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GUIDELINES FOR TERMINOLOGY FOR MICROTECHNOLOGY IN CLINICAL LABORATORIES

(IUPAC Technical Report)

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Guidelines for terminology for microtechnology in clinical laboratories

(IUPAC Technical Report)

Abstract: There is no formal terminology used to describe the scope and use of microtechnology in the clinical laboratory. For many laboratory scientists, the word "microchip" is synonymous with high-density microarrays used primarily for investigating gene expression. The document proposes a system of "categories" and "descriptors" that facilitates the classification of a device in a way that communicates details of its function and analytical role, and describes the analytical principle involved and the methods and materials used for its manufacture. Adoption of this system would enable scientists to employ four descriptors that clearly delineate the function, analytical role, and chemical or physical principle involved in the device. Examples of existing commercial devices are given to illustrate the utility of the system.

Keywords: microtechnology; microfabricated devices; microfabrication; nomenclature; nanotechnology; IUPAC Chemistry and Human Health Division.

1. INTRODUCTION

The global expansion of research and development in microtechnology since the 1980s shows little evidence of slowing down in 2006. Furthermore, the evidence in terms of publications, patent filings, the creation of new companies, and the willingness of federal agencies to fund associated research all point to a continuous expansion for years to come [1–11; <www.gene-chips.com>, <www.biochipnet.com>, <www.amkor.com/ EnablingTechnologies/MEMS/index.cfm>]. With this expansion comes a growing need for the establishment of terminology that will facilitate accurate communication in this exciting field.

These Guidelines establish some key terms and definitions that can be the basis of a set of communication tools for microtechnology in coming years. There is no doubt that microtechnology has already made an impact on the methods of investigation used in many disciplines. It is suggested that virtually every discipline in the physical, chemical, and life sciences will exploit microtechnology at increasing levels in the future, and it is hoped that widespread dissemination of the terminology proposed in this document will enhance those efforts.

The document proposes a system of "categories" and "descriptors" that facilitates the classification of a device in a way that communicates details of its function and analytical role, and describes the analytical principle involved and the methods and materials used for its manufacture.

An important feature is that the scope of science covered by the proposed nomenclature is clearly delineated. This requirement is fundamental because of the widespread misuse of terms used to designate dimensions, activities, products, or applications in microtechnology. As a consequence of this requirement, the proposals presented in these Guidelines will be limited to standards and guidelines for microtechnology used in biological and chemical analysis. Standards and nomenclature for use in nanotechnology are not addressed.

2. DEFINITIONS

Uncontrolled and nonsystematic naming has led to confusion and inconsistency in the naming and description of microfabricated devices (MFDs). Many different names have been applied to MFDs, including microchip, gene chip, etc., and a full list is presented in Appendix 1.

For example, "microchip" is used as a generic term to describe a variety of microfabricated devices made from a range of materials containing key component features with dimensions less than 500 μm. Use of this generic term without qualification is not recommended.

Microfabricated devices can be incorporated into cassettes of different cartridges, or platforms, and can have different reaction chamber volumes. MFDs may even have no reaction volume, as in the case of an MFD at the end of a sensing device. Hence, definitions based on overall size or chamber volumes are not viable.

2.1 microtechnology

Science of microfabrication and microfabricated devices.

Note 1: An MFD must include a key component with at least one dimension between 100 nm to 500 μm.

Note 2: Nanotechnology is considered to involve components with at least one dimension less than 100 nm; see the *Oxford English Dictionary* online at <http://dictionary.oed.com>.

2.2 microfabrication

Name given to fabrication and assembly processes for the production of devices with key components with at least one dimension between 100 nm to 500 μm.

Note: The range of microfabrication technologies is extensive and includes photolithography, chemical/physical etching, embossing, micromachining, stamping, printing, and laser ablation.

2.3 micromachining

Microfabrication technique in which an MFD is produced from a bulk material by processing or removal of unwanted material by ablation or machining.

Note: Sometimes also called "top-down" manufacture as compared to a "bottom-up" process in which a nanodevice is fabricated one atom or molecule at a time.

2.4 microfabricated devices (MFDs)

Devices made by using microtechnology. Hence, such devices must have at least one dimension between 100 nm to 500 μm.

3. EXCLUSIONS

These Guidelines do not address certain types of microdevices:

- MFDs for preparative tasks (e.g., microchemical reactors)
- Microchips used for identification (ID chips)
- Electronic microchips (i.e., incorporated into computers)
- Biosensors (unless the sensor is incorporated into an MFD falling into a category defined in Section 5)

These items were excluded because the focus is biological and chemical analysis only.

4. DESCRIPTION OF MFDs

A system of terminology should also include statements that clearly indicate function (e.g., electrophoresis, hybridization, DNA sizing, PCR, filtration, molecular recognition etc.), active features (e.g., array of molecules, reagents, electrodes, aperture, beads, etc.), and size (e.g., 100 nm to 500 μm).

The spectrum of analytical roles (e.g., analysis of blood, DNA sizing, etc.) currently performed by microchip devices is wide and constantly increasing in scope. The following list exemplifies some of the functions and nature of devices that exist in 2006 and the companies or institutions associated with their development. Most of the devices listed incorporate microfluidic features. The list is not all-inclusive. Some of the listed devices are illustrated in Appendix 2. However, this list fails to adequately categorize the various devices or to provide an adequate description of their function.

Function/analytical role	Nature of MFD	Origin
1. Multiconstituent blood analysis	Ion-selective electrode	Abbott Point of Care (i-STAT Corp.) East Windsor, NJ, USA
2. DNA and RNA separation and sizing and protein separation and sizing	Capillary electrophoresis	Agilent Technologies Palo Alto, CA, USA
3. Olignucleotide hybridization	High-density array	Affymetrix Corp. Santa Clara, CA, USA
4. Flow cytometry	Microfluidic combined with fluorescent detection	Agilent Technologies Santa Clara, CA, USA
5. Ion channel studies	Aperture with electrodes	Aviva Biosciences San Diego, CA, USA
6. Active DNA hybridization	Microelectrodes, immobilized DNA	Nanogen Corp. San Diego, CA, USA
7. Immunoassays	Antibody-coated pillars	Zyomyx Hayward, CA, USA
8. DNA probe assay	Coated microbeads at end of fiber optic	Illumina, Inc. San Diego, CA, USA
9. DNA probe assay and immunoassays	Coated microbeads	Luminex Corp. Austin, TX, USA

5. IUPAC CATEGORIZATION OF MFDs

It is recommended that MFDs be classified in one or more categories (A–F) and further characterized using specific descriptors. It is obvious from the above list (Section 4) that industry and academia would greatly benefit from a system which provides a concise description of the nature and role of a device. This can be achieved if basic descriptors are always used to describe devices that belong to single or multiple MFD categories. Moreover, if the descriptors are used in a specific sequence, then communication about the role, fabrication, and operation will be simplified.

5.1 MFD categories

Currently, all known MFDs can be placed in these categories, but future devices may require additional categories.

5.1.1 microfluidic MFD

Device permitting/providing for fluid movement in channels/chambers/conduits with a dimension less than 500 μm.

5.1.2 micro-electronic MFD

Device based on miniaturization of electronic components and circuits [1]. <http:/www.computeruser.com/resources/dictionary/definition>

5.1.3 microarray MFD

Device based on microscopic, ordered array of nucleic acids, proteins, small molecules, or other substances that enables parallel analysis of complex biochemical samples [12,13].

5.1.4 chemically reactive component-based MFD

Device incorporating immobilized or non-immobilized enzymes, immuno-systems, tissues, organelles, cells, or atoms in an analytical reaction in or on the MFD.

5.1.5 individually addressable MFD

Collection of MFDs, each of which incorporates a coding system to uniquely identify the individual MFDs.

5.1.6 MEMS

Device based on a micro-electromechanical systems (MEMS); i.e., device that combines computers with tiny mechanical devices such as sensors, valves, gears, mirrors, and actuators embedded in semiconductor chips. <www.amkor.com/EnablingTechnologies/MEMS/index.cfm>

5.2 MFD descriptors

The following list of recommended descriptors, to be used in the specified order, provides a concise description of the nature and role of a device.

Descriptor 1 Single or multi-function
Descriptor 2 Analytical role
Descriptor 3 Chemical/physical principle involved
Descriptor 4 Device description including
- 4.1 Fabrication material
- 4.2 Fabrication methods
- 4.3 Physical layout (use of digital images is recommended)
- 4.4 Description of essential peripherals

6. EXAMPLES OF THE USE OF IUPAC CATEGORIES AND RECOMMENDED DESCRIPTORS

These examples are for illustration purposes only.

A. "NanoChip® Electronic Microarray" Nanogen Corp., San Diego, CA, USA

MFD Categories	A, B, C, D, E
Descriptors:	
1. Function	Multi
2. Analytical role	Nucleic acid analysis
3. Chemical/physical principle	Hybridization
4. Device description:	
4.1 Materials	Silicon
4.2 Methods	Lithography
4.3 Physical layout	Digital image (See Appendix 2A)
4.4 Peripherals	Cartridge

B. "Agilent 2100 Bioanalyzer®" Agilent Technologies, Palo Alto, CA, USA

MFD Categories	A
Descriptors:	
1. Function	Multi
2. Analytical role	DNA sizing
3. Chemical/physical principle	Capillary electrophoresis
4. Device description:	
4.1 Materials	Glass
4.2 Methods	Lithography
4.3 Physical layout	Digital image (See Appendix 2B)
4.4 Peripherals	Plastic cartridge

C. "Gene Expression Analysis Array" Affymetrix Corp., Santa Clara, CA, USA

MFD Categories	A, C, D
Descriptors:	
1. Function	Multi
2. Analytical role	Expression analysis
3. Chemical/physical principle	Hybridization
4. Device description:	
4.1 Materials	Silicon, glass
4.2 Methods	Lithography
4.3 Physical layout	Digital image (See Appendix 2C)
4.4 Peripherals	Glass/plastic cartridge

D. "SealChip®" Aviva Biosciences Corp., San Diego, CA, USA

MFD Categories		A, B
Descriptors:		
1.	Function	Single
2.	Analytical role	Ion channel studies
3.	Chemical/physical principle	Patch clamping
4.	Device description:	
4.1	Materials	Glass/plastic
4.2	Methods	Lithography
4.3	Physical layout	Digital image (See Appendix 2D)
4.4	Peripherals	Glass/plastic cartridge

E. "Luminex Microspheres" Luminex Corp., Austin, TX, USA

MFD Categories		C, D, E
Descriptors:		
1.	Function	Multi
2.	Analytical role	Protein or nucleic acid analysis
3.	Chemical/physical principle	Ligand binding
4.	Device description:	
4.1	Materials	Latex
4.2	Methods	Polymerization
4.3	Physical layout	Digital image (See Appendix 2E)
4.4	Peripherals	Glass/plastic

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APPENDIX 1

Examples of names used to describe MFDs [6]:

Assaychip	Lab-on-a-chip
Biochip	Living chip
Bioelectronic chip	Microanalyzer
Chemchip	Microarray
Chip	Microchip
Chiplab	Microdevice
Critters on a chip	Miniaturized total chemical analysis system
DNA chip	PCR chip
Gene chip	Sperm chip
Genome chip	Spotted array
IVF chip	Test tube on a chip

APPENDIX 2

Examples of MFDs:

(2A) NanoChip® Electronic Microarray, Nanogen Corp., San Diego, CA, USA
(2B) Agilent 2100 Bioanalyzer®, Agilent Technologies, Palo Alto, CA, USA
(2C) Gene Expression Analysis Array, Affymetrix Corp., Santa Clara, CA, USA
(2D) Patch clamp chip, Aviva Biosciences Corp., San Diego, CA, USA
(2E) Luminex Microspheres, Luminex Corp., Austin, TX, USA