|  |
| --- |
| **IQ MPS Affiliate** |
| Gastrointestinal Microphysiological System Testing for Specific Contexts of Use in Drug Development |
| REQUEST FOR INFORMATION |

Contents

Contents

[1. Introduction 2](#_Toc42773026)

[a. About IQ MPS Affiliate 2](#_Toc42773027)

[b. Request for Information 2](#_Toc42773028)

[c. Disclaimer 2](#_Toc42773029)

[d. RFI Contact Information 3](#_Toc42773030)

[e. Timelines for RFI 3](#_Toc42773031)

[2. Project Information 3](#_Toc42773032)

[a. Potential Project Sponsors 3](#_Toc42773033)

[b. Project Description 3](#_Toc42773034)

[c. Gastrointestinal MPS Technical Requirements 3](#_Toc42773035)

[d. Availability Requirements 4](#_Toc42773036)

[3. Criteria for Evaluation 4](#_Toc42773037)

[4. Respondent Profile (to be completed by Respondent) 4](#_Toc42773038)

[a. Organization Information 4](#_Toc42773039)

[b. Primary Contact Information 4](#_Toc42773040)

[c. Organization Overview 5](#_Toc42773041)

[d. Summary of Expertise 5](#_Toc42773042)

[e. Miscellaneous 5](#_Toc42773043)

[5. Organization Response to RFI 5](#_Toc42773044)

[a. Overview of Current Gastrointestinal MPS 5](#_Toc42773045)

[b. Functional Capabilities & Specifications of Current Gastrointestinal MPS 6](#_Toc42773046)

# Introduction

## About IQ MPS Affiliate

The IQ MPS is a collaboration of pharmaceutical and biotechnology 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).

## Request for Information

Publication of this ***Request for Information*** (**RFI**) is the first step by the IQ MPS Affiliate to solicit interest in collaborating on the testing of gastrointestinal 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 the IQ MPS Affiliate members to aid in selection of respondent(s) to move forward to the ***Request for Proposal*** (**RFP**) stage. The IQ MPS Affiliate 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 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.

## 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. 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 become property of the IQ Consortium.
* Any questions received and response thereto will be anonymized and made available to all respondents on our 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 is not obligated to contract for any of the products or services described in this RFI.
* The IQ MPS Affiliate reserves 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

## 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

202-230-5661

info@iqmps.org

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

## Timelines for RFI

Issue RFI……………………………………………………………………. June 12, 2020

Responses to RFI due……………………………………………………….. September 14, 2020

# Project Information

## Potential Project Sponsors

One or more members of the IQ MPS Affiliate may elect to serve as project sponsors, to be determined  the RFP stage. Eligible members of the IQ MPS Affiliate 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, Eisai, Inc., Eli Lilly and Company, Genentech, Inc., GlaxoSmithKline, Janssen Pharmaceuticals, Inc., Merck & Co., Inc., Merck Healthcare KGaA, Novartis Pharmaceuticals Corporation, Pfizer, Sanofi, Seattle Genetics, Inc., Takeda, Theravance Biopharma, Vertex Pharmaceuticals Incorporated.

## Project Description

Oral delivery is a conventional route for many drugs. Understanding intestinal absorption and metabolism plays a significant role in assessing the potential for success of an orally administered candidate drug. As an initial site for potential adverse effects, determining the risk for gastrointestinal toxicity is critical. Drug-induced gastrointestinal toxicities encompass a category of common adverse events encountered in clinical trials. They include events such as diarrhea, constipation, vomiting, nausea, and abdominal pain. These events limit both the quality of life of patients and the ability to achieve efficacious drug exposures. Identification of such potential liabilities early in preclinical drug discovery remains a challenge across the industry primarily due to a paucity of adequate human *in* *vitro* models and predictive endpoints.

The IQ MPS Affiliate seeks novel gastrointestinal MPS technology platforms with clear, mechanistically based rationale that not only recapitulate the human intestinal environment in terms of functional capabilities, but also demonstrate improved clinical predictivity for key ADME endpoints and toxicological responses. A single model that addresses all responses, while desirable, is not the sole objective. Emphasis on endpoint-specific predictivity of clinical responses and proven utility will be the most critical for potential future adoption of these systems in drug discovery and development.

## Gastrointestinal MPS Technical Requirements

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

The gastrointestinal MPS would ideally be viable and amenable to multi-day, repeated apical dosing and exhibit segment (i.e. gastric, duodenum, colon, etc.) appropriate barrier function and key ADME-related gene expression, localization, and activity (e.g. P-gp, BCRP, CYP3A4).

For specific technical and functional details of interest to the IQ MPS Affiliate including and beyond minimal requirements, please refer to [Section 5.b](#_Functional_Capabilities_&) of this RFI. Respondents are also encouraged to review recent manuscripts published by the IQ MPS Affiliate on gastrointestinal models ([Peters et al.,](https://pubs.rsc.org/en/content/articlehtml/2020/lc/c9lc01107b) *[Lab on a Chip](https://pubs.rsc.org/en/content/articlehtml/2020/lc/c9lc01107b)*[, 2020,](https://pubs.rsc.org/en/content/articlehtml/2020/lc/c9lc01107b) **[20](https://pubs.rsc.org/en/content/articlehtml/2020/lc/c9lc01107b)**, 1177-1190), and ADME recommendations for MPS ([Fowler et al., *Lab on a Chip*, 2020, **20**, 446](https://pubs.rsc.org/en/content/articlelanding/2020/lc/c9lc00857h/unauth#!divAbstract)-467).

## Availability Requirements

One outcome of this RFI is to prioritize respondent for competition in a subsequent RFP. The ideal candidate model(s) would be readily available (now or within the next 6 months) and exhibit robust reproducibility.

# 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](#_Functional_Capabilities_&) of this RFI.
* Demonstrate expertise in the field of MPS model development and an ability to work collaboratively with the IQ MPS Affiliate to achieve project goals.
* Provide any additional capabilities and/or information that may differentiate them from other potential collaborators.

# Respondent Profile (to be completed by Respondent)

Please provide the following information:

## Organization Information

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

## Primary Contact Information

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

## 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.

|  |
| --- |
|  |

## 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.

|  |
| --- |
|  |

## Miscellaneous

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

|  |
| --- |
|  |

# Organization Response to RFI

## Overview of Current Gastrointestinal MPS

Provide a brief overview/abstract of your gastrointestinal MPS pertaining to the requirements outlined in [Section 2.c](#_Gastrointestinal_MPS_Technical). Include figures/graphs as an addendum if applicable. Please indicate which GI segment(s) your model represents. For developers with multiple models, each representing a unique GI segment, please submit separate documents for each.

|  |
| --- |
|  |

## Functional Capabilities & Specifications of Current Gastrointestinal MPS

The information provided in this section should pertain solely 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 gastrointestinal MPS. It is not required that proposed models demonstrate all listed characteristics and features.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Model Characteristics** | | | | | |
| **Type of Model** | **3D Multi-layered Static** | **Organoid** | **GI-on-a-Chip** | **Organoid-on-a-Chip** | **Other\*** |
| *Response:* |  |  |  |  |  |
| *\*If other, please specify:* |  | | | | |
| **Segment of Gastrointestinal System Modeled:** |  | | | | |
| **Well Throughput**  (for well format models) | **≤6-well** | **12-well** | **24-well** | **48-well** | **≥96-well\*** |
| *Response:* |  |  |  |  |  |
| *\*If ≥96-well, please specify:* |  | | | | |
| **Chip Throughput**  (for chip format models, 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** | **14 Days** | **28 Days** | **3 Months** | **>3Months** |
| *Response:* |  |  |  |  |  |
| **Additional model characteristics not described above:** |  | | | | |

For **Technical Requirements, Features, and/or Capabilities**: Indicate with an “X” whether your gastrointestinal 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****s, Feature****s, and/or Capabilit****ies** | **Yes** | **No** | **Planned** | **Addendum Provided (Y/N)** |
| **Demonstrated Enterocyte Barrier Function (e.g., TEER or other) with ≤5 Test Compounds** |  |  |  |  |
| **Demonstrated Enterocyte Barrier Function (e.g., TEER or other) with 5–20 Test Compounds** |  |  |  |  |
| *If TEER used to assess barrier function,* *please indicate baseline TEER values (Ω cm2)* *and specify intestinal segment evaluated:* |  | | | |
| *If barrier function test other than TEER used**, please specify:* |  | | | |
| *Please list timepoints of barrier function that were assessed:* |  | | | |
| **Demonstrated Ability for Repeat Dosing of Apical (Intestinal Lumen) Surface** |  |  |  |  |
| **Ability to Modulate/Model pH Fluctuations in the System** |  |  |  |  |
| **Stem Cell Renewal Capacity** |  |  |  |  |
| **Demonstrated Epithelial Cell Removal** |  |  |  |  |
| *If yes, please list data demonstrating function, including timepoints assessed:* |  |  |  |  |
| **Goblet Cell Secretions/Mucus Layer Formation** |  |  |  |  |
| *If yes, please list secretions measured and timepoints assessed:* |  | | | |
| **Paneth Cell Secretions** |  |  |  |  |
| *If yes, please list secretions measured and timepoints assessed:* |  | | | |
| **Enteroendocrine Cells Included** |  |  |  |  |
| *If yes, please list data demonstrating function, including timepoints assessed:* |  | | | |
| **Immune Cell Component Included** |  |  |  |  |
| *If yes, please list data demonstrating function, including timepoints assessed:* |  | | | |
| **Demonstrated Inclusion of Microbiome** |  |  |  |  |
| **Enterochromaffin Cells Included** |  |  |  |  |
| *If yes, please list data demonstrating function, including timepoints assessed:* |  | | | |
| **Live Imaging Capable** |  |  |  |  |
|  |  |  |  |  |

For assessment of **Genotypic and/or Biochemical Biomarkers**: Indicate with an “X” whether your gastrointestinal MPS currently include 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 technical characteristics and features.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Genotypic and/or Biochemical Biomarkers Assessed** | **mRNA** | **Protein** | **Secreted Protein (where appropriate)** | **Activity** | **IHC** | **Addendum Provided (Y/N)** |
| **L-citrulline** |  |  |  |  |  |  |
| **Calprotectin** |  |  |  |  |  |  |
| **miR-194** |  |  |  |  |  |  |
| **Pepsinogen** |  |  |  |  |  |  |
| **Diamine Oxidase** |  |  |  |  |  |  |
| **I-FABP** |  |  |  |  |  |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **ADME related (CYP3A, UGTs, P-gp, BCRP, OATP2B1)** |  | |  |  |  |  |  |
| **Other Biomarkers Assessed:**  *Please write-in specific biomarkers for each endpoint* |  | |  |  |  |  |  |
| **Planned Assessments:** |  |  | | | | | |
| *Please indicate if preliminary data addendum* *is provided for planned assessments:* |  |  | | | | | |