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In vitro diagnostic test systems — Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus

Systèmes d'essais de diagnostic in vitro — Exigences relatives aux systèmes d'autosurveillance de la glycémie destinés à la prise en charge du diabète sucré

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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 15197 was prepared by Technical Committee ISO/TC 212, *Clinical laboratory testing and* in vitro *diagnostic test systems*.

Introduction

Blood-glucose monitoring systems are *in vitro* diagnostic medical devices used predominantly by individuals affected by diabetes mellitus. Diabetes mellitus is caused by a relative or absolute deficiency in insulin secretion or by insulin resistance leading to abnormal concentrations of glucose in the blood, which may result in acute and chronic health complications. When used properly, a glucose monitoring system allows the user to monitor and take action to control the concentration of glucose present in the blood.

This International Standard is intended for blood-glucose monitoring systems used by laypersons. The primary objectives are to establish requirements that result in acceptable performance and to specify procedures for demonstrating conformance to this International Standard.

Performance criteria for blood-glucose monitoring systems were established from the accuracy (precision and trueness) required for individual glucose results. System accuracy criteria, also known in the *in vitro* diagnostics (IVD) industry as total error criteria (see NCCLS EP21-P[35]), are used in this International Standard because some of the metrological terms commonly used in International Standards (e.g. uncertainty) would not be familiar to lay users. *System accuracy*, which is affected by systematic bias and measurement uncertainty, describes the degree to which the individual results produced by a glucose monitoring system agree with the true glucose values when the system is used as intended by laypersons.

The criteria for system accuracy are based on three considerations (see References [2] to [21] in the Bibliography):

a) the effectiveness of current technology for monitoring patients with diabetes mellitus, as demonstrated in clinical outcome studies using state-of-the-art monitoring devices;

b) recommendations of diabetes researchers as well as existing product standards and regulatory guidelines;

c) the state-of-the-art of currently available technology, as evidenced by the performance of existing commercial products.

In arriving at the performance criteria, desirable goals had to be weighed against the capabilities of existing devices (the current state-of-the-art) and their effectiveness in clinical outcome studies. It was decided that overly demanding performance requirements would cause manufacturers to focus design improvements on analytical performance at the expense of other important attributes. For example, frequency of testing by diabetic patients can be as important as the accuracy of an individual result, and greater convenience of glucose self-testing improves patient compliance. The system accuracy criteria define the minimum acceptable performance of a blood-glucose measuring device intended for self-monitoring.

Future advances in technology are expected, which should result in improved performance of glucose monitoring devices. Such performance improvements will be driven by the competitive marketplace, particularly through reduction of dependence on user technique.

Requirements that are unique to self-monitoring devices for blood-glucose, including the content of information supplied by the manufacturer, are addressed in this International Standard. General requirements that apply to all *in vitro* diagnostic medical devices and are covered by other standards [e.g. ISO 13485 and ISO 14971] are incorporated by reference where appropriate.

Although this International Standard does not apply to measurement procedures with results on an ordinal scale (e.g. visual, semiquantitative measurement procedures), it may be useful as a guide for developing procedures to evaluate the performance of such systems.

In vitro diagnostic test systems — Requirements for blood-glucose monitoring systems for self-testing in managing diabetes mellitus

1 Scope

This International Standard specifies requirements for *in vitro* glucose monitoring systems that measure glucose concentrations in capillary blood samples and procedures for the verification and the validation of performance by the intended users. These systems are intended for self-testing by laypersons for management of diabetes mellitus.

This International Standard is applicable to manufacturers of such systems and those other organizations (e.g. regulatory authorities and conformity assessment bodies) having the responsibility for assessing the performance of these systems.

This International Standard does not

— provide a comprehensive evaluation of all possible factors that could affect the performance of these systems,

— pertain to glucose concentration measurement for the purpose of *diagnosing* diabetes mellitus,

— address the medical aspects of diabetes mellitus management, or

— apply to measurement procedures with results on an ordinal scale (e.g. visual, semiquantitative test methods).

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 13485, *Medical devices — Quality management systems — Requirements for regulatory purposes*

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

ISO 17511:—[1)], In vitro *diagnostic medical devices — Measurement of quantities in biological samples — Metrological traceability of values assigned to calibrators and control materials*

IEC 60068-2-64:1993, *Environmental testing — Part 2: Test methods — Test Fh: Vibration, broad-band random (digital control) and guidance*

IEC 61010-1:2001, *Safety requirements for electrical equipment for measurement, control, and laboratory use — Part 1: General requirements*

IEC 61010-2-101:2002, *Safety requirements for electrical equipment for measurement, control and laboratory use — Part 2-101: Particular requirements for* in vitro *diagnostic (IVD) medical equipment*

1) To be published.

IEC 61000-4-2, *Electromagnetic compatibility (EMC) — Part 4-2: Testing and measurement techniques — Electrostatic discharge immunity test*

IEC 61000-4-3, *Electromagnetic compatibility (EMC) — Part 4-3: Testing and measurement techniques — Radiated, radio-frequency, electromagnetic field immunity test*

IEC 61326, *Electrical equipment for measurement, control and laboratory use — EMC requirements*

EN 376, *Information supplied by the manufacturer with* in vitro *diagnostic reagents for self-testing*

EN 13612, *Performance evaluation of* in vitro *diagnostic medical devices*

EN 13640, *Stability testing of* in vitro *diagnostic reagents*

3 Terms and definitions

For the purposes of this document, the following terms and definitions apply.

3.1
accuracy
closeness of agreement between a test result and the accepted reference value

[ISO 3534-1:1993]

NOTE 1 The term “accuracy”, when applied to a set of test results, involves a combination of random error components and a common systematic error or bias component. [VIM:1993]

NOTE 2 For a measure of the accuracy of results of a blood-glucose monitoring system, see 3.24.

3.2
bias
difference between the expectation of the test results and an accepted reference value

[ISO 5725-1:1994]

3.3
blood-glucose monitoring system
measuring system consisting of a portable instrument and reagents used for the *in vitro* monitoring of glucose concentrations in blood

NOTE Blood-glucose monitoring systems measure glucose in capillary blood samples, but may express results as either the glucose concentration in blood or the equivalent glucose concentration in plasma. Concentrations in this International Standard refer to the type of results reported by the system.

3.4
blood-glucose meter
component of a blood-glucose monitoring system that converts the result of a chemical reaction into the glucose concentration of the sample

3.5
commutability of a material
ability of a material to yield the same numerical relationships between results of measurements by a given set of measurement procedures, purporting to measure the same quantity, as those between the expectations of the relationships obtained when the same procedures are applied to other relevant types of material

[ISO 15194:2002]

NOTE For reference materials used to calibrate measurement procedures intended for biological samples, “other relevant types of material” include a large number of samples from healthy and relevantly diseased individuals.

3.6
control material
substance, material, or article intended by the manufacturer to be used to verify the performance characteristics of an *in vitro* diagnostic medical device

[EN 375:2001]

3.7
information supplied by the manufacturer with the medical device
all written, printed, or graphic matter on a medical device or any of its containers or wrappers, or accompanying a medical device, relating to the identification, technical description and use of the medical device, but excluding shipping documentation and promotional material

NOTE 1 Adapted from EN 1041:1998.

NOTE 2 In some countries, information supplied by the manufacturer is called “labelling”.

3.8
instructions for use
information supplied by the manufacturer with an *in vitro* diagnostic medical device concerning the safe and proper use of the reagent or the safe and correct operation, maintenance, and basic troubleshooting of the instrument

NOTE 1 Adapted from EN 375:2001 and EN 591:2001.

NOTE 2 Instructions for use for *in vitro* diagnostic reagents for self-testing is described in EN 376.

NOTE 3 Instructions for use for *in vitro* diagnostic instruments for self-testing is described in EN 592.

NOTE 4 Instructions for use may take the form of package insert sheets and/or user manuals.

3.9
intermediate precision
precision under conditions intermediate between reproducibility conditions and repeatability conditions

NOTE The concept of intermediate levels of precision is described in ISO 5725-3:1994.

3.10
intermediate precision conditions
conditions where independent test results are obtained with the same method on identical test items in the same location, but where other variables such as operators, equipment, calibration, environmental conditions and/or time intervals differ

NOTE Intended to measure precision in conditions leading to variability representative of actual use. Quantitative measures of intermediate precision depend on the stipulated conditions.

3.11
label
printed, written, or graphic information placed on a device or container

NOTE Adapted from EN 375:2001.

3.12
layperson
individual who does not have formal training in a specific field or discipline

NOTE 1 Adapted from the definition of “lay user” in EN 376:2002.

NOTE 2 For the purposes of this International Standard, a user of a blood-glucose monitoring device who does not have specific medical, scientific or technical knowledge related to blood-glucose monitoring.

3.13
lot
batch
one or more components or finished devices that consist of a single type, model, class, size, composition, or software version that are manufactured under essentially the same conditions and that are intended to have uniform characteristics and quality within specified limits

NOTE In Directive 98/79/EC[37] and in European Standards the term “batch” is preferred.

3.14
manufacturer's selected measurement procedure
measurement procedure that is calibrated by one or more primary or secondary calibrators and validated for its intended use

NOTE ISO 17511:—, 4.2.2 f), shows the manufacturer's selected measurement procedure in the traceability chain.

3.15
manufacturer's standing measurement procedure
measurement procedure that is calibrated by one or more of the manufacturer’s working calibrators or higher types of calibrator and validated for its intended use

NOTE ISO 17511:—, 4.2.2 h) shows the manufacturer's standing measurement procedure in the traceability chain.

3.16
package insert
instructions for use and other information for the reagent system or control material that is supplied within the package, but not attached to any part of the package

3.17
packed cell volume
volume fraction of the erythrocytes in blood

NOTE 1 Expressed either as a decimal fraction (SI) or as a percentage (conventional). SI units (L/L) are implied.

NOTE 2 Sometimes referred to as “haematocrit” after the instrument originally used to estimate packed cell volume.

3.18
precision of measurement
closeness of agreement between independent test results obtained under stipulated conditions

[ISO 3534-1:1993]

NOTE 1 The degree of precision is expressed numerically by the statistical measures of imprecision of measurements, such as standard deviation and coefficient of variation, that are inversely related to precision. Quantitative measures of precision depend on the stipulated conditions.

NOTE 2 Precision of a given measurement procedure is subdivided according to the specified precision conditions. Particular sets of extreme conditions are termed “repeatability” (3.20) and “reproducibility” (3.22).

3.19
reagent system
part of the *in vitro* diagnostic medical device that produces a signal via a chemical or electrochemical reaction, which allows the analyte (e.g. glucose) in a sample to be detected and its concentration measured

3.20
repeatability
precision under repeatability conditions

[ISO 3534-1:1993]

3.21
repeatability conditions
conditions where independent test results are obtained with the same method on identical test items in the same laboratory by the same operator using the same equipment within short intervals of time

[ISO 3534-1:1993]

NOTE 1 Essentially unchanged conditions, intended to represent conditions resulting in minimum variability of test results.

NOTE 2 For the purposes of this International Standard, “laboratories” should be interpreted as “locations.”

3.22
reproducibility
precision under reproducibility conditions

[ISO 3534-1:1993]

3.23
reproducibility conditions
conditions where test results are obtained with the same method on identical test items in different laboratories with different operators using different equipment

[ISO 3534-1:1993]

NOTE 1 Completely changed conditions, intended to represent conditions resulting in maximum variability of test results.

NOTE 2 For the purposes of this International Standard, “laboratories” should be interpreted as “locations”.

3.24
system accuracy
closeness of agreement of a set of representative test results from a measuring system and their respective reference values

NOTE 1 The term accuracy, when applied to a set of test results, involves a combination of random error components and a common systematic error or bias component. [VIM:1993]

NOTE 2 Reference values are assigned by a measurement procedure traceable to a reference measurement procedure of higher order.

NOTE 3 System accuracy may be expressed as the interval that encompasses 95 % of the differences observed between the results of the system being evaluated and their reference values. This interval also includes measurement uncertainty from the measurement procedure used to assign the reference values.

3.25
traceability
property of the result of a measurement or the value of a standard whereby it can be related to stated references, usually national or international standards, through an unbroken chain of comparisons all having stated uncertainties

[VIM:1993, 6.10]

3.26
trueness
closeness of agreement between the average value obtained from a large series of test results and an accepted reference value

[ISO 3534-1:1993]

NOTE The measure of trueness is usually expressed in terms of bias (3.2).

3.27
type test
test of one or more samples of equipment (or parts of equipment) made to a particular design, to show that the design and construction meet one or more requirements of the applicable standard

NOTE 1 Statistical sampling is not required for blood-glucose monitoring equipment.

NOTE 2 Adapted from IEC 61326.

3.28
user adjustment of blood-glucose monitoring system
procedure described in the instructions for use in which the user enters a number, inserts a code strip or chip, etc., so that the system achieves acceptable performance characteristics

4 Design and development

4.1 General requirements

The requirements specified in ISO 13485 apply.

NOTE Clause 6, 7.2 and 7.3 describe design verification activities, which are intended to provide assurance that the system has the capability of meeting its precision, trueness, safety, and reliability specifications. Clause 8 describes design validation activities, which are intended to provide assurance that system accuracy meets user requirements.

4.2 Safety

The requirements specified in IEC 61010-1 and IEC 61010-2-101 apply.

4.3 Traceability

The requirements specified in ISO 17511 apply to the manufacturer's calibration process.

NOTE 1 The manufacturer's selected or standing measurement procedure may measure glucose in either blood or plasma samples. If plasma samples are used, the blood-glucose monitoring system may report results as plasma glucose equivalents, even though the samples measured by the blood-glucose monitoring system are blood.

NOTE 2 The traceability chain should include as few steps as practical to minimize combined uncertainty.

NOTE 3 A traceability chain for a typical factory-calibrated blood-glucose monitoring system is shown in Annex B. This example is not intended to represent the only possibility of a suitable traceability chain.

4.4 Ergonomic/human factor aspects

The design of the blood-glucose monitoring system shall take into consideration ergonomic and relevant human factors for the following:

a) ease of operation;

b) ease of maintenance;

c) protection from "wear and tear" that might typically be encountered in the use environment;

d) readability of the measured results;

e) unambiguous messages to the user, e.g. "low battery" or "low result", rather than simply "low".

NOTE 1 Blood-glucose monitoring systems intended for self-measurement may be used by laypersons with different physical and mental abilities.

NOTE 2 These systems are often transported by the individual users, who may conduct measurements in a variety of settings.

NOTE 3 It is not expected that a single blood-glucose monitoring system will meet the needs of all possible users or settings.

4.5 Risk analysis

The requirements specified in ISO 14971 apply.

The manufacturer shall decide the acceptability of potential risks from knowledge of factors including but not limited to

a) intended use of the product,

b) users' skills and limitations,

c) protection against unintentional change of essential parameters (e.g. units reported), or

d) influence of interfering substances.

NOTE Guidelines for evaluating potentially interfering substances are found in NCCLS EP7-A[31].

In performing risk analysis, the manufacturer shall evaluate the

e) probability of occurrence of a failure (e.g. insufficient sample volume or incorrect test strip placement),

f) probability of the system not detecting a failure, and

g) consequences of an undetected failure.

NOTE This International Standard does not specify levels of risk and acceptability.

4.6 User verification

The design of the blood-glucose monitoring system shall allow the user to check:

a) correct functioning of the blood-glucose monitoring system, (i.e. system control); and

b) correct execution of the test including the sequence of the procedural steps.

NOTE User verification should be done at the time of use. "At the time of use" means before, during, or immediately after the execution of the test. User verification should be integrated into the test if reasonably possible.

User verification shall give unambiguous information.

5 Information supplied by the manufacturer

5.1 Labels for the blood-glucose meter

The blood-glucose meter shall be identified by labels including, at a minimum, the following information:

a) name or trade name of the manufacturer and address of the manufacturer;

b) product name or designation (this information shall directly appear on a label affixed to the device);

c) intended purpose (a statement that the device is an *in vitro* diagnostic medical device for self-testing shall be included, as well as information regarding the reagent system to be used with the device);

d) lot or serial number appearing directly on a label affixed to the device;

e) conditions for storage and handling, if appropriate;

f) a reference to the user manual or instructions for use.

Where appropriate, information on the label should take the form of symbols. Symbols shall conform to applicable regulations and International Standards. All symbols shall be described in the information supplied with the blood-glucose meter.

5.2 Instructions for use for the blood-glucose monitoring system

The instructions for use shall be presented in a clear and concise manner, using plain terminology that is readily understood by a layperson. The information shall be well organized and easy to read. The print shall be large (e.g. 12-point Courier) and the content shall be readily understandable by persons without a scientific or technical background. Symbols and illustrations shall be used where appropriate.

The instructions for use shall clearly state what actions to take if the verification indicates an invalid result.

The language(s) of the country in which the blood-glucose monitoring system is distributed shall be used. Additional languages are optional.

The instructions for use shall include the following information:

a) name or trade name and address of the manufacturer, the name and address of the distributor (if applicable) (in the European Union, Directive 98/79/EC[37] requires the name and address of the "authorized representative" if the manufacturer is not located in the European Union), and how to access help;

b) product name or designation;

c) intended purpose of the device;

d) the principle of the method;

e) measurement procedures and/or calibrator materials (traceability to a reference measurement procedure and/or reference material of higher order should be indicated, if applicable) used by the manufacturer to establish and evaluate performance characteristics;

f) the type of samples used by the manufacturer for calibration, e.g. blood or plasma;

g) proper reagent system to be used;

h) measurement procedure to be followed when using the device, including:

   — the sequence of adjustment (e.g. use of a number, code strip, code chip, etc.), measurement and verification, and the allocated time intervals between them;

   — the sequence of steps to prepare the instrument for the measurement, to execute the measurement (including the amount and recommended appearance of the sample) and to maintain the instrument after the measurement;

   — the measurement units reported by the device, e.g. mmol/L or mg/dL;

   — whether reported results are equivalent to blood or plasma results;

   — advice on how to proceed when an error message is generated by the meter;

i) environmental conditions (e.g. temperature and humidity range) under which the system shall be used;

j) detailed procedure to be followed by the user in adjusting the device, if applicable;

k) detailed user control procedures, including identification of the appropriate control material to be used to assure that the blood-glucose monitoring system is operating properly and advice on how to proceed if control results are not acceptable;

l) type of sample to be used, as well as any special conditions of collection and pretreatment;

m) precautions to be taken against the risk of infection from prior use of the instrument;

n) precautions to be taken regarding electrostatic discharge, magnetic fields, and other electrical conditions, as well as exposure to temperature, humidity, and other environmental conditions, as applicable (see IEC 61010-2-101:2002, Clause 5);

o) description and explanation of all symbols used on labels and in the instructions for use;

p) guidance on action to be taken by the user as a consequence of the result, including:

— a reference to the instructions given by a physician and/or other qualified healthcare provider, and a warning not to deviate from these instructions on the basis of the result without first consulting the physician or other qualified healthcare provider;

— advice on how to proceed if the result appears to be questionable to the user;

— indication how the monitoring system alerts the user when the result is outside the “measurement interval” (e.g. error messages, fault notifications);

q) information on the safe disposal of the system and its components, where appropriate;

r) the year and month of issue of the instructions for use and/or the revision number.

5.3 Labels for the reagent system and control material

The reagent system and control material shall be identified by a label or labels.

The requirements specified in EN 376 apply.

In addition, the following information shall be included on the label(s):

a) indication of the period of time during which the reagent should be used after the first opening of the immediate reagent container, expressed as months and/or days;

b) a reference to the instructions for use;

c) the blood-glucose meter to be used with the reagents.

Warning statements concerning use of the reagent system with the specified blood-glucose meter and disposal of the reagent system after use should be included on the label to promote reliable measurement results and safe reagent disposal.

The language(s) of the country in which the reagents and control materials are distributed shall be used; additional languages are optional.

5.4 Instructions for use for reagents and control material

The requirements specified in EN 376 apply.

In addition, the following information shall be included:

a) an indication of how to access help from the manufacturer and/or distributor;

b) the specific blood-glucose meter to be used with the reagent system and control material;

c) the storage conditions, (e.g. temperature, humidity, exposure to light, and other environmental factors) (a warning statement concerning the need to tightly seal the cap of the container provided to protect reagent strips or sensors from exposure to air should be included in the instructions for use for reagents);

d) the measurement interval, indicating the upper and lower concentration limits within which the glucose results are accurate and reportable;

e) the performance characteristics (those related to system accuracy are based on the results of testing performed as described in Clause 7) stated in language that is understandable by the intended user and for system accuracy performance (see 7.4.2), the manufacturer shall report:

   — for glucose concentrations $< 4{,}2$ mmol/L (75 mg/dL), the percentage of results within $\pm$ 0,28 mmol/L, $\pm$ 0,56 mmol/L and $\pm$ 0,83 mmol/L ($\pm$ 5 mg/dL, $\pm$ 10 mg/dL and $\pm$ 15 mg/dL) of the reference values;

   — for glucose concentrations $\geqslant 4{,}2$ mmol/L (75 mg/dL), the percentage of results within $\pm$ 5 %, $\pm$ 10 %, $\pm$ 15 % and $\pm$ 20 % of the reference values;

f) any interfering substances, sample conditions (e.g. haemolysis, icterus, lipemia) or physiological conditions (e.g. changes in peripheral circulation) known to affect the accuracy of results;

g) the measurement procedure used to evaluate the performance characteristics of the system, and a statement describing its traceability to a glucose reference measurement procedure or reference material of higher order;

h) the reference interval for capillary blood-glucose concentrations in nondiabetic individuals and the type of samples used for calibration (blood or plasma);

i) the measurement procedure to be followed, including:

   — the sequence of steps to prepare the reagent system and execute the measurement;

   — the timing between the individual steps, if applicable;

j) the detailed control procedures and control materials to be used to verify that the blood-glucose monitoring system is operating within its performance specifications.

The language(s) of the country in which the reagents and control materials are distributed shall be used; additional languages are optional.

Required information regarding reagents and/or control materials may be included in the instructions for use for the instrument or system if the manufacturer of the instrument or system is the same as the manufacturer of the reagents. If there is a change in this information, reagent labels should be used to notify the user, and the changed information shall be placed in the instructions for use for the reagent system.

6 Safety and reliability testing

6.1 General requirements

6.1.1 Protocol

Experimental designs, data analysis procedures and acceptance criteria shall be described in a protocol.

The protocol shall specify the number of meters, reagent units, and replicate measurements per meter.

For performance tests, the protocol shall include statistical rationale.

Specified testing requirements are minimum requirements.

NOTE 1 The tests described in 6.9 to 6.12 are performance tests.

NOTE 2 The tests described in 6.2 to 6.8 are type tests.

6.1.2 Meters and reagent systems

Meters and reagent systems shall be representative of routine production units.

For performance tests, at least ten meters shall be used in each test.

For type tests, three meters should be used in each test.

6.1.3 Acceptance criteria

Acceptance criteria for bias and repeatability for the performance tests in 6.10 to 6.13 should be derived from the system accuracy criteria in 7.4. The rationale shall be documented in the protocol.

The blood-glucose monitoring system shall pass the acceptance criteria in each test protocol. Alternatively, the system shall be rendered nonfunctional and shall not display a numerical glucose result.

Failures to meet acceptance criteria shall be investigated.

6.2 Protection against electric shock

The requirements specified in IEC 61010-1:2001, Clause 6, apply.

6.3 Protection against mechanical hazards

The requirements specified in IEC 61010-1:2001, Clause 7, apply.

6.4 Electromagnetic compatibility

The requirements specified in IEC 61326 apply.

In addition, the requirements specified in Annex A apply.

6.5 Resistance to heat

The requirements specified in IEC 61010-1:2001, Clause 10, apply.

6.6 Resistance to moisture and liquids

The requirements specified in IEC 61010-1:2001, 11.1, 11.2 and 11.3, apply.

6.7 Protection against liberated gases, explosion and implosion

The requirements specified in IEC 61010-1:2001, 13.1 and 13.2.2, apply.

6.8 Meter components

The requirements specified in IEC 61010-1:2001, 14.1, 14.4, 14.5 and 14.6, apply.

6.9 Performance test

The performance test shall be performed before and after each determination of mechanical resistance to shock, vibration and impact (see 6.10) and protection against exposure to temperature and humidity levels (see 6.11 and 6.12). Pass/fail criteria shall be based on the effect of the challenge on system bias and repeatability.

Prior to each performance test the blood-glucose meter shall be equilibrated to 23 °C ± 2 °C.

The manufacturer's recommended control material or a suitable alternative should be used for the performance tests.

It may be difficult to separate the variability due to sample and reagent system components from meter components. This should be taken into consideration when designing the test and developing acceptance criteria.

A check strip, which simulates a reagent strip after reaction with glucose, or other similar alternative to analysing the manufacturer's recommended control material, may be used to verify that measurement system performance has not been affected.

Test samples shall be measured in the order specified in the protocol.

Mean glucose concentration and repeatability shall be calculated before and after each challenge, and the difference compared to the acceptance criteria.

a) Mean glucose concentration: the difference between the mean glucose concentration after the challenge and the mean glucose concentration before the challenge shall be calculated and compared to the acceptance criteria for bias.

b) Repeatability: the square root of the difference between the repeatability variance after the challenge and the repeatability variance before the challenge shall be calculated and compared to the acceptance criteria for repeatability.

6.10 Mechanical resistance to shock, vibration and impact

6.10.1 Vibration test protocol

Perform the performance test described in 6.9.

Perform the vibration test as specified in IEC 60068-2-64:1993, 8.3.

After vibration testing is complete, repeat the performance test.

The requirements specified in IEC 60068-2-64:1993, 8.3, apply.

6.10.2 Drop test protocol

To evaluate drop durability, perform the performance test described in 6.9.

Perform the drop test as specified in IEC 61010-1:2001, 8.2.

After drop testing is complete, repeat the performance test.

The requirements specified in IEC 61010-1:2001, 8.2, apply.

6.11 Equipment temperature exposure limits

6.11.1 High temperature test protocol

Perform the performance test as described in 6.9.

Place each meter in a sealed environmental chamber that can be monitored for internal temperature.

Increase the temperature to 50 °C ± 2 °C and leave at this temperature for 8 h in the sealed chamber.

Remove the meter from the environmental chamber, and allow it to cool to a temperature of 23 °C ± 2 °C and repeat the performance test.

For those systems in which the reagent system is an integral component of the meter and cannot be separated from the device, the high temperature exposure conditions shall be limited to the use conditions specified by the manufacturer.

6.11.2 Low temperature test protocol

Perform the performance test as described in 6.9.

Place the meter in a sealed environmental chamber that can be monitored for internal temperature.

Decrease the temperature to −20 °C ± 2 °C and leave at this temperature for 8 h in the sealed chamber.

Remove the meter from the environmental chamber, allow it to warm until it reaches a temperature of 23 °C ± 2 °C and repeat the performance test.

For those systems in which the reagent system is an integral component of the meter and cannot be separated from the device, the low temperature exposure conditions shall be limited to the use conditions specified by the manufacturer.

6.12 Equipment humidity exposure test protocol

Perform the performance test described in 6.9.

Place the meter in a humidity chamber.

Stabilize the relative humidity, noncondensing to 93 % ± 3 % and a temperature of 32 °C ± 2 °C.

Leave the meter in the humidity chamber for 48 h.

Remove the meter, equilibrate it until it reaches a temperature of 23 °C ± 2 °C and a relative humidity of ⩽ 60 % for 15 min and repeat the performance test.

6.13 Reagent storage and use testing

Conditions for the storage and use of the reagent system and controls shall be defined and validated.

The requirements specified in EN 13640 apply.

7 Analytical performance evaluation

7.1 General requirements

The analytical performance evaluation shall be conducted as part of the manufacturer's design control system.

The requirements specified in ISO 13485 apply.

The performance evaluations shall be performed according to a written protocol. The protocol shall specify the experimental details, data analysis procedures and acceptance criteria.

Statistical designs, including the numbers of meters, reagent units and replicate samples, and the acceptance criteria shall be justified in the protocol.

All components of the system, including meters, reagent system and accessories, shall be representative of product intended for sale.

The blood-glucose monitoring system shall be adjusted prior to the experiment according to the manufacturer's instructions (e.g. via coding, chips). No adjustments shall be made between replicate measurements unless the manufacturer's instructions specify an adjustment before each measurement.

The manufacturer's recommended control procedures shall be performed prior to each evaluation.

NOTE 1 In 7.2 and 7.3, evaluations are design verification activities, which are intended to provide assurance that the product has the capability of meeting precision and trueness specifications set for it. In Clause 8, evaluations are design validation activities, which are intended to provide assurance that system performance meets user requirements.

NOTE 2 The type of samples required for each evaluation is specified.

7.2 Precision evaluation

7.2.1 General

Repeatability and intermediate precision shall be evaluated against performance criteria derived from the system accuracy criteria in 7.3. The acceptance criteria shall be documented in the protocol.

The analysis of variance is the preferred statistical method to use when multiple factors are evaluated.

NOTE 1 Refer to ISO 5725-1[22] for general principles regarding the evaluation of precision of a measurement method.

NOTE 2 The experiments can be designed to evaluate the effect of such factors as different lots, different sample materials, different users, or other variables (e.g. effect of temperature, humidity).

7.2.2 Repeatability evaluation

7.2.2.1 General

Repeatability shall be evaluated at five glucose concentrations spread across the measuring interval.

Repeatability shall be measured over a short span of time, not to exceed one day per meter, with the same user, meter and reagent lot. The experiment shall be designed to minimize the effect of glucose instability in the sample.

The evaluation may be performed on a single lot and/or by a single user if data have demonstrated that the repeatability of the system is not dependent on particular reagent lots and/or users. Otherwise, the experiment shall be designed to evaluate the dependence of repeatability on these factors.

NOTE Refer to ISO 5725-2[23] for guidelines for determining the repeatability of a measurement method.

7.2.2.2 Samples

The repeatability evaluation shall be performed with blood samples. The preferred sample for evaluation of repeatability is venous blood.

Samples shall be prepared from human venous blood collected into tubes containing an anticoagulant specified in the instructions for use. The packed cell volumes (haematocrit) shall be within 0,35 L/L to 0,50 L/L (35 % to 50 %).

Five samples with glucose concentrations in the intervals specified in Table 1 shall be used. The glucose concentration of each sample shall be determined using the blood-glucose monitoring system.

The glucose concentration in venous blood samples may be adjusted by supplementing the sample with an aqueous glucose solution prepared with a 0,9 % saline solution. The dilution should not significantly alter the sample matrix. Spiked samples should be allowed to stand for at least 15 min before use to allow for complete mutarotation and equilibration of the *D* and *L* enantiomers.

A preservative that does not interfere with the glucose measurements (e.g. maleimide, fluoride, or monoiodoacetate) and is in accordance with the manufacturer's recommendations may be added to the sample in sufficient amount to minimize glycolysis.

To achieve lower glucose concentrations, anticoagulated blood samples may be allowed to age until the glucose is depleted to the desired level.

Table 1 — Glucose concentration intervals for repeatability evaluation

Interval	Glucose concentration mmol/L (mg/dL)
1	1,7 to 2,8 (30 to 50)
2	2,9 to 6,1 (51 to 110)
3	6,2 to 8,3 (111 to 150)
4	8,4 to 13,9 (151 to 250)
5	14,0 to 22,2 (251 to 400)

7.2.2.3 Reagent system

At least 500 reagent system units, from at least ten vials or packages, are required.

7.2.2.4 Meters

At least ten meters shall be chosen to evaluate the repeatability of the blood-glucose monitoring system.

7.2.2.5 Evaluation procedure

The following procedure is the minimum experimental design to evaluate repeatability. It requires ten measurements by each meter of samples from each glucose concentration interval in Table 1.

NOTE The procedure may be modified to accommodate multiple reagent lots and/or users.

The samples shall be equilibrated to a temperature of 23 °C ± 5 °C and maintained within ± 2 °C of the starting temperature during the experiments.

The samples shall be gently but thoroughly mixed by inversion before each portion is taken for measurement.

The reagent system units shall be taken from the same vial/package for each meter.

a) Assign a vial/package of reagent system units to each meter.

b) Take one reagent system unit out of a vial/package and apply the sample. Record the result.

   A transfer pipette (i.e. not a repeatable measuring pipette) capable of delivering sample volumes within the manufacturer's recommended interval may be used to simulate routine sample application.

c) Repeat step b) nine more times using the same meter.

d) Using the same sample, repeat steps b) and c) with each of the nine remaining meters and vials or packages. This results in a total of ten measurements per sample per meter.

e) Take the next sample and repeat steps a) to d).

f) Calculate the mean value, the standard deviation and the coefficient of variation (CV) for each meter from the ten measurements.

g) Calculate the grand mean, the pooled variance, the pooled standard deviation (with 95 % confidence interval) and the pooled CV.

NOTE The standard deviation and CV are measures of repeatability.

The experiment may be designed so as to obtain the repeatability standard deviation as well as other variance components by analysis of variance instead of following steps f) and g).

Aliquots shall be removed from each sample immediately before the first and immediately after the last measurement by the blood-glucose monitoring system for measurement (minimum in duplicate) by the manufacturer's selected or standing measurement procedure.

If these results demonstrate the effect of drift based on predetermined stability criteria [e.g. change between the first and last results > 4 % at glucose $> 5{,}5$ mmol/L (100 mg/dL) or $> 0{,}22$ mmol/L (4 mg/dL) at glucose $\leqslant 5{,}5$ mmol/L (100 mg/dL)], then the results for that sample shall not be used and all measurements for that sample shall be repeated.

7.2.3 Intermediate precision evaluation

7.2.3.1 General

Intermediate precision shall be evaluated at three glucose concentrations.

The evaluation shall be designed to measure precision in normal conditions of use, i.e. by an individual user across multiple days with the same meter and reagent system lot.

The evaluation shall be conducted with multiple meters and different users over at least ten days.

The evaluation may be performed on a single lot if data have demonstrated that intermediate precision (including repeatability) is not dependent on the reagent lot. Otherwise, multiple lots should be used and the experiment shall be designed to evaluate lot-to-lot variability.

NOTE Refer to ISO 5725-3 for guidelines for determining the intermediate precision of a measurement method.

7.2.3.2 Samples

The intermediate precision evaluation shall be performed with control materials.

The preferred samples are the control materials provided by the manufacturer. Alternative control materials may be used if approved for use by the manufacturer of the blood-glucose monitoring system.

Control material shall be prepared according to the instructions for use. Sample stability over the evaluation period shall be validated.

Three samples with glucose concentrations in the intervals specified in Table 2 shall be used. The glucose concentration of each sample shall be determined using the blood-glucose monitoring system.

Table 2 — Glucose concentration intervals for intermediate precision evaluation

Interval	Glucose concentration mmol/L (mg/dL)
1	1,7 to 2,8 (30 to 50)
2	5,3 to 8,0 (96 to 144)
3	15,5 to 23,3 (280 to 420)

7.2.3.3 Reagent system

A lot or part of a lot shall be examined. If a complete lot is not available, the part and status of the material shall be recorded.

Three hundred reagent system units from at least ten vials or packages are required.

If multiple lots are used, the experiment shall be designed so that all results from a single meter are obtained using the same lot of reagent system.

7.2.3.4 Meters

At least ten meters shall be selected to evaluate the intermediate precision of the blood-glucose monitoring system.

7.2.3.5 Evaluation procedure

The following procedure is the minimum experimental design to evaluate intermediate precision over multiple days. It requires one measurement per day of a sample from each glucose concentration interval in Table 2 for 10 days for each of ten meters.

The procedure may be modified to accommodate multiple reagent lots.

The reagent system units shall be taken from the same vial/package for each sample.

a) Assign a vial/package of reagent system units to each meter.

b) Take one reagent system unit out of each vial/package and apply the sample. Record the result.

   A transfer pipette (i.e. not a repeatable measuring pipette) capable of delivering sample volumes within the manufacturer's recommended interval may be used to simulate routine sample application.

c) Repeat step b) for each sample.

d) Repeat steps b) and c) once each day with each of the nine remaining meters and vials or packages for a total of ten days. The same vial/package is used for each meter throughout the evaluation period.

e) Calculate the mean value, standard deviation and CV for each meter from the ten measurements.

f) Calculate the grand mean, the pooled standard deviation (with 95 % confidence interval) and the pooled CV. The standard deviation and CV are measures of the intermediate precision of a single system over multiple days.

If the evaluation included multiple lots and/or users, the lot-to-lot and user-to-user variability may be determined as well as the within-meter intermediate precision.

7.2.4 Data analysis and presentation for repeatability and intermediate precision

The mean, standard deviation and coefficient of variation for repeatability and intermediate precision shall be calculated using documented statistical procedures. The analysis of variance is the preferred method for calculating intermediate precision.

The following information shall be reported:

a) glucose concentration of each sample;

b) mean of the observed glucose results for each sample;

c) repeatability standard deviation (with 95 % confidence interval) and coefficient of variation (CV) for each glucose concentration above 4,2 mmol/L (75 mg/dL) and standard deviation (with 95% confidence interval) for each glucose concentration below 4,2 mmol/L (75 mg/dL);

d) intermediate standard deviation (with 95 % confidence interval) and coefficient of variation (CV) for each glucose concentration above 4,2 mmol/L (75 mg/dL) and standard deviation (with 95 % confidence interval) for each glucose concentration below 4,2 mmol/L (75 mg/dL);

e) summary of any outliers (guidelines for identifying outliers are found in ISO 5725-2:1994[23] and in NCCLS EP5-A[30]) identified and excluded from statistical analysis, including the method of identification and the results of the investigation;

f) references to the statistical analysis procedures.

7.3 System accuracy evaluation

7.3.1 Requirements

7.3.1.1 General

System accuracy shall be evaluated with at least 100 different subjects over at least ten days. The evaluation shall be conducted in actual conditions of use, so that the effects of systematic error (bias) and random error (imprecision) that would be experienced by individual users will be included.

Individual measurements from the blood-glucose monitoring system shall be compared to reference glucose concentration values determined by the manufacturer's measurement procedure (i.e. a selected or standing measurement procedure) or by another validated measurement procedure that has been shown to produce equivalent results).

A routine glucose measurement procedure (e.g. in a hospital or outpatient clinic laboratory) that is validated for precision and trueness by comparison to the manufacturer's selected or standing measurement procedure may be used to assign the reference values.

A detailed description of the measurement procedure used to determine the reference values, including its traceability and/or equivalence, shall be documented in the protocol.

7.3.1.2 Samples

The system accuracy evaluation shall be performed with at least 100 fresh capillary blood samples, each with sufficient volume to be measured by two different meters and at least in duplicate by the manufacturer's measurement procedure.

Exclusion criteria, such as packed cell volume (haematocrit), shall be based on the manufacturer's instructions for use.

Capillary blood samples shall be collected by skin puncture (e.g. fingerstick), prepared and processed according to the instructions for use, including sample pretreatment if required. Sample containers designed for the collection of capillary blood should be used.

In some cases, a second skin puncture may be necessary to obtain sufficient sample volume to complete the protocol.

It may be difficult to obtain a sufficient number of fresh capillary blood samples with very low and very high glucose concentrations. In these cases, modified capillary blood samples in which the glucose concentration is elevated or lowered may be substituted (see below).

The glucose concentrations shall be distributed as specified in Table 3. Glucose concentrations shall be determined by the blood-glucose monitoring system.

Once a concentration category is filled, no more samples shall be added to that category.

Table 3 — Glucose concentrations of samples for system accuracy evaluation

Percentage of samples %	**Glucose concentration** mmol/L (mg/dL)
5	< 2,8 (< 50)
15	2,8 to 4,3 (50 to 80)
20	4,4 to 6,7 (80 to 120)
30	6,7 to 11,1 (120 to 200)
15	11,2 to 16,6 (201 to 300)
10	16,7 to 22,2 (301 to 400)
5	> 22,2 (> 400)

Only unaltered capillary blood samples shall be used for glucose concentrations of 2,8 mmol/L to 22,2 mmol/L (50 mg/dL to 400 mg/dL). If necessary to obtain sufficient samples in the lowest and highest concentration intervals, glucose concentrations may be adjusted as follows.

— To obtain additional samples with glucose < 2,8 mmol/L (< 50 mg/dL), capillary blood samples should be collected with an appropriate anticoagulant and incubated to allow glucose to hydrolyse. The incubation conditions (e.g. temperature) to produce samples compatible with the system (e.g. without haemolysis) shall be determined by the manufacturer.

— To obtain additional samples with glucose > 22,2 mmol/L (> 400 mg/dL), capillary blood samples should be collected with an appropriate anticoagulant and then supplemented with glucose.

— Commutability of adjusted samples with the system being evaluated shall be verified.

Aliquots shall be removed from each sample immediately before the first and immediately after the last measurement by the blood-glucose monitoring system for duplicate measurement by the manufacturer's measurement procedure.

If this measurement procedure is not designed for blood samples and it does not specify a procedure to remove cells, the aliquots of the sample shall be centrifuged at 1 000 g for 10 min immediately after collection to obtain plasma.

7.3.1.3 Reagent system

A lot or part of a lot of reagent system units shall be examined. If a complete lot is not available, the parts and status of the material shall be recorded.

At least 200 reagent system units, from at least ten vials or packages, shall be used. Additional units from the same lot shall be available for additional measurements as needed.

A single lot of reagent system units may be used if characterization data have demonstrated that lot-to-lot variability is a minor source of the total variability. Otherwise, multiple reagent lots shall be included in the system accuracy evaluation.

7.3.1.4 Meters

Using more than one meter per subject may be necessary to minimize the time between duplicate measurements. The procedure in 7.3.2 assumes each subject will use two different meters.

If more than two meters are used, the meters shall be rotated through the protocol so that equal numbers of samples are measured with each meter.

NOTE Increasing the number of meters in the experiment reduces the specific influence of each meter (bias), but can increase variability due to meter-to-meter effects (intermediate precision).

If different subjects use the same meter, cleaning the meter may be necessary to avoid the transfer of blood-borne pathogens. It is recommended that manufacturers validate an appropriate cleaning procedure and include cleaning information in the user's manual.

7.3.1.5 Environment

Measurements using the blood-glucose monitoring system shall be performed at 23 °C ± 5 °C.

The measurement of capillary blood samples by the blood-glucose monitoring system should preferably take place in a diabetes mellitus outpatient clinic or hospital setting. The 10 °C temperature interval covers the ambient temperatures that typically exist in these settings.

7.3.2 Evaluation procedure

The following procedure is the minimum experimental design to evaluate system accuracy. It requires at least 100 subjects with glucose concentrations that span the measuring interval as specified in Table 3.

This procedure may be modified to accommodate multiple reagent lots.

The reagent system units shall be taken from the same vial/package for each sample.

Steps a) to f) shall be performed for each sample.

a) Assign numbers to the vials or packages (e.g. 1 to 10).

b) Obtain a sample of fresh capillary blood by skin puncture.

c) Remove an aliquot of the sample for at least duplicate glucose measurements by the manufacturer's measurement procedure. If the manufacturer's measurement procedure is designed for plasma samples, the plasma preparation procedure (e.g. centrifugation at 1 000 g for 10 min to remove cells) shall be performed for each sample.

d) Take two reagent system units out of vial/package number one and measure the glucose concentration in the sample using two different meters.

Samples shall be applied to the reagent system unit in the same manner as described in the manufacturer's instructions (e.g. directly from the subject's skin puncture). If adjusted samples are used, as described in 7.3.1.2, they shall be applied in a manner that simulates the procedure specified in the manufacturer's instructions for use, taking into account possible influences such as sample temperature.

Change vials or packages every ten subjects and ensure that reagent system units from all vials are used in the evaluation. Record the results.

e) Repeat step c) to obtain a second result from the manufacturer's measurement procedure.

f) Evaluate the results from the manufacturer's measurement procedure to verify sample stability.

If these results demonstrate the effect of drift based on predetermined stability criteria [e.g. change between the first and last results > 4 % at glucose $> 5{,}5$ mmol/L (100 mg/dL) or $> 0{,}22$ mmol/L (4 mg/dL) at glucose $\leqslant 5{,}5$ mmol/L (100 mg/dL)], then the results for that subject shall not be included. The rejected sample shall be replaced with another sample in the same glucose concentration interval.

Drift criteria should be related to the intermediate precision capability of the measurement procedure. If criteria are too tight, samples will be discarded unnecessarily. If too loose, the apparent uncertainty of the measurement procedure will be inflated.

g) Obtain a sample from the next subject and repeat steps b) to f).

7.3.3 Data analysis and presentation for system accuracy

7.3.3.1 General

Results shall be plotted and analysed using one of the procedures described below.

The following information shall be reported:

a) total number of samples analysed;

b) range of glucose concentrations;

c) plot of the data;

d) summary of the statistics with confidence intervals;

e) summary of any outliers (guidelines for identifying outliers are found in ISO 5725-2:1994[23] and in NCCLS EP9-A2[32]) identified and excluded from statistical analysis, including the method of identification and the results of the investigation;

Outlier data may not be eliminated from the data set to be used in determining minimum acceptable accuracy (7.4.1), but should be excluded from the calculation of parametric statistics to avoid distorting central tendency and dispersion estimates. Outlier data should be plotted with a different symbol.

f) references for the statistical analysis procedures.

If results of the blood-glucose monitoring system are reported in units of a different sample matrix (e.g. plasma), the manufacturer shall provide details of the conversion and supporting validation data to users upon request.

7.3.3.2 System accuracy analysis

The difference between individual results from the blood-glucose monitoring system and the mean of the reference values shall be plotted as the dependent variable. The mean of the reference values shall be plotted as the independent variable.

Difference plots are the recommended approach for depicting system accuracy because statistical assumptions are minimal and the percentage of data points meeting the system accuracy criteria, as well as estimating bias, are easily calculated. See NCCLS EP9-A2[32] or Bland and Altman[34].

NOTE Plotting percentage difference against concentration at low concentrations is generally not suitable for the graphical evaluation of system accuracy.

EXAMPLE A plot of results from an evaluation of a blood-glucose monitoring system is illustrated in Figure 1. The two bold lines represent the acceptance criteria from 7.4.

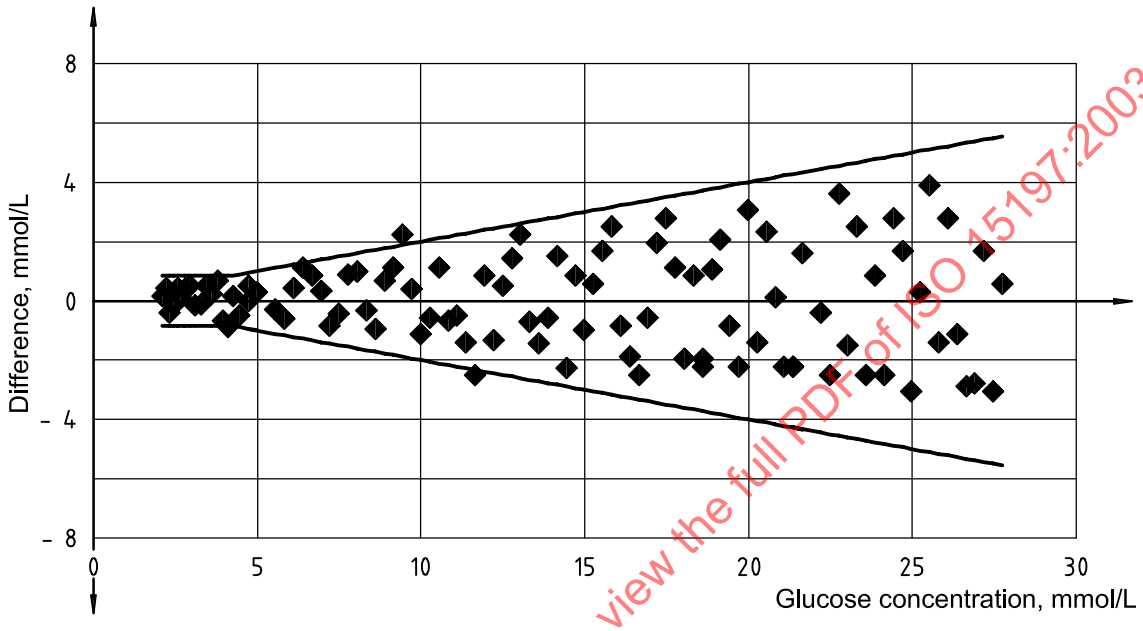


Figure 1 — System accuracy plot

7.3.3.3 Regression analysis

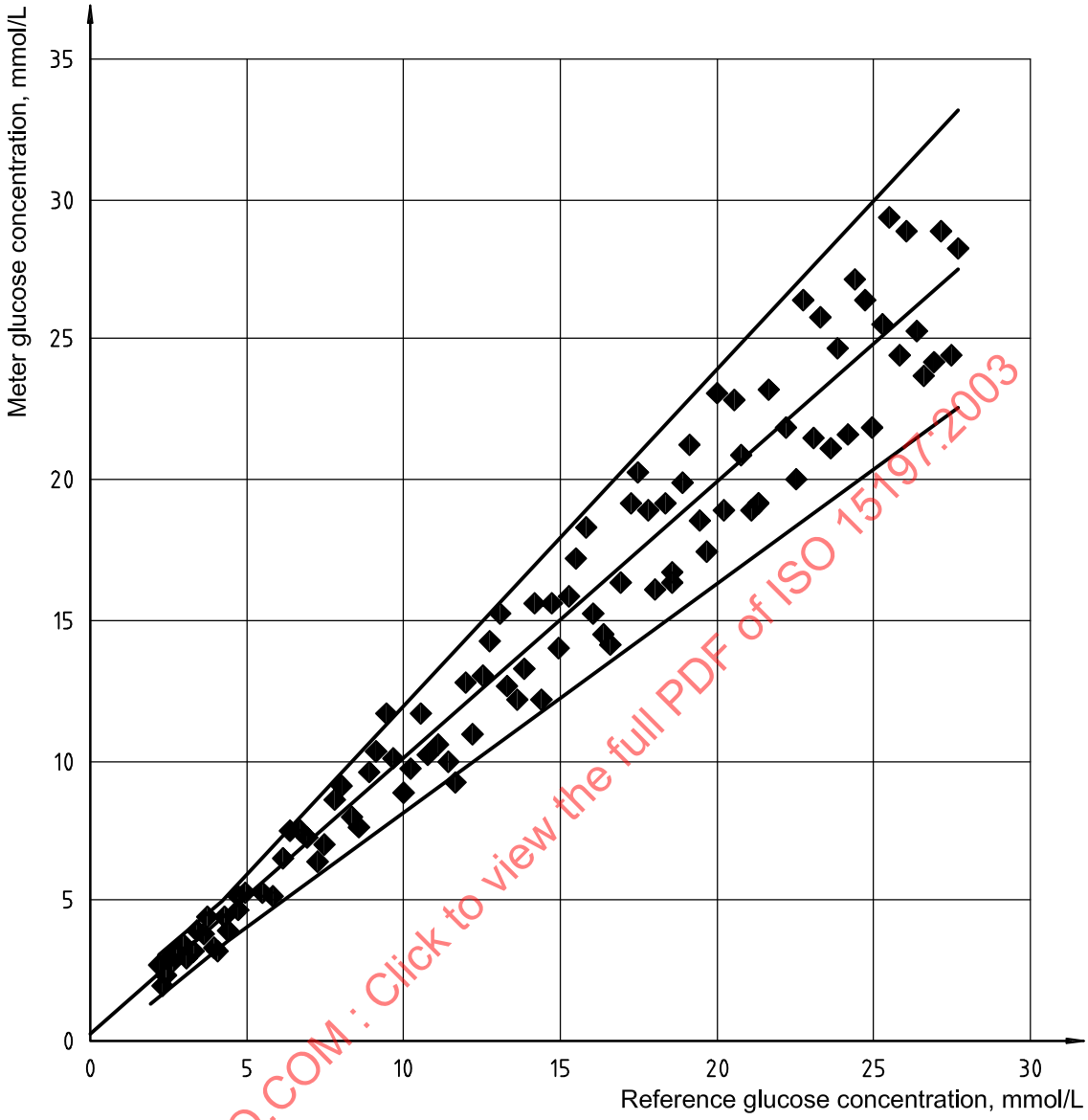
Individual results of the blood-glucose monitoring system shall be plotted as the dependent variable and the mean of the duplicate reference values as the independent variable. Identical scales and intervals shall be used for the x- and y-axes.

Slope and y-intercept shall be calculated by a suitable regression analysis procedure. The estimate of the deviation (standard error) ($s_{y,x}$) should be reported, if linear regression is used. The regression line and the line of identity (y=x) shall be included on the plot.

NOTE 1 Regression analysis depends on the data meeting certain statistical assumptions. For an evaluation of regression procedures for method comparison studies, see Linnet[33] or Stöckl[36].

NOTE 2 Bias can be calculated from the regression equation at selected glucose concentrations (e.g. at medical decision concentrations). See NCCLS EP9-A2[32].

EXAMPLE A regression plot from an evaluation of a blood-glucose monitoring system is illustrated below. The two outer lines represent the acceptance criteria from 7.4. The regression line and the line of equality are superimposed.



y = 0,984x + 0,20

R^2 = 0,959 6

N = 200

Figure 2 — Regression plot

7.4 Minimum acceptable system accuracy

7.4.1 System accuracy requirement

The minimum acceptable accuracy for results produced by a glucose monitoring system shall be as follows.

Ninety-five percent (95 %) of the individual glucose results shall fall within ± 0,83 mmol/L (15 mg/dL) of the results of the manufacturer's measurement procedure at glucose concentrations < 4,2 mmol/L (< 75 mg/dL) and within ± 20 % at glucose concentrations ⩾ 4,2 mmol/L (⩾ 75 mg/dL).

NOTE 1 The minimum acceptable accuracy criteria are based on the medical requirements for glucose monitoring. See the Introduction for additional information.

NOTE 2 The criteria apply to system accuracy evaluations in which users have received proper training, the device has been properly maintained and required adjustment and control procedures have been followed in accordance with the manufacturer's instructions for use.

7.4.2 Data presentation

Results shall be presented separately for the glucose concentration intervals < 4,2 mmol/L (< 75 mg/dL) and ⩾ 4,2 mmol/L (⩾ 75 mg/dL) because different criteria apply.

a) For glucose concentrations < 4,2 mmol/L (75 mg/dL), results shall be expressed as the percentage of values falling within the following intervals: ± 0,28 mmol/L (± 5 mg/dL), ± 0,56 mmol/L (± 10 mg/dL), and ± 0,83 mmol/L (± 15 mg/dL).

b) For glucose concentrations ⩾ 4,2 mmol/L (75 mg/dL), results shall be expressed as the percentage of values falling within the following intervals: ± 5 %, ± 10 %, ± 15 % and ± 20 %.

The results shall be presented in a table for each concentration interval. The recommended format is given in the Example and Tables 4 and 5 below.

EXAMPLE Tables 4 and 5 illustrate the presentation of results for the evaluation illustrated in 7.3.3.2 and 7.3.3.3, in which 200 results were obtained from 100 subjects. The data and criteria to be used in determining acceptability are shown in *italics*.

Table 4 — Example of presentation of system accuracy results for glucose concentration < 4,2 mmol/L (75 mg/dL)

Within ± 0,28 mmol/L (Within ± 5 mg/dL)	**Within ± 0,56 mmol/L** (Within ± 10 mg/dL)	***Within ± 0,83 mmol/L*** *(Within ± 15 mg/dL)*
18/40 (45 %)	28/40 (70 %)	*38/40 (95 %)*

Table 5 — Example of presentation of system accuracy results for glucose concentration ⩾ 4,2 mmol/L (75 mg/dL)

Within ± 5 %	**Within ± 10 %**	**Within ± 15 %**	***Within ± 20 %***
36/160 (22 %)	78/160 (49 %)	136/160 (85 %)	*156/160 (97 %)*

7.4.3 System accuracy assessment

Acceptability of the blood glucose monitoring system shall be determined using all of the 200 results obtained from the 100 subjects, including any results identified as statistical outliers. The number of acceptable results at glucose concentrations < 4,2 mmol/L (< 75 mg/dL) shall be added to the number of acceptable results at glucose concentrations ⩾ 4,2 mmol/L (⩾ 75 mg/dL) to determine the number of acceptable results.

NOTE 1 In the example in 7.4.2, 38 of 40 hypoglycaemic samples were within ± 0,83 mmol/L (± 15 mg/dL) at concentrations < 4,2 mmol/L (< 75 mg/dL) and 156 of the 160 samples with glucose concentrations ⩾ 4,2 mmol/L (⩾ 75 mg/dL) were within ± 20% of the reference values. Therefore, 194 of 200 samples (97,0 %) were within the minimum acceptable performance criteria defined in 7.4.1.

NOTE 2 There are insufficient samples in each concentration interval to permit valid assessment of acceptability at specific concentrations.

8 User performance evaluation

8.1 General

The purpose of the user performance evaluation is to demonstrate that users are able to operate the blood-glucose monitoring system, given only the instructions and training materials routinely provided with the system and obtain valid glucose results.

A user performance evaluation shall be performed by the manufacturer prior to placing a new blood-glucose monitoring system into commercial distribution.

NOTE Healthcare professionals who wish to demonstrate the performance of a blood-glucose monitoring system in a healthcare setting can consult NCCLS C30-A2[11] for guidance.

Results obtained by the lay user shall be compared to results obtained by a validated glucose measurement procedure, as well as to results obtained by a healthcare professional from the same sample, using the same blood-glucose monitoring system.

The evaluation plan shall be documented in a detailed protocol. The requirements specified in EN 13612 apply.

At least 50 subjects, with varying demographics (age, sex, and education level), shall be included for each lot.

Study participants shall meet the requirements of the blood-glucose system (e.g. packed cell volume within the system's specified interval).

User studies shall be conducted using at least three different reagent lots.

8.2 Evaluation sites

Blood-glucose monitoring systems for self-testing shall be evaluated in a setting that allows the lay user to perform the measurements without outside influence, i.e. as described in 8.1.

Rationale for the selection of evaluation sites shall be documented.

The evaluation may be conducted at multiple sites.

8.3 User evaluation

Study participants shall be given the product instructions for use and any training materials that are routinely provided with the blood-glucose monitoring system.

After reviewing the materials, the users shall perform their own fingersticks and test themselves using the blood-glucose monitoring system.

Immediately after the user's self-test, the investigation site's trained healthcare professional shall measure the user's blood with the blood-glucose monitoring system.

Within 5 min, a second blood sample shall be collected. The reference glucose concentrations shall be determined by the manufacturer's measurement procedure (i.e. a selected or standing measurement procedure or by another validated measurement procedure that has been shown to produce equivalent results).

A routine glucose measurement procedure (e.g. in a hospital or outpatient clinic laboratory) that is validated for precision and trueness by comparison to the manufacturer's selected or standing measurement procedure may be used to assign the reference values.

A detailed description of the measurement procedure used to determine the glucose values, including its traceability and/or equivalence to the manufacturer's selected or standing measurement procedure, shall be documented in the protocol.

Study participants shall not receive additional training, instructions, assistance, or training materials other than those routinely provided with the blood-glucose monitoring system.

Study participants may be given a questionnaire to evaluate their understanding of the system.

User techniques in operating and maintaining the system, applying the sample, and reading the result shall be evaluated by the trained healthcare professional participating in the study.

Results shall be documented in a report.

8.4 Evaluation of instructions for use

Instructions for use shall be evaluated by the intended users.

Study participants and healthcare professionals shall review the instructions for use and provide comments regarding the ease of understanding.

This evaluation may be combined with the testing described in 8.3, or may be conducted separately.

User comments may be collected via questionnaires, or as part of human factors studies.