R as the Core Technology to Support Modeling and Simulation in Pharma Research, Development, and Post Approval Activities

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Who We Are

Founded in 2004, Metrum Research Group is a multidisciplinary team.
Model-Informed Drug Development

Just some of the methods and services we provide throughout development programs.

Quantitative Systems Pharmacology, Biomarker Exposure-Response
PK, PK-PD, Probability of Technical Success
Model Based POC, Population PK-PD, Trial Design, Dose Selection
Trial Simulation, Filing Pop PKPD for Safety & Efficacy
Comparative Effectiveness, Real World Evidence

Off-The-Shelf Disease Area Platform Content: Disease Progression, Quantitative Systems Pharmacology, Competitor Model-Based Meta-Analysis, Trial Simulation Tools
<table>
<thead>
<tr>
<th>Understanding Translational &amp; Systems Pharmacology</th>
<th>Probability of Technical Success</th>
<th>Quantitative Due Diligence Assessment</th>
<th>Dose Selection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial Design Evaluation &amp; Optimization</td>
<td>Comparative Effectiveness</td>
<td>Internal Decision Support</td>
<td>Preparation of Regulatory Documents</td>
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</tbody>
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**Strategic Modeling and Simulation**

General Hourly Consulting Services - Fixed Scope Contract Research Projects - Collaborative Scientific Partnership
## Therapeutic Areas and Regulatory Settings

small molecules, biologics, diagnostics, devices

<table>
<thead>
<tr>
<th>&gt;150 Sponsors</th>
<th>&gt;500 Projects</th>
<th>&gt;100 Regulatory Filings</th>
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</thead>
<tbody>
<tr>
<td>Bone Health</td>
<td>Cardiovascular</td>
<td>Neurodegeneration</td>
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<tr>
<td>Ophthalmology</td>
<td>Pediatrics</td>
<td>Pain</td>
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<tr>
<td>Infectious Disease</td>
<td>Hematology</td>
<td>Inflammation</td>
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<tr>
<td>Oncology</td>
<td>Rare &amp; Ultra Rare Disease</td>
<td>Immunology</td>
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<tr>
<td>Growth and Development</td>
<td>CNS</td>
<td>Endocrine &amp; Metabolic Disorders</td>
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Growing the science with open-source tools

At Metrum Research Group, we are strong advocates of open-source software development efforts. We make several of the useful tools we've developed (or co-developed) for our own work available as free, open-source software.

Open Source Tools

- mrgsolve
- metrumrg
- nmqual
- qapply
- fork
- review
- SASexport
- audited
- BUGSModelLibrary
- BUGSParallel
- Torsten (Stan PKPD)
We offer open, free training courses and materials as well as custom, fee-based workshops.

R Programming
Intro & Advanced Pop PKPD
Intro through Advanced Bayesian Data Analysis
Categorical, Count, Time-To-Event Models
Model-Based Meta-Analysis
Exposure-Response Models
Intro and Advanced Stan for PKPD Modeling

Simulation Concepts and Strategies
PKPD Simulation with mrgsolve
Metworx Elastic Cloud Computing
PBPK Modeling (with mrgsolve)
Systems Pharmacology (with mrgsolve)
R-Shiny Web Apps for Decision Making
Communication of M&S to Non-Technical Audiences

On site
YouTube courses
Online/Webinars
Partnerships with scientific meetings
"Using systems pharmacology model we showed that control on hypercalciuria is feasible with more frequent regimen or a slow release PTH profile at lower systemic exposure than 100 µg QD"
Computational Infrastructure and Workflow
Since its foundation in 2004, Metrum Research Group has relied on R as the core technology and central framework for all of the company’s biomedical modeling and simulation (M&S) service activities, spanning more than 475 projects with 150+ different sponsors. Projects include pharmacokinetic-pharmacodynamic modeling, quantitative systems pharmacology models, simulation-based trial design evaluations, disease progression and patient population modeling, model-based meta analysis of competitor data, model-based comparative effectiveness assessments, and data management activities, etc., all within a regulated environment. Analyses were conducted in R or via other software tools which are managed via R scripts, functions, or packages. Key deliverables of M&S projects are routinely provided as R packages or interactive simulation applications, driven by R (and R Shiny). R has also been an essential component of Metrum’s vision for Open Science in biomedical M&S, allowing for accessibility and reproducibility of platform models developed for multiple disease areas.