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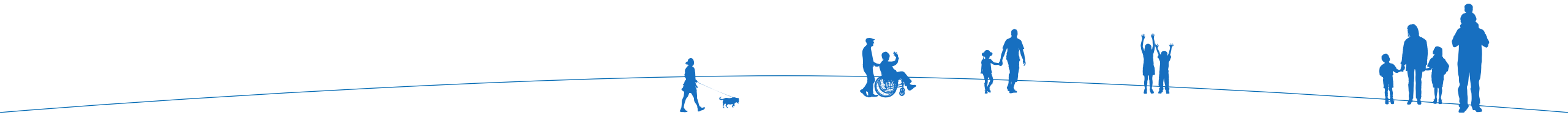
PMDA perspective on acceptance of MPS use for regulatory decision making

Fumito Mikashima

PMDA principle reviewer



Conflicts of Interest（COI） Disclosure

MPS world summit 2025

Institution: Pharmaceuticals and Medical Devices Agency

Name of Speaker : Fumito Mikashima

The speaker has no conflicts of interest related to this presentation.

The speaker is affiliated with Pharmaceuticals and Medical Devices Agency.

The views expressed in this presentation are those of the author and do not necessarily reflect the official views of Pharmaceuticals and Medical Devices Agency.

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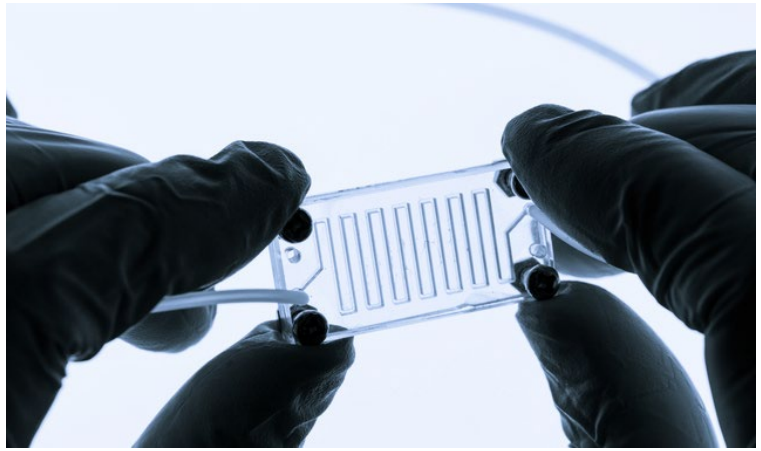
MPS on Drug Discovery

- ✓ MPS are advanced, engineered models that replicate the structure and function of human tissues or organs at a small scale.
- ✓ Organ-on-a-chip is a type of MPS designed to mimic various organ and tissue functions.
- ✓ MPS can be used to assess aspects of pharmacology, toxicology, and ADME that would typically require in vivo testing.



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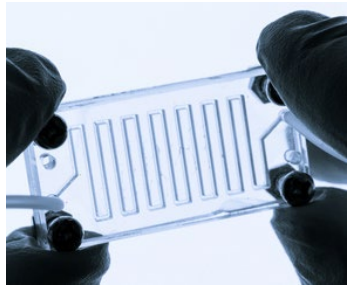
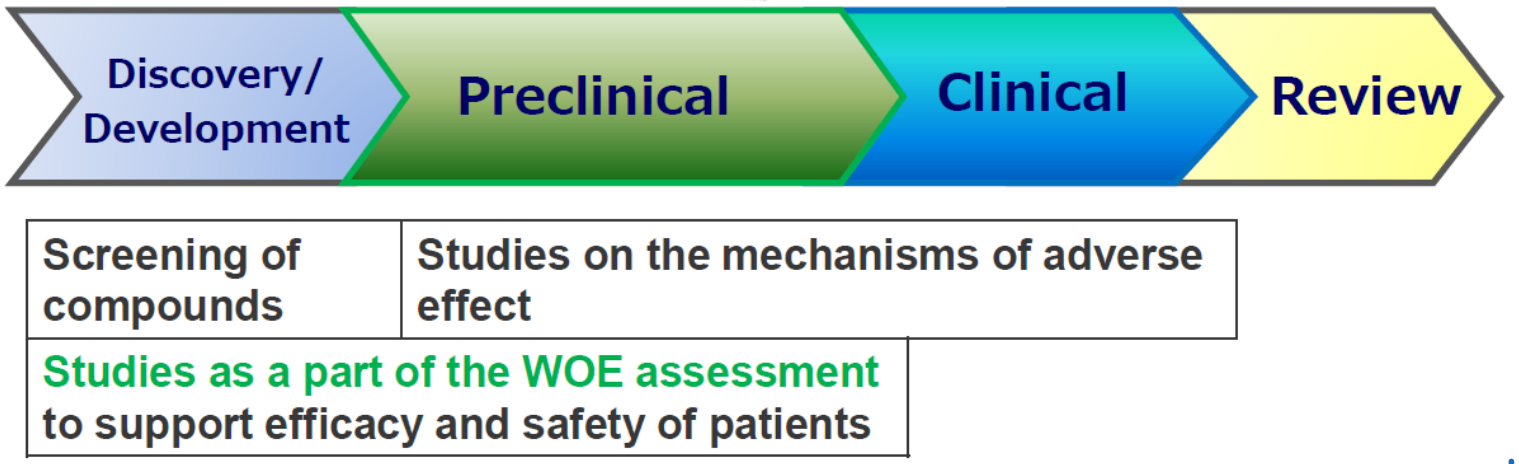
Regulatory use of MPS – future

- ✓ Currently, MPS is mainly used as a supplementary tool to support candidate compound selection, which does not require regulatory acceptance.
- ✓ If MPS-based assays are qualified, they may support non-clinical data in a New Drug Application (NDA) or a Clinical Trial Application (CTA) submissions.
- ✓ In the future, MPS could potentially replace certain in vivo studies rather than merely complementing them.
- ✓ Global acceptance of standardized MPS assays would further enhance their utility.





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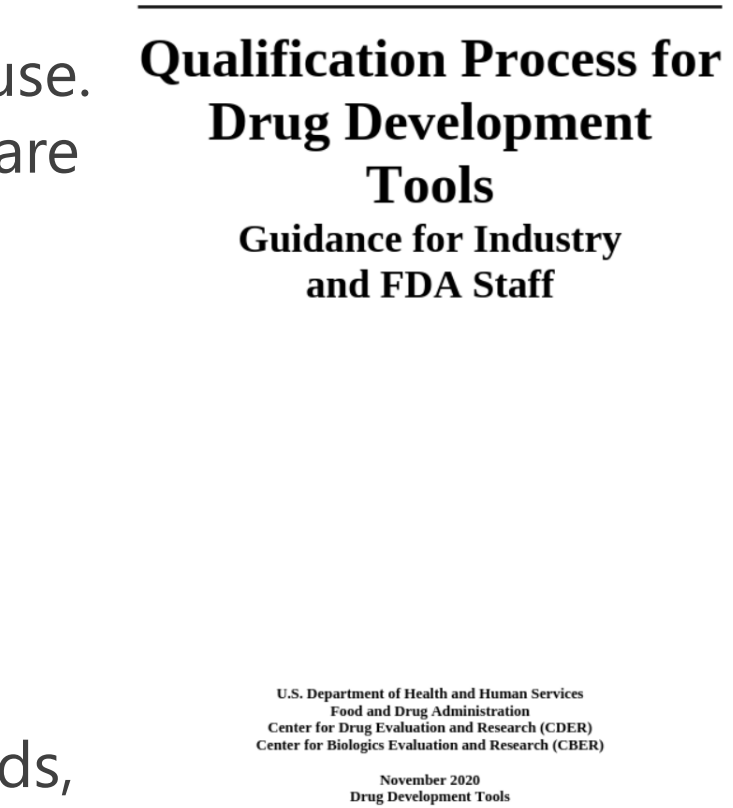
MPS Qualifying process – FDA

- ✓ The DDT program evaluates tools that support drug development and qualifies them for specific contexts of use.
- ✓ It provides a framework to demonstrate that these tools are reliable and useful in drug development and regulatory review.
- ✓ FDA actively engages with applicants to support tool development throughout the qualification process.
- ✓ Once qualified, tools are publicly available for use in any drug development program.
- ✓ This program aims to improve development efficiency, accelerate regulatory review, address unmet medical needs, and promote innovation.


Qualification Process for Drug Development Tools

Guidance for Industry and FDA Staff

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

November 2020
Drug Development Tools

https://www.fda.gov/regulatory-information/search-fda-guidance-documents/qualification-process-drug-development-tools-guidance-industry-and-fda-staff

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MPS Qualifying process – EMA

- ✓ EMA has announced its support for the regulatory acceptance of New Approach Methodologies (NAMs).
- ✓ The CHMP offers a qualification pathway for NAMs developers.
- ✓ Developers can apply for qualification by clearly defining the context of use and submitting robust supporting data.
- ✓ EMA's Qualification Teams, including external experts, assess the scientific validity and regulatory acceptability of the NAMs.
- ✓ They provide advice on protocols and methodologies and plan to publish their qualification assessments.
- ✓ EMA also encourages the voluntary submission of NAMs data.

https://www.ema.europa.eu/en/human-regulatory-overview/research-development/ethical-use-animals-medicine-testing/regulatory-acceptance-new-approach-methodologies-nams-reduce-animal-use-testing

MPS Qualifying process –PMDA

- ✓ Existing consultations are designed to evaluate specific drug development programs.
- ✓ If MPS is used as a pivotal part of the drug's evaluation, its appropriateness can be discussed.
- ✓ However, PMDA does not currently accept consultations from NAMs developers seeking to qualify tools for a specific context of use (CoU), independent of a specific drug.
- ✓ Discussions are ongoing regarding the potential need to establish a system similar to those of the FDA and EMA.

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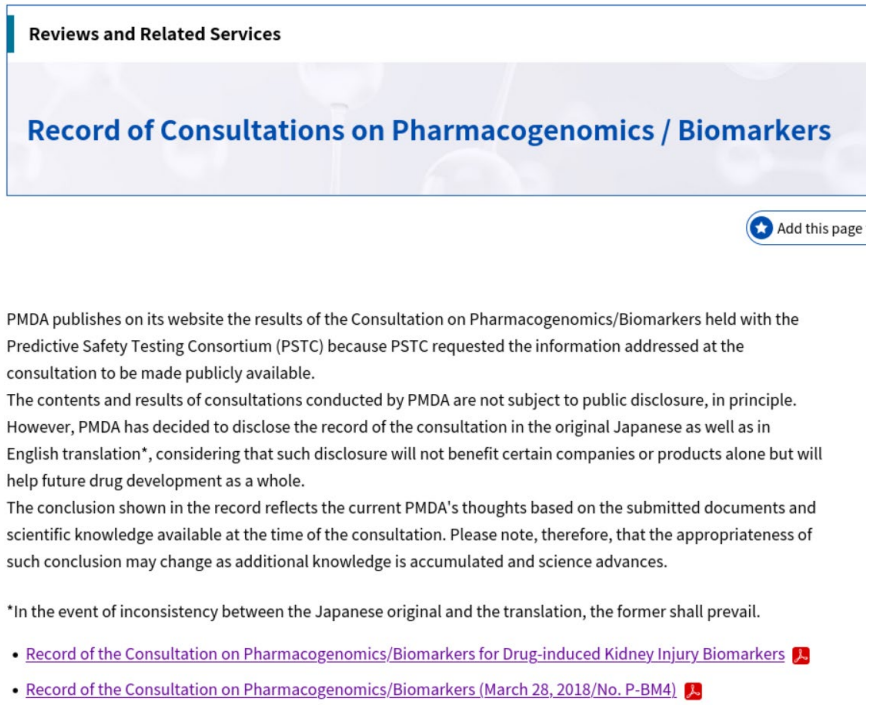
Current consultation system on PMDA

- ✓ Among PMDA's existing consultation systems, the Consultation on Pharmacogenomics/Biomarkers is most similar to a NAMs qualification program.
- ✓ This consultation provides general guidance and advice on the use of pharmacogenomics and biomarkers in drug and medical device development, independent of specific products.
- ✓ It includes evaluation and interpretation of the validity of biomarker-related data.
- ✓ Records of past consultations, including English versions, are publicly available on the PMDA website.


Reviews and Related Services

Record of Consultations on Pharmacogenomics / Biomarkers

Add this page

PMDA publishes on its website the results of the Consultation on Pharmacogenomics/Biomarkers held with the Predictive Safety Testing Consortium (PSTC) because PSTC requested the information addressed at the consultation to be made publicly available.
The contents and results of consultations conducted by PMDA are not subject to public disclosure, in principle. However, PMDA has decided to disclose the record of the consultation in the original Japanese as well as in English translation*, considering that such disclosure will not benefit certain companies or products alone but will help future drug development as a whole.
The conclusion shown in the record reflects the current PMDA's thoughts based on the submitted documents and scientific knowledge available at the time of the consultation. Please note, therefore, that the appropriateness of such conclusion may change as additional knowledge is accumulated and science advances.

*In the event of inconsistency between the Japanese original and the translation, the former shall prevail.

- Record of the Consultation on Pharmacogenomics/Biomarkers for Drug-induced Kidney Injury Biomarkers
- Record of the Consultation on Pharmacogenomics/Biomarkers (March 28, 2018/No. P-BM4)

https://www.pmda.go.jp/english/review-services/consultations/0001.html

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Key challenges of MPS

1. Standardization of MPS Technology

- ✓ Broad adoption of MPS requires reproducible results across different labs and operators.
- ✓ A clearly defined and widely applicable CoU is essential.
- ✓ However, in early development stages, a limited CoU may facilitate clearer interpretation and qualification.
- ✓ Gradual expansion from a qualified limited CoU to a broader one is a realistic path forward.

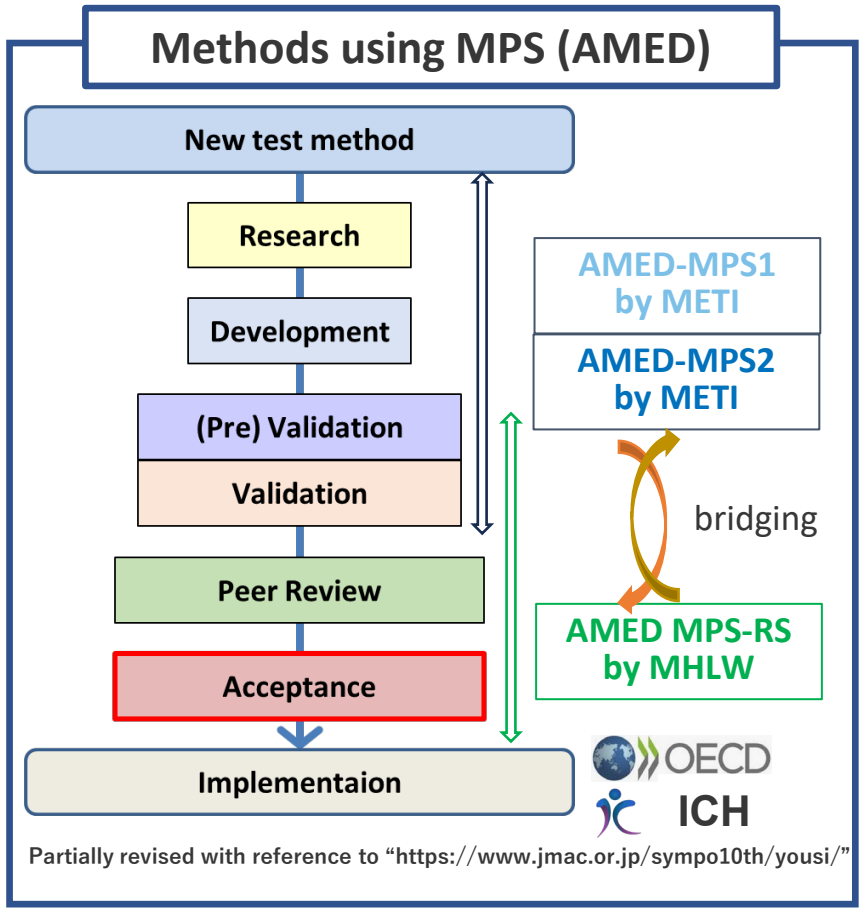
Key challenges of MPS

2. Reliability of Data

- ✓ Regulatory discussions must be based on accurate and reliable data.
- ✓ While Good Laboratory Practice (GLP) is a standard for non-clinical studies, it may not always be required for MPS, depending on the intended use.
- ✓ Clearly defined test system protocols are crucial to support both standardization and reliability.
- ✓ International harmonization efforts (e.g., through OECD and ICH) will be key to establishing these standards.

AMED* MPS RS research group

- ✓ PMDA participates in a research group in Japan that is examining regulatory approaches for the acceptance of MPS.
- ✓ This research group collaborates with the National Institute of Health Sciences (NIHS) and the Japanese Center for the Validation of Alternative Methods (JaCVAM).
- ✓ The aim is to build a framework for future regulatory acceptance of MPS in Japan.



Led by Dr. Daiju Yamazaki

*: Japanese government agency that promotes integrated medical research and development. It supports projects by funding and coordinating efforts among academia, industry, and government.

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Global utilization of MPS

- ✓ MPS qualification programs are under discussion in various countries and regions.
- ✓ However, unlike ICH guidelines, a tool qualified in one region is not automatically considered qualified in Japan.
- ✓ Ideally, the requirements for qualification decisions should be harmonized across regions.
- ✓ Cross-agency dialogue through platforms such as the fNIH VQN or IMRWG3Rs could support this effort.

Global discussion

International Medicines Regulator's Working Group on 3Rs (IMRWG3Rs)

Expectation for future global discussion

ICH

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Future Perspectives

- ✓ In the future, MPS models replicating various organs such as the liver, kidney, heart, and lungs are expected to be fully established.
- ✓ By integrating these systems, it may become possible to comprehensively assess all endpoints currently evaluated through animal-based in vivo studies.
  - ✓ Near or far future…
- ✓ This would enable MPS to serve as a complete alternative to in vivo testing, achieving the principles of the 3Rs: Replacement, Reduction, and Refinement of animal use.

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