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| **IQ MPS Affiliate**  **Critical Path Institute** |
| Kidney Microphysiological System Testing for Specific Contexts of Use in Drug Development |
| REQUEST FOR INFORMATION |

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# Introduction

## About IQ MPS Affiliate

The IQ MPS Affiliate is a collaboration of pharmaceutical and biotechnologies companies created as an Affiliate within the International Consortium for Innovation and Quality in Pharmaceutical Development (also known as the IQ Consortium). The IQ Consortium is a leading science-focused, not-for-profit organization with a mission of advancing science and technology to augment the capability of member companies to develop transformational solutions that benefit patients, regulators and the broader R&D community ([**https://iqconsortium.org**](https://iqconsortium.org/)). The IQ MPS Affiliate was established to provide a venue for appropriate cross-pharma collaboration and data sharing to facilitate the industry implementation and qualification of microphysiological systems (MPS).

1. About Critical Path Institute

[Critical Path Institute](https://c-path.org/) (C-Path) is an independent, nonprofit organization established in 2005 as a public and private partnership. C-Path’s mission is to catalyze the development of new approaches that advance medical innovation and regulatory science, accelerating the path to a healthier world. An international leader in forming collaborations, C-Path has established numerous global consortia that currently include more than 1,600 scientists from government and regulatory agencies, academia, patient organizations, disease foundations, and dozens of pharmaceutical and biotech companies. C-Path US is headquartered in Tucson, Arizona and C-Path, Ltd. EU is headquartered in Dublin, Ireland, with additional staff in multiple other locations. For more information, visit [c-path.org](https://c-path.org/) and [c-path.eu](https://c-path.eu/).

1. Request for Information

Publication of this ***Request for Information (RFI)*** is the first step by the IQ MPS Affiliate and Critical Path Institute to solicit interest in collaborating on the testing of kidney MPS for specific contexts of use (e.g., pharmacology, drug metabolism, toxicology, etc.) in drug development. The information collected during the RFI process will be evaluated by IQ MPS Affiliate and Critical Path Institute members to aid in selection of respondent(s) to move forward to the ***Request for Proposal (RFP)*** stage. The IQ MPS Affiliate and Critical Path Institute may choose respondent(s) to move forward to the RFP stage based solely upon responses to the RFI, or may choose to request clarification on information provided by respondent(s) to the RFI, or request additional technical details. The IQ MPS Affiliate and Critical Path Institute will then release an RFP to selected respondent(s) detailing a study design for a specific context of use. Responses to the RFP will aid in determining study initiation.

1. Disclaimer

The contents and information provided in this RFI are meant to provide general information to parties interested in participating in a study conducted in collaboration with one or more members of the IQ MPS Affiliate and Critical Path Institute. The successful respondent(s) selected at the RFP stage will be expected to execute an Agreement that will govern the terms of the project.

When responding to this RFI, please note the following:

* This RFI is not an offer or contract.
* Materials submitted in response to this RFI will be treated confidentially but will become property of the IQ Consortium and Critical Path Institute.
* Any questions received, and response thereto will be anonymized and made available to all respondents on the IQ MPS Affiliate website.
* Responses to this RFI should not include trade secrets or confidential information, and responses will not be shared with other respondents to this RFI.
* Respondents will not be compensated or reimbursed for any costs incurred as part of the RFI process.
* The IQ MPS Affiliate and Critical Path Institute are not obligated to contract for any of the products or services described in this RFI.
* The IQ MPS Affiliate and Critical Path Institute reserve the right to:
  + Accept or reject any or all responses to the RFI or RFP
  + Modify or cancel this RFI at any time
  + Negotiate with any or all respondents at the RFI and/or RFP stage

1. RFI Contact Information

All questions and inquiries regarding this RFI should be directed to:

IQ MPS Secretariat

c/o Faegre Drinker Biddle & Reath, LLP

1500 K St NW

Washington DC 20005-1209

Phone Number

[info@iqmps.com](mailto:info@iqmps.com)

[www.iqmps.org](http://www.iqmps.org)

1. Project Information
   1. Potential Project Sponsors

One or more members of the IQ MPS Affiliate and Critical Path Institute may elect to serve as project sponsors, to be determined within the RFP stage. Eligible members of the IQ MPS Affiliate and Critical Path Institute that may potentially serve as project sponsor(s) include: AbbVie, Inc., Alnylam Pharmaceuticals, Inc., Amgen, Inc., Astellas Pharma US, Inc., AstraZeneca, Biogen, Bristol-Myers Squibb Company, Daiichi Sankyo, Inc., Eisai, Inc., Eli Lilly and Company, Genentech, Inc., GlaxoSmithKline, Janssen Pharmaceuticals, Inc., Merck & Co., Inc., Merck KGaA, Mitsubishi Tanabe Pharma Corporation, Novartis Pharmaceuticals Corporation, Pfizer, Sanofi, Seattle Genetics, Inc., Takeda, Theravance Biopharma, US, Inc., Vertex Pharmaceuticals Incorporated.

* 1. Project Description

The kidney is a common target organ for drug-induced toxicity and is poorly predicted in nonclinical in vivo studies. Furthermore, due to its critical secretory and filtration activities the kidney plays a role in both drug elimination and maintenance of overall body fluidic content. The structure of the nephron, the functional unit of the kidney and its role in maintaining whole body fluid and electrolyte balance lends the kidney well to MPS model design. Due to the specialized functions of each segment of the nephron (e.g., proximal tubule secretion versus distal tubule Na+/Cl- reabsorption, and glomerular filtration), no single kidney model is required to represent the entirety of needs within pharmaceutical drug development. Rather, the ability to measure specific endpoints with clinical predictivity is of critical importance to the IQ MPS Affiliate and Critical Path Institute.

* 1. Kidney Microphysiological System Technical Requirements

For the purposes of this RFI, MPS refers to models that encompass two or more of the following: multi-cellular/multi-layered tissue, microfluidics, derived of primary or stem cell-derived cells, or inclusion of an immune component. Specifically, this project seeks to investigate models such as organoids, microtissues, organs-on-a-chip, or a combination thereof.

The kidney MPS would ideally be viable and amenable to multi-day, repeated dosing, and exhibit segment (i.e., glomerulus, proximal, distal, collecting duct, etc.) appropriate function and key ADME-related gene expression, localization, and activity (e.g., CYP2B6, CYP2C8, OCT2, MATE1/2, etc.).

For specific technical and functional details of interest to the IQ MPS Affiliate and Critical Path Institute including and beyond minimal requirements, please refer to section 5.b of this RFI. Respondents are also encouraged to review recent manuscripts published by the IQ MPS Affiliate on kidney models and ADME requirements for microphysiological systems (Phillips, et al., Lab on a Chip, DOI: 10.1039/c9lc00925f, 2020; Fowler, et al., Lab on a Chip, DOI: 10.1039/c9lc00857h, 2020).

* 1. Availability Requirements

One outcome of this RFI is to prioritize respondents for competition in a subsequent RFP. The ideal candidate model(s) would be readily available and exhibit robust reproducibility.

1. Criteria for Evaluation

The IQ MPS Affiliate will evaluate the responses to this RFI based on the respondent’s ability to:

* Provide responses reflecting a desire to participate in the collaboration.
* Provide responses to technical queries outlined in section 5.b of this RFI.
* Demonstrate expertise in the field of MPS model development and an ability to work collaboratively with the IQ MPS Affiliate and Critical Path Institute to achieve project goals.
* Provide any additional capabilities and/or information that may differentiate them from other potential collaborators.

1. Respondent Profile (to be completed by Respondent)

Please provide the following information:

* 1. Organization Information

|  |  |
| --- | --- |
| Organization Name |  |
| Address |  |
| City |  |
| State |  |
| Country |  |
| Zip Code |  |
| Website (if applicable) |  |

* 1. Primary Contact Information

|  |  |
| --- | --- |
| Name |  |
| Title |  |
| Email Address |  |
| Phone Number |  |

* 1. Organization Overview

Provide a brief overview of your organization including number of years in the MPS field, number of employees/researchers/trainees involved in the work, models designed, candidate models intended for commercialization within the next 12-18 months, and models commercialized to date.

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Please indicate whether your organization has capabilities to provide your renal MPS model to end users (e.g., ship to customer) and/or is able to conduct studies in-house (e.g., as fee-for-service).

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* 1. Summary of Expertise

Outline your organization’s expertise in the area/field related to this RFI, including any experience working on projects with other consortia.

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* 1. Miscellaneous

Add any additional information about your organization applicable to this RFI to facilitate review of your RFI response.

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1. Organization Response to RFI
   1. Overview of Current Kidney Microphysiological System

Provide a brief overview/abstract of your kidney microphysiological system pertaining to the requirements outlined in Section 2.c include figures/graphs as an addendum if applicable. Please describe material used in device fabrication (e.g., PDMS), surface area available for cell seeding, optical clarity for imaging, volume of media permissible in the system, etc.

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* 1. Functional Capabilities & Specifications of Current Kidney Microphysiological System

The information provided in this section should solely pertain to the system(s) that you would propose to be eligible in a subsequent RFP. It should not be an aspirational test system, but rather one that would be available now or within the next 6 months.

For **Model Characteristics**: Indicate with an “X” all features that apply to your kidney MPS. It is not required that proposed models demonstrate all listed characteristics and features.

| **Model Characteristics** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Type of Model** | **3D Multi-layered Static** | **Organoid** | **Kidney-on-a-Chip** | **Organoid-on-a-Chip** | **Other (please specify)** |
| *Response:* |  |  |  |  |  |
| *If other, please specify:* |  | | | | |
| **Segment of Kidney Modeled (i.e., proximal tubule, glomerulus, distal tubule, etc.):** |  | | | | |
| **Well Throughput**  (for well format models) | **12-well** | **24-well** | **48-well** | **96-well** | **384-well** |
| *Response:* |  |  |  |  |  |
| **Chip Throughput**  (for chip-format models; i.e., number of perfused tissues on a single chip) | **1/chip** | **2/chip** | **3/chip** | **4/chip** | **5+/chip** |
| *Response:* |  |  |  |  |  |
| **For chip models, please comment on how many chips may be run in your perfusion system:** |  | | | | |
| **For chip models, please comment whether the system includes microfluidics, peristaltic stretch, or both***:* |  | | | | |
| **Clinical and Nonclinical Species Availability** | **Human** | **Mouse** | **Rat** | **Dog** | **Primate** |
| *Response:* |  |  |  |  |  |
| **Duration of Tissue Viability and Function** | **<7 Days** | **7 Days** | **14 Days** | **28 Days** | **3 Months** |
| *Response:* |  |  |  |  |  |
| *If duration not shown, please specify:* |  | | | | |
| *Please indicate endpoint used (e.g., ATP, LDH activity, etc.) to measure tissue viability and/or function:* |  | | | | |

For **Technical Requirements, Features, and/or Capabilities:** Indicate with an “X” whether your kidney MPS currently includes the technical requirement (“yes”) or does not (“no”). If your response is “yes”, provide available representative data as an addendum. If providing addended data, please include a brief (<1 page) description of the study design used. If you are currently working to include a technical requirement in your model, but only preliminary data are available, list as “planned.” Inclusion of the preliminary data as an addendum is encouraged. Please note, it is not required that proposed models demonstrate all listed technical characteristics and features.

| **Technical Requirement, Feature, and/or Capability** | **Yes** | **No** | **Planned** | **Addendum Provided (Y/N)** |
| --- | --- | --- | --- | --- |
| **Demonstrated transcript expression of uptake/efflux drug transporters** |  |  |  |  |
| *Please list specific transporters (e.g., OAT, OCT, OATP, URAT1, MATE, P-gp, etc.) for which quantitative expression at the mRNA level has been demonstrated and timepoints assessed:* |  | | | |
| **Demonstrated protein expression of uptake/efflux drug transporters** |  |  |  |  |
| *Please list specific transporters for which qualitative or quantitative expression (verify which) at the protein level has been demonstrated and timepoints assessed:* |  | | | |
| **Demonstrated uptake/efflux drug transporter function** |  |  |  |  |
| *Please list specific compounds used to test function and timepoints assessed:* |  | | | |
| **Demonstrated cellular polarization** |  |  |  |  |
| *Please list specific method (i.e., cellular markers) used to demonstrate polarization:* |  | | | |
| **Demonstrated tubule barrier function (e.g., TEER or other) with ≤5 Test Compounds** |  |  |  |  |
| **Demonstrated tubule barrier function (e.g., TEER or other with 5-20 Test Compounds** |  |  |  |  |
| *If barrier function test other than TEER used (e.g., inulin, FITC-dextran), please specify:* |  | | | |
| *Please list timepoints of barrier function that were assessed:* |  | | | |
| **Presence of primary cilia on epithelial cells** |  |  |  |  |
| *If yes, please describe data demonstrating cilia presence and timepoints assessed:* |  | | | |
| **Demonstrated vitamin D metabolism, bioactivation, and receptor-mediated regulation** |  |  |  |  |
| *If yes, please describe data and timepoints assessed:* |  | | | |
| **Demonstrated GGT (gamma-glutamyl transpeptidase) activity** |  |  |  |  |
| *If yes, please describe data and timepoints assessed:* |  | | | |
| **Demonstrated glucose reabsorption** |  |  |  |  |
| *If yes, please describe data and timepoints assessed:* |  | | | |
| **Demonstrated albumin reabsorption** |  |  |  |  |
| *If yes, please describe data and timepoints assessed:* |  | | | |
| **Demonstrated renal ammoniogenesis** |  |  |  |  |
| *If yes, please describe data and timepoints assessed:* |  | | | |
| **Demonstrated transcript expression of drug metabolizing enzymes** |  |  |  |  |
| *Please list specific enzymes for which expression at the mRNA level has been demonstrated and timepoints assessed:* |  |  |  |  |
| **Demonstrated protein expression of drug metabolizing enzymes** |  |  |  |  |
| *Please list specific enzymes for which expression at the protein level has been demonstrated and timepoints assessed:* |  |  |  |  |
| **Demonstrated drug metabolizing enzyme function** |  |  |  |  |
| *Please list specific compounds (and corresponding enzyme function assessed) used to test function and timepoints assessed:* |  |  |  |  |
| **Live Imaging Capable** |  |  |  |  |

For assessment of **Genotypic and/or Biochemical Biomarkers**: Indicate with an “X” whether your kidney MPS currently includes the biomarker at a specific physiological level (e.g., mRNA expression, protein expression, secreted protein [where appropriate], or immunohistochemistry [IHC]). Please provide available representative data as an addendum. If you are currently working to include a biomarker in your model, but only preliminary data are available, list as “planned”. Inclusion of the preliminary data as an addendum is encouraged. Please note, it is not required that proposed models demonstrate all listed biomarkers.

| **Genotypic and/or Biochemical Biomarkers Assessed** | **mRNA** | **Protein** | **Secreted Protein (where appropriate)** | **IHC** | **Addendum Provided (Y/N)** |
| --- | --- | --- | --- | --- | --- |
| **Clusterin (CLU)** |  |  |  |  |  |
| **Megalin (LRP2)** |  |  |  |  |  |
| **Cubulin (CUBN)** |  |  |  |  |  |
| **PEPT2 (SLC15A2)** |  |  |  |  |  |
| **Glutathione Peroxidase-3 (GPX3)** |  |  |  |  |  |
| **SGLT1 (SLC5A1)** |  |  |  |  |  |
| **SGLT2 (SLC5A2)** |  |  |  |  |  |
| **GLUT2 (SLC2A2)** |  |  |  |  |  |
| **Aquaporin 1 (AQP1)** |  |  |  |  |  |
| **Aquaporin 2 (AQP2)** |  |  |  |  |  |
| **Kidney Androgen Regulated Protein (KAP)** |  |  |  |  |  |
| **KIM-1 (HAVCR1)** |  |  |  |  |  |
| **Heme Oxygenase 1 (HMOX1)** |  |  |  |  |  |
| **Zona Occludens 1 (TJP1)** |  |  |  |  |  |
| **N-Cadherin (CDH2)** |  |  |  |  |  |
| **E-Cadherin (CDH1)** |  |  |  |  |  |
| **Nephrin (NPHS1)** |  |  |  |  |  |
| **Podocalyxin (PODXL)** |  |  |  |  |  |
| **Uromodulin (UMOD)** |  |  |  |  |  |
| **Na+/K+ ATPase (APT1A1)** |  |  |  |  |  |
| **Tubulin** |  |  |  |  |  |
| **Ezrin** |  |  |  |  |  |
| **Cystatin-C** |  |  |  |  |  |
| **N-acetyl-beta-D-glucosaminidase (NAG)** |  |  |  |  |  |
| **Lipocalin (NGAL)** |  |  |  |  |  |
| **Osteopontin (OPN)** |  |  |  |  |  |
| **Other Biomarkers Assessed:**  *Please write-in specific biomarkers for each endpoint* |  |  |  |  |  |
| **Planned Assessments:** |  |  |  |  |  |
| *Please indicate if preliminary data addendum provided for planned assessments:* |  |  |  |  |  |