

ISO/DTR_6037:2023(E)

ISO/TC_48/AG_5

Date: 2023-10-12

Secretariat: DIN

Automated liquid handling systems – Uncertainty of the measurement procedures

iTeh Standards
(<https://standards.itih.ai>)
Document Preview

DTR stage TR 6037

<https://standards.itih.ai/catalog/standards/iso/5006540c-9d69-4513-b3c3-3962f962a9af/iso-dtr-6037>

Warning for WDs and CDs

This document is not an ISO International Standard. It is distributed for review and comment. It is subject to change without notice and may not be referred to as an International Standard.

Recipients of this draft are invited to submit, with their comments, notification of any relevant patent rights of which they are aware and to provide supporting documentation.

A model manuscript of a draft International Standard (known as "The Rice Model") is available at <https://www.iso.org/iso/model-document-rice-model.pdf>

ISO #####-#:####(X)

© ISO 20XX

iTeh Standards
(<https://standards.itih.ai>)
Document Preview

[ISO/DTR 6037](#)

<https://standards.itih.ai/catalog/standards/iso/3606540e-9d69-4513-b3c3-3962f962a9af/iso-dtr-6037>

ISO/DTR 6037:2023(E)2024(en)

© ISO 2024

All rights reserved. Unless otherwise specified, or required in the context of its implementation, no part of this publication may be reproduced or utilized otherwise in any form or by any means, electronic or mechanical, including photocopying, or posting on the internet or an intranet, without prior written permission. Permission can be requested from either ISO at the address below or ISO's member body in the country of the requester.

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

iTeh Standards (<https://standards.iteh.ai>) Document Preview

ISO/DTR 6037

<https://standards.iteh.ai/catalog/standards/iso/3606540e-9d69-4513-b3c3-3962f962a9af/iso-dtr-6037>

© ISO-####_2024 - All rights reserved

Contents

Foreword.....	x
Introduction.....	xi
1 Scope.....	1
2 Normative references.....	1
3 Terms and definitions.....	1
4 General procedure for the uncertainty calculation.....	1
5 Modelling of the measurement.....	2
6 Standard uncertainty components associated with the measuring system.....	2
6.1 General information on standard uncertainty components estimation.....	2
6.2 Specific information on standard uncertainty components estimation.....	3
7 Standard uncertainty components associated with the ALHS.....	3
7.1 General.....	3
7.2 ALHS-type specific influencing parameters.....	3
7.3 Test liquid properties influencing ALHS operation.....	3
7.4 Standard uncertainty of ALHS resolution.....	4
7.5 Standard uncertainty of cubic expansion coefficient (optional).....	4
7.6 Standard uncertainty associated with air cushion effects (optional).....	5
8 Repeatability and reproducibility of the liquid delivery process.....	5
8.1 Repeatability (experimental standard deviation).....	5
8.2 Reproducibility.....	6
9 Combined standard uncertainty of measurement associated with the systematic error of mean volume.....	6
10 Sensitivity coefficients.....	8
11 Coverage factor k	8
12 Expanded uncertainty of measurement associated with the mean volume.....	9
13 Examples for determining the uncertainty of the volume measurement of ALHS.....	10
13.1 Measurement conditions.....	10
13.2 Results.....	10
13.2.1 Standard uncertainty of the ALHS mean volume.....	10
13.2.2 Expanded uncertainty of the measurement.....	10
13.2.3 Result of measurement.....	10
13.2.4 Caution regarding use of numerical values in this report.....	11
13.2.5 Remarks on conformity with ISO/IEC Guide 98-3.....	11
Annex A (informative) Dual-dye radiometric photometric procedure.....	13
A.1 Description of the measurement.....	13
A.2 Modelling the measurement.....	13

A.3	Standard uncertainty components associated with the input quantities to the dual-dye ratiometric photometric procedure.....	14
A.3.1	Absorbance per unit path length of CuCl_2 solution (a_b).....	14
A.3.2	Absorbance per unit path length of Ponceau S test liquid (a_r).....	15
A.3.3	Measured absorbance at 520 nm (A_{520}).....	15
A.3.4	Measured absorbance at 730 nm (A_{730}).....	15
A.3.5	Uncertainty components of the geometric dimensions of microplate wells (D, θ).....	15
A.3.6	Other uncertainty components.....	15
A.4	Sensitivity coefficients.....	15
A.5	Example for determining the uncertainty of the volume measurement of an ALHS with the dual-dye ratiometric photometric procedure.....	17
A.5.1	Measurement conditions.....	17
A.5.2	Results.....	19
Annex B (informative)	Gravimetric procedure.....	21
B.1	Description of the measurement.....	21
B.2	Modelling the measurement.....	21
B.2.1	General gravimetric formula.....	21
B.2.2	Air density.....	23
B.2.3	Test liquid density.....	23
B.2.4	Estimating evaporation.....	24
B.2.5	Modelling the gravimetric single-channel method.....	24
B.2.6	Modelling the gravimetric regression method.....	25
B.3	Standard uncertainty components associated with the measuring system.....	28
B.3.1	Standard uncertainty of weighing.....	28
B.3.2	Standard uncertainty of temperature.....	31
B.3.3	Standard uncertainty of test liquid density.....	32
B.3.4	Standard uncertainty of air density.....	33
B.3.5	Standard uncertainty of weights density.....	34
B.4	Sensitivity coefficients.....	34
B.5	Examples for determining the uncertainty of the volume measurement of the ALHS.....	35
B.5.1	Example of testing a single channel ALHS with multiple replicates.....	35
B.5.2	Example of testing a single channel using gravimetric regression.....	38
Annex C (informative)	Optical image analysis of droplets.....	42
C.1	Description of the measurement.....	42
C.1.1	General.....	42
C.1.2	Optical image analysis of droplets.....	42
C.2	Modelling the measurement.....	42
C.2.1	General.....	42
C.2.2	Analysis of the droplets.....	43

ISO/DTR 6037:2023(E)-2024(en)

C.3	Standard uncertainty components associated with the measuring system	43
C.3.1	Standard uncertainties for the analysis of droplets	44
C.3.2	Standard uncertainty for the magnification factor α	44
C.3.3	Standard uncertainties for determining the number of pixels	45
C.3.4	Standard uncertainty for the spherical shape of the droplet	46
C.3.5	Standard uncertainty for evaporation	49
C.4	Sensitivity coefficients	49
C.5	Example for determining the uncertainty of the volume measurement of the ALHS	50
C.5.1	Measurement conditions for droplets	50
C.5.2	Results for droplets	53
	Bibliography	55

Foreword — vi

Introduction — vii

1 — Scope — 1

2 — Normative references — 1

3 — Terms and definitions — 1

4 — General procedure for the uncertainty calculation — 1

5 — Modelling of the measurement — 2

6 — Standard uncertainty components associated with the measuring system — 2

6.1 — General information on standard uncertainty components estimation — 2

6.2 — Specific information on standard uncertainty components estimation — 3

7 — Standard uncertainty components associated with the ALHS — 3

7.1 — General — 3

7.2 — ALHS type specific influencing parameters — 3

7.3 — Test liquid properties influencing ALHS operation — 3

7.4 — Standard uncertainty of ALHS resolution — 3

7.5 — Standard uncertainty of cubic expansion coefficient (optional) — 4

7.6 — Standard uncertainty associated with air cushion effects (optional) — 4

8 — Repeatability and reproducibility of the liquid delivery process — 5

8.1 — Repeatability (experimental standard deviation) — 5

8.2 — Reproducibility — 5

9 — Combined standard uncertainty of measurement associated with the systematic error of mean volume — 5

10 — Sensitivity coefficients — 6

11 — Coverage factor k — 7

12 — Expanded uncertainty of measurement associated with the mean volume (\bar{V}) — 7

13 — Examples for determining the uncertainty of the volume measurement of ALHS — 7

ISO/DTR 6037:2023(E2024(en)

13.1	Measurement conditions	7
13.2	Results	8
13.2.1	Standard uncertainty of the ALHS mean volume	8
13.2.2	Expanded uncertainty of the measurement	8
13.2.3	Result of measurement	8
13.2.4	Caution regarding use of numerical values in this report	9
13.2.5	Remarks on conformity with ISO/IEC Guide 98	9
Annex A (informative) Dual-dye ratiometric photometric procedure 10		
A.1	Description of the measurement	10
A.2	Modelling the measurement	10
A.3	Standard uncertainty components associated with the input quantities to the dual-dye ratiometric photometric procedure	11
A.3.1	Absorbance per unit pathlength of CuCl_2 solution (α_b)	11
A.3.2	Absorbance per unit pathlength of Ponceau S test liquid (α_r)	11
A.3.3	Measured absorbance at 520 nm (A_{520})	12
A.3.4	Measured absorbance at 730 nm (A_{730})	12
A.3.5	Uncertainty components of the geometric dimensions of microplate wells (D, θ)	12
A.3.6	Other uncertainty components	12
A.4	Sensitivity coefficients	12
A.5	Example for determining the uncertainty of the volume measurement of an ALHS with the dual-dye ratiometric photometric procedure	13
A.5.1	Measurement conditions	13
A.5.2	Results	15
A.5.2.1	Standard uncertainty of the ALHS mean volume	15
A.5.2.2	Expanded uncertainty of the measurement	15
A.5.2.3	Result of measurement	15
A.5.2.4	General remarks	15
Annex B (informative) Gravimetric procedure 17		
B.1	Description of the measurement	17
B.2	Modelling the measurement	17
B.2.1	General gravimetric formula	17
B.2.1.1	Single channel analysis	17
B.2.1.2	Regression analysis	18
B.2.2	Air density	18
B.2.3	Test liquid density	18
B.2.4	Estimating evaporation	19
B.2.5	Modelling the gravimetric single channel method	19
B.2.6	Modelling the gravimetric regression method	19
B.3	Standard uncertainty components associated with the measuring system	21

ISO/DTR 6037:2023(E)-2024(en)

B.3.1	Standard uncertainty of weighing	21
B.3.1.1	Single channel analysis	22
B.3.1.2	Regression analysis	22
B.3.1.3	Standard uncertainty of balance drift	23
B.3.1.4	Standard uncertainty of the calibration of the balance	23
B.3.2	Standard uncertainty of temperature	23
B.3.3	Standard uncertainty of water density	24
B.3.4	Standard uncertainty of air density	25
B.3.5	Standard uncertainty of weights density	25
B.4	Sensitivity coefficients	25
B.5	Examples for determining the uncertainty of the volume measurement of the ALHS	26
B.5.1	Example of testing a single channel ALHS with multiple replicates	26
B.5.1.1	Results	27
B.5.1.1.1	Standard uncertainty of the ALHS mean volume	27
B.5.1.1.2	Expanded uncertainty of the ALHS mean volume	28
B.5.1.1.3	Expression of the measurement result	28
B.5.2	Example of testing a single channel using gravimetric regression	28
B.5.2.1	Measurement conditions	28
B.5.2.2	Results	30
B.5.2.2.1	Standard uncertainty of the ALHS mean volume	30
B.5.2.2.2	Expanded uncertainty of the ALHS mean volume	30
B.5.2.2.3	Expression of the measurement result	30
Annex C (informative)	Optical image analysis of droplets	31
C.1	Description of the measurement	31
C.1.1	General	31
C.1.2	Optical image analysis of droplets	31
C.2	Modelling the measurement	31
C.2.1	General	31
C.2.2	Analysis of the droplets	32
C.3	Standard uncertainty components associated with the measuring system	32
C.3.1	Standard uncertainties for the analysis of droplets	32
C.3.2	Standard uncertainty for the magnification factor α	33
C.3.3	Standard uncertainties for determining the number of pixels	34
C.3.4	Standard uncertainty for the spherical shape of the droplet	34
C.3.5	Standard uncertainty for evaporation	36
C.4	Sensitivity coefficients	36
C.5	Example for determining the uncertainty of the volume measurement of the ALHS	37
C.5.1	Measurement conditions for droplets	37
C.5.2	Results for droplets	39

ISO/DTR 6037:2023(E)2024(en)

C.5.2.1 Standard uncertainty of the ALHS delivered volume 39

C.5.2.2 Expanded uncertainty of the ALHS mean volume 39

C.5.2.3 Expression of the measurement results 39

Bibliography 41

iTeh Standards
(<https://standards.itih.ai>)
Document Preview

ISO/DTR 6037

<https://standards.itih.ai/catalog/standards/iso/3606540e-9d69-4513-b3c3-3962f962a9af/iso-dtr-6037>

© ISO-####_2024 - All rights reserved

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

Field Code Changed

~~Attention is drawn~~ISO draws attention to the possibility that ~~some of the elements~~implementation of this document may ~~be involve~~ the ~~subject~~use of (a) patent(s). ISO takes no position concerning the evidence, validity or applicability of any claimed patent rights ~~in respect thereof. As of the date of publication of this document, ISO had not received notice of (a) patent(s) which may be required to implement this document. However, implementers are cautioned that this may not represent the latest information, which may be obtained from the patent database available at www.iso.org/patents.~~ 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*.

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

The examples given in this document are informative and support the requirement found in [the ISO 23783 series](#) to perform an estimation of measurement uncertainty when calibrating automated liquid handling systems (ALHS) according to the measurement procedures described in ISO 23783-2. The examples in this document are based on the principles of ISO/IEC Guide 98-3.

iTeh Standards (<https://standards.iteh.ai>) Document Preview

[ISO/DTR 6037](#)

<https://standards.iteh.ai/catalog/standards/iso/3606540e-9d69-4513-b3c3-3962f962a9af/iso-dtr-6037>

Automated liquid handling systems – Uncertainty of the measurement procedures

1 Scope

This document describes the measurement uncertainty analysis of the measurement procedures described in ISO 23783-2, following the approach described in ISO/IEC Guide 98-3.

This document also includes the determination of other uncertainty components related to the liquid delivery process and the device under test (DUT) to estimate the overall measurement uncertainty of delivered volumes by an automated liquid handling system (ALHS).

3.2 Normative references

ISO 23783-1, *Automated liquid handling systems – Part 1: Vocabulary and general requirements*

ISO/IEC Guide 98-3, *Uncertainty of measurement – Part 3: Guide to the expression of uncertainty in measurement (GUM:1995)*

ISO/IEC Guide 99, *International vocabulary of metrology – Basic and general concepts and associated terms (VIM)*

4.3 Terms and definitions

For the purposes of this document, the terms and definitions given in ISO 23783-1, ISO/IEC Guide 98-3, and ISO/IEC Guide 99 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/>

5.4 General procedure for the uncertainty calculation

The evaluation of measurement uncertainty in this document follows the ISO/IEC Guide 98-3 “Guide to the Expression of Uncertainty in Measurement (GUM).” The method has the following steps:

- a) ~~1~~-Expressing, in mathematical terms, the relationship between the measurand and its input quantities.
- b) ~~2~~-Determining the expected value of each input quantity.
- c) ~~3~~-Determining the standard uncertainty of each input quantity.
- d) ~~4~~-Determining the degree of freedom for each input quantity.
- e) ~~5~~-Determining all covariance between the input quantities.
- f) ~~6~~-Calculating the expected value for the measurand.
- g) ~~7~~-Calculating the sensitivity coefficient of each input quantity.
- h) ~~8~~-Calculating the combined standard uncertainty of the measurand.

- i) ~~9-~~Calculating the effective degrees of freedom of the combined standard uncertainty.
- j) ~~10-~~Choosing an appropriate coverage factor, k , to achieve the required confidence level.
- k) ~~11-~~Calculating the expanded uncertainty.

In this document, the uncertainty of the measurement procedure is separated in three different clauses:

- ~~—~~the uncertainty components associated with the measuring system, see ~~Clause 6-~~[Clause 6](#);
- ~~—~~the uncertainty components associated with the device under test (ALHS), see ~~Clause 7-~~[Clause 7](#) and ~~Clause 7-~~[Clause 7](#);
- ~~—~~the uncertainty components associated with the liquid delivery process, see ~~Clause 8-~~[Clause 8](#).

65 Modelling of the measurement

Each measurement procedure has specific uncertainty components associated with the measuring system. These uncertainty components are described in the respective annex for each procedure. See ~~Annex A~~[Annex A](#) for the dual-dye radiometric photometric procedure, ~~Annex B~~[Annex B](#) for the gravimetric procedure, and ~~Annex C~~[Annex C](#) for the optical image analysis of droplets.

76 Standard uncertainty components associated with the measuring system

76.1 General information on standard uncertainty components estimation

It is possible to experimentally estimate the standard uncertainty of measurement, $u(x)$, for a quantity x , by performing multiple measurements of x under repeatability conditions. This is called a type A evaluation according to ISO/IEC Guide 98-3. The standard deviation of the obtained values is a measure of the repeatability of the measurement. The standard uncertainty associated with x can be a standard deviation based on previous experience (in the case where a single measurement of x is made), or the standard deviation of the mean equal to $\text{stdev}(x)/\sqrt{n}$ (in the case where x is the average of n readings).

See ISO Guide 98-3:2008, 4.2 for more information on type A evaluation of standard uncertainty.

In addition to repeated measurements, the systematic component of the uncertainty of measurement for a quantity x is estimated by other means. This is called a type B evaluation according to ISO/IEC Guide 98-3. For example, one can obtain information for that estimation by considering the manufacturer's specifications of the ALHS (e.g., resolution, linearity, drift, temperature dependence, etc.).

Often the manufacturer's specifications are given in the form of an interval covering the measurement value, with no additional information regarding distribution or coverage. In those cases, the measurement can be assumed to follow a uniform or rectangular distribution. This distribution is characterised by a constant probability inside the interval while the probability outside the interval is zero.

The interval can be used in a type B evaluation to give the variance of x in the form shown in ~~Formula (1)~~[Formula \(1\)](#):

$$u^2(x) = \frac{(a_+ - a_-)^2}{12} \quad (1)$$

where $u^2(x)$ is the variance of the variable x ;

a_+ and a_- give the upper and lower limits of the interval of the variable x .

$$u^2(x) = \frac{(a_+ - a_-)^2}{12} \quad (1)$$

where