Characterisation and reporting

Chair: Ilka Maschmeyer, TissUse

Roundtable members:

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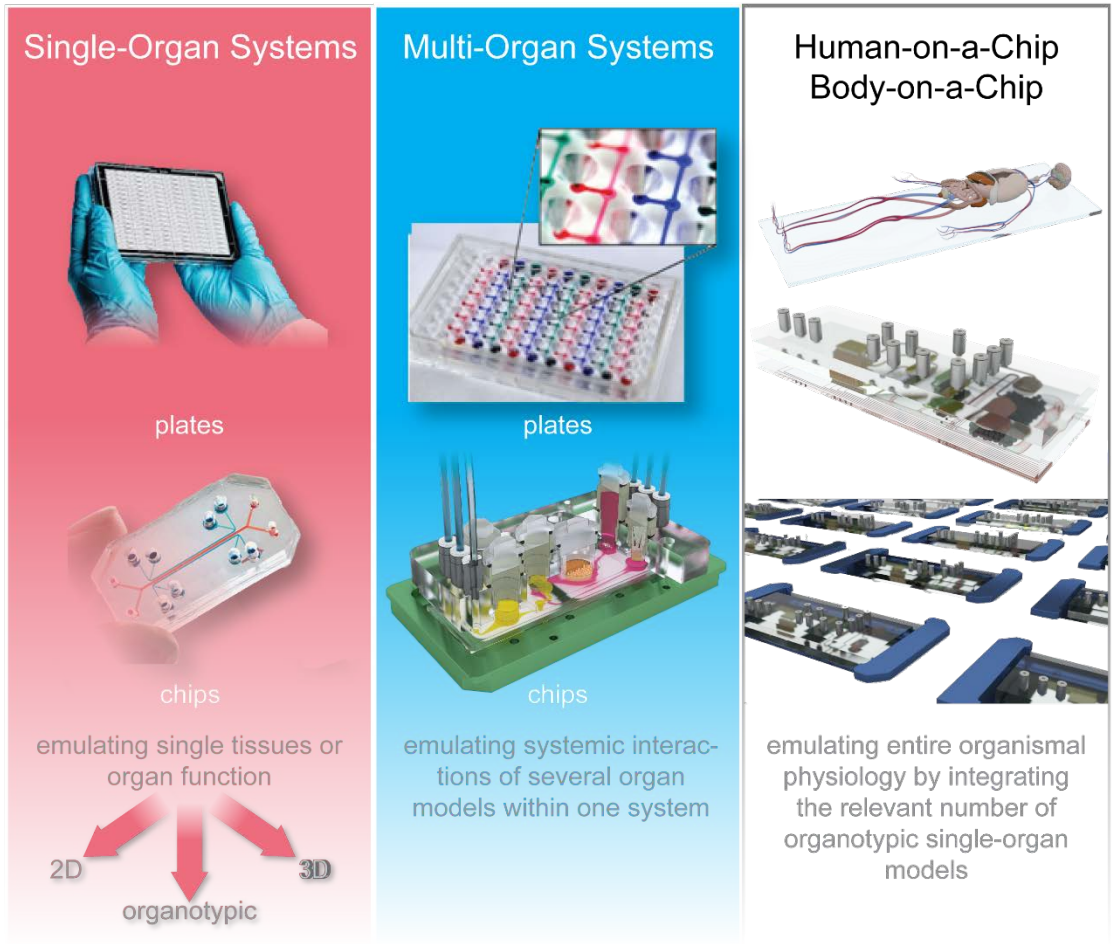
Rapporteur: Monica Piergiovanni

Definitions and terminology – MPS models

- **Microphysiological systems** (MPS) are microfluidic devices capable of emulating human (or any other animal species') biology *in vitro* at the smallest biologically acceptable scale, defined by purpose. The application of fluid flow (dynamic) for the physiological nutrition of the tissues and the creation of microenvironmental biomolecular gradients and relevant mechanical cues (e.g. shear stress) is a major aspect of these systems.
- **MPS-based organ model** or **Organ-on-Chip** stands for a fit-for-purpose microfluidic device, containing living engineered organ substructures (functional unit(s)) in a controlled microenvironment, that recapitulate one or more aspects of the organ's dynamics, functionality and (patho)physiological response *in vivo* under real-time monitoring.
- **MPS-based multi-organ model** or **Multi-Organ-Chip** refers to the combination of two or more different organ models within an MPS-based model emulating systemic organ interactions.
- The term **MPS-based disease model** is used for any single- or multi-organ model mimicking representative elements of the pathophysiology of a disease of a given species, for example, humans.
- The terms **Body-on-Chip** and **Human-on-Chip** are used in scientific literature in the context of MPS-based models envisioned to emulate entire holistic physiological organismal homeostasis.
- The same applies to the term **Patient-on-Chip**, which can be used for MPS-based models envisioned to emulate personalized patient-specific organismal pathophysiology.

Source: Marx et al. ***ALTEX*** 2020,37,3; https://doi.org/10.14573/altex.2001241

Types of Microphysiological Systems



Marx et al. (2016) *ALTEX*

Definitions and terminology – methods, tests and assays

MPS-based methods, tests and assays are used by different stakeholders at three levels of quality:

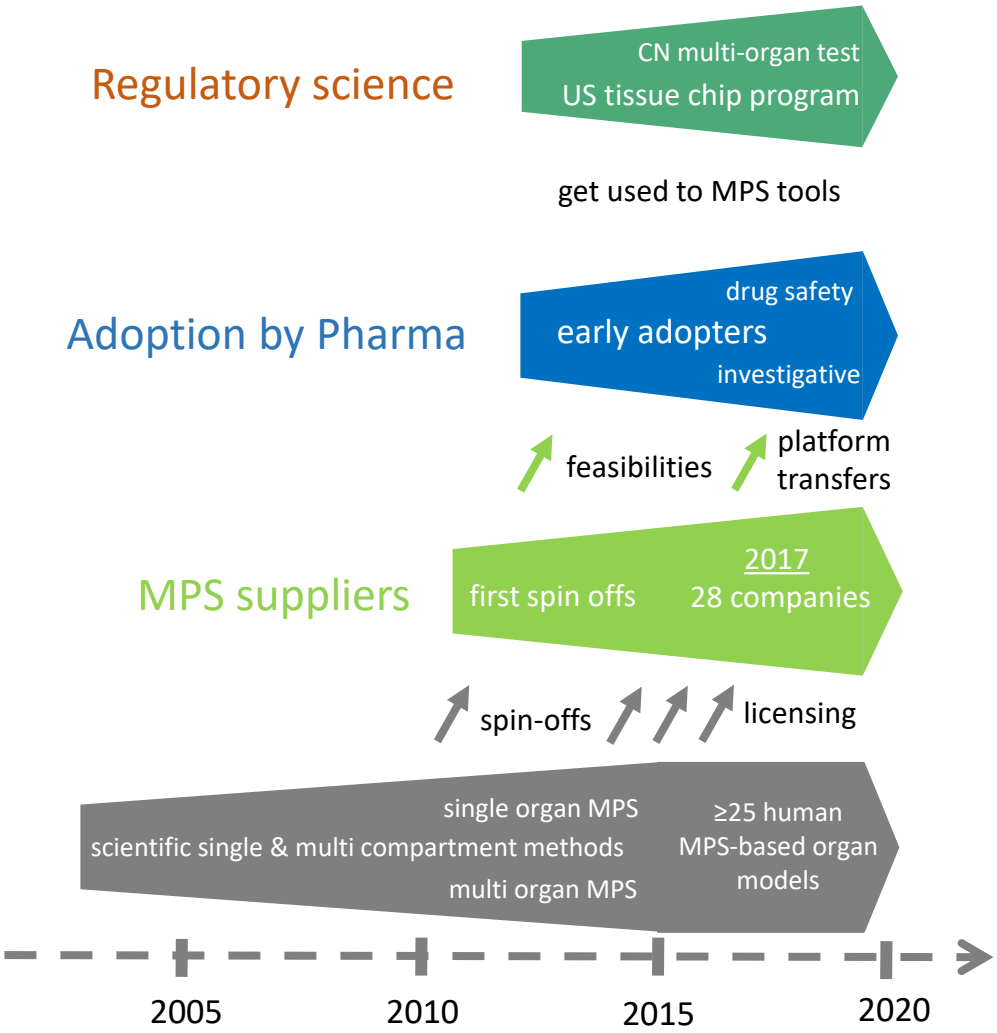
i. The terms **method** or **test** can be used in academia for basic and applied research to make new discoveries in a trial and error fashion. They are supposed to be reproducible scientific methods and tests according to common research standards. Knowledge and scientific publications are the prime outcome from this level of quality of MPS technologies.

ii. The term **qualified assay** can be used for those fit-for-purpose assays which have been adopted by and integrated into end user industries for candidate development and assessment, and, therefore, have been optimized regarding their degree of standardization. Mechanistic understanding of the mode of action and adverse outcome pathways of new leads and investigative data for failed candidates are two examples of the outcome from this level of quality. The data are supporting internal preclinical portfolio decision-making within the end user industries and can become part of an investigational new drug (IND) file or investigational medicinal product dossier (IMPD).

iii. The term **validated assay** can be used for those assays in a specific context of use which have been validated by end users in a setting relevant to regulatory approval processes for new medicines or consumer products. The outcome of this level of quality are assays finally introduced into International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) or Organisation for Economic Co-operation and Development (OECD) guidelines.

Source: Marx et al. ***ALTEX*** 2020,37,3; https://doi.org/10.14573/altex.2001241

Establishment of a Stakeholder Community for MPS



qualified equipment and models
(at least 4 standardized commercial platforms available)

scientific models, methods and tests
(> 1000 scientific papers/y)

GSRS 2020

*model = organ model or disease model

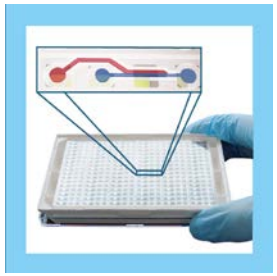
At least four commercially available MPS Platforms

Test throughput
Single tissue/organ models

Biological complexity
Multi tissue/organ models

MIMETAS
the organ-on-a-chip company

OrganoPlate®



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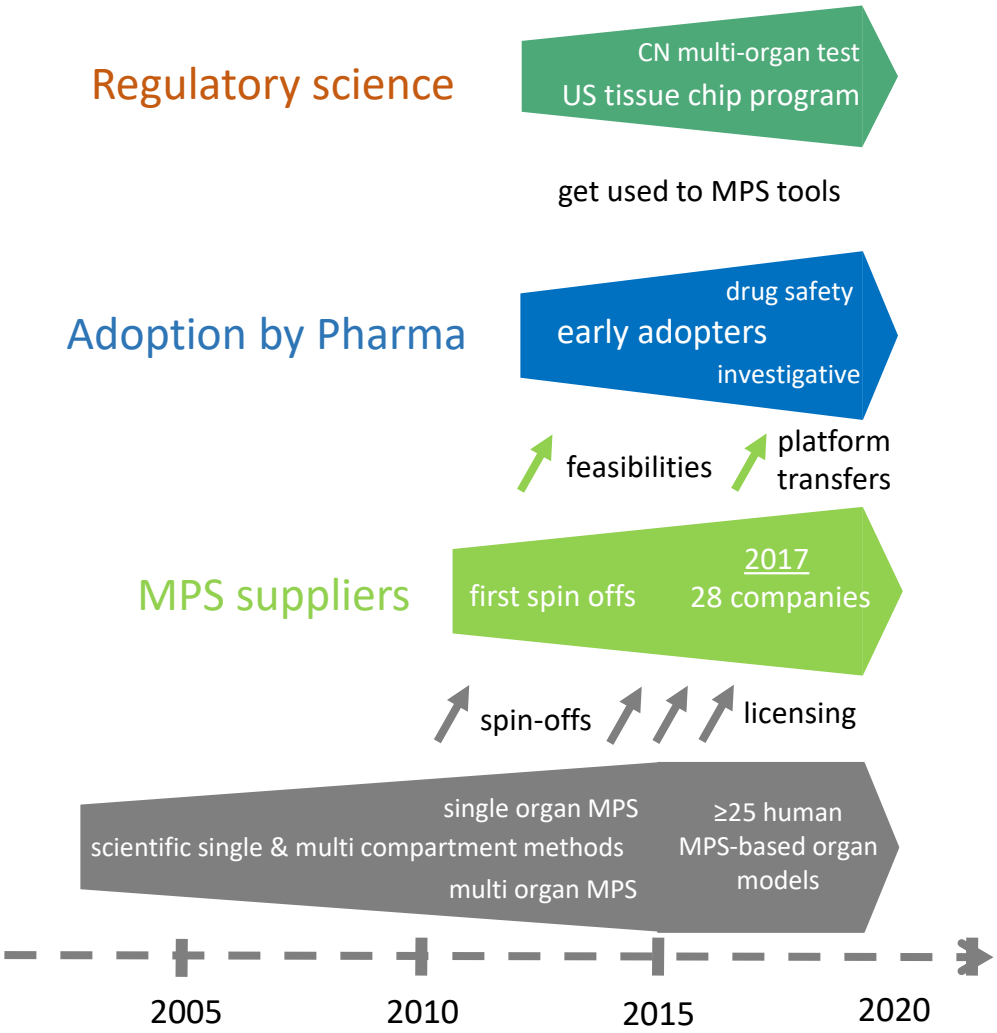
Establishment of a Stakeholder Community for MPS



"23"

fit for purpose assays

internal portfolio decisions

qualified equipment and models

(at least 4 standardized commercial platforms available)

scientific models, methods and tests

(> 1000 scientific papers/y)

*model = organ model or disease model

MPS assays used for internal portfolio decision-making in drug development

MPS-based Organ/Tissue model	Nr. of cases	Area of usage (drug development phase)	MPS-Supplier	End user	Reference (if available)
Blood Vessel, Vasculature	5	Target identification, validation and compound selection	AIST	Daiichi-Sankyo	Satoh et al., 2016
		Discovery (scleroderma)	Mimetas	Galapagos	-
		Systems toxicology for consumer products	Mimetas	Philip Morris	Poussin et al., 2019
		Pharmacokinetics and pharmacology	Mimetas	undisclosed	-
		Target identification and validation	Mimetas	NovoNordisk	-
Bone Marrow	4	Preclinical safety	TissUse	AstraZeneca	Sieber et al., 2018
		Preclinical safety	Emulate	AstraZeneca	Chou et al., 2018
		Preclinical safety	TissUse	Roche	-
		Preclinical safety	TissUse	Bayer	-
Gut Epithelium	4	Discovery (inflammatory bowel disease)	Mimetas	Galapagos	Beaurivage et al., 2019
		Discovery	Mimetas	Roche	-
		Clinical development	Mimetas	Roche	-
		Preclinical Safety	Emulate	Roche	-
Lung	3	Discovery (alveolus)	Wyss	undisclosed	Huh et al., 2012
		Drug efficacy (epithelium)	Wyss	Pfizer, Merck USA	Benam et al., 2016
		Preclinical safety	Emulate	Roche	-
Liver	2	Pharmacological and toxicological effects	Emulate	AstraZeneca	Foster et al., 2019
		Preclinical safety – assessment of species (Rat, Dog & Human)	Emulate	J&J, AstraZeneca	Jang et al., 2019
Ocular compartment	1	Discovery	Fh IGB / EKUT	Roche	Achberger et al., 2019
Kidney Epithelium	1	Pharmacokinetics and pharmacology	Mimetas	undisclosed	Vormann et al., 2018
Liver-Pancreas	1	Target validation / identification	TissUse	AstraZeneca	Bauer et al., 2017
Liver-Thyroid	1	Preclinical safety – assessment of species-specificity (Rat and Human)	TissUse	Bayer	Kuehnlenz et al., 2019
Skin-Tumor	1	Preclinical safety & efficacy	TissUse	Bayer	Huebner et al., 2018

∑ = 23 cases

Marx et al.,
Biology-inspired Microphysiological Systems to Advance Medicines for Patient Benefit and Animal Welfare.
ALTEX 2020

2018

Sieber et al.,
Bone marrow-on-a-chip: Long-term culture of human haematopoietic stem cells in a three-dimensional microfluidic environment

Tissue Eng Regen Med

2017

Bauer et al.,
Sci Rep

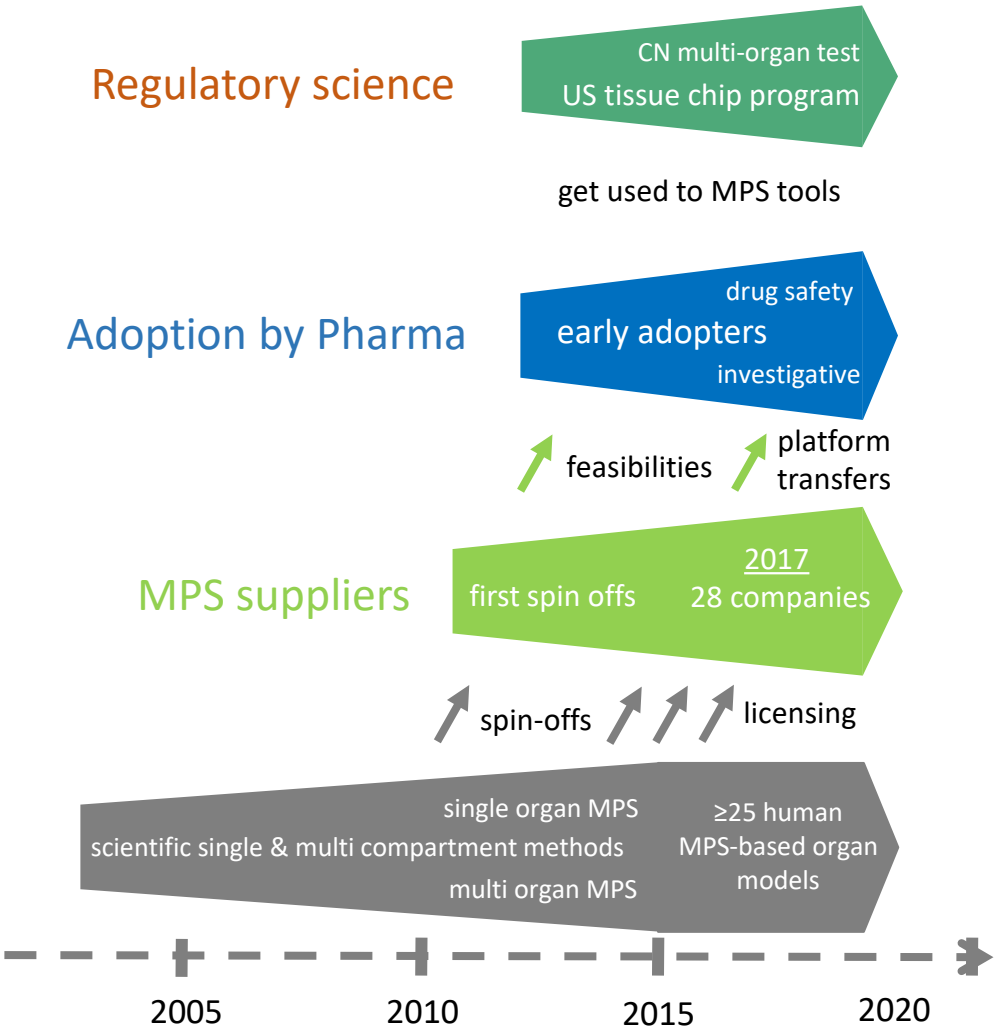
2019

Kühnlenz et al.,
Toxicol Lett (Abstract)

2018

Hübner et al.,
Sci Rep

Establishment of a Stakeholder Community for MPS



"0"

data submission

context of use assays

"23"

fit for purpose assays

internal portfolio decisions

qualified equipment and models

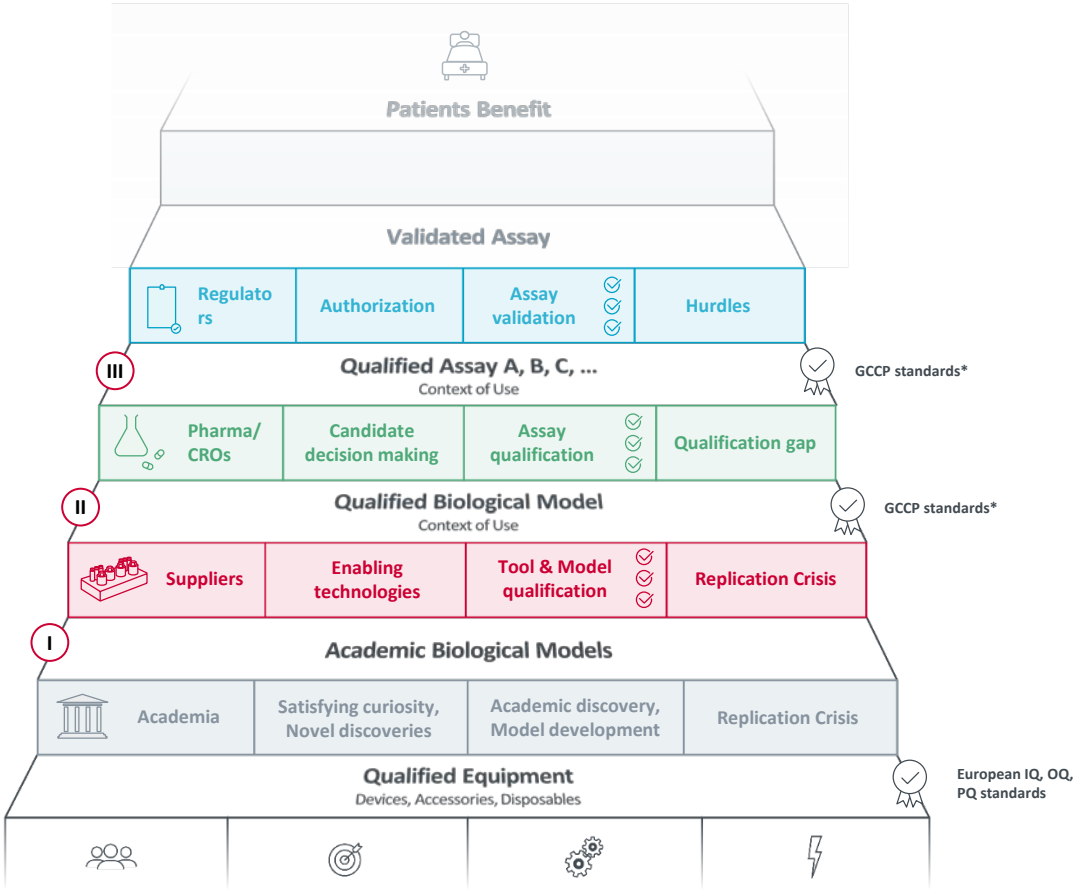
(at least 4 standardized commercial platforms available)

scientific models, methods and tests

(> 1000 scientific papers/y)

*model = organ model or disease model

MPS-based assay value chain



* Pamies et al. 2018

- III Assay established, available for testing/assay transfer
- II Model established, available for assay development
- I Proof of Concept, available for joint development
- Specifications / Features
- Qualification standards

The HUMIMIC® MPS platform – supporting easy transfer!

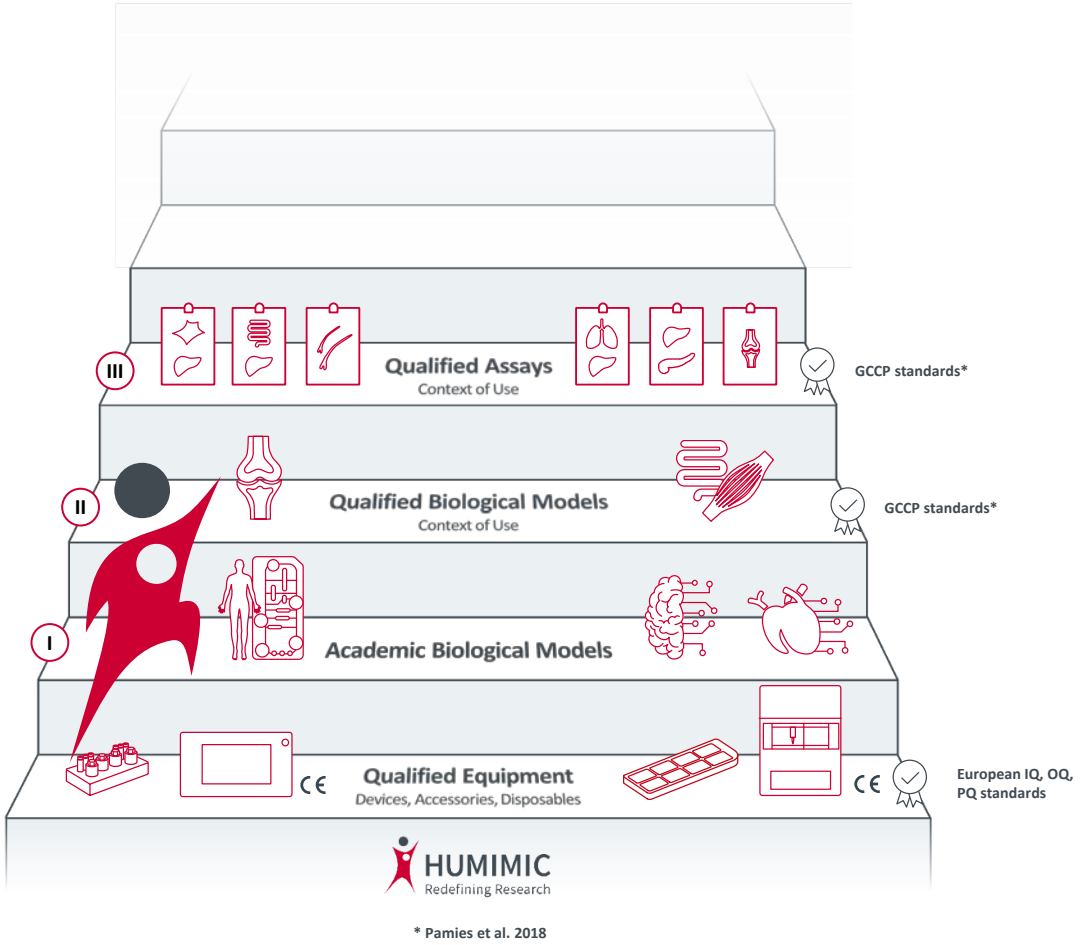
Nr.	Organ model	Schematic	Context of use	Level of readiness
1	Bone marrow		Bone marrow toxicity	III
2	Hair follicle		Hair growth agents	III
3	Skin – Liver		Hazard identification, Tier 3	III
4	Intestine – Liver		Absorption, metabolism	III
5	Lung – Liver		Hazard identification	III
6	Liver – Pancreas		Diabetes drug substances	III
7	Skin – Tumor		Anti-tumor antibodies	III
8	Thyroid – Liver		Hazard identification, safety	II
9	Testis – Liver		Testicular toxicity	II
10	Liver – Neuro		Metabolite neurotoxicity	II
11	Skin – Leukocytes		Allograft rejection therapies	II
12	Intestine – Muscle		Muscle growth agents	II
13	vasc. Pancreas – Tumor		Anti-tumor therapy	II
14	Bone		Nanoparticle toxicity	I
15	Bone marrow		Erythropoiesis	I
16	Skin – Hair follicles		Hair growth agents	I
17	Liver – Cardio		Metabolite cardiotox	I
18	Liver – Kidney		Kidney toxicity	I
19	Skin – Lymph node		Hazard identification, Tier 3	I
20	vasc. Intestine – Lymph node – Tumor		Immuno-Oncology	I
21	ADME-axis + 1		ADME-profile, PBPK, Tox	I
22	Blood-Brain-Barrier		Permeability & Neurotoxicity	I

III **Assay established, available for testing/assay transfer**

II **Model established, available for assay development**

I **Proof of Concept, available for joint development**

Qualification standards



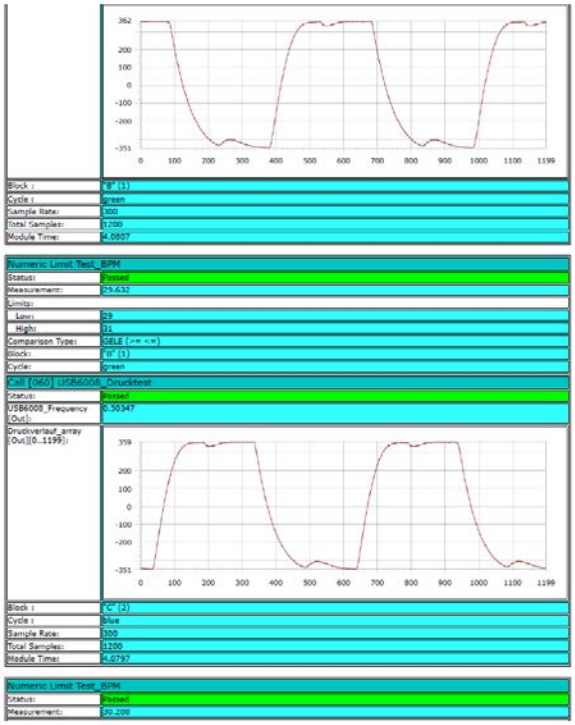
* Pamies et al. 2018

Quality Control

ISO 9001:2015 certified
Quality Management System

HUMIMIC Starter

- Leakage tests
- Test of switching characteristics (e.g. valve switching speed)
- Calibration of all sensors and measurement of signal quality
- Functionality tests of all electric and pneumatic connectors
- Electrical safety tests
- etc…



HUMIMIC Chips

- Casting quality of microfluidics
- Bonding strength
- Configuration of microfluidics and inserts
- Optical inspection of channels and compartments by two different individuals
- etc…

Thank you!

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University of Twente

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Vienna University of Technology

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European Commission, JRC

Rapporteur: **Monica Piergiovanni**