INTERNATIONAL STANDARD

ISO 81060-2

Second edition
2013-05-01

Non-invasive sphygmomanometers —

Part 2: Clinical investigation of automated measurement type

Sphygmomanomètres non invasifs —

Partie 2: Validation clinique pour type à mesurage automatique

Reference number
ISO 81060-2:2013(E)

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Foreword

ISO (the International Organization for Standardization) is a worldwide federation of national standards bodies (ISO member bodies). The work of preparing International Standards is normally carried out through ISO technical committees. Each member body interested in a subject for which a technical committee has been established has the right to be represented on that committee. International organizations, governmental and non-governmental, in liaison with ISO, also take part in the work. ISO collaborates closely with the International Electrotechnical Commission (IEC) on all matters of electrotechnical standardization.

International Standards are drafted in accordance with the rules given in the ISO/IEC Directives, Part 2.

The main task of technical committees is to prepare International Standards. Draft International Standards adopted by the technical committees are circulated to the member bodies for voting. Publication as an International Standard requires approval by at least 75 % of the member bodies casting a vote.

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO shall not be held responsible for identifying any or all such patent rights.

This second edition cancels and replaces the first edition (ISO 81060-2:2009), subclauses 5.2.4.3.1 and 6.2.4 of which have been technically revised. Numerous clarifications have been added and kPa equivalent values for the mmHg values have been included in the standard, including the Criterion 2 requirements of 5.2.4.1.2. It also incorporates the Technical Corrigendum ISO 81060-2:2009/Cor 1:2011.

ISO 81060-2 was prepared by Technical Committee ISO/TC 121, *Anaesthetic and respiratory equipment*, Subcommittee SC 3, *Lung ventilators and related equipment*, in collaboration with Technical Committee IEC/TC 62, *Electrical equipment in medical practice*, Subcommittee 62D, *Electromedical equipment*, in accordance with ISO/IEC mode of cooperation 5.

ISO 81060 consists of the following parts, under the general title *Non-invasive sphygmomanometers*:

— *Part 1: Requirements and test methods for non-automated measurement type*

— *Part 2: Clinical investigation of automated measurement type*

In this document, the following print types are used:

— requirements, compliance with which can be verified, and definitions: roman type;

— notes and examples: smaller roman type;

— test methods: *italic type*;

— terms defined in this document: SMALL CAPITALS TYPE.

Throughout this document, text for which a rationale is provided in Annex A is indicated by an asterisk (*).

The attention of Member Bodies and National Committees is drawn to the fact that equipment manufacturers and testing organizations may need a transitional period following publication of a new, amended or revised ISO or IEC publication in which to make products in accordance with the new requirements and to equip themselves for conducting new or revised tests. It is the recommendation of ISO/TC 121 and IEC/TC 62 that the content of this part of ISO 81060 not be adopted for mandatory implementation nationally earlier than 3 years from the date of publication for equipment newly designed, and not earlier than 5 years from the date of publication for equipment already in production.

Introduction

Determination of BLOOD PRESSURE is an important procedure that is clinically used to assess the status of a PATIENT.

Frequent determination of BLOOD PRESSURE is routine during anaesthesia. BLOOD PRESSURE serves to aid in drug titration and fluid management and to provide warning of conditions that could affect PATIENT morbidity and mortality.

Non-invasive sphygmomanometers —

Part 2:
Clinical investigation of the automated measurement type

1 Scope

This part of ISO 81060 specifies the requirements and methods for the CLINICAL INVESTIGATION of ME EQUIPMENT used for the intermittent non-invasive automated estimation of the arterial BLOOD PRESSURE by utilizing a CUFF.

This part of ISO 81060 is applicable to all SPHYGMOMANOMETERS that sense or display pulsations, flow or sounds for the estimation, display or recording of BLOOD PRESSURE. These SPHYGMOMANOMETERS need not have automatic CUFF inflation.

This part of ISO 81060 covers SPHYGMOMANOMETERS intended for use in all PATIENT populations (e.g. all age and weight ranges), and all conditions of use (e.g. ambulatory BLOOD PRESSURE monitoring, stress testing BLOOD PRESSURE monitoring and BLOOD PRESSURE monitors for the HOME HEALTHCARE ENVIRONMENT for self-measurement as well as use in a professional healthcare facility).

EXAMPLE AUTOMATED SPHYGMOMANOMETER as given in IEC 80601-2-30 undergoing CLINICAL INVESTIGATION according to this part of ISO 81060.

This part of ISO 81060 specifies additional disclosure requirements for the ACCOMPANYING DOCUMENTS of SPHYGMOMANOMETERS that have undergone CLINICAL INVESTIGATION according to this part of ISO 81060.

This part of ISO 81060 is not applicable to CLINICAL INVESTIGATIONS of NON-AUTOMATED SPHYGMOMANOMETERS as given in ISO 81060-1 or INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT as given in IEC 60601-2-34.

2 Normative references

The following documents, in whole or in part, are normatively referenced in this document and are indispensable for its application. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

ISO 14155:2011, *Clinical investigation of medical devices for human subjects — Good clinical practice*

ISO 81060-1, *Non-invasive sphygmomanometers — Part 1: Requirements and test methods for non-automated measurement type*

IEC 80601-2-30:2009, *Medical electrical equipment — Part 2-30: Particular requirements for basic safety and essential performance of automated non-invasive sphygmomanometers*

IEC 60601-1:2005, *Medical electrical equipment — Part 1: General requirements for basic safety and essential performance*
Amendment 1:2012

IEC 60601-1-11:2010, *Medical electrical equipment — Part 1-11: General requirements for basic safety and essential performance — Collateral standard: Requirements for medical electrical equipment and medical electrical systems used in home care applications*

IEC 60601-2-34:2011, *Medical electrical equipment — Part 2-34: Particular requirements for the basic safety and essential performance of invasive blood pressure monitoring equipment*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 14155, IEC 80601-2-30, IEC 60601-1, IEC 60601-1-11, IEC 60601-2-34 and the following apply.

NOTE For convenience, an alphabetized index of defined terms is found beginning on page 40.

3.1
REFERENCE, adj
established accuracy used for the CLINICAL INVESTIGATION of other instruments

3.2
SPHYGMOMANOMETER
ME EQUIPMENT for non-invasive estimation of systemic arterial BLOOD PRESSURE

3.3
SPHYGMOMANOMETER-UNDER-TEST
SPHYGMOMANOMETER undergoing CLINICAL INVESTIGATION

4 General requirements for CLINICAL INVESTIGATIONS

4.1 CLINICAL INVESTIGATION methods

SPHYGMOMANOMETERS other than NON-AUTOMATED SPHYGMOMANOMETERS shall undergo CLINICAL INVESTIGATION either by using a non-invasive (auscultatory) REFERENCE SPHYGMOMANOMETER or by using REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT according to this part of ISO 81060 in each mode of operation.

EXAMPLE 1 Adult and neonatal modes.

EXAMPLE 2 Slow and fast CUFF deflation rate modes.

A CLINICAL INVESTIGATION shall be considered a TYPE TEST.

Consider compliance with the requirements of this subclause to exist when the criteria of the relevant inspections and tests in this part of ISO 81060 are met.

4.2 Good clinical practice

All CLINICAL INVESTIGATIONS shall comply with the requirements of ISO 14155. CLINICAL INVESTIGATION with REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT should not be used for PATIENTS or subjects solely for the purpose of investigating SPHYGMOMANOMETER performance.

NOTE Some authorities having jurisdiction have additional requirements.

The requirements of this International Standard, which are more specific than the corresponding requirements of ISO 14155, shall prevail.

Check compliance by application of the requirements of ISO 14155.

5 CLINICAL INVESTIGATION with an auscultatory REFERENCE SPHYGMOMANOMETER

5.1 Subject requirements

5.1.1 * Number

An auscultatory REFERENCE SPHYGMOMANOMETER CLINICAL INVESTIGATION shall consist of a minimum of 85 subjects. If not otherwise specified, at least three valid BLOOD PRESSURE DETERMINATIONS shall be taken for each subject. There shall be a minimum of 255 valid paired BLOOD PRESSURE DETERMINATIONS.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.1.2 * Gender distribution

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

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.1.3 * Age distribution

For a SPHYGMOMANOMETER intended for use on adults and/or adolescent PATIENTS, the age of every subject included in the CLINICAL INVESTIGATION shall be greater than 12 years.

NOTE 1 Minimum total of 85 subjects.

For a SPHYGMOMANOMETER additionally intended for use in children, 35 child subjects aged between 3 years and 12 years shall be included in the CLINICAL INVESTIGATION.

NOTE 2 Minimum total of 85 subjects.

If the SPHYGMOMANOMETER has a special mode for children, in that mode, children shall be considered a special PATIENT population (see 5.1.6). In such a study, children are exempt from the BLOOD PRESSURE distribution requirements of 5.1.5.

Children aged less than 3 years shall not be included in a CLINICAL INVESTIGATION utilizing auscultatory DETERMINATIONS by observers with a REFERENCE SPHYGMOMANOMETER.

Check compliance by inspection of the ACCOMPANYING DOCUMENT and the CLINICAL INVESTIGATION REPORT.

5.1.4 * Limb size distribution

For a SPHYGMOMANOMETER intended for use with a single CUFF size:

— at least 40 % of the subjects shall have a limb circumference which lies within the upper half of the specified range of use of the CUFF and at least 40 % shall have a limb circumference within the lower half; and

— at least 20 % of the subjects shall have a limb circumference which lies within the upper quarter of the specified range of use of the CUFF and at least 20 % shall have a limb circumference within the lower quarter.

For a SPHYGMOMANOMETER intended for use with multiple CUFF sizes, each CUFF size shall be tested on at least $\frac{1}{2 \times n}$ of the subjects, where n is the number of CUFF sizes.

Check compliance by inspection of the ACCOMPANYING DOCUMENT and the CLINICAL INVESTIGATION REPORT.

5.1.5 * BLOOD PRESSURE distribution

At least 5 % of the REFERENCE BLOOD PRESSURE readings shall have a SYSTOLIC BLOOD PRESSURE ≤ 100 mmHg (13,33 kPa).

At least 5 % of the REFERENCE BLOOD PRESSURE readings shall have a SYSTOLIC BLOOD PRESSURE ≥ 160 mmHg (21,33 kPa).

At least 20 % of the REFERENCE BLOOD PRESSURE readings shall have a SYSTOLIC BLOOD PRESSURE ≥ 140 mmHg (18,66 kPa).

At least 5 % of the REFERENCE BLOOD PRESSURE readings shall have a DIASTOLIC BLOOD PRESSURE ≤ 60 mmHg (8,0 kPa).

At least 5 % of the REFERENCE BLOOD PRESSURE readings shall have a DIASTOLIC BLOOD PRESSURE ≥ 100 mmHg (13,33 kPa).

At least 20 % of the REFERENCE BLOOD PRESSURE readings shall have a DIASTOLIC BLOOD PRESSURE ≥ 85 mmHg (11,33 kPa).

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.1.6 * Special PATIENT populations

A SPHYGMOMANOMETER that is intended for use in special PATIENT populations where there is OBJECTIVE EVIDENCE that the accuracy of the SPHYGMOMANOMETER might be problematic in those PATIENT populations, shall undergo CLINICAL INVESTIGATION in those PATIENT populations.

NOTE Clause 7 has a specific example of a special PATIENT population with specific requirements.

If the SPHYGMOMANOMETER has undergone CLINICAL INVESTIGATION according to the requirements of 5.1.1 and 5.2, it shall then undergo CLINICAL INVESTIGATION in at least an additional 35 special population subjects. If the SPHYGMOMANOMETER has not previously undergone CLINICAL INVESTIGATION according to the requirements of 5.1.1 and 5.2, the CLINICAL INVESTIGATION in accordance with the requirements of 5.1.1 and 5.2 shall consist only of subjects from the special PATIENT population.

The special PATIENT population shall be defined in clear terms and address the following attributes: gender (see 5.1.2), age (see 5.1.3), limb size (see 5.1.4) and BLOOD PRESSURE (see 5.1.5). A summary of this information shall be disclosed in the instructions for use.

Check compliance by inspection of the instructions for use and the CLINICAL INVESTIGATION REPORT.

5.2 CLINICAL INVESTIGATION method with a REFERENCE SPHYGMOMANOMETER

5.2.1 * Subject preparation

Unless otherwise indicated by the instructions for use of the SPHYGMOMANOMETER-UNDER-TEST, position the subject such that the subject:

— is comfortable;

EXAMPLE Comfortably seated with legs uncrossed and feet flat on the floor.

— has the back, elbow and forearm supported;

— has the middle of the CUFF at the level of the right atrium of the heart.

Recommend that the subject be as relaxed as possible and that the subject avoid talking during the entire procedure. Before the first reading is taken, 5 min should elapse.

NOTE Additional details can be found in Reference [32].

5.2.2 * Observer preparation

Observers should be trained in using a proper methodology for performing a resting BLOOD PRESSURE DETERMINATION by utilizing an accepted clinical protocol for BLOOD PRESSURE measurement. References [8], [28], [29], [32] and [45] contain additional information. Observers should have sufficient practice in performing BLOOD PRESSURE DETERMINATIONS.

Each observer's recording of observations of the REFERENCE SPHYGMOMANOMETER shall not be visible to the other observer. The readings of the SPHYGMOMANOMETER-UNDER-TEST shall not be visible to either of these observers.

EXAMPLE 1 Utilizing a third observer for recording the readings of the SPHYGMOMANOMETER-UNDER-TEST.

EXAMPLE 2 Utilizing an electronic means for recording the readings of the SPHYGMOMANOMETER-UNDER-TEST.

Instruct the observers to determine the DIASTOLIC BLOOD PRESSURE as the last audible Korotkoff sound (fifth phase or K5), except when Korotkoff sounds are still audible with the CUFF deflated or in children between 3 years and 12 years of age, where the fourth phase (K4) is used. If K4 is not audible in a child, either K5 is used or the subject is excluded.

NOTE Other than for children, K4 should be reserved for subjects in whom there is a large discrepancy between muffling and disappearance (with the latter at times approaching zero mmHg).

Instruct the observers to record which Korotkoff sound has been used for the DETERMINATION of DIASTOLIC BLOOD PRESSURE.

The Korotkoff sound used for DETERMINATION of DIASTOLIC BLOOD PRESSURE in the CLINICAL INVESTIGATION shall be disclosed in the instructions for use of a SPHYGMOMANOMETER.

EXAMPLE 3 K5 was used on 65 subjects and K4 was used on 20 subjects.

5.2.3 * REFERENCE DETERMINATION

Two observers shall make simultaneous BLOOD PRESSURE DETERMINATIONS on each subject using a double stethoscope.

Unless the SPHYGMOMANOMETER-UNDER-TEST is intended for use during significantly irregular heart rhythm and if either observer detects significantly irregular heart rhythm, that DETERMINATION shall be excluded.

EXAMPLES Bigeminy, trigeminy, isolated ventricular premature beat (VPB), atrial fibrillation.

NOTE 1 Although CLINICAL INVESTIGATION of BLOOD PRESSURE in PATIENTS with atrial fibrillation is clinically important, there are currently no generally accepted guidelines for determining the BLOOD PRESSURE in such individuals.

Any pair of observers' DETERMINATIONS with a difference greater than 4 mmHg (0,53 kPa) shall be excluded. The observers' individual values of each DETERMINATION shall be averaged according to Formula (1) to create the REFERENCE BLOOD PRESSURE DETERMINATION.

$$p_{\mathrm{ref}_i} = \frac{p_{\mathrm{ref}_{i,1}} + p_{\mathrm{ref}_{i,2}}}{2} \tag{1}$$

where

$p_{\mathrm{ref}_{i,1}}$ is the BLOOD PRESSURE determined by observer 1 for the i^{th} DETERMINATION;

$p_{\mathrm{ref}_{i,2}}$ is the BLOOD PRESSURE determined by observer 2 for the i^{th} DETERMINATION;

p_{ref_i} is the REFERENCE BLOOD PRESSURE for the i^{th} DETERMINATION.

The observer-to-observer differences shall be reviewed after completing a set of pairs of test-REFERENCE DETERMINATIONS. If any DETERMINATIONS are excluded, additional pair(s) of DETERMINATIONS shall be taken to ensure that the required number of valid test-REFERENCE pairs are available. A maximum of eight pairs of DETERMINATIONS should be taken.

Use a REFERENCE SPHYGMOMANOMETER that complies with the requirements of ISO 81060-1, except that the maximum permissible error shall be $\pm$ 1 mmHg (0,13 kPa). Reading of the values on the REFERENCE SPHYGMOMANOMETER should be as accurate as possible. When reading the value on the REFERENCE SPHYGMOMANOMETER, the observers should avoid parallax errors and rounding.

NOTE 2 Rounding has a negative effect on the results of the CLINICAL INVESTIGATION.

NOTE 3 For the purposes of this part of ISO 81060, the CUFF is considered part of the REFERENCE SPHYGMOMANOMETER. A CUFF that does not comply with ISO 81060-1 cannot be used.

5.2.4 CLINICAL INVESTIGATION methods

5.2.4.1 Same arm simultaneous method

5.2.4.1.1 * Procedure

This method shall only be used with a SPHYGMOMANOMETER-UNDER-TEST:

— that has a CUFF compliant with ISO 81060-1;

— that is designed for use on the upper arm; and

— where

  — the continuous linear deflation rate is between 2 mmHg/s (0,27 kPa/s) and 3 mmHg/s (0,40 kPa/s) or

  — for a SPHYGMOMANOMETER-UNDER-TEST that controls the deflation as a function of the pulse rate, the deflation rate is between 2 mmHg/pulse (0,27 kPa/pulse) and 3 mmHg/pulse (0,40 kPa/pulse).

Either arm may be utilized.

The SPHYGMOMANOMETER-UNDER-TEST shall not deflate prior to the detection of the REFERENCE DIASTOLIC BLOOD PRESSURE. The SPHYGMOMANOMETER-UNDER-TEST may be modified to meet this criterion.

NOTE Valid same arm simultaneous DETERMINATIONS require the SPHYGMOMANOMETER-UNDER-TEST to inflate the CUFF to at least 20 mmHg (2,67 kPa) higher than the actual SYSTOLIC BLOOD PRESSURE, as determined by the REFERENCE SPHYGMOMANOMETER, and to at least 20 mmHg (2,67 kPa) below the actual DIASTOLIC BLOOD PRESSURE, as determined by the REFERENCE SPHYGMOMANOMETER.

Perform the following:

a) Have the observers using the REFERENCE SPHYGMOMANOMETER and the SPHYGMOMANOMETER-UNDER-TEST simultaneously determine the subject's BLOOD PRESSURE utilizing the same CUFF and inflation/deflation cycle (see Figure 1). These data points are not used in the calculation of accuracy of the SPHYGMOMANOMETER-UNDER-TEST.

b) Clear the SPHYGMOMANOMETER-UNDER-TEST memory of the previous DETERMINATION and then wait at least 60 s.

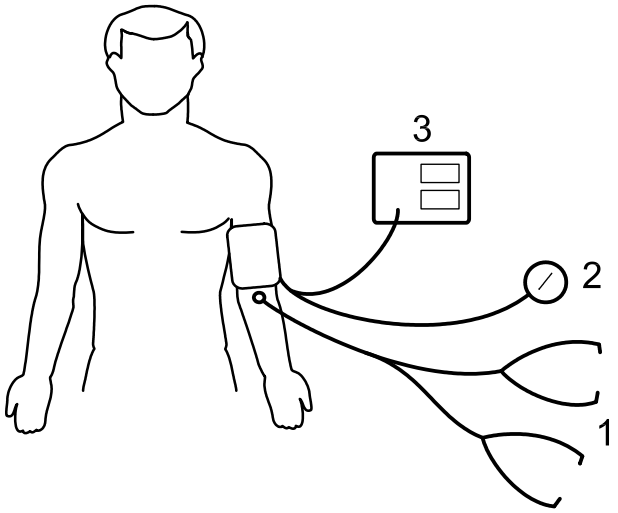
EXAMPLES Switching the power off and on, removing the BLOOD PRESSURE module and reinstalling it or issuing a reset command are methods to clear the memory of the previous DETERMINATION.

c) Have the observers using the REFERENCE SPHYGMOMANOMETER and the SPHYGMOMANOMETER-UNDER-TEST simultaneously determine the subject's BLOOD PRESSURE utilizing the same CUFF and inflation/deflation cycle.

d) Wait at least 60 s between DETERMINATIONS.

e) Repeat c) and d) until the required number of valid DETERMINATIONS has been performed.

All data from a subject shall be excluded if any two REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATIONS differ by more than 12 mmHg (1,60 kPa) or if any two REFERENCE DIASTOLIC BLOOD PRESSURE DETERMINATIONS differ by more than 8 mmHg (1,07 kPa).



Key

1 double stethoscope

2 REFERENCE SPHYGMOMANOMETER display

3 SPHYGMOMANOMETER-UNDER-TEST

Figure 1 — Illustration of same arm simultaneous method

5.2.4.1.2 * Data analysis

The SPHYGMOMANOMETER-UNDER-TEST shall meet the following two criteria.

a) Criterion 1

For SYSTOLIC and DIASTOLIC BLOOD PRESSURES, the mean value of the differences of the DETERMINATIONS, $\bar{x}_n$, of the n individual paired DETERMINATIONS of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' DETERMINATIONS with the REFERENCE SPHYGMOMANOMETER for all subjects shall be within or equal to ± 5,0 mmHg (± 0,67 kPa), with a standard deviation, s_n, no greater than 8,0 mmHg (1,07 kPa) when calculated according to Formula (2) and Formula (3):

$$\bar{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} \left(p_{\mathrm{sut}_i} - p_{\mathrm{ref}_i} \right) \tag{2}$$

$$s_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} \left(x_i - \bar{x}_n \right)^2} \tag{3}$$

where

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

$p_{\text{sut}_i} - p_{\text{ref}_i} = x_i$ difference between a paired BLOOD PRESSURE DETERMINATION [DETERMINATION of the SPHYGMOMANOMETER-UNDER-TEST – REFERENCE BLOOD PRESSURE as calculated according to Formula (1)];

i is the index for the individual element;

n is the number of DETERMINATIONS;

$\bar{x}_n$ and s_n shall be calculated and expressed to 0,1 mmHg (0,01 kPa).

EXAMPLE 1 n = 255 for a SPHYGMOMANOMETER intended for use in adults and/or adolescent PATIENTS (an 85 subject study).

EXAMPLE 2 n = 255 for a SPHYGMOMANOMETER intended for use in adults and/or adolescents and children aged between 3 years and12 years (an 85 subject study).

EXAMPLE 3 n = 105 for a SPHYGMOMANOMETER intended for a special INTENDED USE (a 35 subject study), when the SPHYGMOMANOMETER has previously undergone CLINICAL INVESTIGATION in a separate 85 subject study according to 5.1.1 and 5.2.

b) Criterion 2

For the SYSTOLIC and DIASTOLIC BLOOD PRESSURES for each of the m subjects, the standard deviation, s_m, of the averaged paired DETERMINATIONS per subject of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' DETERMINATIONS with the REFERENCE SPHYGMOMANOMETER shall meet the criteria listed in Table 1 or Table 2 when calculated according to Formula (4):

$$s_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} \left(x_j - \bar{x}_n \right)^2} \tag{4}$$

where

$\bar{x}_n$ is the mean value of the differences as calculated according to Formula (2);

m is the number of subjects;

x_j is the index for the individual element;

m is calculated according to Formula (5).

$$x_j = \frac{1}{d} \times \sum_{k=1}^{d} (p_{\text{sut}_k} - p_{\text{ref}_k}) \tag{5}$$

where

d is the number of DETERMINATIONS per subject;

k is the index for the individual element.

EXAMPLE 4 m = 85 for a SPHYGMOMANOMETER intended for use in adults and/or adolescent PATIENTS (an 85 subject study).

EXAMPLE 5 m = 85 for a SPHYGMOMANOMETER intended for use in adults and/or adolescents and children aged between 3 years and 12 years (an 85 subject study).

EXAMPLE 6 m = 35 for a SPHYGMOMANOMETER intended for (an additional) special INTENDED USE (a 35 subject study), when the SPHYGMOMANOMETER has previously undergone CLINICAL INVESTIGATION in a separate 85 subject study according to 5.1.1 and 5.2.

EXAMPLE 7 m = 85 for a SPHYGMOMANOMETER intended only for a special INTENDED USE (an 85 subject study).

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

$\bar{x}_n$	**Maximum permissible standard deviation, s_m, as 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	—	—	—	—	—	—	—	—	—
EXAMPLE For mean of ± 4,2 mmHg, the maximum permissible standard deviation is 5,49 mmHg.										

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

$\bar{x}_n$	**Maximum permissible standard deviation, s_m, as function of, $\bar{x}_n$** kPa									
	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	—	—
EXAMPLE For mean of ± 0,520 kPa, the maximum permissible standard deviation is 0,7599 kPa.										

5.2.4.2 * Same arm sequential method

5.2.4.2.1 * Procedure

Either arm may be utilized.

Perform the following:

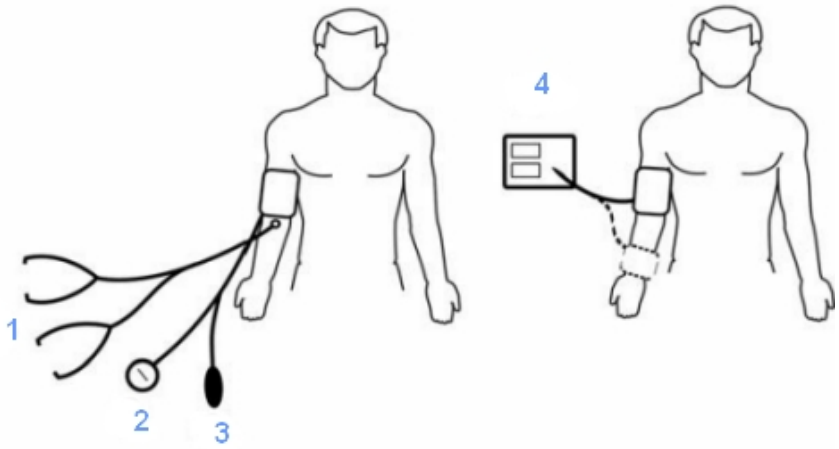
a) *Using the REFERENCE SPHYGMOMANOMETER, have the observers determine the subject's BLOOD PRESSURE (see Figure 2).*

b) *Wait at least 60 s.*

c) *Using the SPHYGMOMANOMETER-UNDER-TEST, have the observers determine the subject's BLOOD PRESSURE.*

d) *Clear the SPHYGMOMANOMETER-UNDER-TEST memory of the previous DETERMINATION and then wait at least 60 s.*

EXAMPLES Switching the power off and on, removing the BLOOD PRESSURE module and reinstalling it or issuing a reset command are methods to clear the memory of the previous DETERMINATION.



Key

1 double stethoscope
2 REFERENCE SPHYGMOMANOMETER display
3 REFERENCE SPHYGMOMANOMETER hand pump
4 SPHYGMOMANOMETER-UNDER-TEST

NOTE Only one CUFF is connected to the SPHYGMOMANOMETER-UNDER-TEST.

Figure 2 — Illustration of the same arm sequential method

e) *Do not use the data points obtained in a) and c) in the DETERMINATION of accuracy.*

f) *Using the REFERENCE SPHYGMOMANOMETER, have the observers determine the subject's BLOOD PRESSURE.*

g) *Have the observers use the SPHYGMOMANOMETER-UNDER-TEST and the REFERENCE SPHYGMOMANOMETER to determine the subject's BLOOD PRESSURE sequentially.*

h) *Wait at least 60 s between each DETERMINATION.*

i) *Repeat g) and h) until the required number of valid DETERMINATIONS has been performed.*

All data from a subject shall be excluded if any two REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATIONS differ by more than 12 mmHg (1,60 kPa) or if any two REFERENCE DIASTOLIC BLOOD PRESSURE DETERMINATIONS

differ by more than 8 mmHg (1,07 kPa). Notwithstanding this requirement, if the REFERENCE BLOOD PRESSURE of an individual subject does not meet these criteria during the period of the test, two compliant consecutive DETERMINATION pairs that meet these criteria may be used. In this case, additional subjects shall be used to complete the minimum number of DETERMINATIONS. No more than 10 % of the subjects shall have fewer than three valid DETERMINATION pairs.

5.2.4.2.2 Data analysis

The SPHYGMOMANOMETER-UNDER-TEST shall meet the following two criteria.

a) Criterion 1

For SYSTOLIC and DIASTOLIC BLOOD PRESSURES, the mean value of the differences of the DETERMINATIONS, $\overline{x}_n$, of the n individual paired DETERMINATIONS of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' DETERMINATIONS with the REFERENCE SPHYGMOMANOMETER for all subjects shall be within or equal to ± 5,0 mmHg (± 0,67 kPa), with a standard deviation, s_n, no greater than 8,0 mmHg (1,07 kPa) when calculated according to Formula (6) and Formula (7):

$$\overline{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} (p_{\mathrm{sut}_i} - p_{\mathrm{ref-sq}_i}) \tag{6}$$

$$s_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} \left(x_i - \overline{x}_n \right)^2} \tag{7}$$

where

$\overline{x}_n$ is the mean value of the differences;

$p_{\mathrm{sut}_i} - p_{\mathrm{ref-sq}_i} = x_i$ difference between the i^{th} paired BLOOD PRESSURE DETERMINATIONS (DETERMINATION of the SPHYGMOMANOMETER-UNDER-TEST – REFERENCE BLOOD PRESSURE);

i is the index for the individual element;

n is the number of DETERMINATIONS;

$p_{\mathrm{ref-sq}_i}$ is the REFERENCE BLOOD PRESSURE for the i^{th} DETERMINATION as calculated according to Formula (8);

$\overline{x}_n$ and s_n shall be calculated and expressed to at least 0,1 mmHg (0,01 kPa).

The REFERENCE BLOOD PRESSURE, $p_{\mathrm{ref-sq}_i}$, (the observers' DETERMINATIONS with the REFERENCE SPHYGMOMANOMETER) shall be the average of the preceding and following REFERENCE BLOOD PRESSURES.

$$p_{\mathrm{ref-sq}_i} = \frac{1}{4} \times (p_{\mathrm{ref}_{i,1}} + p_{\mathrm{ref}_{i,2}} + p_{\mathrm{ref}_{i+1,1}} + p_{\mathrm{ref}_{i+1,2}}) \tag{8}$$

where

$p_{\mathrm{ref}_{i,1}}$ is the BLOOD PRESSURE determined by observer 1 for the i^{th} DETERMINATION;

$p_{\mathrm{ref}_{i,2}}$ is the BLOOD PRESSURE determined by observer 2 for the i^{th} DETERMINATION.

EXAMPLE 1 n = 255 for a SPHYGMOMANOMETER intended for use in adults and/or adolescent PATIENTS (an 85 subject study).

EXAMPLE 2 n = 255 for a SPHYGMOMANOMETER intended for use in adults and/or adolescents and children aged between 3 years and 12 years (an 85 subject study).

EXAMPLE 3 n = 105 for a SPHYGMOMANOMETER intended for a special INTENDED USE (a 35 subject study), when the SPHYGMOMANOMETER has previously undergone CLINICAL INVESTIGATION in a separate 85 subject study according to 5.1.1 and 5.2.

b) Criterion 2

For the SYSTOLIC and DIASTOLIC BLOOD PRESSURES for each of the m subjects, the standard deviation, s_m, of the averaged paired DETERMINATIONS per subject of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' DETERMINATIONS with the REFERENCE SPHYGMOMANOMETER shall meet the criteria listed in Table 1 or Table 2 when calculated according to Formula (9).

$$s_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} (x_j - \overline{x}_n)^2} \tag{9}$$

where

$\overline{x}_n$ is the mean value of the differences as calculated according to Formula (6);

m is the number of subjects;

j is the index for the individual element;

x_j is SPHYGMOMANOMETER-UNDER-TEST error as calculated according to Formula (10);

$$x_j = \frac{1}{d} \times \sum_{k=1}^{d} (p_{\mathrm{sut}_{j,k}} - p_{\mathrm{ref-sq}_{j,k}}) \tag{10}$$

where

d is the number of DETERMINATIONS per subject;

k is the index for the individual element;

$p_{\mathrm{ref-sq}_{j,k}}$ is the REFERENCE BLOOD PRESSURE calculated according to Formula (11).

$$p_{\mathrm{ref-sq}_{j,k}} = \frac{1}{4} \times (p_{\mathrm{ref}_{j,k,1}} + p_{\mathrm{ref}_{j,k,2}} + p_{\mathrm{ref}_{j,k+1,1}} + p_{\mathrm{ref}_{j,k+1,2}}) \tag{11}$$

EXAMPLE 4 m = 85 for a SPHYGMOMANOMETER intended for use in adults and/or adolescent PATIENTS (an 85 subject study).

EXAMPLE 5 m = 85 for a SPHYGMOMANOMETER intended for use in adults and/or adolescents and children aged between 3 years and 12 years (an 85 subject study).

EXAMPLE 6 m = 35 for a SPHYGMOMANOMETER intended for (an additional) special INTENDED USE (a 35 subject study), when the SPHYGMOMANOMETER has previously undergone CLINICAL INVESTIGATION in a separate 85 subject study according to 5.1.1 and 5.2.

EXAMPLE 7 m = 85 for a SPHYGMOMANOMETER intended only for a special INTENDED USE (an 85 subject study).

5.2.4.3 * Opposite limb simultaneous method

5.2.4.3.1 Procedure

The starting arm side of the SPHYGMOMANOMETER-UNDER-TEST and the REFERENCE SPHYGMOMANOMETER DETERMINATIONS shall be alternated between subjects.

Perform the following:

a) Have the observers using the REFERENCE SPHYGMOMANOMETER and the SPHYGMOMANOMETER-UNDER-TEST simultaneously determine the subject's BLOOD PRESSURE in opposite arms (see Figure 3).

b) These data points are not used in the calculation of accuracy.

c) Clear the SPHYGMOMANOMETER-UNDER-TEST memory of the previous DETERMINATION and wait at least 60 s.

EXAMPLES Switching the power off and on, removing the BLOOD PRESSURE module and reinstalling it or issuing a reset command are methods to clear the memory of the previous DETERMINATION.

d) Interchange arm sides of the REFERENCE SPHYGMOMANOMETER and the SPHYGMOMANOMETER-UNDER-TEST.

e) Wait at least 60 s from the completion of the previous determination.

f) Have the observers using the REFERENCE SPHYGMOMANOMETER and the SPHYGMOMANOMETER-UNDER-TEST simultaneously determine the subject's BLOOD PRESSURE in opposite arms.

g) Repeat d) to f) until six paired determinations have been performed.

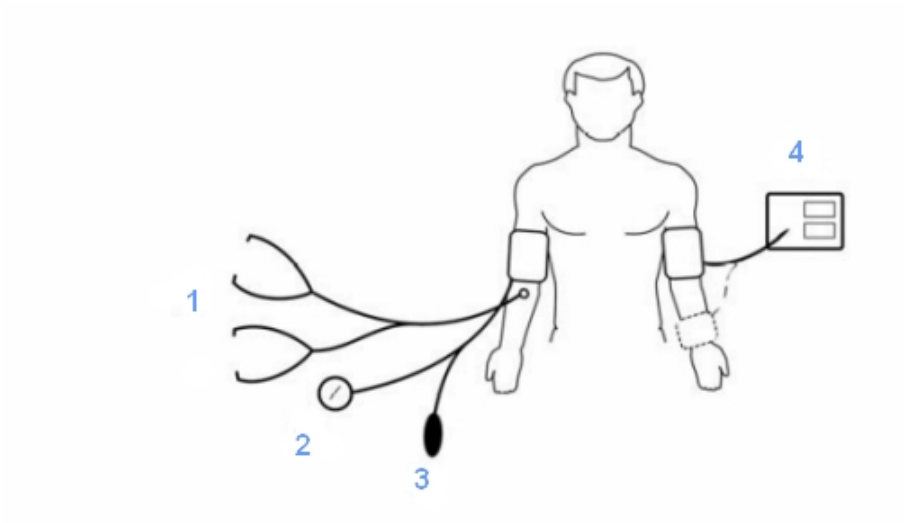
h) If the DETERMINATION by the observers with the REFERENCE SPHYGMOMANOMETER or the SPHYGMOMANOMETER-UNDER-TEST is not successfully completed, repeat the DETERMINATION on the same arm (i.e. without interchanging sides).

i) Repeat a) to h) until the required number of valid subjects and DETERMINATIONS has undergone CLINICAL INVESTIGATION.

All data from a subject shall be excluded if

— any two REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATIONS on the same arm differ by more than 12 mmHg (1,60 kPa) or any two REFERENCE DIASTOLIC BLOOD PRESSURE DETERMINATIONS on the same arm differ by more than 8 mmHg (1,07 kPa).

— the lateral difference of the REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATIONS is more than 15 mmHg (2,00 kPa) or the lateral difference of the REFERENCE DIASTOLIC BLOOD PRESSURE DETERMINATIONS is more than 10 mmHg (1,33 kPa).



Key

1 double stethoscope

2 REFERENCE SPHYGMOMANOMETER display

3 REFERENCE SPHYGMOMANOMETER hand pump

4 SPHYGMOMANOMETER-UNDER-TEST

NOTE Only one CUFF is connected to the SPHYGMOMANOMETER-UNDER-TEST.

Figure 3 — Illustration of opposite arm simultaneous method

The lateral difference, LD, is calculated separately for SYSTOLIC and DIASTOLIC BLOOD PRESSURES, according to Formula (12).

$$LD = \frac{1}{3} \times \left(\sum_{i=1}^{3} p_{\text{ref\_R}_i} - \sum_{j=1}^{3} p_{\text{ref\_L}_j} \right) \tag{12}$$

where

$p_{\text{ref\_R}_i}$ and $p_{\text{ref\_L}_j}$ are REFERENCE BLOOD PRESSURES in the right (R) arm and left (L) arm, respectively.

5.2.4.3.2 * Data analysis

The SPHYGMOMANOMETER-UNDER-TEST error, x, is calculated by taking the difference between the SPHYGMOMANOMETER-UNDER-TEST BLOOD PRESSURE and the REFERENCE SPHYGMOMANOMETER BLOOD PRESSURE and by adding the lateral difference, LD, as calculated according to Formula (13) if the SPHYGMOMANOMETER-UNDER-TEST BLOOD PRESSURE was taken in the left arm or by subtracting the lateral difference, LD, as calculated according to Formula (14) if the SPHYGMOMANOMETER-UNDER-TEST BLOOD PRESSURE was taken in the right arm.

$$x = p_{\text{sut\_L}} - p_{\text{ref\_R}} + LD \tag{13}$$

$$x = p_{\text{sut\_R}} - p_{\text{ref\_L}} - LD \tag{14}$$

where $p_{\text{sut\_R}}$ and $p_{\text{sut\_L}}$ are SPHYGMOMANOMETER-UNDER-TEST BLOOD PRESSURES in right (R) arm and left (L) arm, respectively.

The SPHYGMOMANOMETER-UNDER-TEST shall meet the following two criteria.

a) Criterion 1

For SYSTOLIC and DIASTOLIC BLOOD PRESSURES, the mean value of the differences of the DETERMINATIONS, $\overline{x}_n$, of the n individual paired DETERMINATIONS of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' DETERMINATIONS with the REFERENCE SPHYGMOMANOMETER for all subjects shall be within or equal to ± 5,0 mmHg (± 0,67 kPa), with a standard deviation, s_n, not greater than 8,0 mmHg (1,07 kPa) when calculated according to Formula (15) and Formula (16).

$$\overline{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} x_i \tag{15}$$

$$s_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} \left(x_i - \overline{x}_n \right)^2} \tag{16}$$

where

x_i is the SPHYGMOMANOMETER-UNDER-TEST error as calculated according to Formula (13) and Formula (14);

n is the number of DETERMINATIONS;

i is the index for the individual element.

EXAMPLE 1 n = 510 for a SPHYGMOMANOMETER intended for use in adults and/or adolescent PATIENTS (an 85 subject study).

EXAMPLE 2 n = 510 for a SPHYGMOMANOMETER intended for use in adults and/or adolescents and children aged between 3 years and 12 years (an 85 subject study).

EXAMPLE 3 n = 210 for a SPHYGMOMANOMETER intended for (an additional) special INTENDED USE (a 35 subject study), when the SPHYGMOMANOMETER has previously undergone CLINICAL INVESTIGATION in a separate 85 subject study according to 5.1.1 and 5.2.

b) Criterion 2

For the average of the SYSTOLIC BLOOD PRESSURE and the average of the DIASTOLIC BLOOD PRESSURE for each subject, the standard deviation, s_m, of the m averaged paired DETERMINATIONS of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' DETERMINATIONS with the REFERENCE SPHYGMOMANOMETER, per subject, shall meet the criteria listed in Table 1 or Table 2 when calculated according to Formula (17).

$$s_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} \left(x_j - \overline{x}_n \right)^2} \tag{17}$$

where

$\overline{x}_n$ is the mean value as calculated according to Formula (15);

m is the number of subjects;

j is the index for the individual element;

x_j is the mean per subject calculated according to Formula (18).

$$x_j = \frac{1}{6} \times \sum_{k=1}^{6} x_k \quad (18)$$

where

x_k is the SPHYGMOMANOMETER-UNDER-TEST error for each subject as calculated according to Formula (13) and Formula (14);

k is the index for the individual element.

EXAMPLE 4 m = 85 for a SPHYGMOMANOMETER intended for use in adults and/or adolescent PATIENTS (an 85 subject study).

EXAMPLE 5 m = 85 for a SPHYGMOMANOMETER intended for use in adults and/or adolescents and children aged between 3 years and 12 years (an 85 subject study).

EXAMPLE 6 m = 35 for a SPHYGMOMANOMETER intended for (an additional) special INTENDED USE (a 35 subject study), when the SPHYGMOMANOMETER has previously undergone CLINICAL INVESTIGATION in a separate 85 subject study according to 5.1.1 and 5.2.

EXAMPLE 7 m = 85 for a SPHYGMOMANOMETER intended only for a special INTENDED USE (an 85 subject study).

5.2.5 * Additional requirements for a SPHYGMOMANOMETER intended for use in exercise stress testing environments

For a SPHYGMOMANOMETER intended for use in exercise stress testing, an additional CLINICAL INVESTIGATION shall be performed. During this CLINICAL INVESTIGATION, the subjects shall be stressed by dynamic (aerobic) exercise on a bicycle ergometer or a treadmill so as to increase their heart rate from their resting heart rate to a target heart rate of 50 % to 70 % of their average predicted maximum heart rate (see Annex B). The physical load setting of the ergometer and target heart rate shall be recorded. The arm used for a DETERMINATION shall be supported. The CUFF shall be at the level of the right atrium during the DETERMINATION of BLOOD PRESSURE.

The same arm sequential method of 5.2.4.2 shall not be used. The CLINICAL INVESTIGATION shall consist of a minimum of 35 subjects. A stress testing study shall be exempt from the BLOOD PRESSURE distribution requirements of 5.1.5. At least 10 % of the subjects shall have a resting SYSTOLIC BLOOD PRESSURE ≥ 160 mmHg (21,33 kPa). At least 10 % of the subjects shall have a resting DIASTOLIC BLOOD PRESSURE ≥ 100 mmHg (13,33 kPa).

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.2.6 Additional requirements for a SPHYGMOMANOMETER intended for use in ambulatory monitoring

For a SPHYGMOMANOMETER intended for use in ambulatory monitoring, an additional CLINICAL INVESTIGATION shall be performed. During this CLINICAL INVESTIGATION, the subjects shall be stressed by dynamic (aerobic) exercise on a bicycle ergometer or treadmill so as to increase their heart rate to 10 % to 20 % above their resting heart rate. The physical load setting of the ergometer and heart rate shall be recorded. The arm used for a DETERMINATION shall be supported. The CUFF shall be at the level of the right atrium during the DETERMINATION of BLOOD PRESSURE.

The same arm sequential method of 5.2.4.2 shall not be used. The CLINICAL INVESTIGATION shall consist of a minimum of 35 subjects. An ambulatory monitoring study shall be exempt from the BLOOD PRESSURE distribution requirements of 5.1.5. At least 10 % of the subjects shall have a resting SYSTOLIC BLOOD PRESSURE

> 160 mmHg (21,33 kPa). At least 10 % of the subjects shall have a resting DIASTOLIC BLOOD PRESSURE > 100 mmHg (13,33 kPa).

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

6 CLINICAL INVESTIGATION with REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT

6.1 PATIENT requirements

6.1.1 Number

A REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT CLINICAL INVESTIGATION shall consist of a minimum of 15 PATIENTS. For each PATIENT, no more than 10 valid BLOOD PRESSURE measurements shall be taken. There shall be a minimum of 150 valid BLOOD PRESSURE measurements in the CLINICAL INVESTIGATION.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

6.1.2 * Gender distribution

At least 30 % of the measurements shall be on male PATIENTS and at least 30 % of the measurements shall be on female PATIENTS.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

6.1.3 * Age distribution

6.1.3.1 SPHYGMOMANOMETERS intended for use in adults, adolescents or children

For a SPHYGMOMANOMETER intended for use in adult and/or adolescent PATIENTS, the age of every PATIENT included in the CLINICAL INVESTIGATION shall be greater than 12 years.

NOTE 1 Minimum total of 15 subjects.

For a SPHYGMOMANOMETER additionally intended for use in children, at least an additional 5 children aged between 3 years and 12 years shall be included in the CLINICAL INVESTIGATION.

NOTE 2 Minimum total of 20 subjects.

For a SPHYGMOMANOMETER additionally intended for use in children, the data analysis (see 6.1.1) of adults, adolescents and children shall be pooled. Children are exempt from the BLOOD PRESSURE distribution requirements of 6.1.5.

Check compliance by inspection of the ACCOMPANYING DOCUMENT and the CLINICAL INVESTIGATION REPORT.

6.1.3.2 SPHYGMOMANOMETER for neonatal or infant populations

A SPHYGMOMANOMETER intended for use in neonates, infants and children of less than 3 years of age, shall be investigated in those PATIENT populations.

The following age or weight ranges are required for a neonatal mode CLINICAL INVESTIGATION.

At least 3 PATIENTS shall be < 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 $>$ 2 000 g in weight.

At least 3 PATIENTS shall be ≥ to 29 days and $<$ 1 year of age.

At least 3 PATIENTS shall be ≥ 1 year and $<$ 3 years of age.

The remaining PATIENTS may be from any of the above age or weight groups in order to complete the sample size of 18.

NOTE 1 Minimum total of 18 PATIENTS.

NOTE 2 A PATIENT can be in more than one category simultaneously.

Neonates, infants and children of less than 3 years of age are exempt from the BLOOD PRESSURE distribution requirements of 6.1.5, the gender distribution requirements of 6.1.2 and the limb size distribution requirements of 6.1.4.

Check compliance by inspection of the ACCOMPANYING DOCUMENT and the CLINICAL INVESTIGATION REPORT.

6.1.4 * Limb size distribution

For a SPHYGMOMANOMETER intended for use with a single CUFF size, at least 40 % of the subjects shall have a limb circumference that lies within the upper half of the specified range of use of the CUFF and at least 40 % shall have a limb circumference within the lower half.

For a SPHYGMOMANOMETER intended for use with multiple CUFF sizes, at least $\frac{1}{2 \times n}$ of the subjects shall be tested with each CUFF size, where n is the number of CUFF sizes.

Check compliance by inspection of the ACCOMPANYING DOCUMENT and the CLINICAL INVESTIGATION REPORT.

6.1.5 * BLOOD PRESSURE distribution

At least 10 % of the subjects shall have a REFERENCE SYSTOLIC BLOOD PRESSURE ≤ 100 mmHg (13,33 kPa).

At least 10 % of the subjects shall have a REFERENCE SYSTOLIC BLOOD PRESSURE ≥ 160 mmHg (21,33 kPa).

At least 10 % of the subjects shall have a REFERENCE DIASTOLIC BLOOD PRESSURE ≤ 70 mmHg (9,33 kPa).

At least 10 % of the subjects shall have a REFERENCE DIASTOLIC BLOOD PRESSURE ≥ 85 mmHg (11,33 kPa).

These requirements shall be met by calculating the mean of the REFERENCE SYSTOLIC and DIASTOLIC BLOOD PRESSURE measurements taken during the study. Additional REFERENCE measurements may be taken prior to the study to aid in determining inclusion criteria.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

6.1.6 Special PATIENT populations

A SPHYGMOMANOMETER that is intended for use in special PATIENT populations where there is OBJECTIVE EVIDENCE that the accuracy of the SPHYGMOMANOMETER might be problematic in those PATIENT populations shall undergo CLINICAL INVESTIGATION in those PATIENT populations.

NOTE Clause 7 has a specific example of a special PATIENT population.

If the SPHYGMOMANOMETER has undergone CLINICAL INVESTIGATION according to the requirements of 6.1.1, then only seven additional special population PATIENTS shall be included in the CLINICAL INVESTIGATION. Otherwise,

the CLINICAL INVESTIGATION in accordance with the requirements of 6.1.1 shall consist only of PATIENTS from the special population.

Check compliance by inspection of the ACCOMPANYING DOCUMENT and the CLINICAL INVESTIGATION REPORT.

6.2 CLINICAL INVESTIGATION methods with REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT

6.2.1 * REFERENCE measurement

REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT shall comply with the requirements of IEC 60601-2-34:2011, except that the maximum allowable error shall be ± 2 mmHg (± 0,27 kPa). The resonant frequency and damping coefficient of the REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT shall be characterized. The transducer for the intra-arterial catheter and the SPHYGMOMANOMETER-UNDER-TEST CUFF should both be kept at the level of the right atrium of the heart.

NOTE 1 References [18] and [44] contain additional information regarding characterization of INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT.

Unless the SPHYGMOMANOMETER-UNDER-TEST is intended for use during a clinically significant irregular heart rhythm or if the REFERENCE intra-arterial recording indicates the presence of a significantly irregular heart rhythm, that intra-arterial BLOOD PRESSURE recording and its associated SPHYGMOMANOMETER-UNDER-TEST BLOOD PRESSURE DETERMINATION shall be excluded. The intra-arterial blood recordings shall be checked for the occurrence of dysrhythmias against the MANUFACTURER'S exclusion criteria. The instructions for use shall indicate that the effectiveness of this SPHYGMOMANOMETER has not been established in the presence of any dysrhythmias included in the exclusion criteria. The effect of isolated premature ventricular beats (VPBs) may be addressed by removing the pressure pulse associated with the VPB and the following compensatory beat.

EXAMPLES Bigeminy, trigeminy, isolated VPB, atrial fibrillation.

NOTE 2 Although CLINICAL INVESTIGATION of BLOOD PRESSURE in PATIENTS with atrial fibrillation is clinically important, there are currently no generally accepted guidelines for determining the BLOOD PRESSURE in such individuals.

6.2.2 * Arterial REFERENCE site

No arterial site is excluded, but the instructions for use of the SPHYGMOMANOMETER shall disclose the arterial site used as the REFERENCE site.

NOTE Different sites produce different results due to the pressure difference between the central aorta and other arteries.

Sites on the same limb, a central, subclavian or femoral REFERENCE may be used for simultaneous comparison of intra-arterial BLOOD PRESSURE recordings and SPHYGMOMANOMETER-UNDER-TEST BLOOD PRESSURE DETERMINATION. The arterial transducer should be at the level of the right atrium. The REFERENCE site may be on the opposite limb. If the opposite limb is used, the results shall be corrected for the lateral difference. Formula (A.1) provides an example of a non-invasive correction method. Simultaneous non-invasive DETERMINATIONS may be used to determine the lateral difference. The lateral difference in BLOOD PRESSURE shall be calculated prior to taking the invasive data. All data from a subject shall be excluded from the CLINICAL INVESTIGATION if the lateral difference of the REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATIONS is more than 15 mmHg (2,00 kPa) or the lateral difference of the REFERENCE DIASTOLIC BLOOD PRESSURE DETERMINATIONS is more than 10 mmHg (1,33 kPa).

Check compliance by inspection of the ACCOMPANYING DOCUMENT.

6.2.3 Procedure

Appropriate measures should be taken to remove air bubbles and clots from the system prior to taking the REFERENCE measurements.

NOTE The ability to accurately measure arterial BLOOD PRESSURE can be degraded by the presence of air bubbles and/or blood clots in the catheter/transducer system.

Perform the following:

a) Have the observers using the SPHYGMOMANOMETER-UNDER-TEST determine the subject's BLOOD PRESSURE.

b) Remove the CUFF from the subject.

c) Clear the SPHYGMOMANOMETER-UNDER-TEST memory of the previous DETERMINATION and wait at least 3 min.

EXAMPLE Switching the power off and on, removing the BLOOD PRESSURE module and reinstalling it or issuing a reset command are methods to clear the memory of the previous DETERMINATION.

d) Do not use the data points obtained in a) in the calculation of accuracy.

e) Have the observers using the REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT and the SPHYGMOMANOMETER-UNDER-TEST simultaneously record and determine the subject's BLOOD PRESSURE.

f) Wait at least 60 s between DETERMINATIONS or, for neonatal PATIENTS, 3 min.

g) Repeat e) and f) until the required number of recordings and DETERMINATIONS has been performed.

6.2.4 * Determining the REFERENCE BLOOD PRESSURE

The invasive SYSTOLIC and DIASTOLIC BLOOD PRESSURE values shall be determined from the recordings of 6.2.3 e). Determine the mean and standard deviation of the SYSTOLIC and DIASTOLIC BLOOD PRESSURE from the recordings.

In those cases, where the recording

a) is not interrupted due to the CUFF inflation, the REFERENCE BLOOD PRESSURE ranges shall be determined from the recording of the invasive BLOOD PRESSURE for a duration of at least 30 s that includes the period of the DETERMINATION of the SPHYGMOMANOMETER-UNDER-TEST;

b) is interrupted due to the CUFF inflation, the REFERENCE BLOOD PRESSURE ranges shall be determined from the recording of the invasive BLOOD PRESSURE for a duration of at least 30 s (approximately 40 s to 10 s) before the cuff inflation starts and for a duration of at least 30 s (approximately 10 s to 40 s) after the CUFF has been deflated.

The REFERENCE SYSTOLIC BLOOD PRESSURE is defined as the range of $\pm$ 1 experimental standard deviation around the mean value of the invasive BLOOD PRESSURE values obtained during the DETERMINATION performed by the SPHYGMOMANOMETER-UNDER-TEST. The REFERENCE DIASTOLIC BLOOD PRESSURE is defined in the same way.

NOTE These ranges of BLOOD PRESSURES ($\pm$ 1 experimental standard deviation around the mean value) represent the actual BLOOD PRESSURE variations while the SPHYGMOMANOMETER-UNDER-TEST has determined the PATIENT'S BLOOD PRESSURE. As a result, the SPHYGMOMANOMETER-UNDER-TEST error is considered to be 0 mmHg (0 kPa) when a reading is within these ranges.

Unless the SPHYGMOMANOMETER-UNDER-TEST is intended for use during significantly irregular heart rhythm, during the recording

— all data from a subject shall be excluded if the invasive REFERENCE SYSTOLIC BLOOD PRESSURE range is more than 20 mmHg (2,67 kPa) or if the invasive REFERENCE DIASTOLIC BLOOD PRESSURE range is more than 12 mmHg (1,6 kPa);

— isolated premature ventricular beats (VPBs) shall be addressed by removing the pressure pulse associated with the VPB and the following compensatory beat.

As the calculation of the MEAN ARTERIAL PRESSURE (MAP) from the recording requires a special algorithm, the REFERENCE MEAN ARTERIAL PRESSURE range may be read from the values displayed on the REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT or manually calculated for each individual beat.

Record the range of the REFERENCE BLOOD PRESSURE for all three BLOOD PRESSURE values (SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE, MAP) as determined by this subclause.

Check compliance by inspection of the ACCOMPANYING DOCUMENT and the CLINICAL INVESTIGATION REPORT.

6.2.5 Determining the error of the BLOOD PRESSURE measurement

If the value obtained from the SPHYGMOMANOMETER-UNDER-TEST DETERMINATION lies within the range of the REFERENCE BLOOD PRESSURE as determined in 6.2.4, assign an error of 0 mmHg (0 kPa) to this DETERMINATION.

If the value obtained from the SPHYGMOMANOMETER-UNDER-TEST DETERMINATION lies outside the range of the REFERENCE BLOOD PRESSURE as determined in 6.2.4, subtract the value of the DETERMINATION from the adjacent limit of the range of the variation of BLOOD PRESSURE. That difference represents the error for this DETERMINATION.

EXAMPLE 1 The range of the REFERENCE DIASTOLIC BLOOD PRESSURE is 73 mmHg (9,73 kPa) to 82 mmHg (10,93 kPa). The DIASTOLIC BLOOD PRESSURE value determined by the SPHYGMOMANOMETER-UNDER-TEST is 76 mmHg (10,13 kPa). The error for this DETERMINATION is 0 mmHg (0 kPa).

EXAMPLE 2 The range of the REFERENCE DIASTOLIC BLOOD PRESSURE is 73 mmHg (9,73 kPa) to 82 mmHg (10,93 kPa). The DIASTOLIC BLOOD PRESSURE value determined by the SPHYGMOMANOMETER-UNDER-TEST is 70 mmHg (9,33 kPa). The error for this DETERMINATION is -3 mmHg (-0,40 kPa).

From the errors of each DETERMINATION for each PATIENT, calculate the arithmetic mean of the error and its experimental standard deviation.

6.2.6 Data analysis

For SYSTOLIC and DIASTOLIC BLOOD PRESSURES, the mean value of the errors of the DETERMINATIONS, $\overline{x}_n$, of the n individual paired DETERMINATIONS of the SPHYGMOMANOMETER-UNDER-TEST as determined in 6.2.5 for all subjects shall be within or equal to ± 5,0 mmHg (± 0,67 kPa), with an experimental standard deviation, s_n, no greater than 8,0 mmHg (1,07 kPa) when calculated according to Formula (19) and Formula (20).

$$\overline{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} x_i \tag{19}$$

$$s_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} \left(x_i - \overline{x}_n \right)^2} \tag{20}$$

where

x_i is the error of the i^{th} individual DETERMINATION as determined in 6.2.5;

n is the total number of DETERMINATIONS;

i is the index for the individual DETERMINATION.

EXAMPLE 1 n = 150 for a SPHYGMOMANOMETER intended for use in adults and/or adolescent PATIENTS (a 15 subject study).

EXAMPLE 2 n = 200 for a SPHYGMOMANOMETER intended for use in adults and/or adolescents and children aged between 3 years and 12 years (a 20 subject study).

6.2.7 MEAN ARTERIAL PRESSURE (MAP)

If a SPHYGMOMANOMETER displays a value for MEAN ARTERIAL PRESSURE (MAP), the ACCOMPANYING DOCUMENT shall disclose the method used to determine and verify the MEAN ARTERIAL PRESSURE.

Check compliance by inspection of the ACCOMPANYING DOCUMENT and the CLINICAL INVESTIGATION REPORT.

7 * Pregnant (including pre-eclamptic) PATIENT populations

A SPHYGMOMANOMETER that is intended for use in pregnant (including pre-eclamptic) PATIENTS shall undergo CLINICAL INVESTIGATION in that PATIENT population.

If the SPHYGMOMANOMETER has undergone CLINICAL INVESTIGATION according to the requirements given in 5.1.1, then at least an additional 45 pregnant (including pre-eclamptic) PATIENTS or, if already having undergone CLINICAL INVESTIGATION according to the requirements given in 6.1.1, then at least an additional 15 pregnant (including pre-eclamptic) PATIENTS, shall separately undergo CLINICAL INVESTIGATION. Otherwise, the CLINICAL INVESTIGATION for the requirements in 5.1.1 or 6.1.1 shall consist only of pregnant (including pre-eclamptic) PATIENTS.

For any CLINICAL INVESTIGATION for pregnant (including pre-eclamptic) PATIENTS, the PATIENT population shall be equally distributed, ± 1 PATIENT, into the following three subgroups:

a) normotensive pregnant PATIENTS with SYSTOLIC BLOOD PRESSURE < 140 mmHg (18,66 kPa) and DIASTOLIC BLOOD PRESSURE < 90 mmHg (12,00 kPa);

b) hypertensive pregnant PATIENTS without proteinuria > 300 mg in 24 h and with SYSTOLIC BLOOD PRESSURE ≥ 140 mmHg (18,66 kPa) or DIASTOLIC BLOOD PRESSURE ≥ 90 mmHg (12,00 kPa);

c) pre-eclampsia, PATIENTS with proteinuria > 300 mg in 24 h and DIASTOLIC BLOOD PRESSURE ≥ 90 mmHg (12,00 kPa).

The PATIENT'S responsible healthcare provider needs to determine whether or not it is safe for a particular PATIENT to participate in a CLINICAL INVESTIGATION.

NOTE Data analysis is performed with the three subgroups pooled.

The instructions for use of a SPHYGMOMANOMETER that has been investigated to operate with pregnant (including pre-eclamptic) PATIENTS shall indicate that the SPHYGMOMANOMETER is suitable for use with pregnant (including pre-eclamptic) PATIENTS. The instructions for use of a SPHYGMOMANOMETER that has not been investigated for use on pregnant (including pre-eclamptic) PATIENTS shall indicate the effectiveness of this SPHYGMOMANOMETER has not been established in pregnant (including pre-eclamptic) PATIENTS.

Check compliance by inspection of the INSTRUCTIONS FOR USE and the CLINICAL INVESTIGATION REPORT.

Annex A
(informative)

Rationale and guidance

A.1 General

This annex provides rationale for some of the requirements of this part of ISO 81060 and is intended for those who are familiar with the subject of this part of ISO 81060 but who have not participated in its development. An understanding of the rationale underlying these requirements is considered to be essential for their proper application. Furthermore, as clinical practice and technology change, it is believed that a rationale will facilitate any revision of this document necessitated by those developments.

The numbering of the following rationale corresponds to the numbering of the clauses and subclauses in this part of ISO 81060. The numbering is, therefore, not consecutive.

5.1.1 Number

The sample size of 85 was determined from the statistics for a normal distribution.

NOTE 1 Reference [6] contains additional information.

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.

NOTE 2 Reference [5] contains additional information.

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.

5.1.2 Gender distribution

While there is no definitive evidence that a SPHYGMOMANOMETER performs differently on male and female PATIENTS, some studies indicate that there might be a bias.

NOTE References [42] and [43] contain additional information.

If bias exists, it is likely caused by differences in limb circumference and body fat distribution. This part of ISO 81060 already requires that the SPHYGMOMANOMETER-UNDER-TEST be tested over a range of arm circumferences. The requirement for gender distribution allows for investigation of gender differences without being difficult to implement.

5.1.3 Age distribution

The division between children and adults at the age of 12 years was based upon the only known publication that compares the utility of the use of either K4 or K5 as the auscultatory estimate of arterial DIASTOLIC BLOOD PRESSURE. In 1963, Moss and Adams[26] studied whether K4 or K5 was a better estimate of aortic BLOOD PRESSURE measured during cardiac catheterization. The data demonstrated that, up to the age of 13 (≤ 12) years old, K4 was superior. In 1987, the Task Force on Blood Pressure Control in Children[11] changed its recommendation to state that K5 could be used in individuals older than 3 years of age. Unfortunately, this recommendation was made in the absence of supporting data. For that reason, this committee continues to utilize evidence-based findings, i.e. that in children from 3 years to 12 years old, auscultatory K4 may be utilized as the non-invasive REFERENCE standard estimate of DIASTOLIC BLOOD PRESSURE in CLINICAL INVESTIGATIONS.

During the growth period from age 3 years to age 12 years, the average child (50th percentile) increases in height from 93 cm to 96 cm (at age 3 years) to 150 cm to 152 cm (at age 12 years). Within the range from the 3rd to the 97th percentiles there can be as much as a 30 cm difference (at age 12 years). Normal growth is remarkably linear during this age range, although there are many different body builds in children, and thus arm circumferences vary significantly. ISO/TC 121 and IEC/TC 62 were not aware of any longitudinal study of children's arm circumferences from age 3 years to age 12 years. Since non-invasive BLOOD PRESSURE accuracy is more strongly influenced by arm circumference than by subject height, ISO/TC 121 and IEC/TC 62 believed that the inclusion of each CUFF size was more important than children of arbitrary ages. For example, a “large” 6 year old can have a significantly greater arm circumference than a “small” 9 year old or 10 year old.

The upper normal SYSTOLIC/DIASTOLIC BLOOD PRESSURE in children increases from about 114/66 mmHg (15,20/8,80 kPa) at age 1 year to 135/91 mmHg (18,00/12,13 kPa) at age 12 years for the tallest children analysed.

NOTE Reference [7] contains additional information.

For this reason, it would not be practical to specify exact “hypertensive” BLOOD PRESSURE values, as can be done in adults for investigations. In addition, the prevalence of essential hypertension in young children is very low, making CLINICAL INVESTIGATIONS requiring hypertensive children extremely difficult to perform. Further, the SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE values in a hypertensive infant are at about the average for normotensive adults. Thus, the SPHYGMOMANOMETER-UNDER-TEST would not be significantly “challenged” with respect to accuracy in this BLOOD PRESSURE range. Thus, ISO/TC 121 and IEC/TC 62 believed there was no valid reason to require hypertensive children in any CLINICAL INVESTIGATION of individuals ≤ 12 years of age and that the data from children > 12 years of age should be pooled with those from adults in the data analysis.

5.1.4 Limb size distribution

This is a compromise between more detailed requirements for limb sizes and the difficulty of conducting the test. For a SPHYGMOMANOMETER with a single CUFF size, it is important to test the full range of limb circumferences intended for use.

5.1.5 BLOOD PRESSURE distribution

These ranges were chosen to ensure that the performance of the SPHYGMOMANOMETER is investigated over the entire clinically relevant BLOOD PRESSURE range. Previous standards required a subject to remain in a single category for all DETERMINATIONS for the data from the subject to be included. This tended to bias the subject selection such that they were far away from the boundaries of the categories, even if the subject’s BLOOD PRESSURE was very stable. This part of ISO 81060 retains the stability criteria for each subject, but categorizes each REFERENCE BLOOD PRESSURE independently.

5.1.6 Special PATIENT populations

In certain PATIENT populations, the accuracy of a SPHYGMOMANOMETER can be problematic. This can be caused by PATIENT characteristics, such as diabetes, peripheral artery disease or other conditions that affect arterial compliance. Similar problems can occur during a CLINICAL INVESTIGATION where PATIENT characteristics that increase the variability of the subject’s BLOOD PRESSURE could affect the accuracy of both the SPHYGMOMANOMETER-UNDER-TEST and the REFERENCE SPHYGMOMANOMETER. Examples include atrial or ventricular arrhythmias.

Although CLINICAL INVESTIGATION of BLOOD PRESSURE in PATIENTS with atrial fibrillation is clinically important, there are currently no generally accepted guidelines to measure BLOOD PRESSURE in such PATIENTS. Since the accuracy of the auscultatory method for the DETERMINATION of BLOOD PRESSURE in PATIENTS with atrial fibrillation is not known, it is desirable to establish another REFERENCE method for SPHYGMOMANOMETERS for PATIENTS with atrial fibrillation.

Although CLINICAL INVESTIGATION of BLOOD PRESSURE in PATIENTS during transport outside a healthcare facility is clinically important, there are currently no generally accepted guidelines to measure BLOOD PRESSURE in such PATIENTS. Since existing clinical standards for BLOOD PRESSURE measurement also can be difficult to use

during PATIENT transport outside a healthcare facility, it is desirable to establish a CLINICAL INVESTIGATION method for a SPHYGMOMANOMETER during such transport.

5.2.1 Subject preparation

Since it is essential to reduce a subject's BLOOD PRESSURE variability during the CLINICAL INVESTIGATION, factors that can cause changes in stability of BLOOD PRESSURE should be controlled.

EXAMPLES The PATIENTS should be asked to empty their bladders prior to taking data and, particularly in older people, measurements should be done at least 2 h after a meal.

5.2.2 Observer preparation

There is now general consensus that the fifth phase should be used for the DETERMINATION of the DIASTOLIC BLOOD PRESSURE, except in situations in which the disappearance of sounds cannot be reliably determined because sounds are audible even after complete deflation of the CUFF, for example, in pregnant women, PATIENTS with arteriovenous fistulas (e.g. for haemodialysis), aortic insufficiency and children between 3 years and 12 years of age.

NOTE 1 Reference [25], the rationale to 5.1.3 and Reference [32] contain additional information.

In the past, there had been some question as to whether the fourth (K4) or fifth (K5) Korotkoff sound should be used to determine the DIASTOLIC BLOOD PRESSURE. The International Society for the Study of Hypertension in Pregnancy currently recommends using K5 for the DETERMINATION of DIASTOLIC BLOOD PRESSURE during pregnancy.

NOTE 2 References [23] and [32] contain additional information.

There is considerable disagreement on how to determine BLOOD PRESSURE in pregnant women. Several national and international groups (e.g. WHO) recommend use of Korotkoff phase IV (K4) as the determinant of DIASTOLIC BLOOD PRESSURE. However, K4 can overestimate intra-arterial pressure by 7 mmHg (0,93 kPa) to 15 mmHg (2,00 kPa) and appears to be more difficult to determine accurately. Furthermore, most healthcare personnel in the US are trained to recognise Korotkoff phase V (K5) as the sound by which they determine DIASTOLIC BLOOD pressure in non-pregnant populations. These considerations led the United States National High Blood Pressure Education Program (NHBPEP) Working Group to recommend use of K5 during pregnancy, reserving K4 for the 10 % or fewer women in whom there is a large discrepancy between muffling and disappearance (with the latter at times approaching zero mmHg).

NOTE 3 References [23] and [32] contain additional information.

5.2.3 REFERENCE DETERMINATION

It was felt that if more than eight DETERMINATIONS are required to get valid readings for a subject then either the observers or the subject were presenting particular problems.

5.2.4.1.1 Procedure

Since the World Health Organization (WHO) recommendations[46] advise performing auscultatory BLOOD PRESSURE DETERMINATIONS at CUFF deflation rates of 2 mmHg/s (0,27 kPa/s) to 3 mmHg/s (0,40 kPa/s) or 2 mmHg/pulse (0,27 kPa/pulse) to 3 mmHg/pulse (0,40 kPa/pulse), the same arm simultaneous method can only be utilized for a SPHYGMOMANOMETER-UNDER-TEST performing a DETERMINATION at these deflation rates on the upper arm.

The DETERMINATION of the REFERENCE DIASTOLIC BLOOD PRESSURE is impossible for the observers if the SPHYGMOMANOMETER-UNDER-TEST, which controls the CUFF pressure, opens the rapid exhaust valve too early, i.e. at a time when the observers are still hearing Korotkoff sounds and have not yet determined the DIASTOLIC BLOOD PRESSURE. To prevent this, the SPHYGMOMANOMETER-UNDER-TEST might need to be modified accordingly, e.g. by disabling the rapid exhaust valve of the SPHYGMOMANOMETER-UNDER-TEST.

The initial measurement by the observers and the SPHYGMOMANOMETER-UNDER-TEST that is not included in the data analysis is required for two reasons:

— it permits the subject to become familiar with the procedure, thereby minimizing any effect on their BLOOD PRESSURE;

— it permits this measurement to be used to modify the maximum CUFF inflation, either manually or automatically, to be slightly above the subject's SYSTOLIC BLOOD PRESSURE.

The 60 s waiting period between the DETERMINATIONS is to allow re-establishment of normal circulation in the limb.

5.2.4.1.2 Data analysis

Criterion 1 is derived from the requirement originating in the early work of the AAMI Sphygmomanometer committee dating from 1987[5]. A t-test of the difference between the two means (test-REFERENCE) was chosen to determine the sample size. The absolute value of the mean value of the differences of DETERMINATIONS, $\overline{x}_n$, $\leq$ 5 mmHg ($\pm$ 0,67 kPa) and standard deviation, s_n, $\leq$ 8 mmHg (1,07 kPa), was chosen based on the review of literature comparing auscultatory to intra-arterial values. The sample size of 85 was then determined from statistics for a normal distribution.

NOTE 1 Reference [6] contains additional information.

A 98 % confidence interval (α = 0,02) and a statistical power of 95 % (β = 0,05) yield a sample size of 85 subjects. 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.

Originally, the mean value of the differences and the standard deviation of DETERMINATIONS was calculated from the average of the three test DETERMINATIONS and three REFERENCE DETERMINATIONS from each of the 85 subjects.

NOTE 2 Reference [5] contains additional information.

Later, the calculation was changed to the individual test-REFERENCE differences for the 255 individual DETERMINATION pairs.

NOTE 3 Reference [4] contains additional information.

In making this change, the AAMI blood pressure committee concluded that the change provided a tighter, more stringent acceptance criterion, since the standard deviation is larger when the values are not averaged by subject.

Criterion 2 is derived from the requirement that originated in more recent work of the AAMI blood pressure committee dating from 2002[3]. In making this change, the AAMI blood pressure committee developed an alternate method to analyse the data in response to the request from clinicians for a more stringent acceptance criterion. This statistical analysis was developed with the goal of limiting the error to $\pm$ 10 mmHg ($\pm$ 1,33 kPa) for 95 % of PATIENTS when the mean of three repeated measurements is used clinically.

Criterion 2 uses the average of the differences of the DETERMINATIONS (test-REFERENCE pairs, per subject) to help reduce the apparent error introduced by changes in the subject's BLOOD PRESSURE during the sequence of BLOOD PRESSURE DETERMINATIONS. The value of 10 mmHg (1,33 kPa) was chosen as a tolerable error based on clinician input.

The sample mean value of the differences of the DETERMINATIONS, $\overline{x}_m$, and sample standard deviation, s_m, refer to the mean and standard deviation of 85 numbers, each being the average of three differences of the DETERMINATIONS on the same subject. These sample statistics are only estimates of the population mean error (also called bias) and of the population standard deviation (also called precision), which could only be determined by testing the SPHYGMOMANOMETER-UNDER-TEST on an unlimited number of subjects.

A SPHYGMOMANOMETER-UNDER-TEST is considered acceptable if its estimated probability of a tolerable error is at least 85 %. This condition requires that the upper limit for an acceptable sample standard deviation depend on the sample mean error.

The calculated probability that the tolerable error of the SPHYGMOMANOMETER-UNDER-TEST is within the limit (10 mmHg) (1,33 kPa) is an estimate of the true probability in the population. As the sample size in the study increases, the estimated probability approaches the true probability. A sample size of n = 85 yields a 90 % chance that the estimated probability of a tolerable error does not differ by more than about 0,07 from the true probability. Thus, if the estimated probability of a tolerable error is 85 %, one can be confident that the true probability of a tolerable error lies between 78 % and 92 %.

In this part of ISO 81060, a SPHYGMOMANOMETER-UNDER-TEST is required to meet both Criterion 1 and Criterion 2.

Comparison of Criterion 1 and Criterion 2.

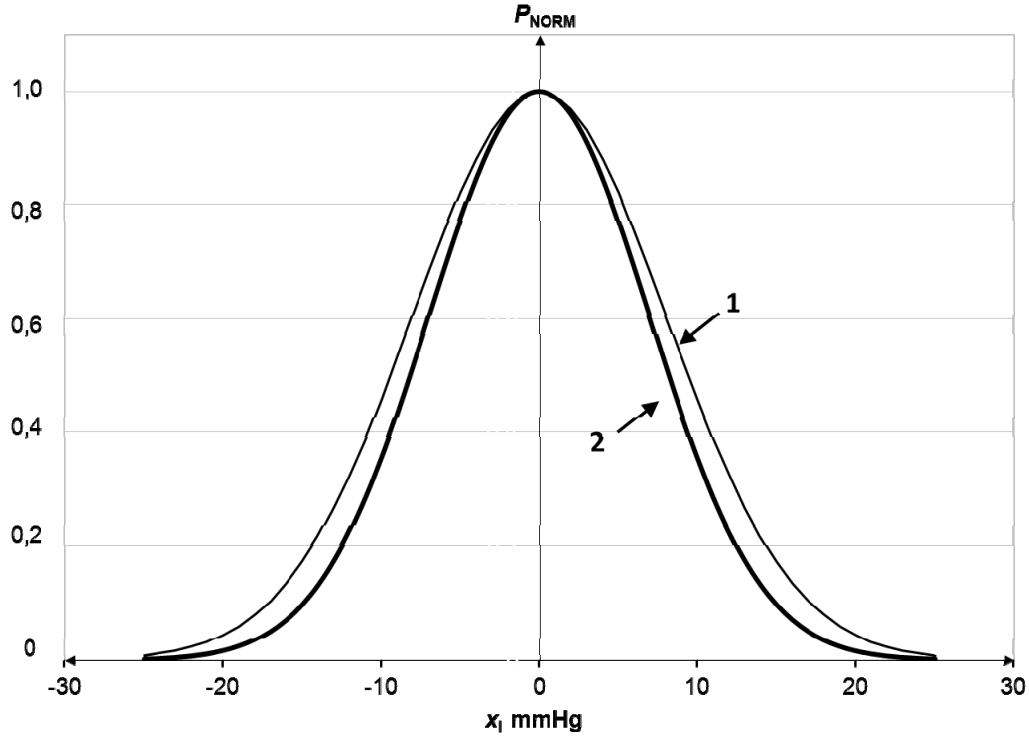
Criterion 1 uses the 255 individual test-REFERENCE differences to determine the performance of the SPHYGMOMANOMETER-UNDER-TEST. As a result, the calculated standard deviation, s_n, (or precision) will reflect both intra-subject and inter-subject variability. However, the allowable standard deviation, s_n, is constant even when the mean of the differences, $\bar{x}_n$, (or bias) is large.

Criterion 2 uses the average of the differences from each subject, so the calculated s_m reflects only inter-subject variability, and a large intra-subject variability can still pass this method. Criterion 2 attempts to prevent that by reducing the allowable s_n as $\bar{x}_n$ increases, (s_n = 8,00 mmHg versus s_m = 6,95 mmHg) (s_n = 1,07 kPa versus s_m = 0,93 kPa), thus addressing both bias and inter-subject precision.

Figure A.1 shows the allowable s for each criterion when $\bar{x}$ = 0.

The difference between the allowable standard deviations of the two methods is larger when $\bar{x}$ = 5,0 mmHg (0,67 kPa), as shown in Figure A.2. Criterion 1 requires an s_n ≤ 8,00 mmHg (1,07 kPa), while Criterion 2 requires an s_m ≤ 4,79 mmHg (0,6386 kPa).

In summary, Criterion 1 evaluates the effect on both intra- and inter-subject variability, but allows for a relatively large error when the bias is large. Criterion 2 does not measure intra-subject variability, but reduces the allowable s_n over the range of allowable $\bar{x}_n$. The use of both criteria ensures that bias and intra- and inter-subject variability are evaluated during the CLINICAL INVESTIGATION the SPHYGMOMANOMETER-UNDER-TEST.

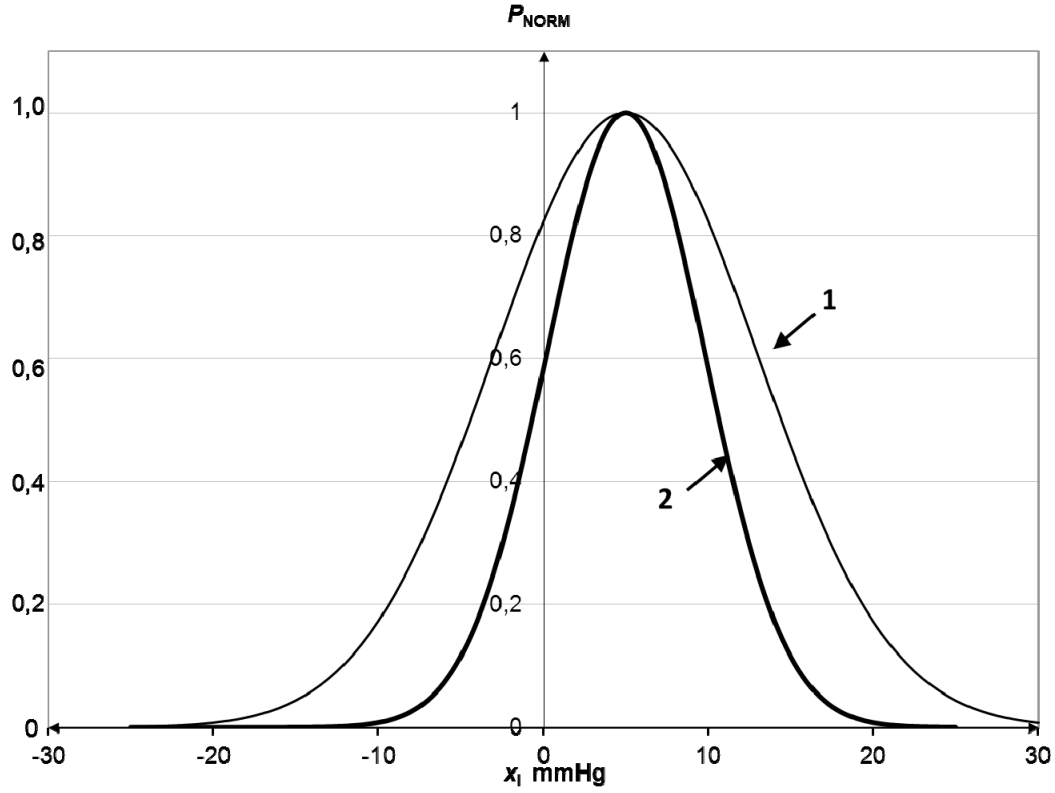


Key

1 criterion 1

2 criterion 2

Figure A.1 — Normalized probability distribution, P_N, for each criterion when the mean is 0,0 mmHg (0,0 kPa)



Key

1 criterion 1

2 criterion 2

Figure A.2 — Normalized probability distribution, P_N, for each criterion when the mean is 5 mmHg (0,67 kPa)

The statistical rationale for criterion 2 was developed based on the use of exactly three DETERMINATIONS per subject. While this ensures an equal contribution from each subject, it can create difficulties in completing the study, particularly in unstable hypertensive subjects.

Relaxing the requirement for exactly three DETERMINATIONS per subject, but maintaining the requirement for 255 DETERMINATIONS in total, requires additional subjects to complete the CLINICAL INVESTIGATION. The use of differing numbers of DETERMINATIONS per subject results in an unequal contribution to the overall error. A compromise is to allow the use of fewer than three DETERMINATIONS per subject, but to require that at least 90 % of the subjects use exactly three DETERMINATIONS.

While criterion 1 uses the individual paired DETERMINATIONS to calculate the mean difference and standard deviation, criterion 2 averages the three REFERENCE and test DETERMINATIONS for each subject. This reduces the impact of the variability of the subject's BLOOD PRESSURE on the apparent SPHYGMOMANOMETER-UNDER-TEST error and also reduces the calculated standard deviation (compared to criterion 1). The reduction in the standard deviation is not as large if subjects with only two DETERMINATIONS are included in the study, making it more difficult for a SPHYGMOMANOMETER-UNDER-TEST to meet the requirements of the CLINICAL INVESTIGATION.

5.2.4.2.1 Procedure

The advantage of the same arm sequential method is that investigation results are not affected by the lateral difference, LD, in BLOOD PRESSURE. However, in this method, BLOOD PRESSURE variability (BPV) is added to the SPHYGMOMANOMETER-UNDER-TEST error and therefore the standard deviation of SPHYGMOMANOMETER-UNDER-TEST error could be overestimated. This hypothesis was experimentally supported by ISO/TC 121 and IEC/TC 62's multiple-centre, independently performed study based on 120 subjects, which showed significant

positive correlation between REFERENCE BLOOD PRESSURE and intra-subject standard deviation of SPHYGMOMANOMETER-UNDER-TEST error.

ISO/TC 121 and IEC/TC 62 carefully considered the various possible methodologies that could be employed to perform same arm sequential investigations. Since the DETERMINATIONS are carried out in temporal succession, it is important that haemodynamically stable conditions exist during the testing period. ISO/TC 121 and IEC/TC 62 had some concern that this condition could be difficult to achieve in hypertensive PATIENTS. As a result of this concern, up to 10 % of the subjects are permitted to have only two measurements if they meet the stability criteria. The following three examples illustrate the intent of this procedure for a particular subject.

EXAMPLE 1 The first REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 122 mmHg. The second REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 128 mmHg. The third REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 132 mmHg. Result: The difference between any two REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATIONS is less than or equal to 12 mmHg; all DETERMINATIONS are included in the study.

EXAMPLE 2 The first REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 120 mmHg. The second REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 134 mmHg. The third REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 107 mmHg. Result: There are no REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATIONS with differences less than or equal to 12 mmHg; all DETERMINATIONS are excluded from the study.

EXAMPLE 3 The first REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 119 mmHg. The second REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 121 mmHg. The third REFERENCE SYSTOLIC BLOOD PRESSURE DETERMINATION equals 134 mmHg. Result: The difference between the first and third DETERMINATIONS is greater than 12 mmHg; all DETERMINATIONS can be excluded from the study. Alternatively, the first and second DETERMINATIONS can be used in the study and the data from the 3rd DETERMINATION can be excluded and an additional PATIENT will need to be recruited.

The use of smaller differences (4 mmHg and 6 mmHg) (0,53 kPa and 0,80 kPa) between consecutive DETERMINATIONS as stability criteria was also discussed, but there was concern that this would cause too many exclusions.

ISO/TC 121 and IEC/TC 62 reviewed the existing protocols and possible sources of bias and error. It was concluded that allowing the choosing of either the preceding or following REFERENCE DETERMINATION based on which one was closer to the value from the SPHYGMOMANOMETER-UNDER-TEST was not scientifically justified. Furthermore, it was concluded that averaging the preceding and following REFERENCE DETERMINATIONS provides a more accurate indication of the subject's BLOOD PRESSURE. Temporal changes in a subject's BLOOD PRESSURE are normal and prove problematic when utilizing a sequential investigation method. ISO/TC 121 and IEC/TC 62 considered using the previous or the following REFERENCE DETERMINATIONS alone as the REFERENCE value; however, it was determined that the average of the previous and the following REFERENCE DETERMINATIONS more accurately estimates the subject's BLOOD PRESSURE during the time that the SPHYGMOMANOMETER-UNDER-TEST makes its DETERMINATION.

This is supported by an analysis of the multiple-centre, independently-performed 120 subject study where the middle observer DETERMINATIONS were treated as the SPHYGMOMANOMETER-UNDER-TEST DETERMINATION.

Table A.1 — Committee's multiple-centre study results

	Prior REFERENCE BLOOD PRESSURE used as REFERENCE BLOOD PRESSURE		Following REFERENCE BLOOD PRESSURE used as REFERENCE BLOOD PRESSURE		Average of prior and following REFERENCE BLOOD PRESSURES used as REFERENCE BLOOD PRESSURE	
	SYSTOLIC BLOOD PRESSURE	DIASTOLIC BLOOD PRESSURE	SYSTOLIC BLOOD PRESSURE	DIASTOLIC BLOOD PRESSURE	SYSTOLIC BLOOD PRESSURE	DIASTOLIC BLOOD PRESSURE
Mean error (mmHg)	-0,8	0,2	0,6	-0,2	-0,1	0,0
Standard deviation (mmHg)	5,7	3,9	5,5	4,0	4,7	3,3
Number of comparisons	234	234	234	234	234	234

The data show that the mean errors in Table A.1 are reduced (and have approached 0,0 mmHg) when the mean value of the preceding and following average is used as the REFERENCE value and that the standard deviation was reduced. The resulting standard deviation reflects observer differences (including observer DETERMINATION error) and subject's temporal BLOOD PRESSURE variations.

5.2.4.3 Opposite limb simultaneous method

The opposite arm simultaneous method is used when the SPHYGMOMANOMETER-UNDER-TEST operates in a manner that does not allow simultaneous DETERMINATION of the auscultatory REFERENCE readings on the same limb. This can be due to the use of a CUFF deflation rate by the SPHYGMOMANOMETER-UNDER-TEST that is outside the allowable range for a manual auscultatory DETERMINATION, the use of a measurement method (e.g. DETERMINATION on inflation) that does not support auscultation or the use of a measurement site that does not support auscultation (e.g. the wrist).

5.2.4.3.2 Data analysis

Standards, such as Reference [2], employ the opposite arm simultaneous method with lateral difference compensation based on three lateral difference measurements prior to, and another three lateral difference measurements after, a series of comparisons using the REFERENCE SPHYGMOMANOMETER and the SPHYGMOMANOMETER-UNDER-TEST. However, via an experiment by ISO/TC 121 and IEC/TC 62, it was demonstrated that the lateral difference compensation in this method was not precise enough. The inaccuracy in the lateral difference compensation could at least be partially explained by long-time lags between lateral difference measurements and REFERENCE SPHYGMOMANOMETER to SPHYGMOMANOMETER-UNDER-TEST comparisons.

This new opposite arm simultaneous method in this part of ISO 81060 was developed to overcome these shortcomings of the currently used methods. Because it compares the REFERENCE SPHYGMOMANOMETER to the SPHYGMOMANOMETER-UNDER-TEST DETERMINATIONS simultaneously, its results are largely immune to BPV. The accuracy of lateral difference compensation is improved by using REFERENCE DETERMINATIONS taken simultaneously with SPHYGMOMANOMETER-UNDER-TEST DETERMINATIONS, i.e. essentially no time lag between the lateral difference measurement and REFERENCE SPHYGMOMANOMETER to SPHYGMOMANOMETER-UNDER-TEST comparison.

Additional advantages of this new opposite arm simultaneous method are:

— the time required per subject is considerably shorter in comparison with the conventional opposite arm simultaneous method (six versus nine DETERMINATIONS except preparatory measurement);

— more paired comparison data are available (six versus three points per subject).

Modification of the number of repetitions per subject could be attempted. However, it was confirmed that the lateral difference compensation was not successful with only four repetitions. This might be because an insufficient number of REFERENCE DETERMINATIONS (only two per side) were used to estimate the lateral difference. If the number of repetitions would be increased to eight, the accuracy of lateral difference might also be reduced because of prolonged time lag and resulting BPV between the first DETERMINATION and the last DETERMINATION. Thus, six repetitions seems to be more appropriate for this method.

5.2.5 Additional requirements for a SPHYGMOMANOMETER intended for use in exercise stress testing environments

The additional CLINICAL INVESTIGATION requirements for exercise stress testing were chosen to assess a SPHYGMOMANOMETER during activity and motion. Achieving a target heart rate of 50 % to 70 % of a subject's predicted maximal heart rate allows an exercise level that can be sustained for the duration of the assessment without subjecting the subject to undue medical risk. Furthermore, the exercise required to cause such a heart rate should not result in a motion artefact so severe as to render the data unacceptable.

NOTE Reference [17] contains additional information.

Although any equipment for exercise can be used in exercise stress testing, the majority of ISO/TC 121 and IEC/TC 62 experts believe that a bicycle ergometer rather than a treadmill is more suitable for SPHYGMOMANOMETER CLINICAL INVESTIGATIONS. This is mainly because the arm can be held at the level of the right atrium more securely. Besides, in exercise with a treadmill, vibration from stepping often causes motion artefact in oscillometric measurement and auscultation is often difficult due to audible noise from stepping and the motor of the treadmill.

6.1.2 Gender distribution

While there is no definitive evidence that a SPHYGMOMANOMETER performs differently on male or female PATIENTS, some studies indicate that there might be a bias.

NOTE References [42] and [43] contain additional information.

If bias exists, it is likely caused by differences in arm circumference and body fat distribution. This part of ISO 81060 already requires that the SPHYGMOMANOMETER-UNDER-TEST be tested over a range of arm circumferences. The requirement for gender distribution allows for investigation of gender differences without being difficult to implement.

6.1.3 Age distribution

The age classifications of paediatric PATIENTS were chosen to be consistent with FDA guidance[6]. The FDA suggested transition from infant to child at 2 years of age has been adjusted to 3 years of age, to be consistent with Korotkoff sound physiology (see rationale to 5.1.3). Table A.2 shows the suggested FDA guidance paediatric subgroups.

Table A.2 — Suggested age ranges of paediatric subgroups from FDA guidance

Paediatric subgroup	Approximate age range
Newborn (neonate)	from birth to 1 month of age
Infant	> 1 month to 2 years of age
Child	> 2 years to 12 years of age
Adolescent	> 12 years to 21 years of age

6.1.4 Limb size distribution

This is a compromise between more detailed requirements for CUFF sizes and the difficulty of conducting the test. For a SPHYGMOMANOMETER with a single CUFF size, it is important to test the full range of limb circumferences intended for use with the CUFF.

6.1.5 BLOOD PRESSURE distribution

These ranges were determined to ensure that the performance of the SPHYGMOMANOMETER is investigated over the entire clinically relevant BLOOD PRESSURE range.

6.2.1 REFERENCE measurement

The intra-arterial pressure can be measured with a saline-filled catheter and external pressure transducer or with a catheter-tip transducer. A catheter-tip transducer is rarely used in clinical practice, but provides an improved dynamic response compared to catheter transducer systems.

The accurate measurement of the intra-arterial REFERENCE requires the use a computerized data collection system (DCS) or a multi-channel strip-chart recorder. The values displayed on the invasive BLOOD PRESSURE (IBP) channel of a PATIENT monitoring system are subject to filtering and do not represent true beat-to-beat values. In addition, the recording of the intra-arterial waveform allows for the recognition of significant arrhythmias or artefacts, which distort the intra-arterial values.

The SPHYGMOMANOMETER-UNDER-TEST should be calibrated with the same manometer as the invasive transducer to avoid any bias between both. All calibration records should be kept on a DCS. The static calibration of both the invasive transducer and the SPHYGMOMANOMETER-UNDER-TEST should be within ± 2 mmHg (± 0,27 kPa) of the REFERENCE.

The frequency response and damping coefficient pair should meet the dynamic requirements proposed by Gardner[18]. The use of short, stiff tubing and the removal of air bubbles from the catheter-transducer system will improve the frequency response characteristics. During the study, any deterioration in the waveform recorded by the intra-arterial catheter should be noted and appropriate corrective measures (e.g. flushing or adjusting the position of the catheter) taken immediately.

The invasive BLOOD PRESSURE transducer needs to be kept at the same level as the BLOOD PRESSURE CUFF to avoid hydrostatic effects. A difference in vertical height of + 1,3 cm between the invasive pressure transducer and the CUFF causes an offset error of -1 mmHg (-0,13 kPa) in measured pressure between the two readings. Both the CUFF and invasive transducer should be at the level of the right atrium of the heart (phlebostatic axis).

During each measurement by the SPHYGMOMANOMETER-UNDER-TEST, the DCS should be recording the intra-arterial pressures and the analogue signals from the SPHYGMOMANOMETER-UNDER-TEST (if these are available).

6.2.2 Arterial REFERENCE site

Some previous standards exclude the radial artery site due to concerns about differences between central and peripheral pressures because of pulse amplification and reflected wave effects. It is unlikely that data taken in the radial artery will have clinical validity for the diagnosis of hypertension, i.e. all morbidity/mortality data are based on DETERMINATIONS performed at the brachial artery, which are not equivalent to measurement performed at the radial artery. However, it is recognized that the more frequent use of radial artery catheters for invasive BLOOD PRESSURE measurement in the operating theatre and intensive care unit reduces the difficulty of obtaining PATIENTS for a study.

NOTE Reference [3] contains additional information.

The lateral difference, LD, measurement can be made using a previously validated AUTOMATED SPHYGMOMANOMETER. The LD should be calculated by simultaneous DETERMINATIONS on both limbs (using two identical AUTOMATED SPHYGMOMANOMETERS). However, LD can also be calculated using a single AUTOMATED SPHYGMOMANOMETER and alternating the site of measurement between the two limbs.

The LD is calculated as the average difference between the DETERMINATIONS made on each limb according to Formula (A.1).

$$LD = \frac{1}{3} \times \left(\sum_{i=1}^{3} p_i - \sum_{j=1}^{3} p_j \right) \quad \text{(A.1)}$$

where

i is the index for the determination on the limb used for the SPHYGMOMANOMETER-UNDER-TEST determination;

j is the index for the determination on the limb used for the REFERENCE determination.

The LD is calculated for each subject and is used according to Formula (13) and Formula (14).

6.2.4 Determining the reference blood pressure

Several options were discussed for defining the REFERENCE SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE. In particular, the normal BLOOD PRESSURE variation that occurs during a non-invasive blood pressure determination (e.g. due to breathing) and the handling of outliers need to be considered. The use of the mean BLOOD PRESSURE would be inappropriate due to the normal BLOOD PRESSURE variation during the non-invasive BLOOD PRESSURE determination, so it was felt that a range was more appropriate. The span derived from all the invasive data measured is not appropriate, because outliers would enlarge the range too much. A range of one experimental standard deviation was chosen as a good compromise to cover all aspects.

Clause 7 Pregnant (including pre-eclamptic) PATIENT populations

Pregnancy is a fundamentally different haemodynamic state and, therefore, there is the potential for SPHYGMOMANOMETERS to work differently. However, the clinical evidence is that most investigation results in non-pre-eclamptic pregnancies are equivalent to the adult CLINICAL INVESTIGATIONS (about 20 studies). Pre-eclampsia has altered haemodynamics (reduced intra-vascular volume, lowered cardiac output, increased interstitial oedema) and the evidence suggests that a majority of AUTOMATED SPHYGMOMANOMETERS underestimate the BLOOD PRESSURE in this PATIENT population. Additional information is found in references [16], [19], [34], [35], [39] and [40]. Although pre-eclampsia only occurs in less than 5 % of an antenatal population, the onset of the hypertension associated with this condition is potentially dangerous. An emphasis on accuracy in this state is essential to ensure the safety of these PATIENTS.

To have sufficient statistical power to separate the two hypertensive subgroups within two standard deviations = 5 mmHg (0,67 kPa) (the maximum permissible mean error) using Student's t distribution, a subgroup size of 15 is required.

Annex B
(normative)

Target heart rates for exercise stress testing

Table B.1 indicates the target heart rate range by age for exercise stress testing.

Table B.1 — Target heart rate table
Additional information can be found in Reference [10]

Age years	**Target heart rate range for exercise investigation 50 % to 70 % of average maximum heart rate** beats/min	**Target heart rate range for exercise 50 % to 85 % of average maximum heart rate** beats/min	**Average maximum heart rate 100 %** beats/min
20	100 to 140	100 to 170	200
25	98 to 137	98 to 166	195
30	95 to 133	95 to 162	190
35	93 to 130	93 to 157	185
40	90 to 126	90 to 153	180
45	88 to 123	88 to 149	175
50	85 to 119	85 to 145	170
55	83 to 116	83 to 140	165
60	80 to 112	80 to 136	160
65	78 to 109	78 to 132	155
70	75 to 105	75 to 128	150
The target heart rate range for exercise CLINICAL INVESTIGATION shall be at least 110 % of the resting heart rate. Target heart rates may be lower for PATIENTS taking medication that lowers the maximum heart rate.			

The following is an example of using Table B.1 to determine the target heart rate and exercise heart rate (see 5.2.5).

The subject is 70 years of age. The subject's resting heart rate is 75 beats/min. The average maximum heart rate from Table B.1 is 150 beats/min. 110 % of 75 beats/min (the subject's resting heart rate) is 83 beats/min. During an exercise stress CLINICAL INVESTIGATION, maintain the subject's heart rate between 83 beats/min and 105 beats/min.

Annex C
(informative)

Reference to the essential principles

This part of ISO/IEC 81060 has been prepared to support the essential principles of safety and performance of electronically controlled, intermittent, AUTOMATED SPHYGMOMANOMETERS as medical devices in accordance with ISO/TR 16142[1]. This part of ISO 81060 is intended to be acceptable for conformity assessment purposes.

Compliance with this part of ISO 81060 provides one means of demonstrating conformance with the specific essential principles of ISO/TR 16142. Other means are possible.

Table C.1 — Correspondence between this document and the essential principles

Corresponding essential principle of ISO/TR 16142:2006, Table A.1, Clause A	Clause(s)/subclause(s) of this document	Qualifying remarks/Notes
9.1	5.1.4, 6.1.4	
13.1	5.1.6, 5.2.2, 6.2.1, 6.2.2, 6.2.7, 7	
14.1	All	

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Terminology — Alphabetized index of defined terms

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