INTERNATIONAL STANDARD

ISO 81060-2

First edition
2009-05-01

Non-invasive sphygmomanometers —

Part 2: Clinical validation of automated measurement type

Sphygmomanomètres non invasifs —

Partie 2: Validation clinique pour type à mesurage automatique

Reference number
ISO 81060-2:2009(E)

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Published in Switzerland

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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.

ISO 81060-2 was prepared by Technical Committee ISO/TC 121, *Anaesthetic and respiratory equipment*, Subcommittee SC 3, *Lung ventilators and related equipment* and Technical Committee IEC/TC 62, *Electrical Equipment in Medical Practice*, Subcommittee 62D, *Electromedical Equipment*.

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 validation of automated measurement type*

Introduction

Determination of **blood pressure** is an important procedure that is clinically used to assess the health of the **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.

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;

— terms defined in this document: **bold type**.

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

Non-invasive sphygmomanometers —

Part 2:
Clinical validation of automated measurement type

1 Scope

This part of ISO 81060 specifies the requirements and methods for the clinical validation of **me equipment** used for the intermittent non-invasive automatic 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** or self-measurement).

EXAMPLE **Automated sphygmomanometer** as given in IEC 80601-2-30 validated by this part of ISO 81060.

This part of ISO 81060 specifies additional disclosure requirements for the **accompanying documents** of **sphygmomanometers** validated according to this part of ISO 81060.

This part of ISO 81060 is not applicable to the validation 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 referenced documents are indispensable for the application 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.

ISO 14155:—[1)], *Clinical investigation of medical devices for human subjects — Good clinical practice*

ISO 81060-1:2007, *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*

IEC 60601-1-11, *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 60601-2-34:2000, *Medical electrical equipment — Part 2-34: Particular requirements for the safety, including essential performance, of invasive blood pressure monitoring equipment*

1) To be published.

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. For convenience, an alphabetized list of the sources of all defined terms used in this document is given in Annex D.

3.1
reference
established accuracy used for clinical evaluation of other instruments

3.2
sphygmomanometer
me equipment for non-invasive estimation of systemic arterial **blood pressure**

3.3
sphygmomanometer-under-test
sphygmomanometer being clinically evaluated

4 General requirements for validation studies

4.1 Validation methods

Sphygmomanometers other than **non-automated sphygmomanometers** shall be clinically validated 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 mode.

EXAMPLE 2 Slow and fast **cuff** deflation rate mode.

A clinical validation study 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 Ethical requirements

All clinical validation studies shall comply with the requirements of ISO 14155. Validation with **reference invasive blood pressure monitoring equipment** should not be used for **patients** or subjects solely for the purpose of validating **sphygmomanometer** performance.

NOTE Some authorities with jurisdiction have additional requirements.

Check compliance by application of the requirements of ISO 14155.

5 Validation with auscultatory reference sphygmomanometer

5.1 Subject requirements

5.1.1 * Number

An auscultatory **reference sphygmomanometer** validation study 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 ages of the subjects included in the validation study shall be > 12 y.

NOTE 1 Minimum total of 85 subjects.

For a **sphygmomanometer** additionally intended for use in children, 35 child subjects aged between 3 y and 12 y shall be included in the validation study.

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 that mode, children are exempt from the **blood pressure** distribution requirements of 5.1.5.

Children < 3 y shall not be included in an auscultatory **reference sphygmomanometer** validation study.

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. At least 20 % of the subjects should have a limb circumference which lies within the upper quarter of the specified range of use of the **cuff** and at least 20 % should 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 $1/(2 \times n)$ 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 readings shall have a **systolic blood pressure** ⩽ 100 mmHg.

At least 5 % of the readings shall have a **systolic blood pressure** ⩾ 160 mmHg.

At least 20 % of the readings shall have a **systolic blood pressure** ⩾ 140 mmHg.

At least 5 % of the readings shall have a **diastolic blood pressure** ⩽ 60 mmHg.

At least 5 % of the readings shall have a **diastolic blood pressure** ⩾ 100 mmHg.

At least 20 % of the readings shall have a **diastolic blood pressure** ⩾ 85 mmHg.

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 be clinically evaluated in those **patient** populations. See also Clause 7.

EXAMPLES Use with **patients** who have atrial fibrillation (AF), premature ventricular beats and peripheral arterial disease (PAD).

If the **sphygmomanometer** has been evaluated according to the requirements of 5.1.1, it shall then be validated in at least an additional 35 special population subjects. Otherwise, the evaluation in accordance with the requirements of 5.1.1 shall only consist of subjects from the special population.

The special 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 Validation method with reference sphygmomanometer

5.2.1 * Subject preparation

See Reference [32].

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 **cuff** at the level of the right atrium of the heart.

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

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. See References [8], [28], [29], [32] and [45]. They 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 **diastolic blood pressure** as the last audible Korotkoff sound (fifth phase or K5), except in children between 3 y and 12 y, pregnant subjects, and subjects during exercise, where the fourth phase (K4) is used.

Instruct the observers to use K4 for the determination of **diastolic blood pressure** when sounds are audible with the **cuff** deflated.

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 validation study shall be disclosed in the instructions for use of a **sphygmomanometer**.

EXAMPLE 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 VPB, atrial fibrillation.

NOTE 1 Although evaluation 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 shall be excluded. The observers' individual values of each determination shall be averaged to create the **reference blood pressure** 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 needed 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. 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. Rounding has a negative effect on the results of the clinical validation.

NOTE 2 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 Validation 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 is designed for use on the upper arm;

— where:

  — the continuous linear deflation rate is 2 mmHg/s to 3 mmHg/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 and 3 mmHg/pulse.

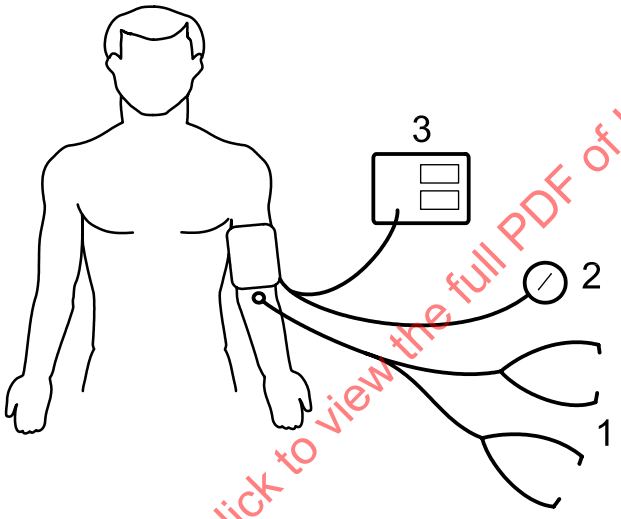
This method shall only be used when the **sphygmomanometer-under-test cuff** meets the requirements of ISO 81060-1.

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 higher than the actual **systolic blood pressure**, as determined by the **reference sphygmomanometer**, and to at least 20 mmHg 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).



Key

1 double stethoscope
2 **reference sphygmomanometer** display
3 **sphygmomanometer-under-test**

Figure 1 — Illustration of same arm simultaneous method

b) Clear the **sphygmomanometer-under-test** memory of the previous determination and then wait at least 60 s.

EXAMPLE Switching the power off and on, removing the **blood pressure** module or issuing a reset command as methods to clear any memory of the previous determination.

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

d) 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.

e) Wait at least 60 s between determinations.

f) Repeat d) and e) until the needed number of determinations have been performed.

If an individual subject is unstable during the period of the test, two valid determination pairs may be used. In this case, additional subjects may be used to complete the method. No more than 10 % of the subjects shall have fewer than three valid determination pairs.

All data from a subject shall be excluded if any two **reference systolic blood pressure** determinations differ by more than 12 mmHg or if any two **reference diastolic blood pressure** determinations differ by more than 8 mmHg.

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 error of determination, $\bar{x}_n$, of the n individual paired determinations of the **sphygmomanometer-under-test** and the **reference sphygmomanometer** for all subjects shall not be greater than 5,0 mmHg, with a standard deviation, s_n, no greater than 8,0 mmHg when calculated according to Equation (1) and Equation (2):

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

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

where

$\bar{x}_n$ is the mean error;

x_i = $p_{\mathrm{sut}_i} - p_{\mathrm{ref}_i}$ of a paired **blood pressure** determination (**sphygmomanometer-under-test** – **reference sphygmomanometer**);

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.

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 y and 12 y (an 85 subject study).

EXAMPLE 3 n = 105 for a **sphygmomanometer** intended for a special intended use (a 35 subject study). The **sphygmomanometer** that has a separate 85 subject study.

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 **reference sphygmomanometer** shall meet the criteria listed in Table 1 when calculated according to Equation (3):

$$s_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} \left(x_j - \bar{x}_n \right)^2} \tag{3}$$

where

$\bar{x}_n$ is the mean error over all subjects (see Equation 1);

m is the number of subjects;

j is the index for the individual element;

x_j is calculated from Equation (4).

$$x_j = \frac{1}{d} \times \sum_{k=1}^{d} (p_{\text{sut}_k} - p_{\text{ref}_k}) \tag{4}$$

where

d is the number of determinations per subject;

k is the index for the individual element.

Table 1 — Averaged subject data acceptance (criterion 2)

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

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 y and 12 y (an 85 subject study).

EXAMPLE 6 m = 35 for a **sphygmomanometer** intended for (an additional) special intended use (a 35 subject study). The **sphygmomanometer** that has a separate 85 subject study.

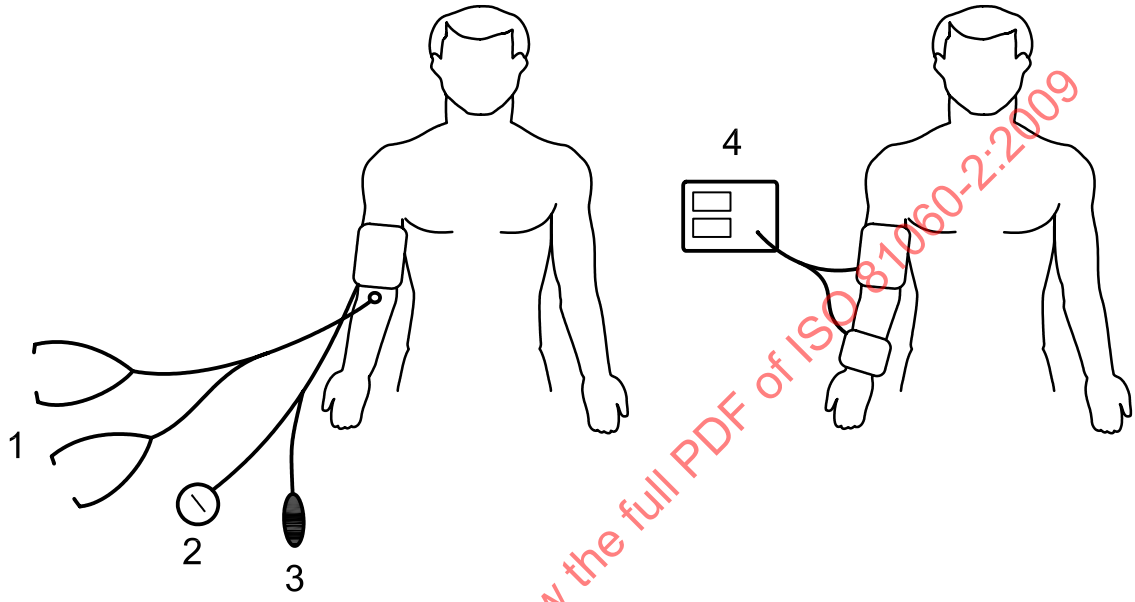
EXAMPLE 7 m = 85 for a **sphygmomanometer** intended only for a special intended use (an 85 subject study).

5.2.4.2 * Same arm sequential method

5.2.4.2.1 Procedure

Perform the following method:

a) Have the observers using the **reference sphygmomanometer** determine the subject's **blood pressure** (see Figure 2).



Key

1 double stethoscope
2 **reference sphygmomanometer** display
3 **reference sphygmomanometer** hand pump
4 **sphygmomanometer-under-test**

Figure 2 — Illustration of same arm sequential method

b) Wait at least 60 s.

c) Have the observers using the **sphygmomanometer-under-test** determine the subject's **blood pressure**.

d) Clear the **sphygmomanometer-under-test** memory of the previous determination and then wait at least 60 s.

EXAMPLE Switching the power off and on, removing the **blood pressure** module or issuing a reset command as methods to clear any memory of the previous determination.

e) These data points shall not be used in the determination of accuracy.

f) The starting order [see g)] of **sphygmomanometer-under-test** and **reference sphygmomanometer** determinations shall be alternated between subjects, or a randomizations procedure may be used to determine the starting order.

g) Have the observers using the **reference sphygmomanometer** and the **sphygmomanometer-under-test** determine the subject's **blood pressure** sequentially.

h) Wait at least 60 s between each determination.

i) Repeat g) and h) until the needed number of 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 or if any two **reference diastolic blood pressure** determinations differ by more than 8 mmHg.

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 error of determination, $\bar{x}_n$, of the n individual paired determinations of the **sphygmomanometer-under-test** and the **reference sphygmomanometer** for all subjects shall not be greater than 5,0 mmHg, with a standard deviation, s_n, no greater than 8,0 mmHg when calculated according to Equation (5) and Equation (6):

$$\bar{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} \left(p_{\text{sut}\,i} - p_{\text{ref}\,i} \right) \tag{5}$$

$$s_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} \left(x_i - \bar{x}_n \right)^2} \tag{6}$$

where

$\bar{x}_n$ is the mean error;

$x_i = p_{\text{sut}} - p_{\text{ref}}$ of a paired **blood pressure** determination (**sphygmomanometer-under-test** – **reference sphygmomanometer**);

n is the number of determinations.

The p_{ref} or **reference sphygmomanometer** determinations shall not be the average of the preceding and following **reference blood pressures**. $\bar{x}_n$ and s_n shall be calculated and expressed to 0,1 mmHg.

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 y and 12 y (an 85 subject study).

EXAMPLE 3 n = 105 for a **sphygmomanometer** intended for a special intended use (a 35 subject study).

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 **reference sphygmomanometer**, shall meet the criteria listed in Table 1 when calculated according to Equation (7).

$$s_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} \left(x_j - \bar{x}_n \right)^2} \quad (7)$$

where

$\bar{x}_n$ is the mean error over all subjects (see Equation 5);

m is the number of subjects;

x_j is calculated from Equation (8).

$$x_j = \frac{1}{d} \times \sum_{k=1}^{d} (p_{\text{sut}_k} - p_{\text{ref}_k}) \quad (8)$$

where d is the number of determinations per subject.

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 y and 12 y (an 85 subject study).

EXAMPLE 6 m = 35 for a **sphygmomanometer** intended for (an additional) special intended use (a 35 subject study).

EXAMPLE 7 m = 85 for a **sphygmomanometer** intended only for a special intended use (an 85 subject study).

5.2.4.3 Opposite arm simultaneous method

5.2.4.3.1 * Procedure

The starting limb 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 determination of accuracy.

c) Clear the **sphygmomanometer-under-test** memory of the previous determination and wait at least 60 s.

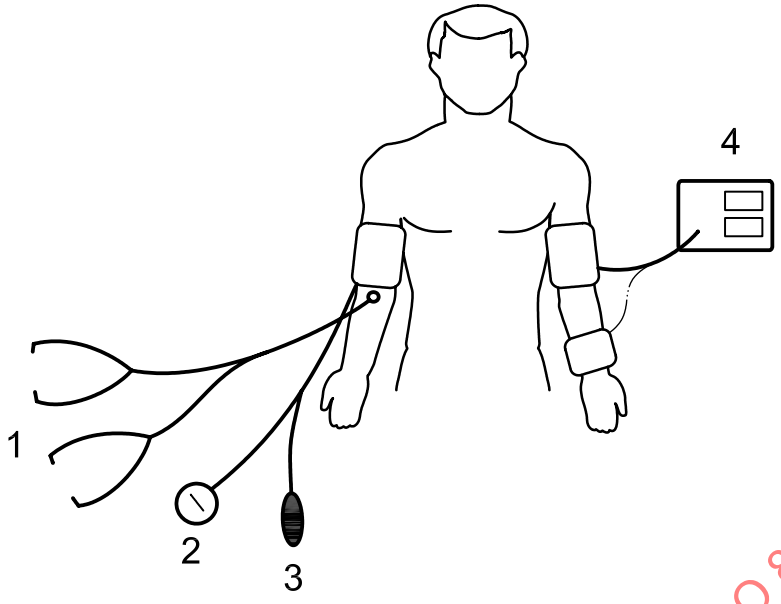
EXAMPLE Switching the power off and on, removing the **blood pressure** module or issuing a reset command as methods to clear any memory of the previous determination.

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) Repeat c) to e) until six paired determinations have been performed.

g) If the determination by the **reference sphygmomanometer** or the **sphygmomanometer-under-test** is not successfully completed, repeat the determination on the same arm sides, i.e., without interchanging limb sides.



Key

1 double stethoscope
2 **reference sphygmomanometer** display
3 **reference sphygmomanometer** hand pump
4 **sphygmomanometer-under-test**

Figure 3 — Illustration of opposite arm simultaneous method

All data from a subject shall be excluded if the lateral difference of the **reference systolic blood pressure** determinations is more than 15 mmHg or the lateral difference of the **reference diastolic blood pressure** determinations is more than 10 mmHg.

The lateral difference, LD, is calculated separately for **systolic** and **diastolic blood pressures**, according to Equation (9).

$$LD = \frac{1}{3} \times \left(\sum_{i=1}^{3} P_{\text{ref\_R}i} - \sum_{j=1}^{3} P_{\text{ref\_L}j} \right) \tag{9}$$

where

$P_{\text{ref\_R}i}$ and $P_{\text{ref\_L}j}$ are **reference blood pressure** in right (R) limb and left (L) limb, respectively.

5.2.4.3.2 * Data analysis

The **sphygmomanometer-under-test** error, x, is computed by taking the difference between the **sphygmomanometer-under-test blood pressure** and **reference sphygmomanometer blood pressure** and by adding the lateral difference, LD, according to Equation (10) if the **sphygmomanometer-under-test blood pressure** was taken in the left arm or by subtracting the lateral difference, LD, according to Equation (11) if the **sphygmomanometer-under-test blood pressure** was taken in the right arm.

$$x = P_{\text{sut\_L}} - P_{\text{ref\_R}} + LD \tag{10}$$

$$x = P_{\text{sut\_R}} - P_{\text{ref\_L}} - LD \tag{11}$$

where P_{sut_R} and P_{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 error of determination, $\bar{x}_n$, of the n individual paired determinations of the **sphygmomanometer-under-test** and the **reference sphygmomanometer** for all subjects shall not be greater than 5,0 mmHg, with a standard deviation, s_n, not greater than 8,0 mmHg when calculated according to Equation (12) and Equation (13).

$$\bar{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} x_i \tag{12}$$

$$s_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} \left(x_i - \bar{x}_n \right)^2} \tag{13}$$

Where n is the number of determinations.

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 y and 12 y (an 85 subject study).

EXAMPLE 3 n = 210 for a **sphygmomanometer** intended for (an additional) special intended use (a 35 subject study).

Criterion 2

For the average of the **systolic** and **diastolic blood pressures** for each subject, the standard deviation, s_m, of the m averaged paired determinations of the **sphygmomanometer-under-test** and the **reference sphygmomanometer**, per subject, shall meet the criteria listed in Table 1 when calculated according to Equation (14).

$$s_m = \sqrt{\frac{1}{m-1} \times \sum_{j=1}^{m} \left(x_j - \bar{x}_n \right)^2} \tag{14}$$

where

m is the number of subjects;

x_j is the mean error per subject calculated from Equation (15).

$$x_j = \frac{1}{6} \times \sum_{k=1}^{6} x_k \tag{15}$$

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 y and 12 y (an 85 subject study).

EXAMPLE 6 m = 35 for a **sphygmomanometer** intended for (an additional) special intended use (a 35 subject study).

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 validation shall be performed. During this evaluation, the subjects shall be stressed by dynamic (aerobic) exercise on a bicycle ergometer so as to increase their heart rate from their resting heart rate to a target heart rate of 50 % to 70 % of their average 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 at heart level during the determination of **blood pressure**.

The same arm sequential method of 5.2.4.2 shall not be used. The validation study 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** $\geqslant$ 160 mmHg. At least 10 % of the subjects shall have a resting **diastolic blood pressure** $\geqslant$ 100 mmHg.

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 validation shall be performed. During this evaluation, 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 at heart level during the determination of **blood pressure**.

The same arm sequential method of 5.2.4.2 shall not be used. The validation study 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. At least 10 % of the subjects shall have a resting **diastolic blood pressure** $>$ 100 mmHg.

Check compliance by inspection of the **clinical investigation report**.

6 Validation with reference invasive blood pressure monitoring equipment

6.1 Patient requirements

6.1.1 Number

A **reference invasive blood pressure monitoring** equipment validation study 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 validation study.

Check compliance by inspection of the **clinical investigation report**.

6.1.2 * Gender distribution

At least 30 % of the measurements shall be from male **patients** and at least 30 % of the measurements shall be from 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 ages of the **patients** included in the validation study shall be > 12 y.

NOTE 1 Minimum total of 15 subjects.

For a **sphygmomanometer** additionally intended for use in children, an additional 5 children aged between 3 y and 12 y shall be included in the validation study.

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 validated in those **patient** populations.

The following age or weight ranges are required for a neonatal mode validation study:

— 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 Minimum total of 18 **patients**. 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 $1/(2 \times n)$ 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 **systolic blood pressure** $\leqslant$ 100 mmHg.

At least 10 % of the subjects shall have a **systolic blood pressure** $\geqslant$ 160 mmHg.

At least 10 % of the subjects shall have a **diastolic blood pressure** $\leqslant$ 70 mmHg.

At least 10 % of the subjects shall have a **diastolic blood pressure** $\geqslant$ 85 mmHg.

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 be clinically evaluated in those **patient** populations. See also Clause 7.

EXAMPLES Use with **patients** who have atrial fibrillation (AF), premature ventricular beats, arteriosclerosis obliterans (ASO), arterial calcification at the **cuff** site.

If the **sphygmomanometer** has been evaluated according to the requirements of 6.1.1, then only seven additional special population **patients** shall be included in the validation study. Otherwise, the evaluation 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 Validation methods with reference invasive blood pressure monitoring equipment

6.2.1 * Reference measurement

Use **reference invasive blood pressure monitoring equipment** that complies with the requirements of IEC 60601-2-34, except that the maximum allowable error shall be $\pm$ 1 mmHg. The resonant frequency and damping coefficient of the **reference invasive blood pressure monitoring equipment** shall be characterized. See References [16] and [42]. The intra-arterial (IA) transducer and the **sphygmomanometer-under-test cuff** should both be kept at the level of the right atrium of the heart.

Unless the **sphygmomanometer-under-test** is intended for use during a clinically significantly 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 records of the invasive pressure values 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 Bigemeny, trigemeny, isolated VPB, atrial fibrillation.

NOTE Although evaluation 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 heart. The **reference** site may be on the opposite limb. If the opposite limb is used, the results shall be corrected for the lateral difference [see Equation (A.1)]. Simultaneous non-invasive determinations may be used to determine the lateral difference. The lateral difference in pressure shall be calculated prior to validation. **Patients** with a **systolic** or **diastolic** lateral difference greater than 12 mmHg shall be excluded from the study.

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 or issuing a reset command as methods to clear any memory of the previous determination.

d) These data points shall not be used in the determination 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 needed 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. Compute the mean and standard deviation of the **systolic** and **diastolic blood pressure** from the recordings. Isolated premature ventricular beats (VPBs) may be addressed by removing the pressure pulse associated with the VPB and the following compensatory beat. The mean **systolic blood pressure** values $\pm$ 1 standard deviation of the invasive **blood pressure** curve obtained during the determination performed by the **sphygmomanometer-under-test** shall be used to determine the range of the variation of **systolic blood pressure**. The range of the variation of **diastolic blood pressure** shall be determined in the same way.

NOTE These ranges of variation of **blood pressures** represent an experimental uncertainty. The **sphygmomanometer-under-test** has determined the **patient's blood pressure** when it was somewhere within these ranges.

Unless the **sphygmomanometer-under-test** is intended for use during significantly irregular heart rhythm, all data from a subject shall be excluded if the range of **systolic blood pressure** differs by more than 20 mmHg or if the range of **diastolic blood pressure** differs by more than 12 mmHg.

In those cases, where the arterial curve is interrupted due to the **cuff** inflation, the **reference blood pressure** ranges shall be determined from the curve of the invasive **blood pressure** 30 s before and 30 s after the interruption.

As the determination of the **mean blood pressure** (MAP) from the curve of the recording requires a special algorithm, the **reference mean blood pressure** range may be read from the values displayed on the **reference invasive blood pressure monitoring equipment** or manually determined for each individual beat.

Record the range of the variation of **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 blood pressure error

If the value obtained from the **sphygmomanometer-under-test** determination lies within the range of the variation of **blood pressure** (see 6.2.4), assign an error of 0 mmHg to this determination.

If the value obtained from the **sphygmomanometer-under-test** determination lies outside the range of the variation of **blood pressure**, 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 variation of **diastolic blood pressure** is 73 mmHg to 82 mmHg. **Diastolic blood pressure** value determined by the **sphygmomanometer-under-test** is 76 mmHg. The error for this determination is 0 mmHg.

EXAMPLE 2 The range of the variation of **diastolic blood pressure** is 73 mmHg to 82 mmHg. **Diastolic blood pressure** value determined by the **sphygmomanometer-under-test** is 70 mmHg. The error for this determination is –3 mmHg.

From the errors of each determination of each **patient**, calculate the arithmetic mean of the error and its standard deviation.

6.2.6 Data analysis

For **systolic** and **diastolic blood pressures**, the mean error of determination, $\bar{x}_n$, of the n individual paired determinations of the **sphygmomanometer-under-test** and the **reference sphygmomanometer** for all subjects shall not be greater than 5,0 mmHg, with a standard deviation, s_n, no greater than 8,0 mmHg when calculated according to Equation (16) and Equation (17).

$$\bar{x}_n = \frac{1}{n} \times \sum_{i=1}^{n} x_i \tag{16}$$

$$s_n = \sqrt{\frac{1}{n-1} \times \sum_{i=1}^{n} \left(x_i - \bar{x}_n \right)^2} \tag{17}$$

where n is the number of determinations.

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 y and 12 y (a 20 subject study).

6.2.7 Mean blood pressure (MAP)

If a **sphygmomanometer** displays a value for **mean blood pressure** (MAP), the **accompanying document** shall disclose the method used to determine and verify the **mean blood 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 be clinically evaluated in that **patient** population.

If the **sphygmomanometer** has been evaluated according to the requirements given in 5.1.1, then at least an additional 45 pregnant, including pre-eclamptic, **patients** or, if evaluating according to the requirements given in 6.1.1, then at least an additional 15 pregnant, including pre-eclamptic, **patients**, shall be separately validated. Otherwise, the evaluation according to the requirements given in 5.1.1 shall consist only of pregnant, including pre-eclamptic, **patients**.

For a validation study for pregnant, including pre-eclamptic, **patients**, the **patient** population shall be equally distributed, ± 1, into the following three subgroups:

a) normotensive pregnant **patients** with **systolic blood pressure** < 140 mmHg and **diastolic blood pressure** < 90 mmHg;

b) hypertensive pregnant **patients** without proteinuria > 300 mg in 24 h and with **systolic blood pressure** ⩾ 140 mmHg or **diastolic blood pressure** ⩾ 90 mmHg;

c) pre-eclampsia, **patients** with proteinuria > 300 mg in 24 h and **diastolic blood pressure** ⩾ 90 mmHg.

The **patient's** responsible healthcare provider needs to determine whether or not it is safe for a particular **patient** to participate in a validation study.

NOTE Data analysis is performed with the three subgroups pooled.

The instructions for use of a **sphygmomanometer** that has been validated 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 validated 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

General

This annex provides a rationale for some 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 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. See Reference [6]. 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. See Reference [5].

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. See References [42] and [43]. 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.

5.1.3 Age distribution

The division between children and adults at the age of 12 y was based upon the only known publication that compares the utility of the use of either K4 or K5 as the auscultatory estimate of intra-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 ($\leqslant$ 12) y 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 y 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 y to 12 y old, auscultatory K4 may be utilized as the non-invasive **reference** standard estimate of **diastolic blood pressure** in validation studies.

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

The upper normal **blood pressure** in children increases from about 114/66 mmHg at age 1 y to 135/91 mmHg at age 12 y for the tallest children analysed. See Reference [7]. For this reason, it would not be practical to specify exact "hypertensive" **blood pressure** values, as can be done in adults for validation testing. In addition, the prevalence of essential hypertension in young children is very low, making validation studies 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, the committee believed there was no valid reason to require hypertensive children in any validation study of individuals $\leqslant$ 12 y of age and that children $>$ 12 y of age should be pooled with adults.

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 evaluated over the entire clinically relevant **blood pressure** range. Previous standards required a subject to remain in a single category for all measurements. This tended to bias the subject selection such that they were far away from the boundaries of the categories, even if the subject 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

Although evaluation 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 evaluation method for **sphygmomanometers** in **patients** with atrial fibrillation.

Although evaluation 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 can also be difficult to use during **patient** transport outside a healthcare facility, it is desirable to establish an evaluation method for a **sphygmomanometer** in **patients** during such transport.

5.2.1 Subject preparation

Since it is essential to reduce a subject's **blood pressure** variability during the study, 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 validation 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, 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 in children between 3 y and 12 y of age. See Reference [25] (see also rationale to 5.1.3) and Reference [32]. 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** in pregnancy. See References [23] and [32].

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 to 15 mmHg and appears to be more difficult to determine accurately. Furthermore, most health 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 NHBPEP Working Group to recommend use of K5 in pregnancy, reserving K4 for the 10 % or fewer gravidas in whom there is a large discrepancy between muffling and disappearance (with the latter at times approaching zero). See References [23] and [32].

5.2.3 Reference determination

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

5.2.4.1.1 Procedure

Since WHO recommendations [46] advise performing auscultatory **blood pressure** determinations at **cuff** deflation rates of 2 mmHg/s to 3 mmHg/s or 2 mmHg/pulse to 3 mmHg/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 validation 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 near the subject's **systolic blood pressure**.

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 mean error of determination, $\bar{x}_n$, of $\pm$ 5 mmHg and standard deviation, s_n, of 8 mmHg, 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. See Reference [6]. 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 error of determination was calculated from the average of the three test determinations and three **reference** determinations from each of the 85 subjects. See Reference [5]. Later, the calculation was changed to the individual test-**reference** differences for the 255 individual determination pairs. See Reference [4]. In making this change, the AAMI blood pressure committee concluded that the change provided a slighter, 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 for 95 % of **patients** when the mean of three repeated measurements is used clinically.

Criterion 2 uses the average of the error 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 was chosen as a tolerable error based on clinician input.

The sample mean error of the determination, $\bar{x}_m$, and sample standard deviation of errors, s_m, refer to the mean and standard deviation of 85 numbers, each being the average of three errors of the determination on the same subject. These sample statistics are only estimates of the true mean error (also called bias) and of the true standard deviation of errors (also called precision), which can 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) 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.

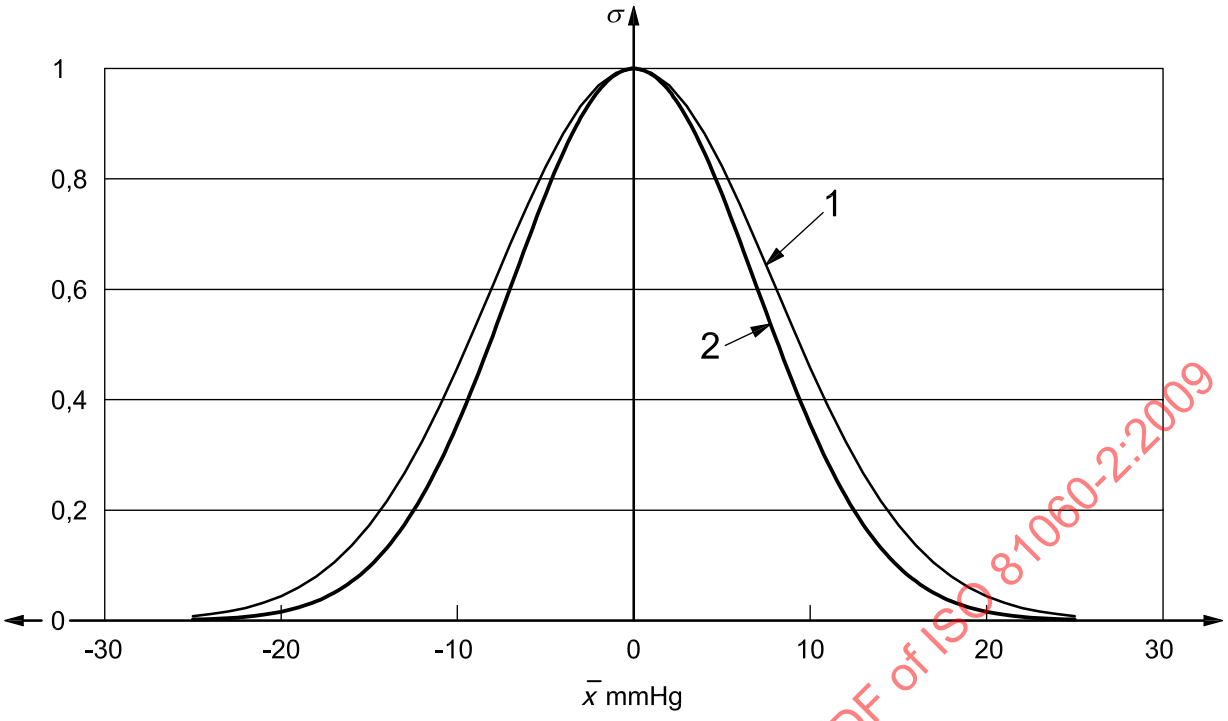
Criterion 1 uses the 255 individual test-**reference** differences to determine the performance of the **sphygmomanometer-under-test**. As a result, the calculated standard deviation, s_n, (or precision) will reflect both intra-subject and inter-subject variability. However, the allowable s_n is independent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

Criterion 2 uses the average error 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 vs. s_m = 6,95 mmHg), 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 mmHg, as shown in Figure A.2. Criterion 1 requires an $s_n \leqslant$ 8,00 mmHg, while Criterion 2 requires an $s_m \leqslant$ 4,81 mmHg.

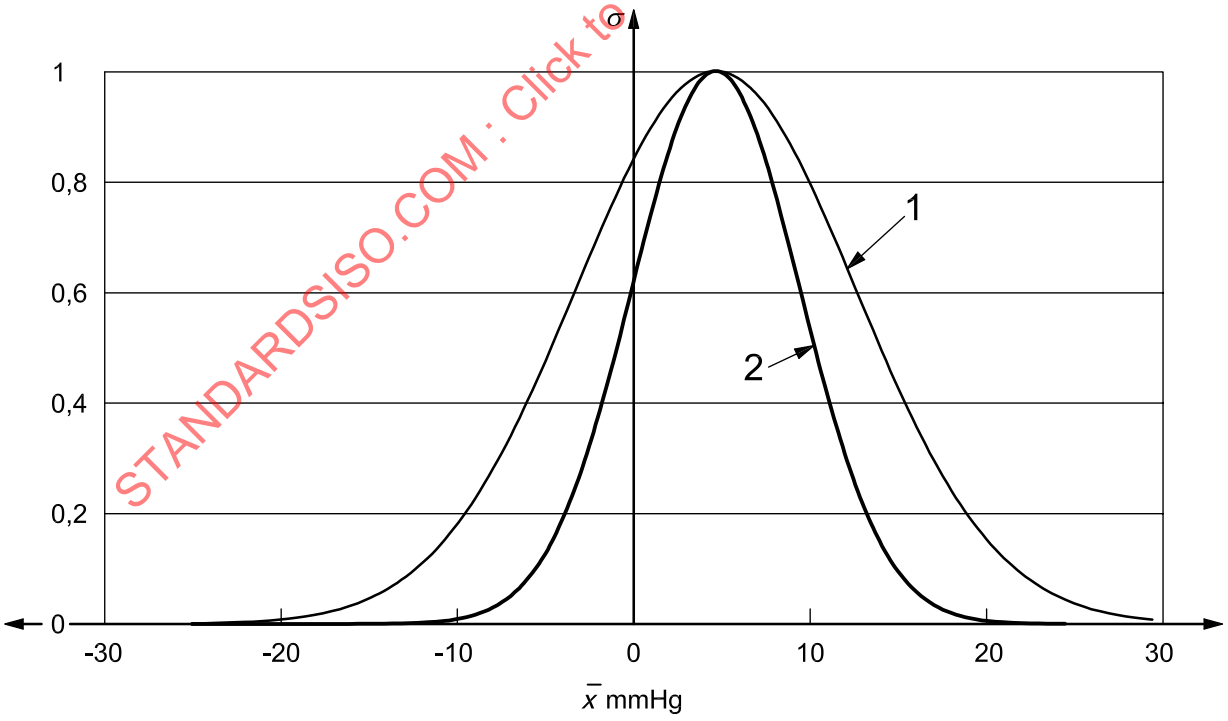
In summary, Criterion 1 evaluates the effect on both intra- and inter-subject variability, but allows for a relatively large error when the bias is large. Criterion 2 does not measure intra-subject variability, but reduces the allowable s_n over the range of allowable $\bar{x}_n$. The use of both criteria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



Key
1 criterion 1
2 criterion 2

NOTE The mean error of the determinations = 0.

Figure A.1 — Allowable standard deviation for each criterion when the mean error is zero



Key
1 criterion 1
2 criterion 2

NOTE The mean error of the determinations = 5 mmHg.

Figure A.2 — Allowable standard deviation for each criterion when the mean error is 5 mmHg

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.

One assumption of this method is that averaging the three values from each subject helps to reduce an apparent error caused by changes in the subject's **blood pressure** during the sequence of **blood pressure** determinations. This reduction in error is reduced if fewer determinations from each subject are used.

Relaxing the requirement for exactly three determinations per subject, but maintaining the requirement for 255 determinations, requires additional subjects to complete a study. The use of differing numbers of determinations per subject results in 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.

5.2.4.2 Same arm sequential method

Since the determinations are carried out in temporal succession, it is important that haemodynamically stable conditions exist during the testing period. The working group had some concern that this condition could be difficult to achieve in hypertensive **patients**. The use of smaller differences (4 mmHg and 6 mmHg) between consecutive determinations was also discussed, but there was concern that this would cause too many exclusions.

5.2.4.3.1 Procedure

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. This can be due to the use of a 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

The advantage of the same arm sequential method (see 5.2.4.2) is that validation results are not as affected by lateral difference, LD, in **blood pressure**. However, in this method, **blood pressure** variability (BPV) is added to **sphygmomanometer-under-test** error and therefore the standard deviation of **sphygmomanometer-under-test** error could be overestimated. This hypothesis was experimentally supported by this committee'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.

Other 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 **reference sphygmomanometer** to **sphygmomanometer-under-test** comparisons. However, via the same experiment by the committee, 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.

The 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 **reference sphygmomanometer** to **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 method are:

— the experimental time needed per subject is considerably shorter in comparison with the conventional opposite arm simultaneous method (six vs. nine determinations except preparatory measurement);

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

Modification of the number of repetitions per subject could be attempted. However, the committee 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 lateral difference. If the repetition was 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 validation requirements for exercise stress testing were chosen to assess a **sphygmomanometer** during simulated activity and motion. Achieving a target heart rate of 50 % to 70 % of a subject's average maximum 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 needed to cause such a heart rate should not result in a motion artefact so severe as to render the data unacceptable. See Reference [17].

6.1.2 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. See References [42] and [43]. 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 y of age has been adjusted to 3 y of age, consistent with Korotkoff sound physiology (see rationale to 5.1.3). Table A.1 shows the suggested FDA guidance paediatric subgroups.

Table A.1 — 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 y of age
Child	> 2 y to 12 y of age
Adolescent	> 12 y to 21 y 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 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 evaluated 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 determination of the intra-arterial **reference** requires the use a computerized data collection system or a multi-channel strip-chart recorder (DCS). 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 error. All calibration records should be kept on a DCS. The static calibration of both the invasive and the **sphygmomanometer-under-test** should be within ± 2 mmHg 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 taken immediately (e.g., flushing or adjusting the position of the catheter).

The **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 pressure transducer and the **cuff** causes an offset error of 1 mmHg in measured pressure between the two readings. Both the **cuff** and transducer should be at the level 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 radial **reference** data will have clinical validity for the diagnosis of hypertension, i.e., all morbidity/mortality data are based on brachial artery pressures, which are not equivalent to radial artery pressures. However, it is recognized that the more frequent use of radial artery catheters for invasive pressure measurement in the operating theatre and intensive care unit reduces the difficulty of obtaining **patients** for a study. See Reference [3].

The lateral difference, LD, measurement can be made using a previously validated **automated sphygmomanometer**. The LD should be determined by simultaneous determinations on both limbs (using two identical **automated sphygmomanometers**). However, LD can also be determined using a single **automated sphygmomanometer** and alternating the site of measurement between the two limbs.