject blood pressure demographic has already been filled		
12. The subject has severe contact allergy to sensors or cuff material		

13. The subject has 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.		
14. The subject whose arm circumference falls within the unusable range for the refence cuffs		
15. The subject has no audible k5 sound.		
16. Subject is pregnant and/or breastfeeding.		

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

Therefore, the subject is eligible to participate in the study.

☐ The subject does not meet all inclusion criteria and/or meets at least one of the exclusion criteria. Therefore, the subject is not eligible to participate in the study.

PI / Clinician (Print): _____ **Date:** _____

PI / Clinician (Sign): _____