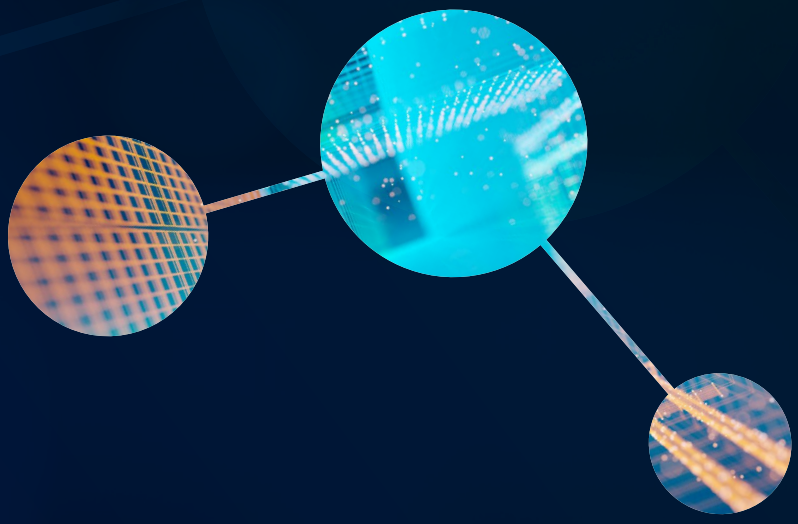


2021 IQ MPS AFFILIATE YEAR-END REPORT

IQ MPS
IQ Microphysiological Systems Affiliate

INTERNATIONAL CONSORTIUM for INNOVATION & QUALITY in PHARMACEUTICAL DEVELOPMENT

Past Chair (2022-2023)

Jason Ekert PhD, MBA

Senior Director

GlaxoSmithKline Pharmaceutical R&D

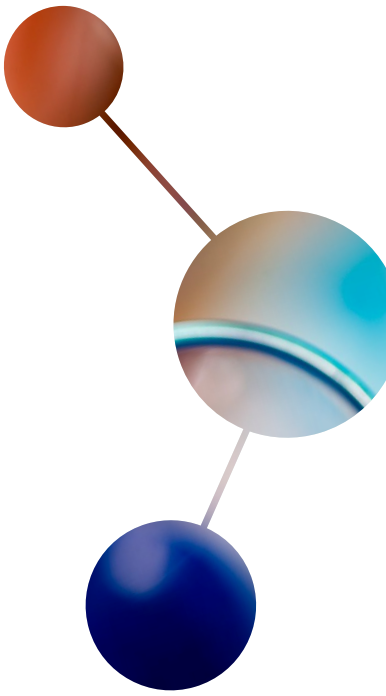
Chair (2022-2023)

Rhiannon Hardwick PhD, DABT

Scientific Associate Director

Bristol Myers Squibb

LETTER FROM THE CHAIRS



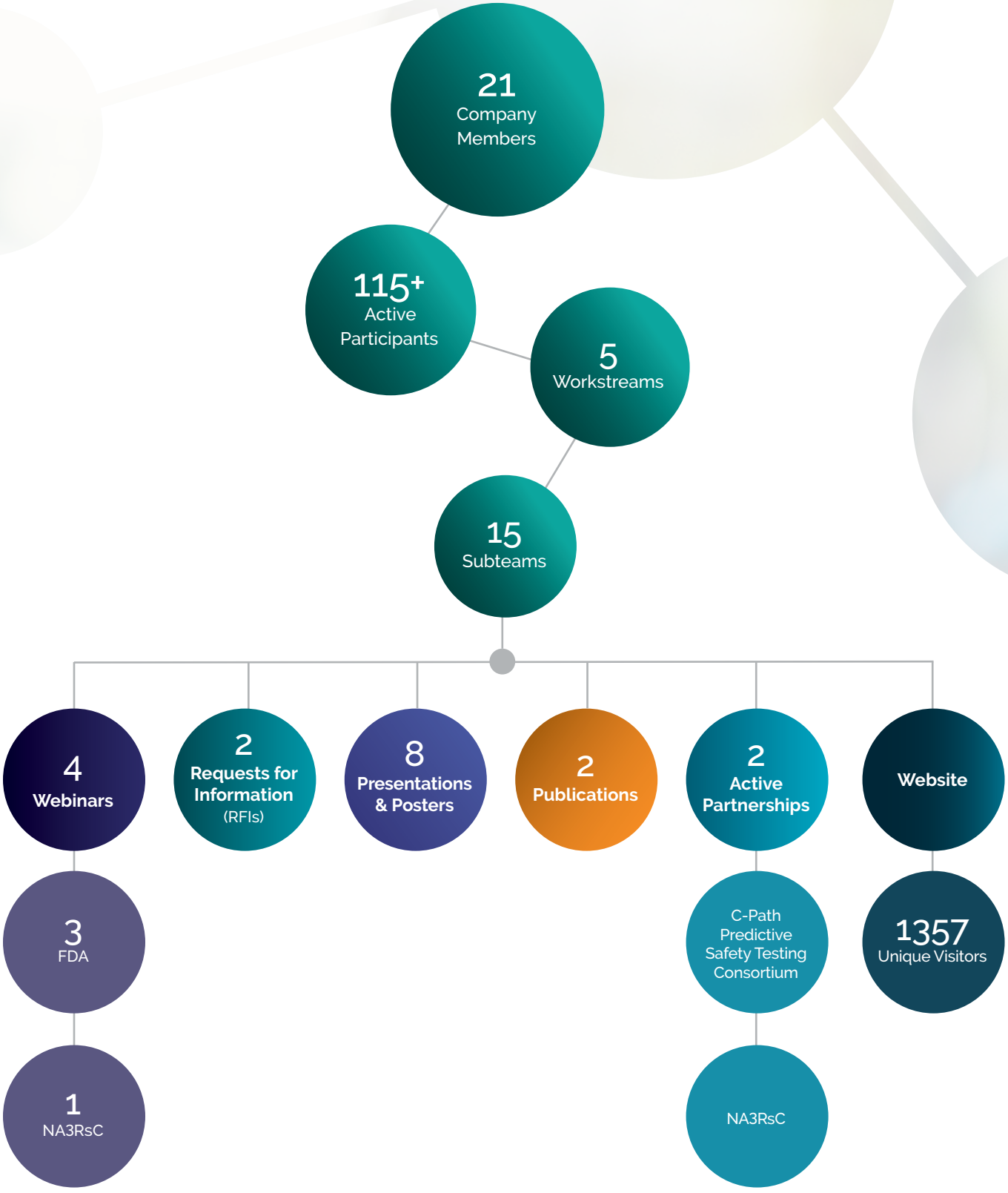
As we recognize and celebrate the accomplishments of the IQ MPS Affiliate in 2021, we also want to acknowledge how much the past two years have tested everyone's resolve and resiliency. The pandemic distanced us from colleagues at a time when our companies needed innovation and collaboration the most. In spite of these challenges, our IQ MPS Affiliate community expanded its collaborations, developed manuscripts, prepared to conduct exciting research, and continued to establish itself as a thought leader in MPS model qualification. Our goals are more ambitious than ever, and we are energized by the rapid adoption of new technologies during the last two years.

Despite being unable to meet in person last year, the IQ MPS Affiliate forged new partnerships and strengthened existing ones by pivoting to virtual meetings and events. We co-organized three webinars with the FDA and laid the foundation for a second joint workshop with FDA in 2022. With the North American 3Rs Collaborative (NA3RsC), we brought together end-users and technology developers to inaugurate an informational webinar series. In addition, the IQ MPS Affiliate presented in eight public and private forums, establishing our organization as a thought leader in MPS model qualification.

We also continued to pursue opportunities for collaborative research. Our teams developed a framework that will allow for new research projects to commence in 2022 and issued a call for developers to submit information to aid in the preparation of proposals. Work on manuscripts also continued and in the coming year we anticipate publishing an additional seven manuscripts capturing industry best practices for building confidence in these novel *in vitro* technologies for evaluating preclinical drug safety and disposition and investigating human relevant toxicities.

With our members' support, we look forward to continuing to grow the IQ MPS network and mission. We wish everyone good health and safety in the coming year and hope for more productivity in 2022!

2021 YEAR IN REVIEW



ORGANOTYPIC MANUSCRIPT TEAM

Over the past three years, the Organotypic Manuscript Team has collectively published 11 manuscripts outlining organ- and context-specific recommendations for developing, evaluating, and characterizing MPS models for use in drug discovery and development. These manuscripts have been cited over 150 times and referenced by regulatory and government agencies in efforts to forge a path to industry adoption, helping to establish the IQ MPS Affiliate as a thought leader for MPS model qualification. In 2021, the Organotypic Manuscript Team made great strides to initiate the second collection of manuscripts and successfully published recommendations for applying MPS in oligonucleotide therapy development and a report of the inaugural IQ/FDA workshop. In the coming year, the team anticipates publishing another seven manuscripts focused on *in vitro* models of the immune, central nervous, ocular, and reproductive systems as well as MPS applications in disease modeling, gene editing, and cell therapies.

Key Accomplishments

- Published two manuscripts in ALTEX
- Presented summaries of prior manuscripts at five conferences

Next Steps

- Complete the 2.0 Organotypic Manuscript Series by publishing remaining seven manuscripts in ALTEX

LANDSCAPE ASSESSMENT SURVEY TEAM

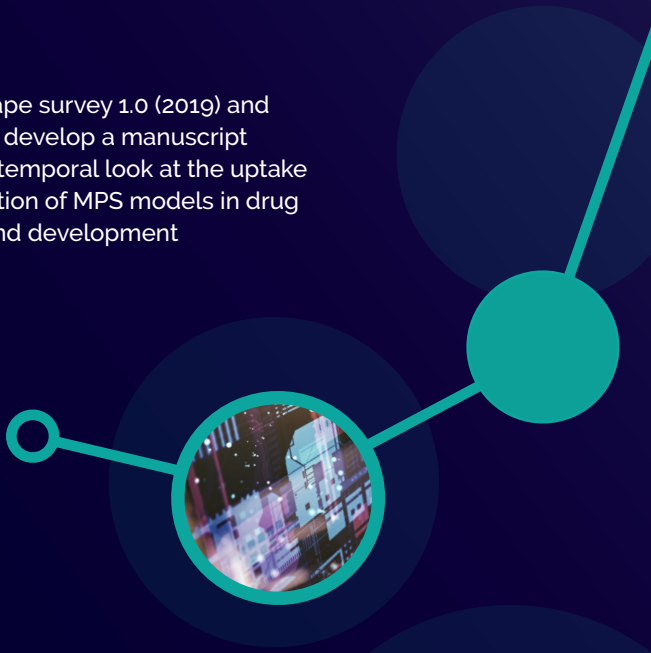
In 2021, the Survey Team focused on analyzing and disseminating the results of their second Landscape Assessment Survey, which evaluates trends in MPS model applications across the pharmaceutical industry. In this recent iteration, 25 companies participated, answering over 100 questions on company resourcing, organs of interest, compound modalities tested, and organ-specific questions, including preclinical species needs and cell types. A comparison of the 2019 and 2021 results also provided a glimpse into the evolution and future direction of the field. The Survey Team presented a summary of these findings in three public conferences (11th World Congress on Alternatives and Animal Use in the Life Sciences, Predict: 8th Annual 3D Tissue Models Summit, and MPS World Summit) as well as in two webinars, one with the C-Path Predictive Safety Consortium (PSTC) and another with FDA. The webinar with FDA featured the results of questions on MPS data use in regulatory filings and was attended by over 100 representatives from across the agency.

Key Accomplishments

- Performed in-depth analysis of the 2021 Survey 2.0 results and longitudinal changes by comparison with 2019 Survey 1.0 results
- Provided a rich data set for Affiliate members to share within their organizations and a summary slide deck to present externally
- Presented survey results at three conferences, one FDA webinar, and one PSTC webinar

Next Steps

- Use landscape survey 1.0 (2019) and 2.0 (2021) to develop a manuscript providing a temporal look at the uptake and application of MPS models in drug discovery and development



MPS CHARACTERIZATION (RFI/RFP) TEAM

The MPS Characterization (RFI/RFP) Team experienced tremendous growth this year, expanding to 34+ active members and splitting into two subteams, one focusing on gastrointestinal models and the other on kidney models. After successfully releasing a Request for Information (RFI) for gastrointestinal models last year, this year the team identified two Contexts of Use (COUs) - Toxicology Biomarkers and Stem Cell Toxicology - and developed the study design for their first Request for Proposal (RFP). In parallel, the team also prepared an RFI for kidney models, received responses from seven MPS developers, and collaborated with the C-Path Predictive Safety Testing Consortium (PSTC) Kidney Biomarker team to prepare an RFP to characterize MPS for proximal tubule damage evaluations. In the coming year, the team will use the responses from these two RFPs to initiate its first two MPS characterization studies.

Key Accomplishments

Gastrointestinal MPS Characterization Projects

- Released RFI and received eleven responses
- Interviewed MPS developers and selected five to advance to RFP phase
- Conducted rank order context of use (COU) poll with Steering Committee & identified top two COUs for initial RFP phase
- Prepared draft Toxicology Biomarkers RFP

Kidney MPS Characterization Projects

- Released RFI and received seven responses
- Established regular meetings with PSTC and prepared working draft of RFP

Next Steps

Gastrointestinal MPS Characterization Projects

- Invite developers to respond to Toxicology Biomarkers RFP, execute contract, and initiate study
- Draft study design for Stem Cell Toxicology RFP and invite responses

Kidney MPS Characterization Projects

- Collaborate with PSTC to complete study design for Proximal Tubule Damage Biomarkers RFP and invite responses
- Identify COU for second RFP opportunity

RFI/RFP Workstream General

- Identify organ system for new RFI/RFP
- Continue to streamline RFI/RFP workflow to enable faster identification of new projects (i.e., COUs) and nimble execution
- Develop core publication strategy, outline data management/processing, authoring roles, publication venues (e.g., conferences, manuscripts)

STRATEGIC PARTNERSHIPS & COMMUNICATIONS TEAM

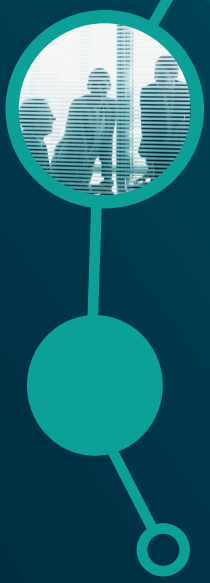
To better reflect its growing mission, in 2021, the Communications Working Group became the Strategic Partnerships and Communications (SPAC) Working Group. The team has focused on refreshing key forms of communication for the IQ MPS Affiliate such as the IQ MPS website (www.iqmps.org), and maintaining previously established connections with organizations, such as the National Center for Advancing Translational Sciences (NCATS), the European Organ-on-Chip Society (EUROoCs), and the United Kingdom-based National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs). The team also established new connections by organizing introductions with the Advanced Regenerative Manufacturing Institute (ARMI), the Health and Environmental Sciences Institute (HESI), and the National Institute of Standards and Technology (NIST). To facilitate communication between developers and end users, a partnership was forged with North American 3Rs Collaborative (NA3RsC) to develop a webinar and workshop series.

Key Accomplishments

- Refreshed IQ MPS Affiliate website and master slide deck
- Hosted presentations from NCATS, NA3RsC, ARMI, and NIST
- Established jointly sponsored webinar series with NA3RsC
- Initiated work on IQ MPS-coordinated Society of Toxicology (SOT) symposium proposal

Next Steps

- Support foundational activities by maintaining and enhancing website and ready-to-use master slide deck
- Facilitate public webinars by leveraging partnership established with NA3RsC to highlight use of MPS and/or IQ MPS Affiliate
- Continue to build networks that promote and facilitate the use of MPS by maintaining relationship with EUROoCS, HESI, NC3Rs, NA3RsC, ARMI, NCATS and reaching out to newly identified organizations
- Lead development of IQ MPS-coordinated conference symposia proposal (e.g., SOT)



REGULATORY ENGAGEMENT TEAM

Building on a successful in person workshop with FDA in 2020, this year, the Regulatory Engagement Team organized three successful webinars with FDA, each attended by over 40 subject matter experts from various FDA divisions. These events offered an opportunity for IQ MPS Affiliate members to continue dialogue initiated at the 2020 workshop on overcoming hurdles to the adoption of MPS technologies and submitting MPS data in regulatory submissions. These webinars were also used to initiate new discussions around the importance of animal cell-based MPS in building confidence in the translatability of MPS models, which has led to the initiation of efforts to publish complementary IQ MPS and FDA commentaries on the importance of bridging between animal models and MPS technologies. The team also developed a draft roadmap towards harmonization and standardization of MPS use, which has led to joint planning with the FDA of a similarly focused workshop with global regulators.

Key Accomplishments

- 2020 IQ MPS FDA Workshop proceedings accepted for publication by ALTEX and included in organotypic 2.0 manuscript series
- Held three successful webinars, each with over 100 attendees
    - **JAN 2021**
      Deeper dive of 2020 Workshop case studies
      (Attendees: 50 FDA/36 Industry)
    - **JUN 2021**
      Animal Cell-Based MPS
      (Attendees: 44 FDA/41 Industry)
    - **DEC 2021**
      Current Status and Use of MPS:
      Pharmaceutical Industry Survey
      (Attendees: 34 FDA/29 Industry)
- Initiated planning for 2022 IQ MPS FDA Workshop: Towards Development of Performance Standards and Guidelines for Microphysiological Systems in Drug Development
- Established team with FDA to draft commentaries on the value of animal cell-based MPS
- Developed draft roadmap towards establishing recommendations for harmonizing and standardizing MPS applications
- Expanded outreach to global regulatory agencies

Next Steps

- Execute a successful workshop with FDA and global regulatory agencies
- With FDA, co-author a manuscript on performance criteria and standards for MPS
- Publish commentaries on the value of animal cell-based MPS
- Continue IQ MPS FDA Joint Webinar Series

WHAT OUR MEMBERS ARE SAYING...

"Participation in the IQ MPS Affiliate has enabled broad learning about complex *in vitro* models – information that can be shared internally. Not only has it helped us benchmark our internal efforts, but it has also permitted us to tap into the knowledge and experience of other experts in the field. The consortium acts as a unified voice to interface with regulatory agencies and other organizations. Finally, it has been particularly exciting to see some of the specific aims and objectives in various workstreams come to fruition this year. The hard work and engagement of the consortium members have been truly outstanding."

David Stresser, PhD
Senior Principal
Research Scientist
AbbVie

"It has been an eye-opening experience coming from the MPS developer community to now joining pharma and this IQ MPS Affiliate group. The community is very welcoming, and I felt equally able to add a developer perspective while learning about the translational challenges from multiple pharma partners and regulators. I am excited that the upcoming RFPs on GI and Kidney MPS will provide much needed cross-model and cross-species comparisons to push the field forward and help realize our collective potential to reduce animal use and be more predictive by employing MPS."

Kimberly Homan, PhD
Director of the Complex
in Vitro Systems Group
Genentech

EXECUTIVE COMMITTEE

The Executive Committee provides leadership and guidance in the management of the business and affairs of the consortium, implements strategic plans recommended by the Steering Committee, and provides general counsel and tactical advice in support of IQ MPS's Working Groups.

Past Chair 2020-2021
Terry Van Vleet
AbbVie, Inc.

Chair 2020-2021
Jason Ekert
GlaxoSmithKline

Vice Chair 2020-2021
Szczepan Baran
Novartis

Vice Chair Elect 2020-2021
Rhiannon Hardwick
Theravance Biopharma[‡]

Congratulations to our incoming 2022 leaders:

Chair
Rhiannon Hardwick
Bristol Myers Squibb

Vice Chair
Anna Kopec
Pfizer

STEERING COMMITTEE

The Steering Committee provides strategic oversight of the initiative's portfolio and is the primary decision-making body for the IQ MPS Affiliate. The Steering Committee has representation from all member companies and acts on the recommendations of working groups and member companies to establish objectives, policies, and plans of action on a consensus basis.

AbbVie, Inc.
David Stresser
Terry Van Vleet

Alnylam Pharmaceuticals, Inc.
Saket Agarwal
Sarah Hyde

Amgen
Xiaoting Wang

Astellas
Qun Li

AstraZeneca
Kainat Khan
Rhiannon David

Biogen
Chris Hinckley
Sandra Engle

Boehringer Ingelheim
Gaurav Kaushik
Thomas Chan

Bristol Myers Squibb
Myrtle Davis
Silvi Chacko

Eisai, Inc.
Rongrong Jiang
Tushar Kokate

Eli Lilly and Company
Mike Mohutsky
Thomas Baker

Genentech, Inc.
Kimberly Homan
Aaron Fullerton

GlaxoSmithKline
Jason Ekert
Josie McAuliffe

Janssen Research & Development, LLC
Onyi Irrechukwu
Raymond Evers

Merck & Co., Inc.
Jocelyn Yabut
Wen Kang

Merck Healthcare KGaA
Philip Hewitt
Sakshi Garg

Novartis
Patrick Devine
Szczepan Baran

Pfizer Inc.
Anna Kopec
Jennifer Liras

Sanofi
Karissa Adkins
Piyush Bajaj

Takeda
Matthew Wagoner

Theravance Biopharma
Rhiannon Hardwick[‡]
Aaron Navratil

Vertex Inc.
Arek Raczynski
Sanjeev Kumar

[‡] Currently Bristol Myers Squibb

MEMBER BENEFITS AND SECRETARIAT SUPPORT

IQ MPS is an Affiliate of the International Consortium for Innovation and Quality in Pharmaceutical Development (IQ). The law firm of Faegre Drinker Biddle & Reath LLP serves as Legal Counsel and Secretariat to IQ and its Affiliates.

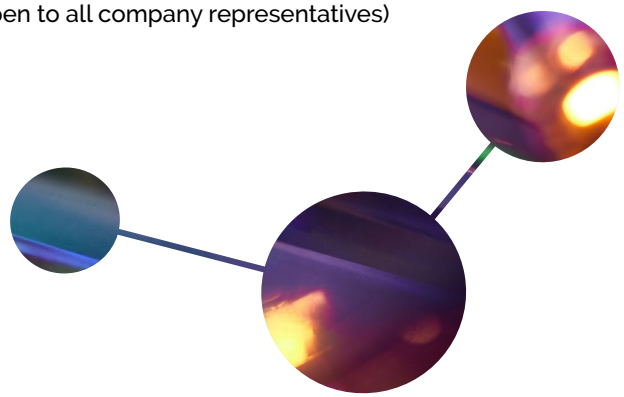
Composed of attorneys, scientists, and project managers, Faegre Drinker Biddle & Reath's Consortium Management Team forms and supports life sciences industry collaborations that help companies throughout the world to address topics of mutual interest. For the past 25 years, the team's work with these collaborations has yielded new scientific knowledge; sound, data-driven policies; and technological advances that improve the drug-development process.

The Secretariat Supports the Affiliate By:

- Developing consensus positions on strategic initiatives and projects by facilitating member company decision-making processes within the IQ MPS
- Ensuring antitrust compliance by providing training, oversight, and ad hoc legal counsel
- Providing broad scientific, project management, legal, and administrative support
- Providing the Steering Committee with robust strategic, operational, and planning support, including agendas, minutes, and presentations for meetings and teleconferences
- Supporting the exploration and scoping of data-sharing initiatives
- Reviewing manuscripts under development to ensure antitrust compliance
- Facilitating IQ MPS's external collaborations
- Managing internal and external communications
- Managing IQ MPS's website
- Providing venue and logistical support for in-person meetings

Member Companies Are Entitled To:

- Two seats on the Steering Committee
- Participate in all in-person meetings and teleconferences of the IQ MPS Affiliate
- Shape data-sharing and prospective collaboration projects
- Access to the IQ MPS Collaboration Site
- Nominate representatives to all workstreams and project teams (open to all company representatives)
- Contribute to ongoing organotypic manuscripts and propose new topics (open to all company representatives)



For further information regarding IQ MPS and membership opportunities please contact:

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Reed Abrahamson, JD
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Secretariat
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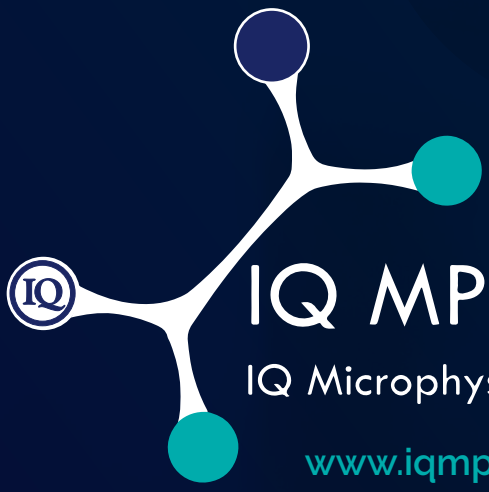
Catherine Graveline Mattia
Project Manager
Secretariat
catherine.graveline@faegredrinker.com

IQ MPS AFFILIATE MEMBERSHIP INQUIRIES

2022 Membership in the IQ MPS Affiliate is open to all members of the IQ Consortium. If you are not a member of the IQ Consortium but would like to learn more, we welcome the opportunity to provide an overview of membership options. For questions about the IQ MPS Affiliate and its priorities, progress and membership, please email **Catherine Graveline Mattia** at **catherine.graveline@faegredrinker.com**.



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