INTERNATIONAL STANDARD

ISO 23783-1

First edition
2022-08

Automated liquid handling systems —

Part 1: Vocabulary and general requirements

Systèmes automatisés de manipulation de liquides —

Partie 1: Vocabulaire et exigences générales

Reference number
ISO 23783-1:2022(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

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.

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 ISO documents should be noted. This document was drafted in accordance with the editorial rules of the ISO/IEC Directives, Part 2 (see www.iso.org/directives).

Attention is drawn to the possibility that some of the elements of this document may be the subject of patent rights. ISO 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).

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

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

This document was prepared by Technical Committee ISO/TC 48, *Laboratory equipment*.

This first edition of ISO 23783-1, together with ISO 23783-2 and ISO 23783-3, cancels and replaces IWA 15:2015.

A list of all parts in the ISO 23783 series can be found on the ISO website.

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

Introduction

Globalization of laboratory operations requires standardized practices for operating automated liquid handling systems (ALHS), communicating test protocols, as well as analysing and reporting of performance parameters. IWA 15:2015 was developed to provide standardized terminology, test protocols, and analytical methods for reporting test results. The concepts developed for, and described in, IWA 15 form the foundation of the ISO 23783 series.

Specifically, this document addresses the needs of:

— users of ALHS, as a basis for calibration, verification, validation, optimization, and routine testing of trueness and precision;

— manufacturers of ALHS, as a basis for quality control, communication of acceptance test specifications and conditions, and issuance of manufacturer's declarations (where appropriate);

— test houses and other bodies, as a basis for certification, calibration, and testing.

The tests established in this document should be carried out by trained personnel.

Automated liquid handling systems —

Part 1:
Vocabulary and general requirements

1 Scope

This document defines terms relating to automated liquid handling systems (ALHS). This document also specifies general requirements for the use of ALHS. It describes types of ALHS and specific use requirements, settings, and adjustments for each ALHS type. It also specifies environmental requirements for the use of ALHS.

This document is applicable to all ALHS with complete, installed liquid handling devices, including tips and other essential parts needed for delivering a specified volume, which perform liquid handling tasks without human intervention into labware.

NOTE Measurement procedures for the determination of volumetric performance are given in ISO 23783-2. The determination, specification, and reporting of volumetric performance of automated liquid handling systems are described in ISO 23783-3.

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 23783-2, *Automated liquid handling systems — Part 2: Measurement procedures for the determination of volumetric performance*

ISO 23783-3:2022, *Automated liquid handling systems — Part 3: Determination, specification, and reporting of volumetric performance*

3 Terms and definitions

For the purposes of this document, the following terms and definitions 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
accuracy
accuracy of liquid delivery
<ALHS> closeness of agreement between the delivered volume and the target volume

Note 1 to entry: The concept "accuracy" is not given a numerical value. A liquid delivery is said to be more accurate when it is made with a smaller error.

Note 2 to entry: The term "accuracy" shall not be used for "trueness" and the term "precision" should not be used for 'accuracy,' which, however, is related to both of these concepts.

Note 3 to entry: The relationship between accuracy, systematic error, and random error of an automated liquid handling system is explained further in ISO 23783-3:2022, 5.1.

[SOURCE: ISO/IEC Guide 99:2007, 2.13, modified — definition and Notes 1 and 2 were modified for the context of automated liquid handling and Note 3 was replaced.]

3.2
air displacement
<piston-operated ALHS> liquid handling principle in which a body of air is contained between the piston and the test liquid

Note 1 to entry: It is possible to have a large air gap (piston systems), or a smaller air gap between the test liquid and the system liquid (liquid filled systems).

3.3
air gap
captive air volume
dead air volume
<piston-operated ALHS> air volume between the lower part of the piston and the surface of the aspirated liquid

Note 1 to entry: It is possible to have a large air gap (piston systems), or a smaller air gap for liquid filled systems.

3.4
automated liquid handling system
ALHS
system with a complete, installed liquid handling device, including tips and other essential components needed for delivering a specified volume without human intervention into labware

Note 1 to entry: Examples of automated liquid handling systems include automated pipetting systems (APS), and automated dispensing systems (ADS).

3.5
calibration
<ALHS> operation that, under specified conditions, establishes a relation between the target volume of the ALHS and the delivered volume

Note 1 to entry: A calibration may be expressed by a statement, a calibration curve or a calibration table. It may include a correction, but correction or adjustment is not a required element of a calibration.

[SOURCE: ISO/IEC Guide 99:2007, 2.39, modified — definition was simplified and modified for the context of automated liquid handling; Note 1 was simplified and Notes 2 and 3 were deleted.]

3.6
correction
mathematical compensation for a systematic effect

Note 1 to entry: The mathematical compensation can take different forms, such as an addend or a factor, or can be deducted from a table.

[SOURCE: ISO/IEC Guide 99:2007, 2.53, modified – added mathematical to the definition and Note 2, deleted estimated from the definition, and Note 1 was deleted.]

3.7
delivered volume
quantity delivered by a liquid handling system

Note 1 to entry: Delivered volume is a conceptual term and cannot be known with complete certainty due to measurement error.

3.8
dispense height
initial distance at which the test liquid is dispensed relative to a stated reference

Note 1 to entry: Dispensing from an initial fixed distance relative to the liquid surface will decrease the dispense height as the liquid level rises.

Note 2 to entry: Dispensing from a fixed distance relative to the well bottom will not change the dispense height over the course of the dispense.

Note 3 to entry: Dispensing and adjusting the distance relative to the liquid surface will not change the dispense height over the course of the dispense. This is an operational mode possible with some ALHS liquid level detection systems.

Note 4 to entry: Dispensing and adjusting the distance relative to the well bottom will increase the dispense height over the course of the dispense. This is an operational mode possible with some ALHS liquid level detection systems.

3.9
dispensing system
device for delivering liquids from a pre-filled liquid reservoir

3.10
disposable tip
component to transfer liquid, which is attached once and after use, as defined by the manufacturer, detached and intended to be discarded

Note 1 to entry: Disposable tips are usually made of plastic.

Note 2 to entry: Disposable tips are in contrast to *fixed tips* (3.13).

3.11
dry contact dispensing
transferring of liquid while the tip is in contact with a dry surface

3.12
factory acceptance testing
internal testing at the site of ALHS production to ensure ALHS performance to manufacturer's specifications

3.13
fixed tip
component to transfer liquid, which remains attached to the dispense head after use and is cleaned prior to its next use

Note 1 to entry: Fixed tips are in contrast to *disposable tips* (3.10).

3.14
forward mode pipetting
direct mode pipetting
process of liquid transfer where the entire aspirated volume is delivered

3.15
immersion depth
depth of the tip orifice below the liquid surface

Note 1 to entry: Immersion depth can be applied to both aspiration and dispensing (wet contact).

3.16
individually controlled channel
<ALHS> liquid handling channel that can be operated independently of other channels

3.17
inkjet type dispenser
dispensing system which uses technologies that deliver liquid volume as individual, free-flying droplets or jets (e.g. inkjet technology)

Note 1 to entry: For example, multiple volume increments as small as a few picolitres can be added up to dispense volumes of several microlitres.

3.18
labware
<ALHS> materials used in conjunction with liquid handling operations

Note 1 to entry: Labware includes, but is not limited to, disposable tips, reservoirs, receiving vessels, adapters and microplates.

3.19
liquid class
specific liquid or liquid type, which is defined by specific liquid characteristics that require specific settings of the liquid handler to achieve a desired volume delivery

3.20
maximum permissible error
upper or lower permitted extreme value for the deviation of the dispensed volume from the target volume

3.21
maximum specified volume
largest volume for which specifications are provided

3.22
measured volume
quantity reported by a volume measuring system

Note 1 to entry: In practice, all measurements contain some measurement error. The measured volume is a quantity value and serves as an estimate of the delivered volume which is not known with complete certainty.

3.23
minimum specified volume
smallest volume for which specifications are provided

3.24
measurement method
measurement procedure
detailed description of a measurement according to one or more measurement principles

Note 1 to entry: Sometimes, a distinction is drawn between a "‘measurement method" and a "measurement procedure". In this document, the terms are used interchangeably.

Note 2 to entry: The measurement method descriptions in this document detail the steps needed to make a volume measurement and calculate certain descriptive statistics. Additional details needed to operate the ALHS are part of the *test process* (3.51). In this document, the measurement method is one of the components of a test process.

3.25
measurement uncertainty
<delivered volume> non-negative parameter characterizing the statistical dispersion of the delivered volumes

Note 1 to entry: The measurement uncertainty of the mean delivered volume and the measurement uncertainty of a single delivered volume are two distinct applications of this concept.

Note 2 to entry: The measurement uncertainty of the mean delivered volume and the measurement uncertainty of a single delivered volume include contributions from the random errors and uncorrected systematic errors of the ALHS.

Note 3 to entry: The measurement uncertainty includes contributions from the measuring system uncertainty, as well as the ALHS under test.

Note 4 to entry: These measurement uncertainties can be estimated according to ISO/IEC Guide 98-3.

3.26
measuring system uncertainty
non-negative parameter characterizing the statistical dispersion of the volume results of the measurement procedure, which does not include the uncertainty of the ALHS under test

Note 1 to entry: The measuring system uncertainty can be estimated according to ISO/IEC Guide 98-3.

3.27
metrological confirmation
set of operations required to ensure that the ALHS conforms to the requirements for its intended use

Note 1 to entry: Metrological confirmation generally includes calibration or verification, any necessary adjustment or repair, and subsequent recalibration, comparison with the metrological requirements for the intended use of the ALHS, as well as any required sealing and labelling.

Note 2 to entry: Metrological confirmation is not achieved until and unless the fitness of the ALHS for the intended use has been demonstrated and documented.

Note 3 to entry: The requirements for intended use include such considerations as range, resolution and maximum permissible errors.

Note 4 to entry: Metrological requirements are usually distinct from, and are not specified in, product requirements.

[SOURCE: ISO 9000:2015, 3.5.6, modified — the terms 'measurement equipment' and 'equipment' were replaced by 'ALHS.']

3.28
metrological traceability
traceability
property of a measurement result whereby the result can be related to a reference through a documented unbroken chain of calibrations, each contributing to the measurement uncertainty

Note 1 to entry: Additional information can be found in the notes to definition (ISO/IEC Guide 99:2007, 2.41) and the related term 'metrological traceability chain' (ISO/IEC Guide 99:2007, 2.42).

[SOURCE: ISO/IEC Guide 99:2007, 2.41, modified — Notes 1 to 4 were deleted and a new Note 1 to entry was added.]

3.29
microplate
flat plate with an array of wells

Note 1 to entry: Some dimensions of microplates are defined in ANSI/SLAS standards[5–9].

3.30
multichannel head
<ALHS> group of liquid handling channels operated in common

Note 1 to entry: Common arrangements of multichannel heads include 8-, 96-, 384-, and 1 536-channel heads. Other arrangements are possible, e.g. 2-channel to 1 536-channel configurations.

3.31
multi-dispense
repeat dispense
sequential dispense
<ALHS> collection of dispenses without intervening aspiration

Note 1 to entry: First dispense can be different and is frequently wasted.

Note 2 to entry: Repeat dispenses usually dispense repeatedly the same volume, while sequential dispenses usually dispense different volumes.

3.32
non-contact dispensing
contact-free dispensing
free-jet dispensing
dispensing of the liquid without contacting the target or the liquid contained in the target

3.33
outlier
member of a set of values which is inconsistent with the other members of that set

3.34
pipetting system
system for aspirating and dispensing a specified volume of liquid

3.35
positive displacement
direct displacement
<piston-operated ALHS> liquid handling principle in which a piston is in direct contact with the liquid

3.36
precision
<ALHS> closeness of agreement between replicate delivered volumes under specified conditions

Note 1 to entry: Precision is conceptual and not a quantity value.

Note 2 to entry: Measurement precision is usually expressed numerically by measures of random error, such as standard deviation, variance, or coefficient of variation under the specified conditions of measurement.

Note 3 to entry: The "specified conditions" can be, for example, repeatability conditions, intermediate precision, or reproducibility conditions (see ISO 5725-1:1994).

Note 4 to entry: The relationship between accuracy, trueness, precision, systematic error, and random error of an automated liquid handling system is explained further in ISO 23783-3:2022, 5.1.

3.37
random error
<ALHS> component of liquid handling error that in replicate liquid deliveries varies in an unpredictable manner

Note 1 to entry: The relationship between accuracy, systematic error, and random error of an automated liquid handling system is explained further in ISO 23783-3: 2022, 5.1.

[SOURCE: ISO/IEC Guide 99:2007, 2.19, modified — definition was modified for the context of automated liquid handling; Note 1 was replaced and Notes 2 and 3 were deleted.]

3.38
repeatability
liquid delivery repeatability
<ALHS> precision of liquid deliveries under a set of repeatability conditions

Note 1 to entry: Repeatability refers to the variability among liquid deliveries made on the same automated liquid handling system under nearly identical circumstances. It is recognized that, because of unknown or uncontrollable factors which influence the liquid handling process, repeated measurements will usually not agree. The extent of this variability can be expressed by a standard deviation, called the repeatability standard deviation.

[SOURCE: ISO/IEC Guide 99:2007, 2.21, modified — definition was modified for the context of automated liquid handling and Note 1 was added.]

3.39
repeatability condition
repeatability condition of liquid delivery
<ALHS> condition of liquid delivery, out of a set of conditions that includes the same liquid delivery procedure, same operators, same measuring system, same operating conditions and same location, and replicate measurements on the same automated liquid handling system over a short period of time

[SOURCE: ISO/IEC Guide 99:2007, 2.20, modified — definition was modified for the context of automated liquid handling and Notes 1 and 2 were deleted.]

3.40
reproducibility
precision of liquid deliveries under reproducibility conditions

Note 1 to entry: Reproducibility refers to the variability of replicate volume deliveries by identical ALHS under differing conditions. It includes effects caused by differences among the ALHS and measurement instruments, reagents, operators, laboratories, and environmental conditions. The variability of results under these conditions may be described by a standard deviation, called the reproducibility standard deviation.

[SOURCE: ISO/IEC Guide 99:2007, 2.25, modified — definition was modified for the context of automated liquid handling and Note 1 was replaced.]

3.41
reproducibility condition
reproducibility condition of liquid delivery
<ALHS> condition of liquid delivery that includes different locations, environmental conditions, operators, or automated liquid handling systems

3.42
reservoir
liquid container
<ALHS> vessel that contains the liquid

3.43
reverse mode pipetting
pipetting mode where a volume larger than the target volume is aspirated into the tip and only the target volume is delivered

3.44
single dispense
individual dispense
<ALHS> one liquid delivery per aspiration

3.45
site acceptance testing
in-situ testing at the location where the ALHS will be used, typically a part of the installation process

3.46
supplier's declaration
<ALHS> document by which a supplier gives written assurance that an ALHS conforms to the requirements of one or more commonly accepted industry standards

3.47
systematic error
<ALHS> component of liquid handling error that in replicate liquid deliveries remains constant or varies in a predictable manner

Note 1 to entry: Systematic error is estimated by calculating the average volume of a series of deliveries and comparing it to the target volume of the automated liquid handling system. Frequently, this result is expressed as a percentage of the target volume.

Note 2 to entry: Systematic liquid handling error, and its causes, can be known or unknown. A correction can be applied to compensate for a known systematic error.

Note 3 to entry: Some ALHS can be adjusted to compensate for a known systematic error.

Note 4 to entry: The relationship between accuracy, systematic error, and random error of an automated liquid handling system is explained further in ISO 23783-3: 2022, 5.1.

[SOURCE: ISO/IEC Guide 99:2007, 2.17, modified — definition was modified for the context of automated liquid handling; Notes 1 and 3 were replaced and Note 4 was added.]

3.48
system liquid
liquid used to transmit energy between a mechanical actuator and the liquid to be transferred

Note 1 to entry: System liquids can reduce or completely eliminate system dead air volume.

Note 2 to entry: System liquid is usually deionized water. For special applications, organic solvents such as DMSO or aqueous solutions such as saline (e.g. 0,9 % NaCl) can be used.

Note 3 to entry: System liquid can be used for flushing and rinsing tips to minimize cross contamination.

Note 4 to entry: System liquid can be used as a diluent in some applications (e.g. for diluting samples).

3.49
target volume
indicated volume
selected volume
volume which is intended to be delivered

3.50
test liquid
liquid used for the volume measurement

3.51
test process
<ALHS> detailed description of an ALHS testing procedure including system operation and measurement method

Note 1 to entry: The test process includes all details needed to reproduce the test or interpret the results. The *measurement method* (3.24) is only a part of the test process.

3.52
test report
document reporting the result of the testing

Note 1 to entry: Details regarding information to be contained in test reports are specified in ISO 23783-3: 2022, Clause 6.

3.53
test result
value of a characteristic obtained by carrying out a specified test method

Note 1 to entry: Test result is a broader concept than measured volume. The test result can be a single measured volume, a set of measured volumes, or descriptive statistics such as the mean or standard deviation of multiple measurements.

[SOURCE: ISO 5725-1:1994, 3.2, modified — Note 1 was replaced.]

3.54
trueness
<ALHS> closeness of agreement between the average volume delivered in a large series of deliveries and the target volume

Note 1 to entry: Measurement trueness is not a quantity and thus cannot be expressed numerically, but measures for closeness of agreement are given in ISO 5725-1.

Note 2 to entry: Trueness is inversely related to systematic error but is not related to random error.

Note 3 to entry: The term "accuracy" shall not be used for "trueness".

Note 4 to entry: The relationship between accuracy, precision, trueness, systematic error, and random error of an automated liquid handling system is explained further in ISO 23783-3:2022, 5.1.

[SOURCE: ISO/IEC Guide 99:2007, 2.14, modified — definition was modified for the context of automated liquid handling and Note 4 was added.]

3.55
verification
<ALHS> confirmation, through the provision of objective evidence, that volumetric performance specifications have been fulfilled

Note 1 to entry: The term “verified” is used to designate the corresponding status.

3.56
volume increment
discreetly dispensed volumes which are usually added up to achieve larger delivered volumes

Note 1 to entry: Volume increments can be as small as 11 pl in the case of inkjet-type dispensers.

Note 2 to entry: If it is possible to dispense just one increment, the volume increment equals the lowest possible dispense volume.

3.57
wet contact dispensing
dispensing of the test liquid while the tip is in contact with the liquid present in the target

4 Abbreviated terms

See Table 1 for abbreviations used throughout the ISO 23783 series.

Table 1 — Abbreviated terms used in the ISO 23783 series

Abbreviated term	Explanation
AC	Alternating current
ADS	Automated dispensing system
ALHS	Automated liquid handling system
APS	Automated pipetting system
AU	Absorbance unit
BCV	Between class variant
BSA	Bovine serum albumin
CAS	Chemical abstracts service, a division of the American Chemical Society
C2C	Channel-to-channel
CV	Coefficient of variation
DI	De-ionized
DMSO	Dimethylsulfoxide

Table 1 *(continued)*

Abbreviated term	Explanation
DOF	Depth of focus
DUT	Device under test
GA	Grand average
HVAC	Heating, ventilation, and air conditioning
LED	Light-emitting diode
MSU	Measuring system uncertainty
MU	Measurement uncertainty
MW	Molecular weight
ND	Neutral density
4-NP	4-Nitrophenol
OA	Over all
POVA	Piston-operated volumetric apparatus
r/min	Revolutions per minute
rcf	Relative centrifugal force (g-force)
RH	Relative humidity [%]
RSE	Relative systematic error
ROI	Region of interest
SD	Standard deviation
SI	International System of Units

5 Operation of automated liquid handling systems

5.1 Types of automated liquid handling systems

5.1.1 General

Examples of some types of ALHS are provided in 5.1.2 to 5.1.6. This list is not intended to be a comprehensive list as technologies continue to be developed.

Manipulation of the labware on the deck of the ALHS may be achieved automatically, semi-automatically, or manually.

5.1.2 Piston-operated automated liquid handling systems

Piston-operated ALHS can operate as follows:

— variable volume; designed to aspirate and dispense selectable volumes within the specified useable volume range of the dispense head and selected tips (for example, between 10 µl and 100 µl).

— a larger volume can be aspirated into the tips, followed by a series of subsequent dispenses of liquid sub-deliveries.

The dispense head can be:

— permanently attached to the instrument; or

— exchangeable, e.g. to change the usable volume range or number of channels.

The piston can:

— either have a body of air (air gap) contained between the piston and the surface of the liquid (air-displacement); or

— be in direct contact with the surface of the liquid (positive or direct displacement); or

— be in contact with a system liquid (liquid-filled systems are a variation of air-displacement systems).

The system can have:

— a single tip; or

— multiple tips, operated by individual pistons; or

— multiple tips, operated by a single, common drive or moving plate with multiple pistons simultaneously driven by a common drive.

The tip can be:

— permanently attached to the dispense channel of the ALHS; or

— disposable, and used for one or more aspirate and dispense sequences.

5.1.3 Pump operated automated liquid handling systems

Pump-operated ALHS can operate as follows:

— variable volume; designed to dispense selectable volumes within the specified usable volume range of the dispense head.

The dispense head can be:

— permanently attached to the instrument; or

— exchangeable, e.g. to change the usable volume range or number of channels.

The system can have:

— a peristaltic or diaphragm pump to aspirate liquid from a reservoir; or

— a pressurized liquid reservoir and valves to control the liquid delivery.

5.1.4 Automated liquid handling systems using inkjet-type dispensing technologies

Automated liquid handling systems can use inkjet-type dispensing technology, in which a pulsed force is generated to drive fluids through a nozzle, to directly dispense small volumes into microplates. The nozzles in these systems are typically re-filled by capillary action and do not require any pump or pressurized reservoir. Pulsed forces to drive the fluid through the nozzle can be actuated by thermal, piezo-electric, or acoustic technologies.

Different types of dispensing systems cover different volume ranges. Dispensing nozzles can be disposable or reusable.

5.1.5 Automated liquid handling systems using acoustic droplet ejection technology

Acoustic liquid handling systems apply a focused pulse of acoustic energy to the bottom of a source reservoir surface. The source reservoir is frequently a flat-bottomed, multi-welled ANSI/SLAS format microplate. The energy is transmitted through the reservoir and into the liquid to be transferred. A droplet of liquid is ejected from the meniscus of the liquid. The upward bound droplet is captured by a destination or target placed above the source reservoir. Unlike inkjet-type technologies, the technique does not use a nozzle. Usually, volume is dispensed via incremental droplets. The individual droplets can be adjustable or fixed. Additional droplets can be added in rapid succession.

NOTE Typically, single droplet volumes range from 1 nl to 25 nl, which can be delivered at a rate of several hundred droplets per second.

5.1.6 Pin tools

In this type of liquid handler, a metal pin is used to transfer an amount of liquid by first immersing part of the pin into a liquid, then withdrawing and delivering the liquid by contact with the destination.

Pin tools can have various geometric features to promote the retention and delivery of liquid. Solid, slotted and grooved pins, as well as threaded bolts, have been used in pin tools. Pin tools are generally used in arrays, such as 96-, 384-, or 1 536-well designs attached to a base plate. The attachments can be rigidly fixed by pressing or screwing the pins into a base plate. These are called “fixed pins”. Floating pin designs are also employed, where the pin is placed into a guide and can move in the axial direction relative to the base plate.

5.2 Types of pipette tips for ALHS

5.2.1 General

Piston-operated ALHS make use of tips, which fit on the ALHS dispensing head and prevent the instrument from contact with the aspirated liquid. The quality, use, and care of these tips can affect the volumetric performance of the ALHS. The dispensing orifice of the tip shall be shaped in such a way that consistent dispensing of the liquid is achieved. When the pipetting operation is completed, any amount of liquid remaining in or around the dispensing orifice of the tip shall be consistent.

Dispensing heads with multiple channels shall be fitted with tips of the same type, model, and lot on each channel to facilitate uniform volumetric performance between all channels.

In the case of sterilizable tips, the sterilization procedures indicated as appropriate in the user information or on the packaging shall not negatively affect the metrological characteristics of the tips such as shape, seal and wettability.

NOTE This requirement can be assessed by comparing liquid handling errors using tips which have and have not been sterilized under otherwise identical conditions.

5.2.2 Air-displacement tips

Air-displacement tips shall be considered automatically exchangeable parts (see 6.8.1), usually made of plastic.

After use and dismounting from the dispensing head, these tips shall not be cleaned or re-used unless their metrological characteristics are confirmed, and they are shown to be fit for use in the specific application (validation).

NOTE Variability of the amount of externally retained liquid or an incomplete seal will contribute to poor precision when testing with one of the methods described in this document.

5.2.3 Positive displacement tips

Positive displacement tips shall consist of a plunger contained in a rigid tip wall. The rigid tip wall connects to the mandrel of the ALHS dispensing head, and the plunger is actuated through an internal movement mechanism. Various materials can be used for the plunger, such as metal, plastic, or ceramic and for the tip wall, such as plastic or glass. These pipette tips can be reusable or disposable (both plunger and tip wall are changed together, per manufacturer’s instructions), and shall be considered automatically exchangeable parts of the ALHS (see 6.8.1).

5.2.4 Fixed tips

Fixed tips can be manufactured from various materials, such as stainless steel or polymeric materials. These tips can be coated for inertness to pipetted fluids or for specific functionality, e.g. conductivity to sense contact with fluids in receptacles on the deck of the ALHS.

Fixed tips should be examined for damage and tested for proper functionality at regular intervals according to the manufacturer's instructions, which should contain protocols for the maintenance and replacement of such tips (see 5.3).

Fixed tips shall be considered other exchangeable parts according to 6.8.3.

5.3 Cleaning of re-usable components and confirmation of metrological characteristics

Some ALHS contain re-useable components, which come into direct contact with the sample liquids during regular use of the ALHS. These components can include, but are not limited to, tips, valves, and tubing, and can consist of a variety of materials, such as stainless steel or polymeric materials, with or without specific coatings.

Cleaning of re-useable components depends on the chemical, physical and biological properties of the liquids used with these components. Therefore, no generally applicable cleaning protocol can be defined. The basic steps are decontamination, if needed, removal of deposits on the tips, and reconstitution of the component to a similar condition as it was during its prior use. In many cases, flushing and washing with system liquid (often, deionized water) is adequate. For certain applications, an additional cleaning liquid (mostly acidic or basic), which can subsequently be neutralized and rinsed off with the system liquid, is needed. In critical cases, many steps are required; e.g. after an extended flushing, a dedicated decontamination step (e.g. for a certain exposure time) can be followed by a dedicated neutralization and rinsing step. This can even be followed by a dedicated priming step (e.g. BSA coating) to restore the adhesion properties.

The volumetric performance of the ALHS after the cleaning of re-useable components shall be tested as described in this document. Testing of the ALHS volumetric performance is not necessary if the re-useable component is cleaned as part of the validated, automated routine operation of the ALHS (e.g. executing an automated cleaning step of fixed tips after use).

6 Testing and calibration of ALHS

6.1 Metrological confirmation

6.1.1 General

This clause gives requirements and recommendations for metrological confirmation of ALHS. Each channel of the ALHS shall be tested. The ALHS volumetric performance (systematic and random errors, and expanded measurement uncertainty) may be verified against the manufacturer's performance specifications or user requirements. It is permissible to determine the volumetric performance of the ALHS without comparison against specifications or tolerances. Volumetric performance shall be reported in accordance with ISO 23783-3.

6.1.2 Calibration

The calibration of ALHS shall be performed by using one of the methods described in ISO 23783-2. The systematic and random errors and an estimation of the expanded measurement uncertainty shall be calculated and reported.

NOTE The approach given in ISO/IEC Guide 98-3 can be used to fulfil the requirement of estimating the measurement uncertainty.

6.1.3 Routine tests

Routine tests performed in accordance with one of the methods described in ISO 23783-2 can be used to evaluate the volumetric performance of the ALHS and may include an estimation of the expanded measurement uncertainty. In case no estimation of measurement uncertainty is developed, the volumetric performance shall be evaluated by the systematic and random measurement errors according to ISO 23783-3.

NOTE Routine tests include tests while optimizing ALHS performance for a specific use case.

6.2 Channels to test

Each channel of an ALHS shall be tested according to one of the procedures described in ISO 23783-2, and the test results of each channel shall be reported according to ISO 23783-3:2022, Clause 6.

6.3 Test volumes

ALHS volumetric performance shall be tested at a minimum of 2 volume settings. Test volumes should be close to the maximum and minimum of the declared volume range of the tested ALHS configuration. A minimum of 3 volume settings shall be tested to claim linearity over the tested volume range. Other volumes may be tested based on agreement between the concerned parties.

Test volumes delivered by an ALHS, which exceed the volume measurement constraints of the test methods given in ISO 23783-2 shall be tested with a suitable alternative method. If the tested ALHS configuration is capable to deliver volumes within the range of one of the test methods described in ISO 23783-2, at least one volume setting shall be tested according to a suitable method of that International Standard.

If an alternative method is used for testing volumes, that method shall be validated against one of the test procedures described in ISO 23783-2.

6.4 Test liquids

Physical properties of liquids can alter the delivered volume by an ALHS.

Test liquids used for the metrological confirmation of ALHS shall be described in sufficient detail so that the test can be reproduced.

NOTE 1 Examples of physical properties include density, viscosity, surface tension, and vapour pressure.

NOTE 2 The influence of liquid properties on the delivered volume depends on the design of the ALHS.

6.5 Replicate measurements

During the calibration of an ALHS, each volume setting shall be tested with at least 10 replicate deliveries of the test volume. Routine tests or optimization of ALHS settings may be performed with fewer replicates.

6.6 Test frequency

The user of the ALHS should define the calibration interval considering the recommendations of the manufacturer and user requirements.

NOTE User requirements to determine the frequency of calibration or performance verification can include, but are not limited to, the environment in which the ALHS is used, the types of liquids transferred, the frequency of use, frequency and nature of maintenance events, and process tolerances.

