INTERNATIONAL WORKSHOP AGREEMENT

IWA 23

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Interoperability of microfluidic devices — Guidelines for pitch spacing dimensions and initial device classification

Interopérabilité des dispositifs microfluidiques — Lignes directrices pour les dimensions d'un pas d'espacement et le classement initial de l'appareil

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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.

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).

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For an explanation on 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 the following URL: www.iso.org/iso/foreword.html .

The committee responsible for this document is the ISO/TMB, *Technical Management Board*.

International Workshop Agreement IWA 23 was approved at a workshop organized by pan European (ENIAC Joint Undertaking) project MFmanufacturing, in association with Deutsches Institut für Normung (DIN). The workshop was held in British Standards Institution (BSI), London, United Kingdom, on 19 April, 2016. The workshop resolutions and contributors are listed in Annexes A and B, respectively.

Introduction

Microfluidics technology plays an important role for next generation devices. In the last few decades, initial R& D investment in academia has led to the generation of a number of spin out companies. Most of the companies that have flourished are microfluidic foundries or suppliers of microfluidic components. However, the track record associated with the success of actual application devices has been disappointing, with only a small handful of products (such as the ink jet printer) reaching commercial success.

The concern surrounding the lack of commercialization with regards to microfluidic devices has been discussed amongst various interested parties and stakeholders within the Microfluidics Consortium (MC). MC is an ad hoc group that offers a forum for discussion amongst interested parties and stakeholders in the microfluidics community. Such discussions led to the identification of several factors that can potentially hinder commercial success of microfluidics devices. This includes the high R&D and manufacturing costs of devices currently sold into a relatively small market [13]. It has been recognized that in order to reduce costs, there is a need to bring manufacturing of microfluidic devices to the same level of maturity and industrialization as electronic devices. This meant the need to mimic some of the standardization initiatives and outputs from the electronic industry in order to not only reduce costs but at the same time increase interoperability, thus promoting plug-and-play. The standardization initiative that had begun in the MC led to the development of several internal documents, such as a guideline on how to design microfluidic devices [14]. The standardization initiative and knowledge base gained through the MC eventually led to the formation of a pan-European project MFmanufacturing consisting of 20 project partners.

In identifying what standards should be proposed, consideration must be given to current market needs and trends. This led MFmanufacturing to develop, implement and analyse a survey (of 134 respondents), in order to identify those items that are in need of standardization to ultimately enhance the commercialization of microfluidic devices. Attention was given to those items that have been identified as being of highest priority, which are

a) terminology of relevance,

b) geometrical specifications on pitch dimensions,

c) device classification.

These items are further discussed in the relevant paragraphs below.

Interoperability of microfluidic devices — Guidelines for pitch spacing dimensions and initial device classification

1 Scope

This International Workshop Agreement is a consensus document developed by the workshop participants and observers in response to the need for standardization and harmonization of pitch spacing dimension, initial device classification and terminology of relevance.

This International Workshop Agreement will serve as a guideline and is applicable to various interested parties and stakeholders in the microfluidics community.

This International Workshop Agreement

— specifies geometrical standards in relation to pitch connector dimensions of microfluidic devices,

— specifies an initial device classification rules, and

— defines terms of relevance.

2 Terms and definitions

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

2.1
classification
method of sorting into categories

[SOURCE: ISO 22935-1:2009, 3.7]

2.2
connector
component that allows one part of the set to be connected to another

[SOURCE: ISO 3826-4:2015, 3.4]

2.3
device
component or assembly of components to perform a required function

[SOURCE: ISO 10209:2012, 2.30, modified]

2.4
end-users
person or persons who will ultimately be using the system for its intended purpose

[SOURCE: ISO/IEC 19770-5:2015, 3.13]

2.5
integration
process of physically and functionally combining lower-level functional elements (hardware or software) to obtain a particular functional configuration considered to be of a much higher-level entity

[SOURCE: ISO 10795:2011, 1.117, modified]

2.6
interconnect
device used to connect two things together

2.7
interested party and stakeholders
person or organization that can affect, be affected by or perceive themselves to be affected by a decision or activity

[SOURCE: ISO 28007-1:2015, 3.6]

2.8
interoperability
characteristic of providing an intended function in coordination with other components, the characteristic of sharing information with other system functions or components to provide additional functionality

[SOURCE: ISO 22902-1:2006, 3.1.42]

2.9
microfluidics
handling of fluids in technical apparatus having internal dimensions in the range of micrometres up to a few millimetres

[SOURCE: ISO 10991:2009, 2.5, modified]

2.10
miniaturization
making things on a smaller or miniature scale

2.11
pitch
mean distance between corresponding features in a regular array of features on a surface

[SOURCE: ISO 18115-2:2013, 5.106]

2.12
plug and play
denoting or relating to software or devices that are intended to work perfectly when first used or connected, without reconfiguration or adjustment by the user and thereby enable automatic configuration

[SOURCE: ISO/IEC/IEEE 21451-4:2010, 3.1.31, modified]

2.13
reliability
capability of a device to function without a failure in all specified conditions

[SOURCE: ISO 16972:2010, 3.158]

2.14
verification
confirmation, through the provision of objective evidence, that specified requirements have been fulfilled

[SOURCE: ISO 14025:2006, 3.9]

3 Geometrical pitch specifications

3.1 General

One of the main outputs of the survey is to address the need for geometrical specifications associated with connectors that will ultimately support an increasing trend towards highly integrated complex devices (that may require connections to electrical or optical elements) and miniaturization [15]. Interestingly, this output from the MFmanufacturing survey coincided with the result of an earlier finding from a survey conducted by Semiconductor Equipment and Materials International (SEMI). The SEMI survey (of 85 respondents) also concluded the need for industry to cater for complex and highly integrated devices. It is important to highlight that although the two surveys have reached the same conclusion, the SEMI survey focused on Micro- Electro- Mechanical Systems (MEMS)/sensors rather than microfluidics [16].

In order to support the drive towards highly integrated complex microfluidic based devices, geometrical specifications associated with pitch positions must be considered. Much of the early discussions within MFmanufacturing started in evaluating what has been done with regards to this. Figure 1 summarizes potential possibilities in relation to port pitch spacing dimensions.

Dimensions in millimetres

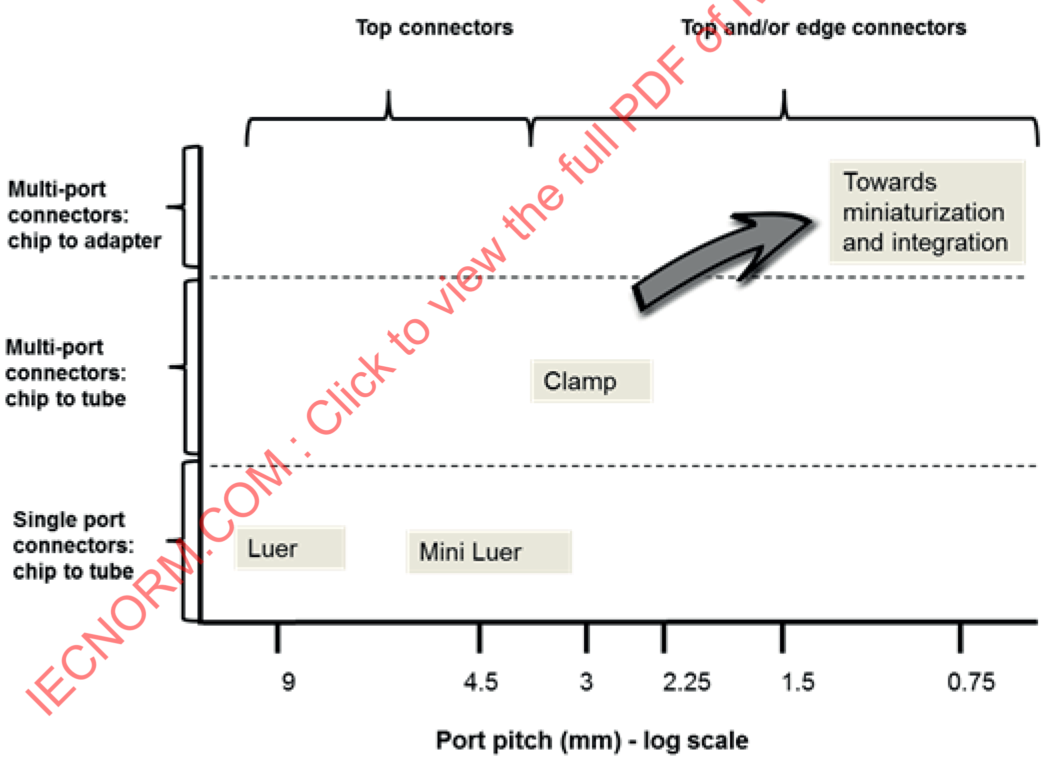


Figure 1 — Port pitch dimension possibilities

Figure 1 clearly shows for the purpose of integration and miniaturization, the trend towards smaller pitches must be realized. In further defining the geometrical specifications for pitch, several factors must be taken into consideration to include the need to:

a) adapt to what the majority of microfluidic manufacturers and users are currently using, such as existing standards already found in laboratory equipment [17];

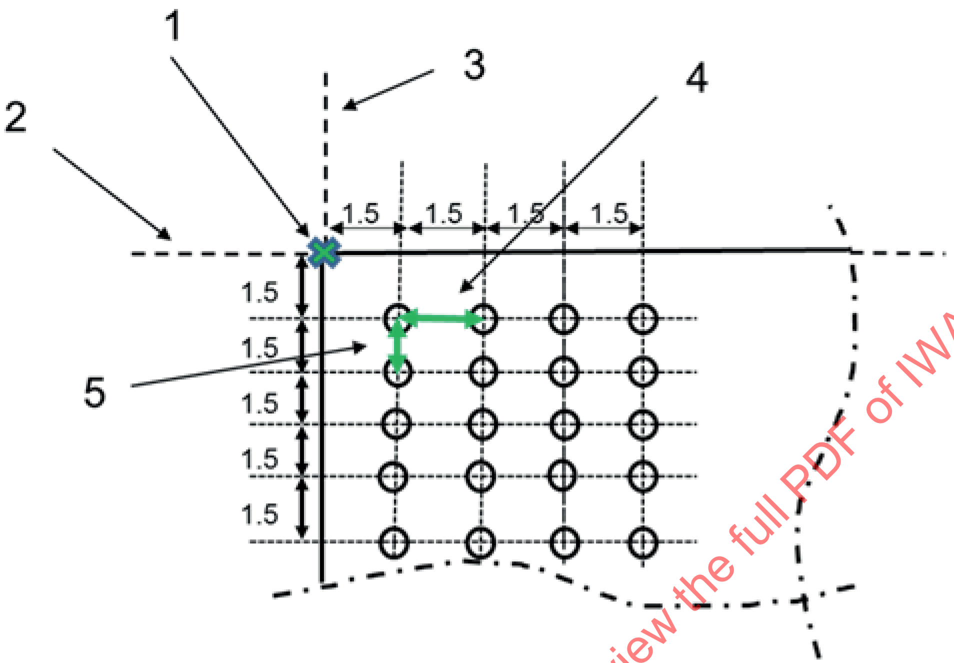
b) have a reliable leakage-free fluidic connections using the currently available multiport connection technologies.

3.2 Geometrical specifications on pitch dimensions

The purpose of this Clause is to specify the geometrical connector pitch dimensions for microfluidic devices.

Designs of microfluidic devices shall be based on a metric multiple pitch concept of $n \times 1{,}5$ mm, where $n \geq 1$. An example layout for the $n \times 1{,}5$ mm grid is shown in Figure 2.

Dimensions in millimetres



Key

1 reference point

2 *x*-axis

3 *y*-axis

4 distance between the centres of two ports on the *x*-axis

5 distance between the centres of two ports on the *y*-axis

Figure 2 — Top view (of top or bottom connections) that shows possible port pitch positions based on the $n \times 1{,}5$ mm grid, where n is an integer ≥ 1

The following considerations should be taken into account in relation to the use of the $n \times 1{,}5$ mm grid concept:

a) only the positions of the ports are prescribed;

b) all prescribed pitch positions in the 1,5 mm grid need not to be used in a design;

c) designation of port pitches shall be independent of the fabrication process and supplier.

If the above criteria are not reached, then the pitch dimensions in the design cannot be considered as standard.

The standard geometrical specifications need not apply if microfluidic chip is of the same size as normal microtitre plate and microscope slides.

4 Device classification

4.1 General

The ability to classify microfluidic devices is important because it allows the interested party and stakeholders to identify and group devices with similar properties via a standardized system [18]. The ability to classify will enhance harmonization of research activity and speed up the process of testing on a global scale, e.g. for standardized verification tests, to ultimately give a certain level of assurance to the customer [19].

Potentially, microfluidic devices can be classified in several ways. However, in order to propose an initial device classification system, there is a need to consider common generic entities common to all microfluidic devices. At the very basic level, all devices have pre-determined operating temperature and pressure ranges in which they are able to perform reliably. As such, the operating temperature and pressure considerations can be used as a basis for device differentiation and thus classification. Furthermore, common to all microfluidic devices are sub–components such as pumps, mixers, valves, flow controllers, tubings, fittings and connectors. These sub-components in turn will have their own respective temperature and pressure limitations, which quite often are restricted on the basis of their material type. Finally, another aspect to consider with regards to classification is the need to understand what microfluidic devices are actually being used in real world applications. Through a combination of a literature research and carrying out the MFmanufacturing survey [20] on standardization issues, the following key findings have been highlighted:

— A 4 °C – 50 °C temperature range is commonly used by suppliers for off-the-shelf micro pumps, valves and liquid flow sensors. There are however, a handful of subcomponents that can go beyond the 50 °C mark, with only a few that can go up to the 100 °C mark.

— Most end-users (i.e. > 95 %) are operating their devices below 100 °C and 7 bar. The high temperature range included a microfluidic device that is based on polymerase chain reaction (PCR) technology, in which a maximum operating temperature of 100 °C is needed.

— The maximum temperature at which a device can operate is mainly restricted by material choice. Tubings, fittings and connectors are among the most critical parts, due to leakage risks. Materials used for these components can vary tremendously. Those that are often used are not recommended to be used above 100 °C or even 75 °C limit.

— Supplier's high temperature devices do not operate beyond the 100 °C mark.

— Applications based on aqueous samples, do not go below the 0 °C mark generally, as this may cause freezing and do not go above the 100 °C mark, as this may cause boiling.

— Pressures of 2 bar and 7 bar maximum are widely used in industry and laboratory environments. Having said this, a few microfluidic devices can operate up to 30 bar.

All the above factors and observations should ideally be taken into account in any attempts to clarify and define classification boundaries.

4.2 Initial device classification

The purpose of this Clause is to give guidelines on the initial device classification scheme for microfluidic devices.

An initial device classification scheme based on operating temperature and pressure limits should be considered, as shown in Table 1.

Table 1 — Initial classification scheme for microfluidic devices; PT denotes pressure and temperature, respectively

Class type	Maximum pressure (bar)	Maximum temperature (°C)	Minimum temperature (°C)
PT 2/50	2	50	4
PT 2/75	2	75	4
PT 2/100	2	100	4
PT 7/50	7	50	4
PT 7/100	7	100	4
PT 30/50	30	50	4

The classification system in Table 1 can be refined or developed further to take into account other types of microfluidic devices. It can also be used to further develop sub-classification systems.

5 Potential future work

A number of participants in the IWA expressed an interest in continued technical work of standardization, integration, and miniaturization. This work has been pioneered by the Micro-electrical Mechanical Systems (MEMS) Committee of SEMI.

— Some possibly relevant guidance and specification towards integration of microfluidics and semiconductors can be found in SEMI MEMS SEMI MS6-0308 [21], and SEMI MS7-0708 [22],

— Some possibly relevant specifications for permanent connections between microfluidic devices can be found in SEMI MS9-0611 [23].

Annex A
(informative)

Workshop resolutions

Resolution 1

The International Workshop on Microfluidics recognizes that standardization has been an essential component for industry growth, which subsequently resulted in several benefits. As in the electronic industry, it promotes interoperability, plug and play and the harmonization of research activity. Because of that, the International Workshop on Microfluidics recommends the identification of those standardization items in order to enhance the commercialization of microfluidic devices.

Resolution 2

The International Workshop on Microfluidics recognizes the importance of miniaturization and to subsequently cater for high level complex integrations in devices. Because of that, the International Workshop on Microfluidics recommends the need to standardize pitch connector dimensions.

Resolution 3

The International Workshop on Microfluidics recognizes that specifications of pitch dimensions should take into consideration, whenever possible, what the majority of microfluidic manufacturers/users are currently using, such as pitch requirements for (mini)Leurs connectors and Society for Biomolecular Screening (SBS) microwell plates.

Resolution 4

The International Workshop on Microfluidics recommends the acceptability:

a) for all designs to adhere to certain dimensions for pitches,

b) for the allowable pitch positions to be based on a metric multiple pitch concept of $n \times 1{,}5$ mm where n is an integer ≥ 1.

The International Workshop on Microfluidics recognizes that the specification is not too restrictive and that:

a) only the positions of the ports are prescribed,

b) not all of the positions in the 1,5 mm grid need to be used in a design,

c) designation of port positions is to be independent of the fabrication process and supplier,

d) an exception is justified if the microfluidic chip is of the same size as the normal microtitre plate or microscope slides.

Resolution 5

The International Workshop on Microfluidics recognizes:

a) the need to have a classification system that will allow for the identification and grouping of similar devices with similar properties via a standardized system,

b) that such a classification system will promote the development of standard test methods, for the purpose of device qualification. Such standard protocols can help speed up device testing, such as for reliability assessment.

Because of that, the International Workshop on Microfluidics recommends:

a) the acceptability of an initial device classification scheme,

b) that the initial classification scheme is based on grouping that takes into account basic operating conditions such as temperature and pressure range,

c) that future research be conducted to develop test methods that adequately address the need for reliability testing of microfluidic devices.

Resolution 6

The International Workshop on Microfluidics recognizes that the initial device classification may not fully reflect all of the microfluidic devices as seen in the field, as there are hundreds of microfluidic devices and classification may be dependent on other factors (such as sample and analysis type). Because of that, the International Workshop on Microfluidics recommends the further development of the initial classification system, to take into account other types of microfluidic devices.

Resolution 7

The International Workshop on Microfluidics recognizes the importance of terminology, which will enable interested parties and stakeholders (such as researchers, manufacturers, regulators, consumers) in the community to communicate clearly and avoid misunderstandings. The International Workshop Agreement on Microfluidics recommends the adoption or refinement of existing terms already published in standard documents and those commonly used in literature, whenever possible.

Annex B
(informative)

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