INTERNATIONAL STANDARD

ISO 81060-3

First edition
2022-12

Non-invasive sphygmomanometers —

Part 3: Clinical investigation of continuous automated measurement type

Sphygmomanomètres non invasifs —

Partie 3: Investigation clinique pour type à mesurage automatique continu

Reference number
ISO 81060-3:2022(E)

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

Published in Switzerland

Contents

Page

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 or www.iec.ch/members_experts/refdocs).

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 https://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. In the IEC, see www.iec.ch/understanding-standards.

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 62D, *Electromedical equipment*, in collaboration with the European Committee for Standardization (CEN) Technical Committee CEN/TC 205, *Non-active medical devices*, in accordance with the Agreement on technical cooperation between ISO and CEN (Vienna Agreement).

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

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 and www.iec.ch/national-committees.

Introduction

The number of continuously measuring non-invasive *automated sphygmomanometers* has increased significantly in the last 10 years. This document is intended to provide the necessary requirements for *clinical investigation* to ensure that the *essential performance* of these *sphygmomanometers* is at an adequate level, similar to those standards on *intermittent automated non-invasive sphygmomanometer*.

Non-invasive sphygmomanometers —

Part 3:
Clinical investigation of continuous automated measurement type

1 Scope

This document specifies the requirements and methods for the *clinical investigation* of *continuous automated non-invasive sphygmomanometers* used for the measurement of the *blood pressure* of a patient.

This document does not cover usability aspects such as the form and manner of the data display or output. This document does not specify a numerical threshold on the *minimum output period*. A *continuous automated non-invasive sphygmomanometer* providing *blood pressure* parameters (e.g., *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*) with an *output period* considerably larger than 30 s is not typically considered a *continuous automated non-invasive sphygmomanometer*.

This document covers both trending *continuous automated non-invasive sphygmomanometers* and absolute accuracy *continuous automated non-invasive sphygmomanometers* and focuses solely on requirements for the *clinical investigation*. Representation of output is not covered by this document.

NOTE 1 IEC 62366-1 provides requirements on the application of usability engineering to medical devices. The usability engineering *process* can be used to clarify for the intended user whether the displayed data concerns absolute accurate values or trending values.

The requirements and methods for the *clinical investigation* of *continuous automated non-invasive sphygmomanometers* provided in this document are applicable to any subject population, and any condition of use of the *continuous automated non-invasive sphygmomanometers*.

NOTE 2 Subject populations can, for example, be represented by age or weight ranges.

NOTE 3 This document does not provide a method to assess the effect of artefacts during the *clinical investigation* (e.g. motion artefacts induced by the movement of the subject or the movement of the platform supporting the subject).

This document specifies additional disclosure requirements for the *accompanying documents* of *continuous automated non-invasive sphygmomanometers* that have undergone *clinical investigation* according to this document.

This document is not applicable to:

— the *clinical investigation* of a *non-automated sphygmomanometer* as given in ISO 81060-1,

— the *clinical investigation* of an *intermittent automated non-invasive sphygmomanometer* as given in ISO 81060-2,

— an *automated non-invasive sphygmomanometer* as given in IEC 80601-2-30, 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.

ISO 14155:2020, *Clinical investigation of medical devices for human subjects — Good clinical practice*

ISO 14971:2019, *Medical devices — Application of risk management to medical devices*

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

ISO 81060-2:2018+Amd 1:2020, *Non-invasive sphygmomanometers — Part 2: Clinical investigation of intermittent automated measurement type*

IEC 60601-1:2005+AMD1:2012+AMD2:2020, *Medical electrical equipment — Part 1: General requirements for basic safety and essential performance*

IEC 60601-2-34:2011, *Medical electrical equipment — Part 2-34: Particular requirements for the safety, including 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 14155:2020, ISO 14971:2019, ISO 81060-1:2007, ISO 81060-2:2018+Amd 1:2020, IEC 60601-1:2005+AMD1:2012+AMD2:2020, IEC 60601-2-34:2011, IEC 80601-2-30:2018, and the following apply.

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

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

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

3.1
change evaluation interval
time period for which a *continuous automated non-invasive sphygmomanometer* is demonstrated to track changes in *blood pressure*

3.2
continuous automated non-invasive sphygmomanometer
ME equipment estimating *blood pressure* from each cardiac cycle without arterial puncture and providing a continual series of *blood pressure* parameters

Note 1 to entry: While the *continuous automated non-invasive sphygmomanometer* analyses each heart cycle, this does not mean the *continuous automated non-invasive sphygmomanometer* always uses data from each heart cycle to estimate the *blood pressure*. Not using data from a specific heart cycle can be useful, for example, to omit data from premature ventricular contractions.

Note 2 to entry: The only *blood pressure* parameters considered in this document are *systolic blood pressure*, *diastolic blood pressure* and *mean arterial pressure*.

Note 3 to entry: This document does not cover usability aspects such as the form and manner of the data display or output. Hence, this document does not specify a numerical threshold on the *minimum output period*. However, a *continuous automated non-invasive sphygmomanometer* providing *blood pressure* parameters (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*) with an *output period* considerably larger than 30 s are not typically considered a *continuous automated non-invasive sphygmomanometer*.

Note 4 to entry: There is guidance or rationale for this definition contained in Clause A.2.

3.3
determination
determination value
result of the *process* of estimating *blood pressure* by the *continuous automated non-invasive sphygmomanometer*

[SOURCE: IEC 80601-2-30:2018, 201.3.203; modified: replaced *automated sphygmomanometer* by *continuous automated non-invasive sphygmomanometer*]

3.4
initialization
re-initialization
process of the *continuous automated non-invasive sphygmomanometer* to determine subject- or condition-specific parameters needed to estimate *blood pressure*

Note 1 to entry: In this document, the term *initialization* is used for the initial *initialization; re-initialization* is used for the repeated *initialization process* during the measurement period.

3.5
intermittent automated non-invasive sphygmomanometer
ME equipment estimating *blood pressure* from a number of cardiac cycles without arterial puncture and providing a single set of *blood pressure* parameters

Note 1 to entry: The only *blood pressure* parameters considered in this document are *systolic blood pressure*, *diastolic blood pressure* and *mean arterial pressure*.

Note 2 to entry: There is guidance or rationale for this definition contained in Clause A.2.

3.6
output period
period of time after which a specific *continuous automated non-invasive sphygmomanometer* provides updated values for *blood pressure* parameters (e.g. *systolic blood pressure, diastolic blood pressure* or *mean arterial pressure*)

Note 1 to entry: The *output period* may be constituted by a number of heart beats.

3.7
paired measurements
two measurements of a subject's *blood pressure*, one of which is recorded with the *continuous automated non-invasive sphygmomanometer* and the other with the *reference* method from the same cardiac cycles

Note 1 to entry: The two measurements of *blood pressure* can be two measurements of *systolic blood pressure*, two measurements of *diastolic blood pressure* or two measurements of *mean arterial pressure*.

3.8
paired values
pair of *blood pressure* values as a result of a *paired measurement*

Note 1 to entry: The pair of *blood pressure* values can be a pair of *systolic blood pressure*, a pair of *diastolic blood pressure* or a pair of *mean arterial pressure* values.

3.9
reference measurement
procedure with established accuracy used for the *clinical investigation* of a *continuous automated non-invasive sphygmomanometer*

3.10
reference reading
result of the *process* of measuring *blood pressure* using a *reference* method

Note 1 to entry: The result can be a *systolic blood pressure*, a *diastolic blood pressure* or a *mean arterial pressure*.

4 General requirements for the *clinical investigation*

4.1 Good clinical practice

The *clinical investigation* shall conform with the requirements of ISO 14155.

NOTE Some authorities having jurisdiction can have additional requirements.

Check conformance by application of the requirements of ISO 14155.

4.2 General

NOTE 1 There is guidance or rationale for this subclause contained in Clause A.2.

a) The conditions of the *clinical investigation* shall represent as closely as possible the intended conditions of use of the *continuous automated non-invasive sphygmomanometers.*

   1) If a target population is specified in the instructions for use, the subjects of the *clinical investigation* shall represent that target population as closely as possible.

      NOTE 2 Since a *clinical investigation* as described in this document requires an invasive *reference, reference invasive blood pressure monitoring equipment* will be inserted in all subjects included in the *clinical investigation*. However, some target populations for the *continuous automated non-invasive sphygmomanometers* can include patients who would not be monitored by *reference invasive blood pressure monitoring equipment* (e.g. invasive monitoring is contraindicated or not recommended for the patient's critical care due to local infection at site, prior surgery/stents in intended vasculature, etc.). Therefore, there is a limit as to how representative the subjects of the *clinical investigation* can be for the target population.

b) For the *clinical investigation*, different postures (e.g. supine or sitting) shall be evaluated to determine if they affect the performance of the *continuous automated non-invasive sphygmomanometer*.

   1) If different postures affect the performance of the *continuous automated non-invasive sphygmomanometer*, any *clinical investigation* shall be performed with all subjects in the same posture.

c) Set up the *continuous automated non-invasive sphygmomanometer* according to the instructions for use.

d) *Continuous automated non-invasive sphygmomanometers* that continuously and non-invasively provide accurate *blood pressure determinations* are classified as Type A.

e) In contrast to Type A, *continuous automated non-invasive sphygmomanometers* that continuously and non-invasively provide *blood pressure* values that can have an unknown constant subject-specific offset are classified as Type T.

   NOTE 3 Type T *continuous automated non-invasive sphygmomanometers* (trending *continuous automated non-invasive sphygmomanometers*) provide *blood pressure* values that are not intended to be absolutely accurate. However, since these *blood pressure* values have an unknown constant subject-specific offset, these *continuous automated non-invasive sphygmomanometers* enable representations of accurate *blood pressure* changes over time.

   NOTE 4 Since the *blood pressure* values provided by Type T *continuous automated non-invasive sphygmomanometers* (trending *continuous automated non-invasive sphygmomanometers*) have an unknown constant subject-specific offset, users of the *continuous automated non-invasive sphygmomanometers* could be misled to think the values displayed on the screen are intended to be absolutely accurate, when in reality they are not. This document does not cover usability study that would be used to address this matter.

f) *Continuous automated non-invasive sphygmomanometer* tests shall be performed according to Table 1.

g) If *initialization* of the *continuous automated non-invasive sphygmomanometer* is necessary, the *reference* device may not be used for this *initialization* during the *clinical investigation*.

Table 1 provides different sets of tests for Type A and Type T *continuous automated non-invasive sphygmomanometers*.

Table 1 — Applicable testing depending on functionality

		Type A	Type T
Performance assessments	5.1 Method for the accuracy of *blood pressure determination*	applicable	—
	5.2 Method for stability	applicable	applicable
	5.3 Method for *blood pressure* changes	applicable	applicable

4.3 *Reference* method

4.3.1 *Reference invasive blood pressure monitoring equipment*

NOTE 1 There is guidance or rationale for this subclause contained in Clause A.2.

a) A *continuous automated non-invasive sphygmomanometer* shall be clinically investigated by using *reference invasive blood pressure monitoring equipment*.

b) *Reference invasive blood pressure monitoring equipment* shall conform with the requirements of IEC 60601-2-34.

c) The natural frequency and damping coefficient of the *reference invasive blood pressure monitoring equipment* shall be examined and optimised to meet dynamic requirements for each subject. See Reference [1].

d) The *reference invasive blood pressure monitoring equipment* shall be referenced to the level of the right atrium.

e) Appropriate measures shall be taken to remove air bubbles and clots from the system prior to taking the *reference measurements*.

NOTE 2 The ability to accurately measure *blood pressure* could be degraded by the presence of air bubbles or blood clots in the catheter/transducer system.

f) *Reference invasive blood pressure monitoring equipment* that does not directly output the *blood pressure* waveform or beat-to-beat data may be modified to permit such data collection.

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

4.3.2 Subject requirements

4.3.2.1 Number

NOTE There is guidance or rationale for this subclause contained in Clause A.2.

a) A *clinical investigation* shall consist of repeated measurements performed on test subjects.

b) The number of repeated measurements per subject shall be determined according to the *procedure* in 4.5.3.

c) The number of subjects shall be determined according to the *procedure* in 4.5.3.

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

4.3.2.2 Gender distribution

NOTE There is guidance or rationale for this subclause contained in Clause A.2.

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

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

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

4.3.2.3 Age distribution

NOTE There is guidance or rationale for this subclause contained in Clause A.2.

4.3.2.3.1 General

If a *continuous automated non-invasive sphygmomanometer* is intended for use in more than one of the age groups defined in 4.3.2.3.2, 4.3.2.3.3 and 4.3.2.3.4, each applicable age group shall be investigated separately.

4.3.2.3.2 *Sphygmomanometers* intended for use in subjects aged greater than 12 years

For a *continuous automated non-invasive sphygmomanometer* intended for use in subjects aged greater than 12 years, the age of every subject included in the *clinical investigation* shall be greater than 12 years, with the following age distribution:

a) 40 % shall be at least 50 years of age;

b) 25 % shall be at least 60 years of age; and

c) 10 % shall be at least 70 years of age.

Check conformance by inspection of the *accompanying document* and the *clinical investigation report*.

4.3.2.3.3 *Sphygmomanometers* intended for use in subjects aged between 1 year and 12 years

a) For a *continuous automated non-invasive sphygmomanometer* intended for use in subjects aged between 1 year and 12 years, the age of every subject included in the *clinical investigation* shall be between 1 year and 12 years.

b) Subjects aged between 1 year and 12 years are exempt from

   1) the gender distribution requirements of 4.3.2.2, and

   2) the *blood pressure* distribution requirements of 4.3.3.

Check conformance by inspection of the *accompanying document* and the *clinical investigation report*.

4.3.2.3.4 *Sphygmomanometers* intended for use in subjects of less than 1 year of age

a) A *continuous automated non-invasive sphygmomanometer* intended for use in subjects of less than 1 year of age, shall be investigated in that subject population.

b) The following age or weight ranges are required for a *clinical investigation* of *continuous automated non-invasive sphygmomanometers* intended for use in subjects of less than 1 year of age:

   1) at least 20 % of the subjects shall be less than 2 000 g in weight;

   2) at least 20 % of the subjects shall be 2 000 g to 3 000 g in weight;

   3) at least 20 % of the subjects shall be more than 3 000 g in weight; and

4) at least 20 % of the subjects shall be at least 29 days of age.

c) The remaining subjects may be from any of the above age or weight groups in order to fulfil the sample size requirement.

NOTE A subject can be in more than one category simultaneously.

d) Subjects of less than 1 year of age are exempt from

1) the gender distribution requirements of 4.3.2.2, and

2) the *blood pressure* distribution requirements of 4.3.3.

Check conformance by inspection of the *accompanying document* and the *clinical investigation report*.

4.3.2.4 Special subject populations

NOTE There is guidance or rationale for this subclause contained in Clause A.2.

a) When there is evidence that a certain subject characteristic might affect the performance of a *continuous automated non-invasive sphygmomanometer*, and if this is within its *intended use*, that population (which is well defined by such subject characteristics) shall be considered a special subject population.

b) The *continuous automated non-invasive sphygmomanometer* shall be investigated across the range of the subject characteristics that is within its *intended use*.

c) Unless otherwise justified, each special subject population identified shall be investigated separately.

d) The instructions for use of the *continuous automated non-invasive sphygmomanometer* shall disclose a summary of the definition of all special subject populations identified per clause 4.3.2.4 a).

Check conformance by inspection of the *accompanying document* and the *clinical investigation report*.

4.3.3 *Blood pressure* distribution

For the data included in the analysis of the method for the accuracy of *blood pressure determination* (see 5.1) the following requirements apply.

a) If the *continuous automated non-invasive sphygmomanometer* is intended to output *systolic blood pressure*, the following shall be fulfilled.

1) At least 5 % of the *reference readings* shall have a *systolic blood pressure* less than or equal to 90 mmHg (12,00 kPa).

2) At least 20 % of the *reference readings* shall have a *systolic blood pressure* less than or equal to 110 mmHg (14,67 kPa).

3) At least 20 % of the *reference readings* shall have a *systolic blood pressure* greater than 110 mmHg (14,67 kPa) and less than 140 mmHg (18,67 kPa).

4) At least 20 % of the *reference readings* shall have a *systolic blood pressure* greater than or equal to 140 mmHg (18,67 kPa).

5) At least 5 % of the *reference readings* shall have a *systolic blood pressure* greater than or equal to 160 mmHg (21,33 kPa).

b) If the *continuous automated non-invasive sphygmomanometer* is intended to output *diastolic blood pressure*, the following shall be fulfilled.

1) At least 5 % of the *reference readings* shall have a *diastolic blood pressure* less than or equal to 50 mmHg (6,67 kPa).

2) At least 20 % of the *reference readings* shall have a *diastolic blood pressure* less than or equal to 60 mmHg (8,00 kPa).

3) At least 20 % of the *reference readings* shall have a *diastolic blood pressure* greater than 60 mmHg (8,00 kPa) and less than 80 mmHg (10,67 kPa).

4) At least 20 % of the *reference readings* shall have a *diastolic blood pressure* greater than or equal to 80 mmHg (10,67 kPa).

5) At least 5 % of the *reference readings* shall have a *diastolic blood pressure* greater than or equal to 90 mmHg (12,00 kPa).

c) If the *continuous automated non-invasive sphygmomanometer* is intended to output *mean arterial pressure*, the following shall be fulfilled.

1) At least 5 % of the *reference readings* shall have a *mean arterial pressure* less than or equal to 65 mmHg (8,67 kPa).

2) At least 20 % of the *reference readings* shall have a *mean arterial pressure* less than or equal to 75 mmHg (10,00 kPa).

3) At least 20 % of the *reference readings* shall have a *mean arterial pressure* greater than 75 mmHg (10,00 kPa) and less than 100 mmHg (13,33 kPa).

4) At least 20 % of the *reference readings* shall have a *mean arterial pressure* greater than or equal to 100 mmHg (13,33 kPa).

5) At least 5 % of the *reference readings* shall have a *mean arterial pressure* greater than or equal to 115 mmHg (15,33 kPa).

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

4.3.4 Arterial *reference* site

NOTE 1 There is guidance or rationale for this subclause contained in Clause A.2.

a) Any *reference* site may be used for simultaneous comparison of intra-arterial *blood pressure* readings and *continuous automated non-invasive sphygmomanometer blood pressure determinations*.

NOTE 2 Different sites can produce different results due to the pressure difference between the central aorta and other arteries.

b) The instructions for use of the *continuous automated non-invasive sphygmomanometer* shall disclose the arterial site used as the *reference* site;

NOTE 3 While this document does not address technical requirements, it is expected that any values output by the *continuous automated non-invasive sphygmomanometer* always correspond to the *reference site* chosen. This does, however, not mean that the *continuous automated non-invasive sphygmomanometer blood pressure determinations* need to be taken at the same site as the *reference* site.

c) The lateral difference in *blood pressure* may be established.

1) If the lateral difference is determined, it shall be determined in accordance with 4.4.

2) If the lateral difference is determined, subjects shall be excluded if:

   i) the average lateral difference of the auscultatory *systolic blood pressure* readings is more than 15 mmHg (2,00 kPa), or

   ii) the average lateral difference of the auscultatory *diastolic blood pressure* readings is more than 10 mmHg (1,33 kPa).

   NOTE 4 High lateral differences are an indication that this subject might have a stenosis in one artery.

d) Application of lateral difference for adjustment of data in accordance with 4.4.4 may be used.

   1) However, as described in 4.4.1 a), if adjustments for the lateral difference are made, the same *procedure* shall be applied to all subjects for which the *continuous automated non-invasive sphygmomanometer determinations* are intended to be an estimate of the opposite limb of the *reference* site.

   NOTE 5 There is no method in this document to adjust for lateral difference of *mean arterial pressure*.

Check conformance by inspection of the *accompanying document*.

4.4 Lateral difference

4.4.1 General

a) Any lateral differences shall be determined by non-invasive auscultatory readings.

   1) The *reference sphygmomanometer* used in this *procedure* shall be in accordance with ISO 81060-1, except that the maximum permissible error shall be ±1 mmHg (0,13 kPa).

b) If the *reference readings* and *continuous automated non-invasive sphygmomanometer determinations* are representing opposite arms, the lateral difference may be:

   1) calculated for each subject; and

   2) used to adjust the differences x_j in 5.1.3 as well as the differences x_j and x_j,T in 5.2.3.

      i) If adjustments for the lateral difference are made, the same *procedure* shall be applied to all subjects for which *reference readings* and *continuous automated non-invasive sphygmomanometer determinations* are representing opposite arms.

c) If the lateral difference is determined, either the sequential *procedure* (see 4.4.2) or the simultaneous *procedure* (see 4.4.3) shall be applied in accordance with the following *procedure*.

   1) Measurement of the upper mid-arm circumference.

      i) 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 ° at the elbow with the palm facing up.

      ii) The subject's upper mid-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.

   2) *Cuffs* for the *sphygmomanometer* used to determine the auscultatory readings shall have:

      i) a *bladder* length of 75 % to 100 % of the upper mid-arm circumference, and

      ii) a *bladder* width of 37 % to 50 % of the upper mid-arm circumference.

   3) Before the first auscultatory reading is taken, the subject should rest for at least 5 min.

4) Two observers shall simultaneously determine the *blood pressure* on each subject using a stethoscope that allows listening simultaneously to the Korotkoff sounds (e.g. a double stethoscope).

5) Any pair of observers' individual values of an auscultatory measurement with a difference greater than 4 mmHg (0,53 kPa) shall be excluded.

6) The observers' individual values of each auscultatory measurement shall be averaged according to Formula (1) to create the auscultatory reading.

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

where

$P_{\mathrm{aus}_{i,1}}$ is the *blood pressure* determined by observer 1 for the i^{th} *measurement*;

$P_{\mathrm{aus}_{i,2}}$ is the *blood pressure* determined by observer 2 for the i^{th} *measurement*; and

P_{aus_i} is the auscultatory reading for the i^{th} *measurement.*

7) When reading the value on the *sphygmomanometer* used to determine the auscultatory readings, the observers should avoid parallax errors and rounding.

NOTE Rounding has a negative effect on the results of the *clinical investigation*.

d) Calculate the lateral difference, d_{l}, separately for *systolic blood pressure* or *diastolic blood pressure*, according to Formula (2).

$$d_{\mathrm{l}} = \frac{1}{3} \cdot \left(\sum_{m=1}^{3} P_{\mathrm{aus\_R}_m} - \sum_{n=1}^{3} P_{\mathrm{aus\_L}_n} \right) \quad (2)$$

where $P_{\mathrm{aus\_R}_m}$ and $P_{\mathrm{aus\_L}_n}$ are auscultatory readings in the right (R) arm and left (L) arm, respectively.

4.4.2 Sequential *procedure*

a) Alternate the starting arm side between subjects.

b) Have two observers determine the subject's *blood pressure* in the starting arm.

c) Wait at least 60 s from the completion of the previous measurement.

d) Have two observers determine the subject's *blood pressure* in the opposite arm.

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

f) Repeat b) to e) until 3 auscultatory readings on the right arm $P_{\mathrm{aus\_R}_m}$ and 3 auscultatory readings on the left arm $P_{\mathrm{aus\_L}_n}$ have been gathered.

4.4.3 Simultaneous *procedure*

a) Determine the subject's *blood pressure* simultaneously in both arms with two observers per arm.

b) Wait at least 60 s from the completion of the previous measurement.

c) Repeat a) and b) until 3 auscultatory readings on the right arm $P_{\mathrm{aus\_R}_m}$ and 3 auscultatory readings on the left arm $P_{\mathrm{aus\_L}_n}$ have been gathered.

4.4.4 Application of lateral difference

a) Depending on from which arm the *reference reading* was taken, the correction of Formula (3) or Formula (4) is carried out for the difference of the individual *paired values* separately for *systolic blood pressure* or *diastolic blood pressure*.

b) Calculate the *continuous automated non-invasive sphygmomanometer* error, x, by taking the difference between the *continuous automated non-invasive sphygmomanometer blood pressure* and the *reference sphygmomanometer blood pressure* and by adding the lateral difference, d_l, as calculated according to Formula (3) if the *continuous automated non-invasive sphygmomanometer blood pressure* was taken in the left arm or by subtracting the lateral difference, d_l, as calculated according to Formula (4) if the *continuous automated non-invasive sphygmomanometer blood pressure* was taken in the right arm.

$$x = P_{\text{sut\_L}} - P_{\text{ref\_R}} + d_l \tag{3}$$

$$x = P_{\text{sut\_R}} - P_{\text{ref\_L}} - d_l \tag{4}$$

where

$P_{\text{sut\_R}}$ and $P_{\text{sut\_L}}$ are *continuous automated non-invasive sphygmomanometer blood pressures* in the right (R) arm and the left (L) arm, respectively; and

$P_{\text{ref\_R}}$ and $P_{\text{ref\_L}}$ are *reference readings* in the right (R) arm and the left (L) arm, respectively.

4.5 Statistical considerations

4.5.1 General

a) The method for the accuracy of *blood pressure determination* of the *continuous automated non-invasive sphygmomanometer* shall be based on r repeated *paired measurements* performed on k subjects.

1) For the method for the accuracy of *blood pressure determination* in 5.1, r and k shall be chosen so that $N_{\text{ind}} \geq 278$ [see Formula (6)].

2) For the method for stability in 5.2 the number of:

i) repeated *paired measurements* per subject shall be the same r as in 5.1; and

ii) subjects shall be at least k.

3) For the method for *blood pressure* changes in 5.3 the number of subjects shall be at least k.

NOTE 1 Measurements performed on different subjects are generally completely independent.

NOTE 2 *Continuous automated non-invasive sphygmomanometers* are able to perform repeated measurements on the same subject. Repeated measurements on the same subject are never completely independent, but are usually also not completely dependent.

b) The following additional requirements shall be met by the *clinical investigation*:

1) the number of repeated *paired measurements* per subject, r, shall be equal for each subject;

2) the number of repeated *paired measurements* per subject, r, shall be lower than the number of subjects, k; and

3) the number of subjects, k, shall be at least 30.

4.5.2 Intra-class correlation coefficient and number of independent measurements

The intra-class correlation coefficient, I_{cc}, compares the between subject and within subject variances, thus quantifying the distribution of errors that are sampled by measuring on multiple subjects versus repeated measures on the same subject as shown by Formula (5).

$$I_{CC} = \frac{\frac{\mu_{SB} - \mu_{SW}}{f_{BA}}}{\frac{\mu_{SB} - \mu_{SW}}{f_{BA}} + \mu_{SW}} \tag{5}$$

where

f_{BA} is a Bland-Altman factor calculated according to Formula (10);

μ_{SB} is the mean of the squares between subjects calculated according to Formula (11); and

μ_{SW} is the mean of the squares within subjects calculated according to Formula (12).

The number of independent measurements, N_{ind}, obtained by performing r repeated measurements on k subjects with a *continuous automated non-invasive sphygmomanometer* with an intra-class correlation coefficient is given by Formula (6).

$$N_{ind} = k(1+(1-I_{CC})(r-1)) \tag{6}$$

where

I_{CC} is the intra-class correlation coefficient according to Formula (5);

r is the number of repeated *paired measurements* per subject; and

k is the number of subjects.

4.5.3 *Procedure* to derive the number of subjects and number of repeated *paired measurements* per subject

a) To determine the number of repeated *paired measurements* and subjects, the following *procedure* shall be performed.

1) Estimate the intra-class correlation coefficient for the *continuous automated non-invasive sphygmomanometer* for each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*);

NOTE 1 The intra-class correlation coefficient is usually estimated based on prior knowledge, e.g. available data, or based on results from *clinical investigations* performed on similar technology.

NOTE 2 For Type T *continuous automated non-invasive sphygmomanometers*, estimation of the intra-class correlation coefficient, I_{cc_est}, based on prior knowledge and calculation of the intra-class correlation coefficient, I_{cc}, is done without subtracting any subject-specific offsets.

2) Choose the maximum intra-class correlation coefficient, I_{cc_est}, from all intra-class correlation coefficients estimated in 1).

3) Determine the number of repeated *paired measurements* per subject, r.

4) Determine the number of subjects, k, for the maximum intra-class correlation coefficient chosen in 2) from:

i) Formula (6); or

ii) Table 2,

such that $N_{ind} \geq 278$.

Table 2 — Relationship between *r* and the minimum *k* depending on the estimated intra-class correlation coefficient

$I_{cc\_est} \leq 0{,}6$		$0{,}6 < I_{cc\_est} \leq 0{,}7$		$0{,}7 < I_{cc\_est} \leq 0{,}8$		$0{,}8 < I_{cc\_est} \leq 0{,}9$		$0{,}9 < I_{cc\_est} \leq 0{,}95$		$0{,}95 < I_{cc\_est} \leq 0{,}98$		$0{,}98 < I_{cc\_est} \leq 0{,}99$		$0{,}99 < I_{cc\_est} \leq 1{,}0$	
r	*k*	*r*	*k*	*r*	*k*	*r*	*k*	*r*	*k*	*r*	*k*	*r*	*k*	*r*	*k*
1	278	1	278	1	278	1	278	1	278	1	278	1	278	1	278
10	60	10	75	10	99	10	146	10	192	10	236	10	255	10	278
20	32	20	41	20	58	20	96	20	143	20	201	20	234	20	278
22	30	29	30	30	41	30	71	30	113	30	176	30	216	30	278
-	-	-	-	35	36	40	57	40	94	40	156	40	200	40	278
-	-	-	-	-	-	48	49	50	81	50	140	50	187	50	278
-	-	-	-	-	-	-	-	60	70	60	128	60	175	60	278
-	-	-	-	-	-	-	-	65	66	70	117	70	164	70	278
-	-	-	-	-	-	-	-	-	-	80	108	80	155	80	278
-	-	-	-	-	-	-	-	-	-	90	100	90	147	90	278
-	-	-	-	-	-	-	-	-	-	95	97	100	140	100	278
-	-	-	-	-	-	-	-	-	-	-	-	110	133	110	278
-	-	-	-	-	-	-	-	-	-	-	-	120	127	120	278
-	-	-	-	-	-	-	-	-	-	-	-	124	125	130	278

5 Methods for *clinical investigation*

5.1 Method for the accuracy of *blood pressure determination*

5.1.1 General

a) Set up the *continuous automated non-invasive sphygmomanometer* according to the instructions for use.

b) Select the control settings of the *continuous automated non-invasive sphygmomanometer* reflecting the worst case for the accuracy of *blood pressure determination*. The worst case control settings shall include selection of the minimum *output period*.

c) The number of repeated *paired measurements*, *r*, and the number of subjects, *k*, shall be determined in accordance with 4.5.

5.1.2 *Procedure*

a) For each subject, the following *procedure* shall be performed:

b) For each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure, diastolic blood pressure* or *mean arterial pressure*) simultaneously record beat-to-beat data obtained with the *reference invasive blood pressure monitoring equipment* and the output values of the *continuous automated non-invasive sphygmomanometer* at the minimum *output period.*

NOTE The intent is to simultaneously record data from the same cardiac cycles.

5.1.3 Data analysis

NOTE 1 There is guidance or rationale for this subclause contained in Clause A.2.

For the data of each subject, perform the following *procedure*:

a) Divide the data recorded from the *reference invasive blood pressure monitoring equipment* into non-overlapping segments of approximately equal duration.

   1) he segment duration shall match the minimum *output period* specific to the *continuous automated non-invasive sphygmomanometer* as closely as possible.

   2) The end time of each segment shall match as closely as possible the initial time the respective output value is provided by the *continuous automated non-invasive sphygmomanometer.*

      NOTE 2 This document does not address usability aspects, such as time delays, of *continuous automated non-invasive sphygmomanometers*.

b) For each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*), perform the following:

   1) If the segment contains more than one *reference reading*, average the *reference readings* of each segment.

      NOTE 3 In some *continuous automated non-invasive sphygmomanometers* the segment duration equates to one cardiac cycle which makes averaging unnecessary.

   2) Match the (averaged) *reference reading* with the output value provided by the *continuous automated non-invasive sphygmomanometer* at the end of the segment. This results in one set of *paired values* of (averaged) *reference reading* and output value for each segment.

c) Without considering values provided by the *continuous automated non-invasive sphygmomanometer* select *r* non-overlapping segments for analysis such that the *reference readings* conform with 4.3.3.

d) No *re-initialization* shall occur within the *r* non-overlapping segments.

e) For each selected segment, *j*, and for each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*), calculate the difference, x_j, of the *paired values* as given by Formula (7):

$$x_j = P_{\mathrm{sut}_j} - P_{\mathrm{ref}_j} \tag{7}$$

f) For each *blood pressure* parameter (i.e., *systolic blood pressure*, *diastolic blood pressure*, and *mean arterial pressure*), the *clinical investigation report* shall include a scatter plot for the data included in the accuracy analysis, where the Y axis shows all *reference blood pressure* values (in mmHg or kPa) and the X axis shows the time elapsed (in s) between the *re-initialization* and the time the *reference blood pressure* values were measured at.

NOTE 4 These plots help to visualize whether certain ranges of *reference blood pressure* values were chosen close to the *initialization* time of the *continuous automated non-invasive sphygmomanometer*.

5.1.4 Acceptance criteria

NOTE 1 There is guidance or rationale for this subclause contained in Clause A.2.

a) For each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*) and over the totality of subjects, calculate

   1) the mean value of the differences of the *paired values,* $\bar{x}$, using Formula (8); and

   2) the corrected experimental standard deviation, s_{corr}, using Formula (9) to Formula (12)[2]; and

   3) the intra-class correlation coefficient, I_{cc}, using Formula (10) to Formula (12) followed by Formula (5); and

4) the number of independent measurements, N_{ind}, using Formula (6).

b) It is important to calculate I_{cc} from the data of the *clinical investigation* using Formula (10) to Formula (12) and not to use I_{cc_est} for the following calculations.

$$\bar{x} = \frac{1}{n}\sum_{j=1}^{n} x_j \tag{8}$$

where

n is the total number of *paired measurements* of all subjects;

j is the index of each individual *paired measurement*;

x_j is the difference of the j^{th} *paired values*; and

$$s_{corr} = \sqrt{\frac{\mu_{SB} - \mu_{SW}}{f_{BA}} + \mu_{SW}} \tag{9}$$

where

f_{BA} is a Bland-Altman factor calculated according to Formula (10);

μ_{SB} is the mean of the squares between subjects calculated according to Formula (11); and

μ_{SW} is the mean of the squares within a subject calculated according to Formula (12).

NOTE 2 In the case where subjects each provide more than one data pair for the analysis (i.e. repeated measurements per subject which are by definition interrelated and therefore not independent), this fact is accounted for by Formula (9)[2].

$$f_{BA} = \frac{n^2 - \sum m_i^2}{(k-1)\cdot n} = r \tag{10}$$

NOTE 3 $f_{BA} = r$, since all k subjects contribute equally.

$$\mu_{SB} = \frac{1}{k-1}\cdot\sum_{i=1}^{k} m_i\cdot(\bar{x}_i - \bar{x})^2 = \frac{1}{k-1}\cdot\sum_{i=1}^{k} r\cdot(\bar{x}_i - \bar{x})^2 \tag{11}$$

$$\mu_{SW} = \frac{1}{n-k}\sum_{i=1}^{k}(m_i - 1)\cdot\sigma_i^2 = \frac{1}{n-k}\cdot\sum_{i=1}^{k}(r-1)\cdot\sigma_i^2 \tag{12}$$

NOTE 4 $m_i = r$, since all k subjects contribute equally.

where

k is the total number of subjects;

r is the number of repeated *paired measurements* of each subject;

m_i is the number of repeated *paired measurements* of the i^{th} individual subject;

$\bar{x}_i$ is the mean of the differences of all *paired values* of the i^{th} individual subject;

$\bar{x}$ is the mean of the differences of all *paired values* of all subjects; and

σ_i^2 is the variance of the differences of the *paired values* of the i^{th} individual subject.

NOTE 5 The variance is defined as the square of the standard deviation.

a) The mean value of the differences of the *paired values,* $\bar{x}$, shall be within or equal to ±6,0 mmHg (±0,80 kPa).

b) The corrected experimental standard deviation, s_{corr}, shall be less than or equal to 10,0 mmHg (1,33 kPa).

c) N_{ind} shall be greater than or equal to 278.

d) If c) and d) are fulfilled, but N_{ind} is below 278, additional subjects may be added, if afterwards the requirements of c), d) and e) are fulfilled.

5.2 Method for stability

NOTE There is guidance or rationale for this subclause contained in Clause A.2.

5.2.1 General

a) The method for stability is designed to repeatedly perform the *procedure* for accuracy in the same number of subjects.

   1) For Type A *continuous automated non-invasive sphygmomanometers* the number of:

      i) subjects shall be at least *k* (see 4.5); and

      ii) repeated *paired measurements* per subject shall be the same *r* as used in 5.1.

   2) For Type T *continuous automated non-invasive sphygmomanometers,* based on the estimated intra-class correlation coefficient, I_{cc_est}, in accordance with 4.5 without subtracting any subject-specific offsets, determine:

      i) the number of repeated *paired measurements*, *r*; and

      ii) the number of subjects, *k*.

b) Set up the *continuous automated non-invasive sphygmomanometer* according to the instructions for use.

c) Select the control settings of the *continuous automated non-invasive sphygmomanometer* reflecting the worst case for the accuracy of *blood pressure determination*.

   1) The worst-case control settings shall include selection of the minimum *output period*.

   2) The *re-initialization process* described in the instructions for use of the *continuous automated non-invasive sphygmomanometer* shall be used in the *clinical investigation*.

d) If the *continuous automated non-invasive sphygmomanometer* allows variable *re-initialization* periods, the use the maximum *re-initialization* period.

   NOTE It is assumed that this represents the worst case for the verification of the stability.

e) If the *continuous automated non-invasive sphygmomanometer* needs *re-initialization*, the maximum *re-initialization* period shall be disclosed in the instructions for use.

f) If the *continuous automated non-invasive sphygmomanometer* does not need *re-initialization*, the maximum time of application shall be disclosed in the instructions for use.

5.2.2 *Procedure*

For each subject, perform the following *procedure*:

a) Depending on the need for *re-initialization* of the *continuous automated non-invasive sphygmomanometer* as defined in the instructions for use, perform the *procedure* of the test method for the accuracy of *blood pressure determination* according to 5.1.2 at the following times.

   1) For any maximum *re-initialization* period up to 1,5 h, perform 5.1.2 over one test period with a duration equal to the maximum *re-initialization* period.

   2) For any maximum *re-initialization* period greater than 1,5 h but not greater than 5 h, perform 5.1.2 at a minimum of 6 (approximately) equally distributed test periods of at least 15 min each over the maximum *re-initialization* period.

   3) For any maximum *re-initialization* period greater than 5 h but not greater than 24 h, perform 5.1.2 at a minimum of 5 (approximately) equally distributed test periods of at least 15 min each in the first 5 h, plus once at the end of the maximum *re-initialization* period.

   4) For any maximum *re-initialization* period greater than 24 h, do the following.

      i) Perform 5.1.2 at a minimum of 5 (approximately) equally distributed test periods of at least 15 min each in the first 5 h.

      ii) Afterwards, up to the end of the maximum *re-initialization* period, perform 5.1.2 at a minimum of two test periods of at least 15 min each:

         I) on day 2; and

         II) day 3.

      Any two consecutive test periods shall be at least 6 h apart.

      iii) Afterwards, perform 5.1.2 at a minimum of one test period of at least 15 min every day up to the end of the maximum *re-initialization* period.

      iv) If 5.1.2 has not been performed at the end of the maximum *re-initialization* period in either ii) or iii), perform 5.1.2 at the end of the maximum *re-initialization* period.

      NOTE It is typically not feasible to use an invasive *reference* for longer than a few days. It could be challenging to perform the stability test for maximum *re-initialization* periods longer than a few days.

b) If the *continuous automated non-invasive sphygmomanometer* does not need a *re-initialization*, then the maximum time of application as specified in the instructions for use shall be used for 1) to 4) instead of the *re-initialization* period.

5.2.3 Data analysis

a) For each test period, divide the data recorded from the *reference invasive blood pressure monitoring equipment* into non-overlapping segments of approximately equal duration.

   1) The segment duration shall match the *minimum output period* specific to the *continuous automated non-invasive sphygmomanometer* as closely as possible.

   2) The end time of each segment shall match as closely as possible the initial time the respective output value is provided by the *continuous automated non-invasive sphygmomanometer.*

      NOTE 1 This document does not address usability aspects, such as time delays, of *continuous automated non-invasive sphygmomanometers.*

b) For each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*), perform the following:

1) If the segment contains more than one *reference reading*, average the *reference readings* of each segment.

NOTE 2 In some *continuous automated non-invasive sphygmomanometers* the segment duration equates to one cardiac cycle which makes averaging unnecessary.

2) Match the (averaged) *reference reading* with the output value provided by the *continuous automated non-invasive sphygmomanometer* at the end of the segment. This results in one set of *paired values* of (averaged) *reference reading* and output value for each segment.

c) Divide each test period into as many non-overlapping analysis periods as possible such that each analysis period consists of r consecutive data pairs per subject.

d) A histogram of the *reference readings* of the analysis periods of all the test periods which are segmented in accordance with a) and averaged over the minimum *output period* in accordance with b) shall be included in the *clinical investigation report* for each *blood pressure* parameter investigated.

NOTE 3 The method for stability does not include a *blood pressure* distribution requirement.

e) For a Type A *continuous automated non-invasive sphygmomanometer* perform the following for each parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*):

1) For each data pair, j, within each analysis period from each test period calculate the difference, x_j, of the *paired values* as given in Formula (13)

$$x_j = P_{\mathrm{sut}_j} - P_{\mathrm{ref}_j} \tag{13}$$

NOTE 4 Formula (13) is identical to Formula (7) and is only repeated here to improve the readability of the document.

f) For a Type T *continuous automated non-invasive sphygmomanometer* perform the following for each parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*):

1) For each data pair, j, of each subject i, within each analysis period from each test period, calculate the difference of the *paired values*, x_j, using Formula (13);

2) For each analysis period from each test period calculate over the totality of subjects:

i) the intra-class correlation coefficient, I_{cc}, using Formula (10) to Formula (12) followed by Formula (5); and

ii) the number of independent measurements, N_{ind}, using Formula (6).

It is important to calculate I_{cc} from the data of the *clinical investigation* using Formula (10) to Formula (12) and not to use I_{cc_est} for the following calculations.

3) For each subject, i, calculate the subject-specific offset o_i according to Formula (14) by taking the average of the differences between the *reference readings* and the *blood pressure determinations* from the first analysis period of the subject's first test period according to 5.2.2;

$$o_i = \frac{1}{r}\sum_{j=1}^{r}\left(P_{\mathrm{sut}_{i,j}} - P_{\mathrm{ref}_{i,j}}\right) \tag{14}$$

where

$P_{\mathrm{sut}_{i,j}}$ is the j^{th} *blood pressure determination* from the first analysis period of the first test period of the i^{th} subject;

$P_{\mathrm{ref}_{i,j}}$ is the j^{th} *reference reading* from the first analysis period of the first test period of the i^{th} subject; and

4) For each data pair, j, of each subject i, within each analysis period from each test period, calculate the offset corrected difference of the *paired values*, $x_{j,T}$, using Formula (15) considering the subject-specific offset o_i as calculated in Formula (14) as

$$x_{j,\mathrm{T}} = P_{\mathrm{sut}_j} - P_{\mathrm{ref}_j} - o_i \tag{15}$$

5) For each analysis period from each test period calculate over the totality of subjects:

i) the mean value of the differences of the *paired values*, $\bar{x}$, using Formula (8), but replacing x_j with $x_{j,T}$ in all related formulae; and

ii) the corrected experimental standard deviation, s_{corr}, using Formula (9) to Formula (12), but replacing x_j with $x_{j,T}$ in all related formulae.

5.2.4 Acceptance criteria

a) For a Type A *continuous automated non-invasive sphygmomanometer*, confirm that the criteria 5.1.4 b), c), d) and e) are met for the differences of the *paired values*, x_j, pooled over all subjects, of each analysis period from each test period.

NOTE For the Type A *continuous automated non-invasive sphygmomanometer* this ensures that accuracy is maintained until the next *re-initialization* or the maximum time of application.

b) For a Type T *continuous automated non-invasive sphygmomanometer*, confirm that the following criteria are met for each analysis period from each test period:

1) The corrected experimental standard deviation, s_{corr}, shall be less than or equal to 6,0 mmHg (1,33 kPa);

2) N_{ind} shall be greater than or equal to 278; and

3) If 1) is fulfilled, but N_{ind} is below 278, additional subjects may be added, if afterwards the requirements of 1) and 2) are fulfilled.

5.3 Method for *blood pressure* changes

5.3.1 *Change evaluation interval*

NOTE There is guidance or rationale for this subclause contained in Clause A.2.

a) The validation of the ability of the *continuous automated non-invasive sphygmomanometer* to track *blood pressure* changes is performed by analysing a number of *blood pressure* changes as defined in 5.3.2.

1) The *blood pressure* changes used to validate the ability to track changes shall occur within time intervals shorter than or equal to the *change evaluation interval*.

2) This *change evaluation interval* shall be disclosed in the instructions for use based on the *intended use* of the *automated sphygmomanometer*.

b) The specified *change evaluation interval* shall be disclosed in the instructions for use.

c) The instructions for use shall disclose a justification for the intended specified *change evaluation interval*.

d) The specified *change evaluation interval* shall not be longer than the maximum *re-initialization* period.

5.3.2 General

NOTE 1 There is guidance or rationale for this subclause contained in Clause A.2.

a) The *continuous automated non-invasive sphygmomanometer* shall be set up according to the instructions for use.

b) A mode of the *continuous automated non-invasive sphygmomanometer* reflecting the worst case for measuring *blood pressure* changes shall be selected.

   1) The worst-case control settings shall include selection of the minimum *output period*.

c) The number of subjects shall be at least k (see 4.5).

d) The minimum number of changes included for each individual subject shall be 50.

e) If a subject provides fewer than 50 changes that subject shall be excluded for the method for *blood pressure* changes and replaced with another subject until at least k subjects with at least 50 changes each are included in the analysis.

f) The distribution of *reference blood pressure* changes should be such that at least 30 % of changes should be increases in *blood pressure* and at least 30 % of changes shall be decreases in *blood pressure*.

g) The required absolute changes for *systolic blood pressure* shall be at least 15 mmHg (2,00 kPa).

h) The required absolute changes for *diastolic blood pressure* shall be at least 10 mmHg (1,33 kPa).

i) The required absolute changes for *mean arterial pressure* shall be at least 12 mmHg (1,60 kPa).

NOTE 2 The limits for the required absolute changes defined in h), i) and j) refer to both the invasive *reference blood pressure* and the *blood pressure* determined with the *continuous automated non-invasive sphygmomanometer.* For further details on data analysis, see 5.3.4.

5.3.3 *Procedure*

For each subject, the following *procedure* shall be performed:

a) For a minimum duration of 30 min, simultaneously record for each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*) the beat-to-beat data obtained with the *reference invasive blood pressure monitoring equipment* and the output values of the *continuous automated non-invasive sphygmomanometer* at the minimum *output period*.

b) If the maximum *re-initialization* period of the *continuous automated non-invasive sphygmomanometer* is at least 30 min, ensure that no *re-initialization* of the *continuous automated non-invasive sphygmomanometer* occurs during the test.

c) If the maximum *re-initialization* period of the *continuous automated non-invasive sphygmomanometer* is less than 30 min, select the maximum *re-initialization* period for the *continuous automated non-invasive sphygmomanometer*.

5.3.4 Data analysis

NOTE 1 There is guidance or rationale for this subclause contained in Clause A.2.

For the data of each subject, perform the following *procedure*:

a) Divide the data recorded from the *reference invasive blood pressure monitoring equipment* into non-overlapping segments of approximately equal duration.

   1) Match the segment duration of the minimum *output period* specific to the *continuous automated non-invasive sphygmomanometer* as closely as possible.

   2) Match the end time of each segment to the initial time the respective output value provided by the *continuous automated non-invasive sphygmomanometer* as closely as possible.

      NOTE 2 This document does not address usability aspects, such as time delays, of *continuous automated non-invasive sphygmomanometers*.

b) For each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*), perform the following:

   1) If the segment contains more than one *reference reading*, average the *reference readings* of each segment.

      NOTE 3 In some *continuous automated non-invasive sphygmomanometers* the segment duration equates to one cardiac cycle which makes averaging unnecessary.

   2) Match the (averaged) *reference reading* with the output value provided by the *continuous automated non-invasive sphygmomanometer* at the end of the segment. This results in one set of *paired values* of (averaged) *reference reading* and output value for each segment. The set of *paired values* is assigned the time stamp t representing the time at which the output value is produced by the *continuous automated non-invasive sphygmomanometer*.

   3) For each set of *paired values* perform the following:

      i) Each set of *paired values* is considered a starting point for change analysis.

      ii) For each starting point for change analysis with time stamp t_{start}, determine all end points for change analysis based on their time stamps t_{end} where $t_{end} > t_{start}$ and the difference $t_{end} - t_{start}$ is less than or equal to the *change evaluation interval*, I_{CE}, as shown by Formula (16).

$$t_{end} - t_{start} \leq I_{CE} \tag{16}$$

where

t_{end} is the time stamp at the end of the *blood pressure* change;

t_{start} is the time stamp at the start of *blood pressure* change; and

I_{CE} is the *change evaluation interval.*

      iii) Discard any changes for which a *re-initialization* has occurred between t_{start} and t_{end}.

      NOTE 4 iii) does only apply to the continuous automated non-invasive sphygmomanometer with a maximum re-initialization period of less than 30 min, since no re-initialization is permitted for continuous automated non-invasive sphygmomanometer with a maximum re-initialization period of at least 30 min. See also 5.3.3.

      iv) Calculate the change in blood pressure ΔP for the reference sphygmomanometer, ΔP_{ref}, and the continuous automated non-invasive sphygmomanometer, ΔP_{sut}, according to Formula (17).

$$\Delta P = P_{end} - P_{start} \quad (17)$$

where

ΔP is the change in *blood pressure* for the *reference sphygmomanometer* (ΔP_{ref}) or the *continuous automated non-invasive sphygmomanometer* (ΔP_{sut});

P_{end} is the *blood pressure* at t_{end}; and

P_{start} is the *blood pressure* at t_{start}.

v) If either ΔP_{ref} or ΔP_{sut} fulfil the corresponding requirements of 5.3.2 h) to j), calculate the absolute error, $E_{percent}$, according to Formula (18).

$$E_{percent} = \frac{|\Delta P_{sut} - \Delta P_{ref}|}{max(|\Delta P_{sut}|, |\Delta P_{ref}|)} \cdot 100\ \% \quad (18)$$

where

ΔP_{ref} is the change in *blood pressure* for the *reference sphygmomanometer*; and

ΔP_{sut} is the change in *blood pressure* for the *continuous automated non-invasive sphygmomanometer.*

4) After pooling all $E_{percent}$ values of each subject, calculate the 50th percentile of all the $E_{percent}$ values per subject.

5) After pooling all $E_{percent}$ values of each subject, calculate the 85th percentile of all the $E_{percent}$ values per subject.

c) For each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*) a histogram of all *reference readings* P_{ref} included in the analysis shall be included in the *clinical investigation report*.

d) For each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*) a histogram of all ΔP_{ref} values included in the analysis shall be included in the *clinical investigation report*.

NOTE 5 The method for *blood pressure* changes does not include a *blood pressure* distribution requirement.

5.3.5 Acceptance criteria

For each *blood pressure* parameter to be investigated (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*), confirm separately that the following criteria are fulfilled:

a) After averaging the calculated 50th percentiles over all subjects, this average shall be less than or equal to 25 %.

b) After averaging the calculated 85th percentiles over all subjects, this average shall be less than or equal to 50 %.

Annex A
(informative)

Rationale and guidance

A.1 General guidance

This Annex provides a rationale for some 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 rationales 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.

A.2 Rationale for particular clauses and subclauses

The following are rationales for specific clauses and subclause in this document, with clause and subclause numbers parallel to those in the body of the document. The numbering is, therefore, not consecutive.

— 3.2 – ***Continuous automated non-invasive sphygmomanometer*** and

— 3.5 – ***Intermittent automated non-invasive sphygmomanometer***

The definition of *continuous automated non-invasive sphygmomanometers* is not based on a specific numerical threshold for the time resolution of the series of *blood pressure* parameters (e.g. *systolic blood pressure*, *diastolic blood pressure* or *mean arterial pressure*) which are provided by a *continuous automated non-invasive sphygmomanometer*. For example, a *continuous automated non-invasive sphygmomanometers* does not need to provide *blood pressure* parameters for every heartbeat for it to be considered a *continuous automated non-invasive sphygmomanometer*. However, this standard provides specifications to compare the output of the *continuous automated non-invasive sphygmomanometer* with an invasive *reference*, which provides *blood pressure* parameters for every heartbeat.

An invasive *reference* also provides *blood pressure* (in mmHg or kPa) waveform as a function of time, using time discretization that is much smaller than the duration of a single heart cycle (i.e., << 1 s), and that is only limited by the sampling frequency of the *continuous automated non-invasive sphygmomanometers*. However, this standard does not provide test methods to validate such *blood pressure* waveform outputs of non-invasive *continuous automated non-invasive sphygmomanometers*.

A *continuous automated non-invasive sphygmomanometer* would typically be designed to continuously collect physiological data from the patient; however, a *continuous automated non-invasive sphygmomanometer* could also have short temporal interruptions of physiological data collection if those are clinically insignificant for the *intended use*. But, in all cases, the *clinical investigation* of a *continuous automated non-invasive sphygmomanometer* involves an uninterrupted comparison of the time series output of the *continuous automated non-invasive sphygmomanometer* with the time series output of the invasive *reference*. Typically, long temporal interruptions in physiological data collection would make it harder for the *continuous automated non-invasive sphygmomanometer* to demonstrate its performance supporting its *intended use*.

Whereas, an *intermittent automated non-invasive sphygmomanometer* is not intended to continuously monitor the patient's *blood pressure* variations over time. It is only intended to provide accurate snapshot of the patient's *blood pressure* upon a single request. A *clinical investigation* of *intermittent automated non-invasive sphygmomanometer* only supports the accuracy of a single requested output

at a specific time. On the other hand, a *clinical investigation* of *continuous automated non-invasive sphygmomanometer* supports the use of the time-series output for monitoring the patient over time.

It is important to validate a *continuous automated non-invasive sphygmomanometer* under conditions that are representative of the *intended use*. For example, *continuous automated non-invasive sphygmomanometers* that are intended to be used in the OR would be tested in the OR when the patient's *blood pressure* variations are recorded by both the *reference* and the *continuous automated non-invasive sphygmomanometer* simultaneously.

— **4.2 – General**

A novelty of this document is the introduction of two types of *continuous automated non-invasive sphygmomanometers*: Type A and Type T. The committees have observed new trends in clinical practice and new technological solutions that have motivated this decision.

As described in 4.2, Type A *continuous automated non-invasive sphygmomanometers* are *continuous automated non-invasive sphygmomanometers* that provide *blood pressure determinations* expressed in mmHg or kPa, as did medical electrical equipment (ME equipment) investigated following ISO 81060-2.

For Type A *continuous automated non-invasive sphygmomanometers* it is therefore necessary to fulfil the requirements of all three methods for the *clinical investigation* provided in Clause 5: method for the accuracy of *blood pressure determination*, method for *blood pressure* changes and method for stability.

Alternatively, Type T *continuous automated non-invasive sphygmomanometers* are *continuous automated non-invasive sphygmomanometers* that provide *blood pressure determinations* expressed in mmHg or kPa but for which an unknown subject-specific offset can be present. This is typically the case for cuffless *continuous automated sphygmomanometers* that are not initialized prior to their first use. Although these *continuous automated non-invasive sphygmomanometers* are not able to provide "absolute" *blood pressure determinations*, they are accurate in tracking *blood pressure* changes and can be relevant for therapeutic applications.

For Type T *continuous automated non-invasive sphygmomanometers* it is only necessary to fulfil the requirements of two methods for the *clinical investigation* as provided in Clause 5: method for *blood pressure* changes and method for stability.

NOTE The method for stability applicable to Type T *continuous automated non-invasive sphygmomanometers* introduces an offset-correction algorithm that allows uniform analysis of data with that of Type A *continuous automated non-invasive sphygmomanometers*.

— **4.3.1 – *Reference invasive blood pressure monitoring equipment***

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

The accurate measurement of the intra-arterial *reference blood pressure* requires the use of a computerized data collection system (DCS). The values displayed on the invasive *blood pressure* (IBP) channel of a subject 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 frequency response and damping coefficient pair should meet the dynamic requirements proposed by Gardner[1]. 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.

During each measurement by the *continuous automated non-invasive sphygmomanometer*, the DCS should be recording the intra-arterial pressures and the analogue signals from the *continuous automated non-invasive sphygmomanometer* (if these are available).

— **4.3.2.1 –Number**

Mean error of the *continuous automated non-invasive sphygmomanometer* must be estimated to within an acceptable standard error. The Bland-Altman[3] formulation for the standard error, E_S [see Formula (A.1)], of the estimate of the mean error, which assumes a normal distribution and 95 % confidence, is applicable:

$$E_S = \sqrt{\frac{s_{corr}^{\,2}}{n}} \tag{A.1}$$

where

s_{corr}, is the corrected standard deviation, and

n is the number of independent measurements.

ISO 81060-2 with auscultation *reference* provides a benchmark to determine an acceptable E_S. ISO 81060-2 with auscultation *reference* prescribes 85 subjects with 3 measurements per subject. The 3 measurements per subject are neither perfectly independent nor perfectly dependent. However, if perfectly independent, then 255 independent measurements, and a worst-case acceptable standard deviation of 8 mmHg are assumed the lower limit on the acceptable E_S is 0,5 mmHg. 0,5 mmHg is 10 % of the minimum Mean Error allowed by ISO 81060-2. 0,6 mmHg is 10 % of the minimum Mean Error allowed by this document, so an E_S of 0,6 mmHg is used for this document.

This document allows a maximum (worst-case) acceptable corrected standard deviation of s_{corr} = 10 mmHg. Then, the required number of independent measurements is 278.

This document seeks to give clear and simple-to-apply directions to determine the number of test subjects required, while taking advantage of the additional power that can be gained by taking many repeated measurements on a single subject.

The effective number of independent measurements obtained by performing r repeated measures on k subjects must be determined. The intra-class correlation coefficient compares the between subject and within subject variances, thus quantifying the distribution of errors that are sampled by measuring on multiple subjects versus repeated measures on the same subject[4] and allowing the calculation of the effective number of independent measurements obtained by performing r repeated measures on k subjects [see Formula (A.2)]:

$$n = k(1+(1-I_{CC})(r-1)) \tag{A.2}$$

The absolute agreement, one-way random effects model I_{cc} is given by Formula (A.3):

$$I_{CC} = \frac{S_b^{\,2}}{S_b^{\,2} + S_w^{\,2}} = \frac{\frac{\mu_{SB} - \mu_{SW}}{r}}{\frac{\mu_{SB} - \mu_{SW}}{r} + \mu_{SW}} \tag{A.3}$$

assumes there is no prescribed pattern to the within-subject measurements. The one-way random effects model I_{cc} has the advantage that it is calculated from the same Mean Squares Between (μ_{SB}) and Mean Squares Within (μ_{SW}) already used by this document to calculate the corrected standard deviation.

Continuous automated non-invasive sphygmomanometers covered by this document perform an *initialization* followed by continuous measurement. Drift in the information obtained during the

initialization will introduce a time dependence to the measured errors. Thus, the I_{cc} can depend upon both the sample interval (time between measurements) and sample duration (time over which measurements are performed). This is acceptable as long as the same test conditions – sample interval and sample duration – used to determine the number of subjects and number of repeated measures per subjects are used for the *clinical investigation*. In other words, the I_{cc} is a characteristic of the testing conditions as well as the *continuous automated non-invasive sphygmomanometer*.

Furthermore, the power of the test is verified by calculating the I_{cc} of the test data and confirming that it is less than or equal to the I_{cc} assumed when calculating the number of subjects.

Type T *continuous automated non-invasive sphygmomanometers* provide *blood pressure* values that are not intended to be absolutely accurate, thus when assessing the stability of Type T *continuous automated non-invasive sphygmomanometers*, it is correct to remove constant subject-specific offsets. However, when calculating I_{CC} absolute *blood pressure* values must be used in order to assess the relative contributions of between and within subject errors. Due to the unknown constant subject-specific offsets Type T *continuous automated non-invasive sphygmomanometers* will in general have larger between subject errors and larger I_{CC}'s than Type A *continuous automated non-invasive sphygmomanometers*.

If a Type T *continuous automated non-invasive sphygmomanometer* only outputs relative *blood pressure* values, e.g. the value at t = 0 is 0 mmHg and subsequent values are only relative increases or decreases from that initial 0 mmHg, those relative *blood pressure* values shall be used as absolute *blood pressure* values when calculating I_{CC}.

— **4.3.2.2– Gender distribution**

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

NOTE References [5] and [6] contain additional information.

— **4.3.2.3 – Age distribution**

The age classifications of subjects were suggested by the committees considering the exclusive use of the invasive *reference* in this document. FDA guidance documents (see Reference [7] and [8]) provide age ranges of paediatric subgroups.

As stated in ISO 81060-2, the upper normal *systolic/diastolic blood pressure* in paediatrics 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 paediatrics analysed. Reference [9] contains additional information.

For this reason, it would not be practical to specify exact "hypertensive" *blood pressure* values, as can be done in adults for investigations. In addition, the prevalence of essential hypertension in young children is very low, making *clinical investigations* requiring hypertensive children extremely difficult to perform. Further, the *systolic blood pressure* and *diastolic blood pressure* values in a hypertensive infant are at about the average for normotensive adults. Thus, the *continuous automated non-invasive sphygmomanometer* would not be significantly "challenged" with respect to accuracy in this *blood pressure* range. Thus, there is no valid reason to require hypertensive children paediatrics in any *clinical investigation* of individuals less than 12 years of age.

— **4.3.2.4 – Special subject populations**

In certain subject populations, the accuracy of a *sphygmomanometer* can be problematic. This can be caused by subject characteristics such as age, pregnancy, vasoactive drug therapy, diabetes, peripheral artery disease or other conditions that affect arterial compliance. Similar problems can occur during a *clinical investigation* where subject characteristics that increase the variability of the subject's *blood pressure* could affect the accuracy of both the *continuous automated non-invasive sphygmomanometer* and the *reference sphygmomanometer*. Examples include atrial or ventricular arrhythmias.

Although *clinical investigation* of *blood pressure* in subjects with atrial fibrillation is clinically important, there are currently no generally accepted guidelines to measure *blood pressure* in such subjects.

— **4.3.4 – Arterial *reference* site**

Arterial pressure is not constant throughout the arterial tree; although *diastolic blood pressure* and *mean arterial pressure* will be lower at more distal sites from the heart as compared to sites more proximal to the heart, the same does not always apply to *systolic blood pressure*. The cause for this so-called pulse amplification can be found in the vascular properties of the arterial tree[10]. This means that *systolic blood pressure*, *diastolic blood pressure* and *mean arterial pressure* are different in the central aorta, brachial artery and radial artery. Hence, for the user it is important to know the *reference* site in order to interpret the measurements correctly.

— **4.4 – Lateral difference**

It is assumed that in a normal situation, the *blood pressure* in both arms is the same, arms having a mirrored physiology with respect to the heart. However, there might be subjects with an anatomical variance (e.g. arterial stenosis) which might cause a difference in *blood pressure* between the two arms. Therefore, in cases where *reference readings* and *continuous automated non-invasive sphygmomanometer determinations* are representing opposite arms the user is allowed to correct for a lateral difference.

— **5.1.3 – Data analysis**

Within the recorded data used for determining accuracy, theoretically a difference between values taken from each beat cycle (i.e. *systolic blood pressure*, *diastolic blood pressure* and *mean arterial pressure*) of the invasive *reference* waveform and the time-corresponding output of the *continuous automated non-invasive sphygmomanometer* can be obtained. Data from the same subject, especially beat-to-beat data, are intrinsically highly correlated. In order to reduce this correlation and to account for the fact that most *continuous automated non-invasive sphygmomanometer* output values with a device-specific averaging over a window of, for example, 5 s to 10 s, the recorded data is divided into segments for which the *reference* values are averaged. The segment duration is selected to match the minimum *output period* specific to the *continuous automated non-invasive sphygmomanometer* as closely as possible.

NOTE For instance, if the *continuous automated non-invasive sphygmomanometer* provides output values every 10 heart beats, then the segment duration can be selected as 10 s.

— **5.1.4 – Acceptance criteria**

The intention of this document is that *continuous automated non-invasive sphygmomanometer*s as clinically tested according to this document have a level of performance and safety comparable to an intermittent non-invasive *sphygmomanometer* as clinically tested according to ISO 81060-2. The statistical methods to calculate the standard deviation of error are different for the two categories of sphygmomanometesr:

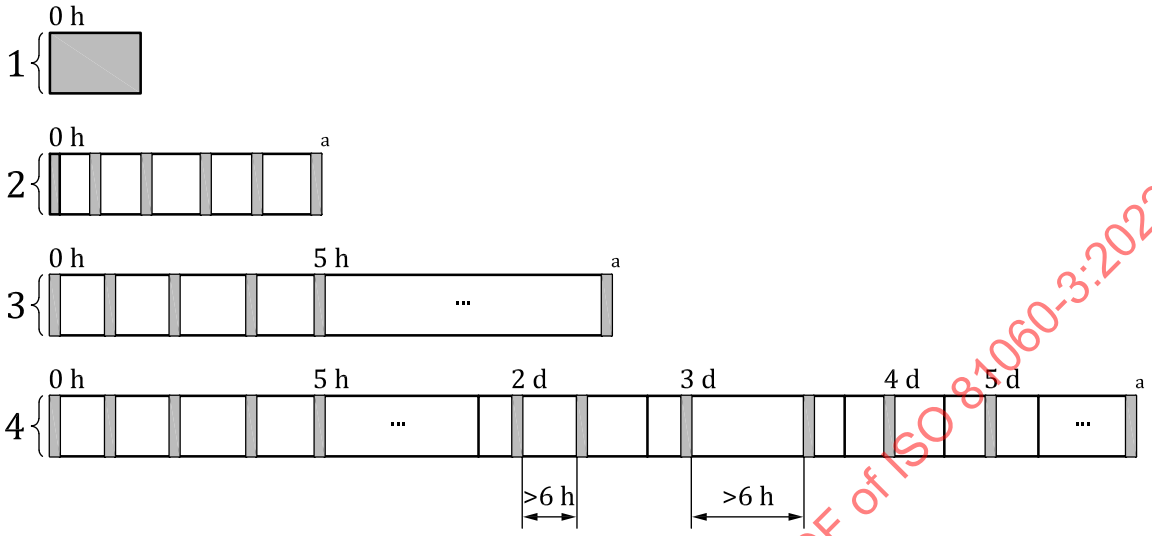
a) ISO 81060-2 sets all error differences between *continuous automated non-invasive sphygmomanometer* estimates and *reference measurements* that are within one standard deviation to 0 mmHg. This document does not set any error differences to zero.

b) Within this document, the calculation of the experimental standard deviation of error differences takes into account that multiple measurements are taken in each patient, because data are partly dependent, and the experimental standard deviation of error is widened accordingly. For more information see Reference [11].

Thus, the statistical methods used by this document produce standard deviations of error larger than those produced by ISO 81060-2 when applied to identical data sets. Therefore, the criteria limits of this document (±6 mmHg mean error and 10 mmHg corrected standard deviation of error) are substituted for the criteria limits of ISO 81060-2 (±5 mmHg mean error and 8 mmHg standard deviation of error).

— **5.2 – Method for stability**

Figure A.1 provides a graphical representation of the *procedure* for the stability method given in 5.2.2. The first line of Figure A.1 relates to 5.2.2 b), the second line to 5.2.2 c), the third line to 5.2.2 d) and the last line to 5.2.2 e).



Key

1 maximum *re-initialization* period of up 1,5 h

2 maximum *re-initialization* period greater than 1,5 h and not greater than 5 h

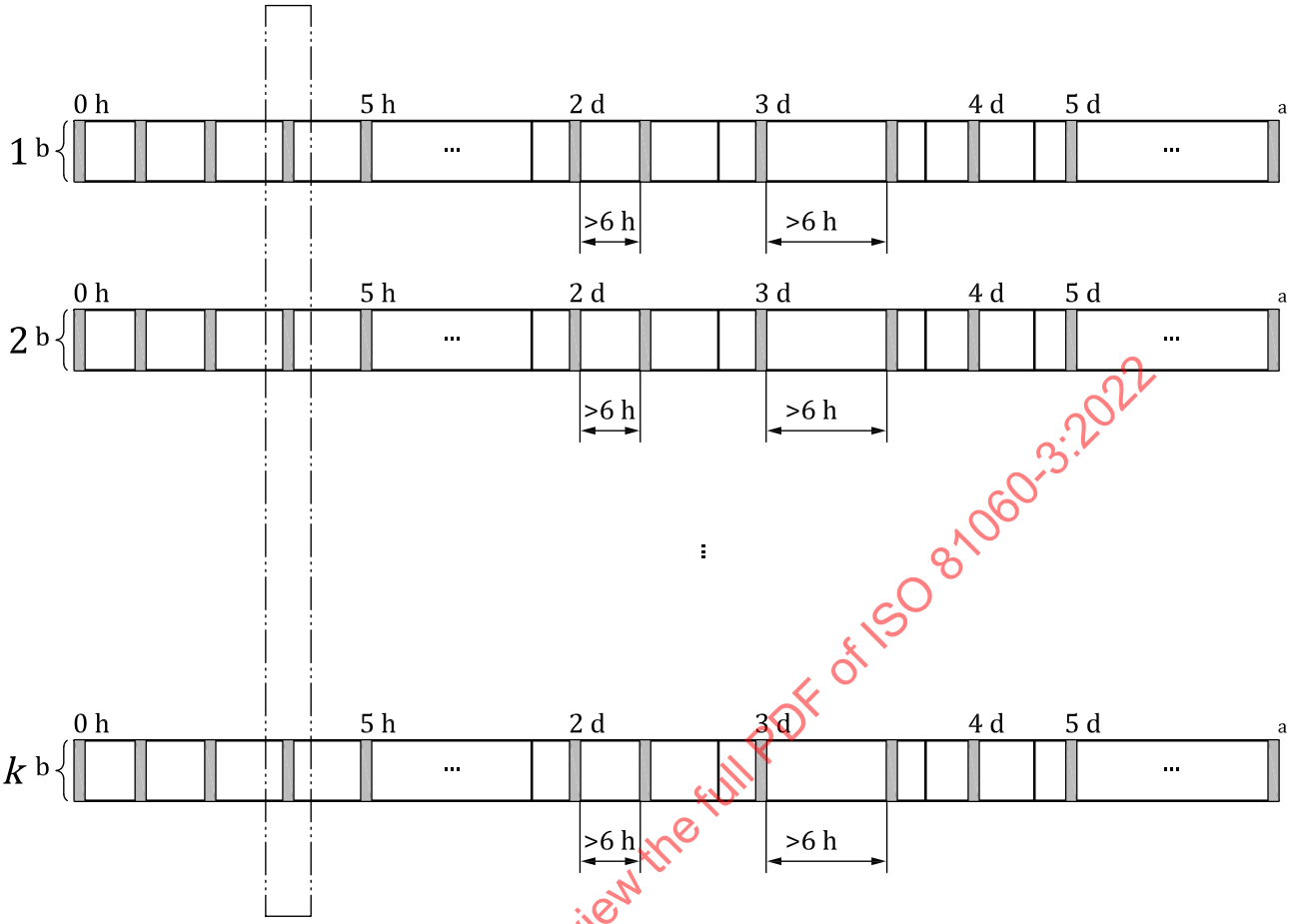
3 maximum *re-initialization* period greater than 5 h and not greater than 24 h

4 maximum *re-initialization* period greater than 24 h

[a] Maximum *re-initialization* period.

Figure A.1 — Graphical representation of test periods at which the stability *procedure* needs to be carried out according to 5.2.2

Figure A.2 provides a graphical representation of the data analysis for the stability method described in 5.2.3. Figure A.2 emphasizes that the data from one test period is analysed over all k subjects. The detailed data analysis for each test period can be found in 5.2.3 c) to f).



a Maximum *re-initialization* period.

b Subject number.

Figure A.2 — Graphical representation of data analysis according to 5.2.3

— **5.3.1 – *Change evaluation interval***

The committees considered specifying a maximum value for the choice of the *change evaluation interval*; in particular, the committees considered various potential maximum values such as the minimum *output period* of the *continuous automated non-invasive sphygmomanometer*, 30 s, 2 min, etc. However, there is no consensus regarding the time over which a *blood pressure* change is clinically significant. Therefore, a framework was developed whereby the *manufacturer* sets the clinically relevant time scale by declaring the *change evaluation interval* and performing clinical tests according to this document to validate the change tracking ability within that interval. Thus, this document is applicable to as wide a range of use cases and clinical settings as possible.

In general, choice of a short or long *change evaluation interval* could affect the result of the change analysis. There could also be uncertainties about the correct interpretation of the *change evaluation interval* that is disclosed in the instructions for use. This document does not provide methods to be used to demonstrate the appropriateness of the disclosed *change evaluation interval* for the *intended use* of the *continuous automated non-invasive sphygmomanometer*.

— **5.3.2 – General**

The *continuous automated non-invasive sphygmomanometer*s to be investigated according to this document are typically intended to measure continuous *blood pressure* changes in clinical settings where changes in *blood pressure* have therapeutic consequences. Thus, this document requires