INTERNATIONAL STANDARD

ISO 81060-2

Third edition
2018-11

Non-invasive sphygmomanometers —

Part 2: Clinical investigation of intermittent automated measurement type

Sphygmomanomètres non invasifs —

Partie 2: Investigation clinique pour type ponctuel à mesurage automatique

Reference number
ISO 81060-2:2018(E)

ISO copyright office
CP 401 • Ch. de Blandonnet 8
CH-1214 Vernier, Geneva
Phone: +41 22 749 01 11
Fax: +41 22 749 09 47
Email: copyright@iso.org
Website: www.iso.org

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Foreword

ISO (the International Organization for Standardization) and IEC (the International Electrotechnical Commission) form the specialized system for worldwide standardization. National bodies that are members of ISO or IEC participate in the development of International Standards through technical committees established by the respective organization to deal with particular fields of technical activity. ISO and IEC technical committees collaborate in fields of mutual interest. Other international organizations, governmental and non-governmental, in liaison with ISO and IEC, also take part in the work.

The procedures used to develop this document and those intended for its further maintenance are described in the ISO/IEC Directives, Part 1. In particular, the different approval criteria needed for the different types of document should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO and IEC shall not be held responsible for identifying any or all such patent rights. Details of any patent rights identified during the development of the document will be in the Introduction and/or on the ISO list of patent declarations received (see www.iso.org/patents) or the IEC list of patent declarations received (see http://patents.iec.ch).

Any trade name used in this document is information given for the convenience of users and does not constitute an endorsement.

For an explanation of the voluntary nature of standards, the meaning of ISO specific terms and expressions related to conformity assessment, as well as information about ISO's adherence to the World Trade Organization (WTO) principles in the Technical Barriers to Trade (TBT) see www.iso.org/iso/foreword.html.

This document was prepared jointly by Technical Committee ISO/TC 121, *Anaesthetic and respiratory equipment*, Subcommittee SC 3, *Respiratory devices and related equipment used for patient care*, and Technical Committee IEC/TC 62, *Electrical equipment in medical practice*, Subcommittee SC D, *Electromedical equipment*.

This third edition cancels and replaces the second edition (ISO 81060-2:2013), which has been technically revised.

The main changes compared to the previous edition are as follows:

— same arm simultaneous method has been deleted;

— numerous clarifications have been added and kPa equivalent values for the mmHg values have been included.

A list of all parts in the ISO/IEC 81060 series can be found on the ISO website.

Any feedback or questions on this document should be directed to the user's national standards body. A complete listing of these bodies can be found at www.iso.org/members.html.

Introduction

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

BLOOD PRESSURE serves as aid to control the drug titration and fluid management and to provide warning about the changes in PATIENT'S state of health.

Frequently determining BLOOD PRESSURE is routine during anaesthesia. BLOOD PRESSURE serves to aid to control drug titration and fluid management and to provide warning about the changes in the PATIENT'S state of health.

In this document, the following print types are used:

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

— informative material appearing outside of tables, such as notes, examples and references: in smaller roman type. Normative text of tables is also in a smaller roman type;

— *test methods: italic type;* and

— TERMS DEFINED IN CLAUSE 3 OF THE GENERAL STANDARD, IN THIS DOCUMENT OR AS NOTED: SMALL CAPITALS TYPE.

In this document, the conjunctive "or" is used as an "inclusive or" so a statement is true if any combination of the conditions is true.

The verbal forms used in this document conform to usage described in Annex H of the ISO/IEC Directives, Part 2. For the purposes of this document, the auxiliary verb:

— "shall" means that compliance with a requirement or a test is mandatory for compliance with this document;

— "should" means that compliance with a requirement or a test is recommended but is not mandatory for compliance with this document;

— "may" is used to describe a permissible way to achieve compliance with a requirement or test.

An asterisk (*) as the first character of a title or at the beginning of a paragraph or table title indicates that there is guidance or rationale related to that item in Annex A.

Annex B maps the clauses and subclauses of this document with the ESSENTIAL PRINCIPLES of ISO 16142-1:2016.

Non-invasive sphygmomanometers —

Part 2:
Clinical investigation of intermittent automated measurement type

1 Scope

This document 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 document 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 document 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 document.

This document specifies additional disclosure requirements for the ACCOMPANYING DOCUMENTS of SPHYGMOMANOMETERS that have passed a CLINICAL INVESTIGATION according to this document.

This document 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 are referred to in the text in such a way that some or all of their content constitutes requirements of this document. For dated references, only the edition cited applies. For undated references, the latest edition of the referenced document (including any amendments) applies.

NOTE 1 The way in which these referenced documents are cited in normative requirements determines the extent (in whole or in part) to which they apply.

NOTE 2 Informative references are listed in the Bibliography.

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

ISO 14971:2007, *Medical devices — Application of risk management to medical devices*

ISO 16142-1:2016, *Medical devices — Recognized essential principles of safety and performance of medical devices — Part 1: General essential principles and additional specific essential principles for all non-IVD medical devices and guidance on the selection of standards*

ISO 81060-1:2007, *Non-invasive sphygmomanometers — Part 1: Requirements and test methods for non-automated measurement type*

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

IEC 60601-1-11:2015, *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*

IEC 80601-2-30:2018, *Medical electrical equipment — Part 2-30: Particular requirements for basic safety and essential performance of automated non-invasive sphygmomanometers*

3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 14155:2011, ISO 14971:2007, ISO 16142-1:2016, ISO 81060-1:2007, IEC 60601-1:2005+AMD1:2012, IEC 60601-1-11:2015, IEC 60601-2-34:2011 and IEC 80601-2-30:2018, and the following apply.

ISO and IEC maintain terminological databases for use in standardization at the following addresses:

— ISO Online browsing platform: available at https://www.iso.org/obp

— IEC Electropedia: available at http://www.electropedia.org/

NOTE For convenience, an alphabetized index of defined terms is found in Annex C.

3.1
intermittent
<non-invasive SPHYGMOMANOMETER> utilizing a PROCESS of estimating BLOOD PRESSURE that provides a single set of pressure values from a number of heart beats

3.2
reference
ref
established accuracy used for the CLINICAL INVESTIGATION of other instruments

3.3
sphygmomanometer
ME EQUIPMENT for non-invasive estimation of systemic arterial BLOOD PRESSURE

3.4
sphygmomanometer-under-test
sut
AUTOMATED SPHYGMOMANOMETER undergoing CLINICAL INVESTIGATION

4 General requirements for CLINICAL INVESTIGATIONS

4.1 CLINICAL INVESTIGATION methods

a) AUTOMATED SPHYGMOMANOMETERS shall undergo CLINICAL INVESTIGATION according to this document in each mode of operation by either using:

   1) a non-invasive auscultatory REFERENCE SPHYGMOMANOMETER at the upper arm; or

   2) a REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT.

      EXAMPLE 1 Adult and neonatal modes.

      EXAMPLE 2 Slow and fast CUFF deflation rate modes.

b) A clinical investigation shall be considered a type test.

中央和主动脉血压

c) An automated sphygmomanometer intending to display central or aortic blood pressure shall utilize a central or aortic invasive reference site for clinical investigation (see 6.2.2).

NOTE Such an automated SPHYGMOMANOMETER is investigated according to Clause 6.

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

4.2 Good clinical practice

a) All CLINICAL INVESTIGATIONS shall comply with the requirements of ISO 14155:2011.

b) 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.

c) The requirements of this document, which are more specific than the corresponding requirements of ISO 14155:2011, shall prevail.

Check compliance by application of the requirements of ISO 14155:2011.

4.3 Status of previous CLINICAL INVESTIGATIONS

The CLINICAL INVESTIGATION results for SPHYGMOMANOMETERS that have been successfully clinically investigated according to previous versions of ISO 81060-2 remain valid and a CLINICAL INVESTIGATION need not be repeated to comply with this document.

4.4 Disclosure of summary of CLINICAL INVESTIGATION

The technical description of a SPHYGMOMANOMETER shall contain contact information permitting the RESPONSIBLE ORGANIZATION to acquire a copy of the summary of the CLINICAL INVESTIGATION.

5 CLINICAL INVESTIGATION with an auscultatory REFERENCE SPHYGMOMANOMETER

5.1 Subject requirements

5.1.1 * Number

a) An auscultatory REFERENCE SPHYGMOMANOMETER CLINICAL INVESTIGATION shall consist of a minimum of 85 subjects.

b) If not otherwise specified, at least three valid paired BLOOD PRESSURE values shall be taken for each subject [see 5.2.4.1.1 o)].

c) There shall be a minimum of 255 valid paired BLOOD PRESSURE values.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.1.2 * Gender distribution

a) At least 30 % of the subjects shall be male.

b) At least 30 % of the subjects shall be female.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.1.3 * Age distribution

a) For a SPHYGMOMANOMETER intended for use on adults 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.

b) 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 (35 children aged 3-12 years and 50 subjects older than 12 years).

c) 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.

d) Children aged less than 3 years shall not be included in a CLINICAL INVESTIGATION utilizing auscultatory REFERENCE readings 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

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

1) 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;

2) at least 40 % of the subjects shall have a limb circumference within the lower half of the specified range of use of the CUFF;

3) 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;

4) at least 20 % of the subjects shall have a limb circumference within the lower quarter of the specified range of use of the CUFF; and

5) at least 10 % of the subjects shall have a limb circumference which lies within the upper octal of the specified range of use of the CUFF; and

6) at least 10 % of the subjects shall have a limb circumference within the lower octal of the specified range of use of the CUFF.

b) For a SPHYGMOMANOMETER intended for use with multiple CUFF sizes:

1) each CUFF size shall be tested on at least $\frac{1}{2\times n}$ of the total number of subjects, where n is the number of CUFF sizes; and

2) 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

3) at least 40 % of the subjects shall have a limb circumference within the lower half of the specified range of use of the CUFF.

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

5.1.5 Blood pressure distribution

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

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

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

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

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

f) 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) 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.

b) If the SPHYGMOMANOMETER has passed 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.

c) If the SPHYGMOMANOMETER has not successfully 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.

d) The special PATIENT population shall be defined in clear terms and address the following attributes:

1) gender (see 5.1.2);

2) age (see 5.1.3);

3) limb size (see 5.1.4); and

4) BLOOD PRESSURE (see 5.1.5).

e) A summary of the definition of the special PATIENT population 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

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

1) is comfortable;

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

2) has the back, elbow and forearm supported;

3) has the measurement site at the level of the left ventricle of the heart.

b) It is recommended that:

1) the subject be as relaxed as possible; and

2) the subject avoids talking during the entire PROCEDURE.

c) The CUFF shall be applied on the bare arm and there shall be no arm compression proximal to the CUFF.

d) Before the first REFERENCE reading is taken, 5 min should elapse.

NOTE Additional details can be found in Reference [16].

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

5.2.2 * Observer preparation

a) Observers shall be trained in using a proper methodology for performing a resting BLOOD PRESSURE reading by utilizing an accepted clinical protocol for BLOOD PRESSURE measurement. References [15], [16], and [25] contain additional information.

b) Observers shall have sufficient practice in performing BLOOD PRESSURE readings.

c) Each observer's recording of observations of the REFERENCE SPHYGMOMANOMETER shall not be visible to the other observer.

d) The DETERMINATIONS of the SPHYGMOMANOMETER-UNDER-TEST shall not be visible to either of these observers.

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

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

e) The Korotkoff sound [fifth phase (K5)] shall be used by the observers for determining the REFERENCE DIASTOLIC BLOOD PRESSURE.

f) If the Korotkoff sound [fifth phase (K5)] for determining REFERENCE DIASTOLIC BLOOD PRESSURE is not audible, the subject shall be excluded.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.2.3 * REFERENCE readings

a) Two observers shall simultaneously determine the SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE on each subject using a double stethoscope.

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

EXAMPLE 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.

c) Any pair of observers' SYSTOLIC BLOOD PRESSURE VALUE or DIASTOLIC BLOOD PRESSURE VALUE with a difference greater than 4 mmHg (0,53 kPa) shall be excluded.

d) The observers' individual values of each reading shall be averaged according to Formula (1) to create the REFERENCE BLOOD PRESSURE value.

$$p_{\mathrm{REF}_i} = \frac{p_{\mathrm{REF}_{i,1}} + p_{\mathrm{REF}_{i,2}}}{2} \quad (1)$$

where

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

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

p_{REF_i} is the REFERENCE BLOOD PRESSURE value for the i^{th} reading.

e) The observer-to-observer differences shall be reviewed after completing a set of pairs of test-REFERENCE values.

1) If any readings are excluded, additional pair(s) of readings shall be taken to ensure that the required number of valid test-REFERENCE pairs are available.

2) A maximum of eight pairs of readings per subject shall be taken.

f) Use a REFERENCE SPHYGMOMANOMETER that complies with the requirements of ISO 81060-1, except that the maximum permissible error shall be ±1 mmHg (0,13 kPa).

1) Reading of the values on the REFERENCE SPHYGMOMANOMETER should be as accurate as possible.

2) 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.

g) Measurement of the upper arm circumference:

1) The upper arm midpoint is first determined by marking the arm posteriorly at a point halfway between the acromion and olecranon, measured while the arm is flexed 90 degrees at the elbow with the palm facing up.

2) The subject's upper arm circumference shall be determined by measuring at the midpoint of the upper arm while the elbow is relaxed and the arm is dangling freely to the side.

h) *CUFFS for the reference SPHYGMOMANOMETER shall have:

1) a bladder length of 75 % to 100 % of the upper arm circumference; and

2) a bladder width of 37 % to 50 % of the upper arm circumference.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.2.4 CLINICAL INVESTIGATION methods

5.2.4.1 Same arm sequential method

5.2.4.1.1 * PROCEDURE

a) Either arm may be utilized.

Perform the following:

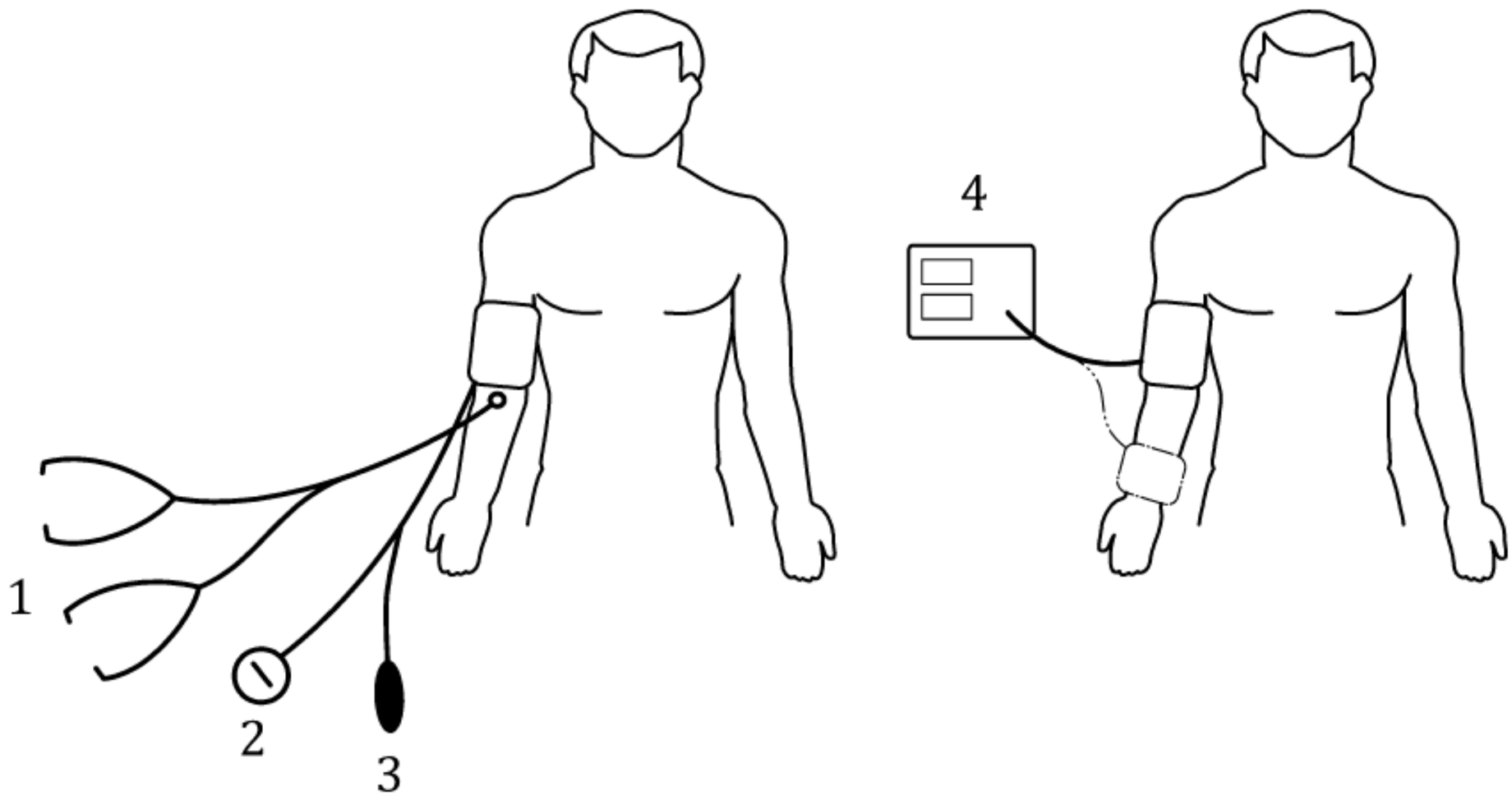
b) *Using the REFERENCE SPHYGMOMANOMETER, have the observers determine the subject's BLOOD PRESSURE (see Figure 1).*

c) *Interchange CUFFS and wait at least 60 s.*

d) *Use the SPHYGMOMANOMETER-UNDER-TEST to determine the subject's BLOOD PRESSURE.*

e) *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 1 — Illustration of the same arm sequential method

f) *Do not use the data points obtained in b) and d) in the calculation of accuracy.*

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

h) *Interchange CUFFS and wait at least 60 s.*

i) *Use the SPHYGMOMANOMETER-UNDER-TEST to determine the subject's BLOOD PRESSURE.*

j) *Interchange CUFFS and wait at least 60 s.*

k) *Have the observers use the REFERENCE SPHYGMOMANOMETER to determine the subject's BLOOD PRESSURE REFERENCE reading.*

l) *Interchange CUFFS and wait at least 60 s.*

m) *Repeat i) to l) until the required number of valid REFERENCE readings and DETERMINATIONS have been performed.*

n) *All data from a subject shall be excluded if:*

1) *any two REFERENCE SYSTOLIC BLOOD PRESSURE VALUES differ by more than 12 mmHg (1,60 kPa); or*

2) *any two REFERENCE DIASTOLIC BLOOD PRESSURE VALUES differ by more than 8 mmHg (1,07 kPa).*

o) *Notwithstanding the requirement in n), if the REFERENCE BLOOD PRESSURE of an individual subject does not meet these criteria during the period of the test, two compliant consecutive pairs of REFERENCE readings and DETERMINATIONS that meet these criteria may be used.*

1) *In this case, additional subjects shall be used to complete the minimum number of readings and DETERMINATIONS.*

2) *No more than 10 % of the subjects shall have fewer than three valid pairs of REFERENCE reading and DETERMINATION.*

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.2.4.1.2 Data analysis

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

a) Criterion 1

1) The differences of the n individual paired DETERMINATIONS of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' readings with the REFERENCE SPHYGMOMANOMETER for all subjects, calculated separately for SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE, shall:

i) according to Formula (2), have the mean value of the differences, $\bar{x}_n$, be within or equal to ±5,0 mmHg (±0,67 kPa); and

ii) according to Formula (3), have a standard deviation, s_n, no greater than 8,0 mmHg (1,07 kPa).

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

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

where

$\bar{x}_n$	is the mean value of the differences;
$p_{\mathrm{SUT}_i} - p_{\mathrm{REF-sq}_i}$	is the difference between the i^{th} paired BLOOD PRESSURE values (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} value as calculated according to Formula (4).

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

2) The REFERENCE BLOOD PRESSURE value, $p_{\mathrm{REF-sq}_i}$, shall be the average of the observers' readings with the REFERENCE SPHYGMOMANOMETER preceding and following the SPHYGMOMANOMETER-UNDER-TEST DETERMINATION.

$$p_{\mathrm{REF-sq}_i} = \frac{1}{4} \times \left(p_{\mathrm{REF}_{i,1}} + p_{\mathrm{REF}_{i,2}} + p_{\mathrm{REF}_{i+1,1}} + p_{\mathrm{REF}_{i+1,2}} \right) \quad (4)$$

where

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

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

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

EXAMPLE 2 n = 255 for a SPHYGMOMANOMETER intended for use in adults 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 passed a CLINICAL INVESTIGATION in a separate 85 subject study according to 5.1.1 and 5.2.

b) Criterion 2

1) For the SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE for each of m subjects, the standard deviation s_m of the averaged paired DETERMINATIONS per subject of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' readings with the REFERENCE SPHYGMOMANOMETER shall meet the criteria listed:

i) in Table 1; or

ii) in Table 2

when calculated according to Formula (5).

$$s_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} (x_j - \overline{x}_n)^2} \quad (5)$$

where

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

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 (6);

$$x_j = \frac{1}{d} \times \sum_{k=1}^{d} \left(p_{\mathrm{SUT}_{j,k}} - p_{\mathrm{REF-sq}_{j,k}} \right) \quad (6)$$

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 (7).

$$p_{\mathrm{REF-sq}_{j,k}} = \frac{1}{4} \times \left(p_{\mathrm{REF}_{j,k,1}} + p_{\mathrm{REF}_{j,k,2}} + p_{\mathrm{REF}_{j,k+1,1}} + p_{\mathrm{REF}_{j,k+1,2}} \right) \quad (7)$$

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	0,926 6	0,926 6	0,926 6	0,926 6	0,926 6	0,924 6	0,923 3	0,922 3	0,921 3	0,920 3
±0,1	0,919 3	0,918 3	0,917 3	0,916 3	0,915 2	0,913 8	0,911 9	0,909 9	0,907 9	0,905 9
±0,2	0,903 9	0,900 7	0,898 9	0,897 0	0,894 6	0,890 6	0,887 8	0,885 5	0,882 6	0,878 5
±0,3	0,875 6	0,872 3	0,867 9	0,864 1	0,860 1	0,856 2	0,851 9	0,847 1	0,841 4	0,837 4
±0,4	0,833 3	0,828 3	0,822 6	0,816 9	0,811 9	0,805 9	0,799 9	0,793 3	0,785 3	0,779 3
±0,5	0,773 9	0,766 9	0,759 9	0,753 1	0,746 3	0,738 8	0,731 9	0,723 7	0,715 7	0,707 7
±0,6	0,699 9	0,689 1	0,680 2	0,672 3	0,667 0	0,659 5	0,648 8	0,638 6	—	—
EXAMPLE For mean of ±0,520 kPa, the maximum permissible standard deviation is 0,759 9 kPa.										

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

EXAMPLE 5 m = 85 for a SPHYGMOMANOMETER intended for use in adults 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 passed a 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).

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.2.4.2 * Opposite limb simultaneous method

5.2.4.2.1 Procedure

a) The starting arm side of the SPHYGMOMANOMETER-UNDER-TEST DETERMINATION and the REFERENCE SPHYGMOMANOMETER reading shall be alternated between subjects.

Perform the following:

b) *Have the observers using the REFERENCE SPHYGMOMANOMETER and the SPHYGMOMANOMETER-UNDER-TEST simultaneously determine the subject's BLOOD PRESSURE in opposite arms (see Figure 2).*

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

d) *Clear the SPHYGMOMANOMETER-UNDER-TEST memory of the previous DETERMINATION.*

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.*

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

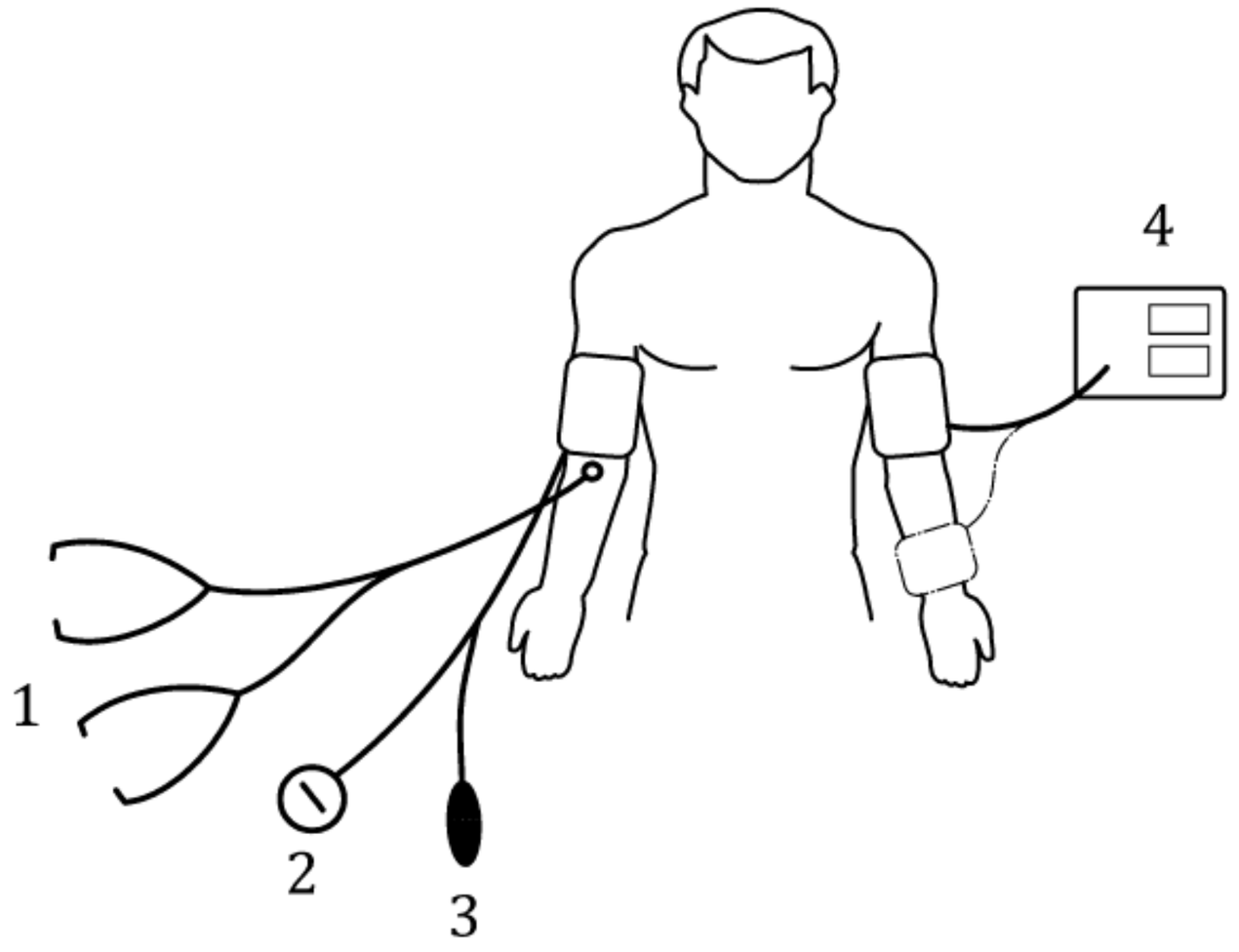
f) *Wait at least 60 s from the completion of the previous REFERENCE reading or DETERMINATION.*

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

h) *If the reading by the observers with the REFERENCE SPHYGMOMANOMETER or the DETERMINATION by the SPHYGMOMANOMETER-UNDER-TEST is not successfully completed, wait at least 60 s and repeat on the same arm (i.e. without interchanging sides).*

i) *Repeat e) to g) until six paired REFERENCE readings and DETERMINATIONS have been performed.*

j) *Repeat b) to i) until the required number of valid subjects and DETERMINATIONS have been obtained.*



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 opposite arm simultaneous method

k) All data from a subject shall be excluded if:

1) any two REFERENCE SYSTOLIC BLOOD PRESSURE VALUES on the same arm differ by more than 12 mmHg (1,60 kPa);

2) any two REFERENCE DIASTOLIC BLOOD PRESSURE VALUES on the same arm differ by more than 8 mmHg (1,07 kPa);

3) the lateral difference of the REFERENCE SYSTOLIC BLOOD PRESSURE VALUES is more than 15 mmHg (2,00 kPa); or

4) the lateral difference of the REFERENCE DIASTOLIC BLOOD PRESSURE VALUES is more than 10 mmHg (1,33 kPa).

l) The lateral difference, *LD*, is calculated separately for SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE, according to Formula (8).

$$LD = \frac{1}{3} \times \left(\sum_{i=1}^{3} p_{\mathrm{REF\_R}_i} - \sum_{j=1}^{3} p_{\mathrm{REF\_L}_j} \right) \tag{8}$$

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

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

5.2.4.2.2 * Data analysis

a) 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 (9) 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 (10) if the SPHYGMOMANOMETER-UNDER-TEST BLOOD PRESSURE was taken in the right arm.

$$x = p_{SUT\_L} - p_{REF\_R} + LD \quad (9)$$

$$x = p_{SUT\_R} - p_{REF\_L} - LD \quad (10)$$

where p_{SUT_R} and p_{SUT_L} are SPHYGMOMANOMETER-UNDER-TEST BLOOD PRESSURES in right (R) arm and left (L) arm, respectively.

b) The SPHYGMOMANOMETER-UNDER-TEST shall meet both:

1) criterion 1; and

2) criterion 2.

c) Criterion 1

1) The differences, $\overline{x}_n$, of the *n* individual paired DETERMINATIONS of the SPHYGMOMANOMETER-UNDER-TEST and of the observers' readings with the REFERENCE SPHYGMOMANOMETER for all subjects shall:

i) according to Formula (11), have the mean value of the differences, $\overline{x}_n$, be within or equal to ±5,0 mmHg (±0,67 kPa);

ii) according to Formula (12), have a standard deviation, s_n, not greater than 8,0 mmHg (1,07 kPa).

$$\overline{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} x_i \quad (11)$$

$$s_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} (x_i - \overline{x}_n)^2} \quad (12)$$

where

x_i is the SPHYGMOMANOMETER-UNDER-TEST error as calculated according to Formula (9) and Formula (10);

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 or adolescent PATIENTS (an 85 subject study).

EXAMPLE 2 n = 510 for a SPHYGMOMANOMETER intended for use in adults 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 passed a CLINICAL INVESTIGATION in a separate 85 subject study according to 5.1.1 and 5.2.

d) Criterion 2

1) 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' readings with the REFERENCE SPHYGMOMANOMETER, per subject, shall meet the criteria listed:

i) in Table 1; or

ii) in Table 2

when calculated according to Formula (13).

$$s_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} \left(x_j - \bar{x}_n \right)^2} \tag{13}$$

where

$\bar{x}_n$ is the mean value of the differences over all subjects as calculated according to Formula (11);

m is the number of subjects;

j is the index for the individual element;

x_j is the mean value of the differences per subject calculated according to Formula (14).

$$x_j = \frac{1}{6} \times \sum_{k=1}^{6} x_k \tag{14}$$

where

x_k is the SPHYGMOMANOMETER-UNDER-TEST error for each subject as calculated according to Formula (9) and Formula (10);

k is the index for the individual element.

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

EXAMPLE 5 m = 85 for a SPHYGMOMANOMETER intended for use in adults 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 passed a 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).

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

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

a) For a SPHYGMOMANOMETER intended for use in exercise stress testing, an additional CLINICAL INVESTIGATION shall be performed.

1) During this CLINICAL INVESTIGATION, the subjects shall be stressed by dynamic (aerobic) exercise on a bicycle ergometer so as to increase their heart rate to at least 30 % above their resting heart rate.

2) The resting heart rate shall be recorded.

3) The heart rate for each DETERMINATION shall be recorded.

4) Any arm used for the REFERENCE reading and DETERMINATION shall be supported.

5) The CUFF shall be at the level of the left ventricle during the REFERENCE reading and DETERMINATION of BLOOD PRESSURE.

b) Any one of the CLINICAL INVESTIGATION methods described in 5.2.4 may be used.

1) The CLINICAL INVESTIGATION shall consist of a minimum of 35 subjects.

2) A stress testing study shall be exempt from the requirements of 5.1.1, 5.1.3, 5.1.4 and 5.1.5.

3) At least 10 % of the subjects shall have a resting SYSTOLIC BLOOD PRESSURE ≥140 mmHg (18,66 kPa).

4) An exercise stress monitoring study need not be evaluated with acceptance criterion 2 of 5.2.4.1.2 or 5.2.4.2.2.

c) For the same arm sequential method of 5.2.4.1 replace the REFERENCE BLOOD PRESSURE variation exclusion criteria of 5.2.4.1.1 n) with the following:

1) Data from the subject shall be excluded, if any two sequential:

i) REFERENCE SYSTOLIC BLOOD PRESSURE readings differ by more than 8 mmHg (1,07 kPa); or

ii) any two sequential REFERENCE DIASTOLIC BLOOD PRESSURE readings differ by more than 6 mmHg (0,80 kPa).

2) The subject need not be excluded from the CLINICAL INVESTIGATION, but the series of REFERENCE readings and DETERMINATIONS may be continued.

3) The initial resting REFERENCE reading and DETERMINATION need not be repeated.

Check compliance by inspection of the CLINICAL INVESTIGATION REPORT.

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

a) For a SPHYGMOMANOMETER intended for use in ambulatory monitoring, an additional CLINICAL INVESTIGATION shall be performed.

1) During this CLINICAL INVESTIGATION, the subjects shall be stressed by dynamic (aerobic) exercise on a bicycle ergometer so as to increase their heart rate to at least 15 % above their resting heart rate.

2) The resting heart rate shall be recorded.

3) The heart rate for each DETERMINATION shall be recorded.

4) During the REFERENCE reading and the SUT DETERMINATION any elbow and forearm shall be supported.

5) The CUFF shall be at the level of the left ventricle during the REFERENCE reading and DETERMINATION of BLOOD PRESSURE.

b) Any one of the CLINICAL INVESTIGATION methods described in 5.2.4 may be used.

1) The CLINICAL INVESTIGATION shall consist of a minimum of 35 subjects.

2) An ambulatory monitoring study shall be exempt from the requirements of 5.1.1, 5.1.3, 5.1.4 and 5.1.5.

3) At least 30 % of the subjects shall have a resting SYSTOLIC BLOOD PRESSURE >140 mmHg (18,66 kPa).

4) An ambulatory monitoring study shall be exempt from the acceptance criterion 2 of 5.2.4.1.2 or 5.2.4.2.2.

c) For the same arm sequential method of 5.2.4.1, replace the REFERENCE BLOOD PRESSURE variation exclusion criteria of 5.2.4.2.1 with the following:

1) Data from the subject shall be excluded, if any two sequential:

i) REFERENCE SYSTOLIC BLOOD PRESSURE readings differ by more than 8 mmHg (1,07 kPa); or

ii) REFERENCE DIASTOLIC BLOOD PRESSURE readings differ by more than 6 mmHg (0,80 kPa).

2) The subject need not be excluded from the CLINICAL INVESTIGATION, but the series of REFERENCE readings and DETERMINATIONS may be continued.

3) The initial resting REFERENCE reading and DETERMINATION need not be repeated.

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) A REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT CLINICAL INVESTIGATION shall consist of a minimum of 15 PATIENTS.

b) For each PATIENT, no more than 10 valid BLOOD PRESSURE measurements shall be taken.

c) 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

The measurements shall be made from:

a) at least 30 % male PATIENTS; and

b) at least 30 % 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

a) For a SPHYGMOMANOMETER intended for use in adult 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 and 150 DETERMINATIONS.

b) 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 and 200 DETERMINATIONS.

c) For a SPHYGMOMANOMETER additionally intended for use in children, the data analysis (see 6.2.6) of adults, adolescents and children shall be pooled.

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

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

1) At least 3 PATIENTS shall be <1 000 g in weight.

2) At least 3 PATIENTS shall be 1 000 g to 2 000 g in weight.

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

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

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

6) 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 and 180 DETERMINATIONS.

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

c) Neonates, infants and children of less than 3 years of age are exempt from:

1) the BLOOD PRESSURE distribution requirements of 6.1.5;

2) the gender distribution requirements of 6.1.2; and

3) 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

a) For a SPHYGMOMANOMETER intended for use with a single CUFF size,

1) 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

2) at least 40 % shall have a limb circumference within the lower half of the specified range of use of the CUFF.

b) For a SPHYGMOMANOMETER intended for use with multiple CUFF sizes, at least $\frac{1}{2\times n}$ of the total number of 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

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

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

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

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

e) 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) 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 shall undergo CLINICAL INVESTIGATION in those PATIENT populations.

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

b) If the SPHYGMOMANOMETER has passed CLINICAL INVESTIGATION according to the requirements of 6.1.1, then only seven additional special population PATIENTS need be included in the CLINICAL INVESTIGATION.

NOTE Minimum total of 22 PATIENTS and 220 DETERMINATIONS.

c) 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

a) 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).

b) The resonant frequency and damping coefficient of the REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT shall be characterized.

NOTE 1 References [9] and [23] contain additional information regarding characterization of INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT.

c) The transducer for:

1) the intra-arterial catheter; and

2) the SPHYGMOMANOMETER-UNDER-TEST CUFF

should both be kept at the level of the left ventricle of the heart.

d) 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.

1) The intra-arterial BLOOD PRESSURE recordings shall be checked for the occurrence of dysrhythmias against the MANUFACTURER'S exclusion criteria for the SPHYGMOMANOMETER-UNDER-TEST.

2) 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.

3) 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

a) 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.

b) 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.

1) The arterial transducer should be at the level of the left ventricle of the heart.

2) The REFERENCE site may be on the opposite limb.

3) If the opposite limb is used, the results shall be corrected for the lateral difference.

4) Formula (A.1) provides an example of a non-invasive correction method.

5) Simultaneous non-invasive auscultatory readings performed by observers may be used to determine the lateral difference.

6) The lateral difference in BLOOD PRESSURE shall be calculated prior to taking the invasive data.

7) All data from a subject shall be excluded from the CLINICAL INVESTIGATION if:

   i) the lateral difference of the REFERENCE SYSTOLIC BLOOD PRESSURE readings is more than 15 mmHg (2,00 kPa); or

   ii) the lateral difference of the REFERENCE DIASTOLIC BLOOD PRESSURE readings is more than 10 mmHg (1,33 kPa).

NOTE For a SPHYGMOMANOMETER-UNDER-TEST that utilizes a measurement site other than a limb, it might be possible to ignore the lateral difference considerations in this subclause. However, at present the Committee does not have enough information to draw this conclusion for all future SPHYGMOMANOMETERS-UNDER-TEST.

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

6.2.3 PROCEDURE

a) 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 or blood clots in the catheter/transducer system.

Perform the following:

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

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 b) in the calculation of accuracy.*

e) *In each measurement session of interest, start recording the REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT at least 40 s before the SPHYGMOMANOMETER-UNDER-TEST starts to inflate the CUFF for the DETERMINATION. Stop the recording of the REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT when at least 40 s have elapsed after the SPHYGMOMANOMETER-UNDER-TEST CUFF has deflated.*

NOTE *It is acceptable for the REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT to continue recording the subject's BLOOD PRESSURE for the entire study.*

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 have been performed.*

6.2.4 * Determining the REFERENCE BLOOD PRESSURE

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

b) In those cases, where the recording

1) is not interrupted due to 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;

2) is interrupted due to 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 (e.g. approximately from 40 s to 10 s) before the CUFF inflation starts.

c) The REFERENCE SYSTOLIC BLOOD PRESSURE is defined as the range of ±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 (±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 DETERMINATION is within these ranges.

d) Unless the SPHYGMOMANOMETER-UNDER-TEST is intended for use during significantly irregular heart rhythm and no exclusion criteria for irregular heart rhythm is disclosed in the instructions for use, during the recording:

1) 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) during or before a DETERMINATION by the SPHYGMOMANOMETER-UNDER-TEST; and

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

e) As the calculation of the MEAN ARTERIAL PRESSURE (MAP) from the recording requires a special algorithm, the REFERENCE MEAN ARTERIAL PRESSURE range may:

1) be read from the values displayed on the REFERENCE INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT; or

2) be manually calculated for each individual beat by using the area under the BLOOD PRESSURE curve divided by the duration of the heartbeat.

f) 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

a) 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.

b) 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 adjacent limit of the REFERENCE BLOOD PRESSURE from the value of the SPHYGMOMANOMETER-UNDER-TEST DETERMINATION. 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).

c) Calculate the arithmetic mean of the error and its experimental standard deviation from the errors of each DETERMINATION for each PATIENT and for each BLOOD PRESSURE value (SYSTOLIC BLOOD PRESSURE, DIASTOLIC BLOOD PRESSURE, MAP).

6.2.6 Data analysis

For SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE, the mean value of the errors $\overline{x}_n$ 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 (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 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 or adolescent PATIENTS (a 15 subject study).

EXAMPLE 2 n = 200 for a SPHYGMOMANOMETER intended for use in adults 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 [see 6.2.4 e)].

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

7 * Pregnant PATIENT populations

a) A SPHYGMOMANOMETER that is intended for use in pregnant PATIENTS shall undergo CLINICAL INVESTIGATION in that PATIENT population.

b) If the SPHYGMOMANOMETER has passed the CLINICAL INVESTIGATION according to the requirements given in 5.1 and 5.2, then it shall undergo CLINICAL INVESTIGATION according to 5.2 in at least an additional 45 pregnant PATIENTS.

c) If the SPHYGMOMANOMETER has passed the CLINICAL INVESTIGATION according to the requirements given in 6.1 and 6.2, then it shall undergo CLINICAL INVESTIGATION according to 6.2 in at least an additional 15 pregnant PATIENTS.

d) If the SPHYGMOMANOMETER has not successfully undergone a CLINICAL INVESTIGATION described in either 5.1 and 5.2 or 6.1 and 6.2, then a CLINICAL INVESTIGATION according to either 5.1.1 and 5.2 or 6.1.1 and 6.2 shall be performed consisting of pregnant PATIENTS only.

e) For any CLINICAL INVESTIGATION for pregnant PATIENTS, the PATIENT population shall be equally distributed, ±1 PATIENT, into the following three subgroups:

   1) normotensive pregnant PATIENTS beyond the first trimester with SYSTOLIC BLOOD PRESSURE <140 mmHg (18,66 kPa) and DIASTOLIC BLOOD PRESSURE <90 mmHg (12 kPa);

   2) hypertensive pregnant PATIENTS beyond the first trimester:

      i) without proteinuria >300 mg in 24 h; and

      ii) with SYSTOLIC BLOOD PRESSURE ≥140 mmHg (18,66 kPa) or DIASTOLIC BLOOD PRESSURE ≥ 90 mmHg (12 kPa);

   3) pre-eclampsia PATIENTS

      i) with proteinuria >300 mg in 24 h; and

      ii) with SYSTOLIC BLOOD PRESSURE ≥140 mmHg (18,66 kPa) or DIASTOLIC BLOOD PRESSURE ≥ 90 mmHg (12,00 kPa).

f) 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.

g) Perform data analysis according to 5.2.4.1.2 or 5.2.4.2.2, using Criterion 1, or 6.2.6, as appropriate, with the three subgroups pooled.

h) The instructions for use of a SPHYGMOMANOMETER that has been investigated to operate with pregnant PATIENTS may indicate that the SPHYGMOMANOMETER is suitable for use with pregnant (including pre-eclamptic) PATIENTS.

i) The instructions for use of a SPHYGMOMANOMETER, which has not been investigated for use on pregnant PATIENTS, shall indicate that 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 document and is intended for those who are familiar with the subject of this document 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 document. 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 [4] 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 [3] 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 [21] and [22] contain additional information.

If bias exists, it is likely caused by differences in limb circumference and body fat distribution. This document 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[14] 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[6] 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.

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 BLOOD PRESSURE/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 [5] 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 VALUE and DIASTOLIC BLOOD PRESSURE VALUE 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.

5.1.6 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 and 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 value 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. 目前房颤患者的血压并没有可接受的指南，因为听诊法对此类患者测量的血压值的准确性是未知的

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 general consensus that the fifth phase should be used for determining the DIASTOLIC BLOOD PRESSURE.

NOTE 1 The rationale to 5.1.3 and Reference [16] 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 for determining the DIASTOLIC BLOOD PRESSURE during pregnancy. The International Society for the Study of Hypertension in Pregnancy currently recommends using K5 for determining DIASTOLIC BLOOD PRESSURE during pregnancy.

NOTE 2 References [13] and [16] contain additional information.

5.2.3 REFERENCE reading

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

Research demonstrates significant error in auscultatory measurement when the CUFF employed is too wide or too narrow for the subject's arm circumference, as compared to an invasive REFERENCE [10]. This phenomenon is widely recognized by experts, and is acknowledged as a leading cause of inaccurate BLOOD PRESSURE measurement worldwide. The data demonstrates good CUFF performance when the width of the CUFF bladder is in the range of 37 % to 50 % of the circumference of the subject's upper arm, as measured at the mid-point of the upper arm. Beyond those upper and lower limits, the data shows increasingly significant error.

Research demonstrates that an arm circumference to CUFF bladder length ratio of <75 % is too low to provide proper occlusion to the subject arm, and that a ratio of >100 % potentially introduces error in the auscultatory reading. The committees conclude that the bladder length ratio needs to fall in the range of 75 % to 100 % to ensure accurate REFERENCE readings.

5.2.4.1.1 PROCEDURE

BLOOD PRESSURE is variable beat to beat, and minute to minute. Therefore, the same arm sequential method is subject to significant temporal BLOOD PRESSURE variability. This phenomenon is greatly mitigated in the opposite-arm, simultaneous method. For this reason, the consensus view is that some tolerance for temporal variability is acceptable in the same arm, sequential method to accommodate such variability.

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/SC 3 and IEC/SC 62D'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/SC 3 and IEC/SC 62D carefully considered the various possible methodologies that could be employed to perform sequential investigations. Since the REFERENCE readings and DETERMINATIONS are carried out in temporal succession, it is important that haemodynamically stable conditions exist during the testing period. There has been 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 reading equals 122 mmHg. The second REFERENCE SYSTOLIC BLOOD PRESSURE reading equals 128 mmHg. The third REFERENCE SYSTOLIC BLOOD PRESSURE reading equals 132 mmHg. Result: The difference between any two REFERENCE SYSTOLIC BLOOD PRESSURE readings is less than or equal to 12 mmHg; all readings are included in the study.

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

EXAMPLE 3 The first REFERENCE SYSTOLIC BLOOD PRESSURE reading equals 119 mmHg. The second REFERENCE SYSTOLIC BLOOD PRESSURE reading equals 121 mmHg. The third REFERENCE SYSTOLIC BLOOD PRESSURE reading equals 134 mmHg. Result: The difference between the first and third REFERENCE readings is greater than 12 mmHg; all REFERENCE readings can be excluded from the study. Alternatively, the first and second readings can be used in the study and the data from the 3rd reading 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 REFERENCE readings as stability criteria was also discussed, but there was concern that this would cause too many exclusions.

The existing protocols and possible sources of bias and error were reviewed. It was concluded that allowing the choosing of either the preceding or following REFERENCE reading 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 readings 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 readings alone as the REFERENCE value; however, it was determined that the average of the previous and the following REFERENCE readings 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 readings were treated as the SPHYGMOMANOMETER-UNDER-TEST DETERMINATION.

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 reading error) and subject's temporal BLOOD PRESSURE variations.

The initial REFERENCE BLOOD PRESSURE reading and DETERMINATION, which are not included in the data analysis, are intended to mitigate the "alerting" or "alarm" response in the subject, which can temporarily increase the initial values in many individuals[12].

Table A.1 — Committees' 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

5.2.4.2 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 REFERENCE reading and DETERMINATION 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 reading, 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).

5.2.4.2.2 Data analysis

Standards, such as Reference [1], 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 document 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 readings 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 readings (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 heart rate of at least 30 % above a subject's resting 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 [8] 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 left ventricle 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.

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

Ambulatory monitoring (e.g. for 24 h or longer) has great value in the diagnosis of hypertension, especially with the white coat effect and masked hypertension. While doing normal daily activities the PATIENT'S BLOOD PRESSURE is taken according to a programmed schedule stored in the AUTOMATED SPHYGMOMANOMETER. Typically a PATIENT'S BLOOD PRESSURE is taken approximately every 15 min during the day and somewhat less often at night so that the PATIENT'S sleep is not interrupted. The daytime heart rate and BLOOD PRESSURE values during ambulatory monitoring are elevated in comparison to baseline resting values. For this reason these additional requirements are designed to evaluate AUTOMATED SPHYGMOMANOMETER performance at mildly elevated heart rates, such as those that would occur during non-strenuous activities. In addition, the bicycle ergometer provides some minor motion artefact that is intended to show that the AUTOMATED SPHYGMOMANOMETER is able to take accurate BLOOD PRESSURE estimates with a minimal level of motion as would be encountered in ambulatory use.

From a clinical basis, ambulatory monitoring is most often done for the diagnosis and management of hypertension. It is for this reason that the requirements call for a percentage of subjects with hypertension at rest.

Each subject should pedal the ergometer at a fixed rate and workload once the criterion of an elevation of at least 15 % above the subject's resting heart rate has been met. That should allow the attainment of a steady state such that the heart rate and BLOOD PRESSURE plateau.

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 [21] and [22] contain additional information.

If bias exists, it is likely caused by differences in arm circumference and body fat distribution. This document already requires that the SPHYGMOMANOMETER-UNDER-TEST is 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[4]. 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

6.2.1 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 BLOOD PRESSURE REFERENCE requires the use of 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 BLOOD PRESSURE.

The frequency response and damping coefficient pair should meet the dynamic requirements proposed by Gardner[9]. 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 left ventricle of the heart (phlebostatic axis).

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

6.2.2 Arterial REFERENCE site

Reference [2] excludes 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 have clinical validity for the diagnosis of hypertension (i.e. all morbidity/mortality data are based on values from 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.

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 REFERENCE readings or DETERMINATIONS made on each limb according to Formula (A.1).

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

where

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

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

The *LD* is calculated for each subject and is used according to Formula (9) and Formula (10).

6.2.4 Determining the REFERENCE BLOOD PRESSURE

Several options were discussed for defining the REFERENCE SYSTOLIC BLOOD PRESSURE and REFERENCE DIASTOLIC BLOOD PRESSURE. In particular, the normal BLOOD PRESSURE variation that occurs during a non-invasive BLOOD PRESSURE reading or 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 reading or 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 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)[24]. Pre-eclampsia has altered haemodynamics (i.e. 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 [7], [11], [17], [18], [19] and [20]. 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 determine the sample size needed for an unbiased SPHYGMOMANOMETER with a true mean difference of 0 mmHg and true standard deviation of 8 mmHg to fail less than 5 % of the time:

— two groups of PATIENTS (n_1 pregnant women without pre-eclampsia, n_2 with pre-eclampsia) are observed, each giving 3 pairs of REFERENCE readings and DETERMINATIONS, leading to 3 measurements of BLOOD PRESSURE difference (error) for each of both SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE per woman.

— Failure occurs only when the observed means of the error of either sets of BLOOD PRESSURES in the 2 groups differ by 5 mmHg or more.

Consider the extreme case: where the standard deviation = 8 mmHg, measurements are highly correlated, so effectively one measurement per woman. In practice the standard deviation would usually be less than 8 mmHg, (if the SPHYGMOMANOMETER is not to have already failed) and there would be some differences within subject measurements; these 2 effects would reduce the chance of a SPHYGMOMANOMETER failing.

The standard requires the sampling distribution of the difference in both SYSTOLIC BLOOD PRESSURE and DIASTOLIC BLOOD PRESSURE to be within –5 mmHg and +5 mmHg. So 2 × SE = 5 mmHg, using the Student's t distribution.

$$SE = 5/1{,}96 = ((1/n_1 + 1/n_2)^{1/2}) \times SD$$

$$(1/n_1 + 2/n_1)^{1/2} = 5/(1{,}96 \times 8)$$

$$(1/n_1)^{1/2} = (5/(1{,}96 \times 8))^{1/3}$$

$$n_1 = 3 \times (1{,}96 \times 8/5)^2 = 30 \text{ and } n_2 = n_1/2 = 15.$$

Therefore 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
(informative)

Reference to the ESSENTIAL PRINCIPLES

This document has been prepared to support the ESSENTIAL PRINCIPLES OF SAFETY AND PERFORMANCE of electronically controlled, INTERMITTENT, AUTOMATED SPHYGMOMANOMETERS as a medical device in accordance with ISO 16142-1:2016. This document is intended to be acceptable for conformity assessment purposes.

Compliance with this document provides one means of demonstrating conformance with the specific ESSENTIAL PRINCIPLES of ISO 16142-1:2016. Other means are possible. Table B.1 maps the clauses and subclauses of this document with the ESSENTIAL PRINCIPLES of ISO 16142-1:2016.

Table B.1 — Correspondence between this document and the ESSENTIAL PRINCIPLES

Corresponding ESSENTIAL PRINCIPLE of ISO 16142-1:2016, Annex B	Clause(s)/subclause(s) of this document	Qualifying remarks/Notes
7.1	All	The part relating to risk/benefit is not addressed.
7.2	All	
13.1	4, 5 and 6	Only the characteristics of the measurement performance (accuracy), as well as the corresponding tests methods, are addressed.
21.1	5.1.6, 5.2.2, 6.2.1, 6.2.2, 6.2.7 and 7	Only certain additional warnings and precautions specific to particular situations and subjects populations are contained in the indicated subclauses.

Annex C
(informative)

Terminology — alphabetized index of defined terms

Term	Source
ACCOMPANYING DOCUMENT	IEC 60601-1:2005+AMD1:2012, 3.4
AUTOMATED SPHYGMOMANOMETER	IEC 80601-2-30:2018, 201.3.201
BLOOD PRESSURE	ISO 81060-1:2007, 3.3
CLINICAL INVESTIGATION	ISO 14155:2011, 3.6
CLINICAL INVESTIGATION REPORT	ISO 14155:2011, 3.8
CUFF	IEC 80601-2-30:2018, 201.3.202
DETERMINATION	IEC 80601-2-30:2018, 201.3.203
DIASTOLIC BLOOD PRESSURE	IEC 80601-2-30:2018, 201.3.204
DIASTOLIC BLOOD PRESSURE VALUE	IEC 80601-2-30:2018, 201.3.204
ESSENTIAL PRINCIPLES	ISO 16142-1:2016, 3.3
ESSENTIAL PRINCIPLES OF SAFETY AND PERFORMANCE	ISO 16142-1:2016, 3.3
HOME HEALTHCARE ENVIRONMENT	IEC 60601-1-11:2015, 3.1
INTENDED USE	IEC 60601-1:2005+AMD1:2012, 3.44
INTERMITTENT	3.1
INVASIVE BLOOD PRESSURE MONITORING EQUIPMENT	IEC 60601-2-34:2011, 3.3
MANUFACTURER	IEC 60601-1:2005+AMD1:2012, 3.55
MEAN ARTERIAL PRESSURE (MAP)	IEC 80601-2-30:2018, 201.3.206
MEDICAL ELECTRICAL EQUIPMENT (ME EQUIPMENT)	IEC 60601-1:2005+AMD1:2012, 3.63
NON-AUTOMATED SPHYGMOMANOMETER	IEC 80601-2-30:2018, 201.3.208
OBJECTIVE EVIDENCE	IEC 60601-1:2005+AMD1:2012, 3.72
PATIENT	IEC 60601-1:2005+AMD1:2012, 3.76
PROCEDURE	ISO 14971:2007, 2.12
REF	3.2
REFERENCE	3.2
RESPONSIBLE ORGANIZATION	IEC 60601-1:2005, 3.101
SPHYGMOMANOMETER	3.3
SPHYGMOMANOMETER-UNDER-TEST	3.4
SUT	3.4
SYSTOLIC BLOOD PRESSURE	IEC 80601-2-30:2018, 201.3.215
SYSTOLIC BLOOD PRESSURE VALUE	IEC 80601-2-30:2018, 201.3.215
TYPE TEST	IEC 60601-1:2005+AMD1:2012, 3.135

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