White Paper

Increase Efficiency and Reduce Risk with a Molecule-to-Market Action Plan

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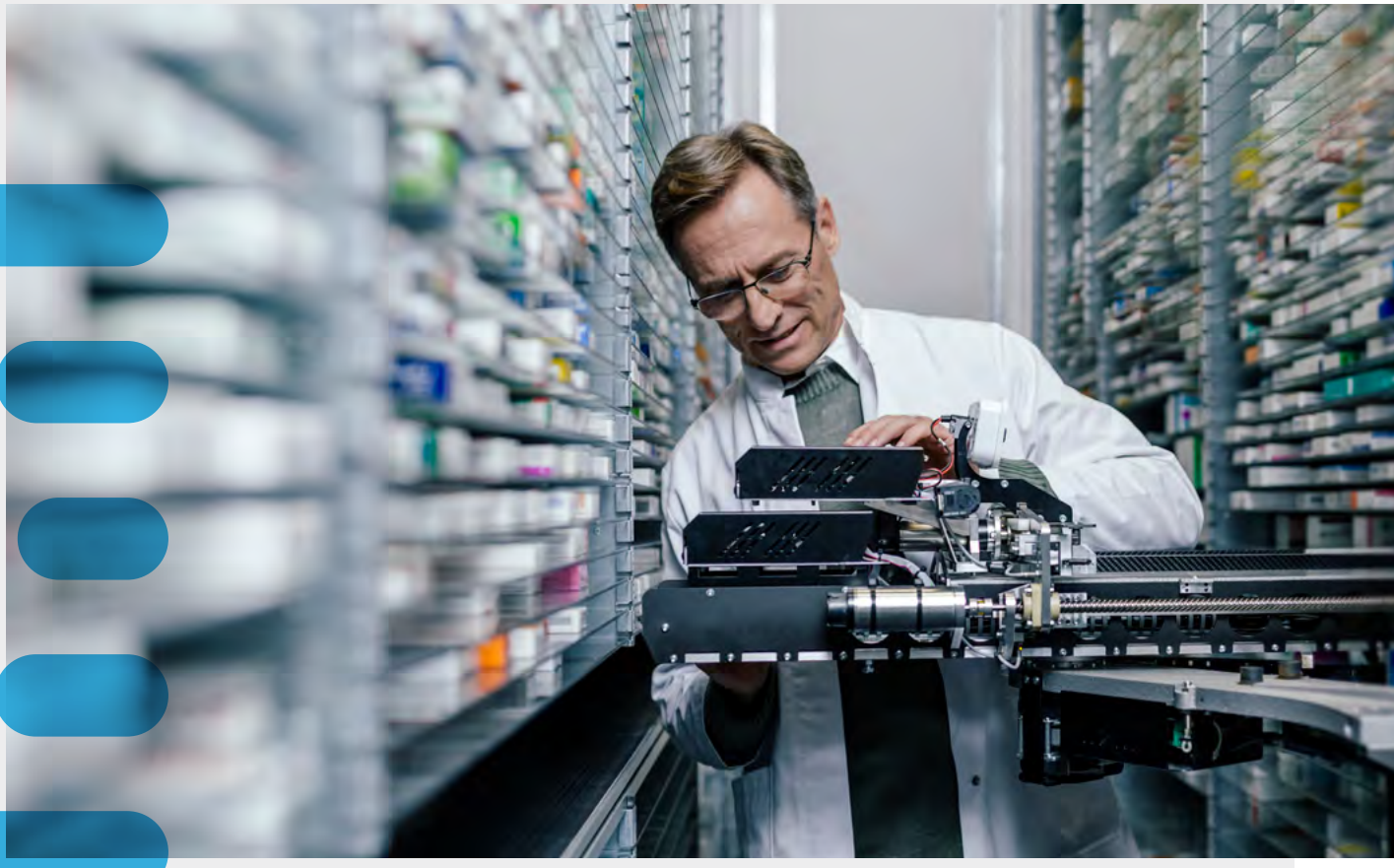

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Introduction

Bringing your drug from molecule to market necessitates expert navigation of the clinical development landscape and its accompanying regulatory systems.

Though a drug sponsor may struggle to identify their best indication for drug development or to meet copious regulatory expectations, the decision to outsource may initially appear equally daunting. However, with careful collaboration and planning, the right outsourcing partner can help you build a streamlined drug development process. Begin your search by familiarizing yourself with the moving parts required to build a scalable, effective outsourcing model.

IQVIA's Regulatory Affairs and Drug Development Solutions (RADDS) group assists companies — emerging biotechs to pharmaceutical giants — with their clinical development and regulatory processes, from the discovery phase through to commercial availability. RADDS equips your team with highly skilled resources and a bespoke outsourcing model designed to drive existing organizational efficiencies. Throughout the process, IQVIA staff provide extensive support, including regulatory intelligence, investigational new drug (IND) and marketed product (NDA/BLA/MAA) application strategies, early- and late-stage gap analyses, market expansion, lifecycle management, regulatory operations, and technology access. For a glimpse inside the mechanisms of end-to-end regulatory engagement, explore an illustrative case study of IQVIA customer, ABC Therapeutics.

Expert resources to guide the way

For each outsourcing customer, IQVIA assigns a program manager with regulatory domain expertise to provide dedicated oversight. Further support is provided by the IQVIA project team, the core team that includes workstream leads that specialize in drug development; chemistry, manufacturing, and controls (CMC); submissions; lifecycle management; and other areas of expertise depending on the customer's requirements. Having a resource pool (large groups of non-dedicated, specialized regulatory experts) as part of the project can provide extended coverage and access to a greater skillset. For the case study referenced below, the resource pool includes global regulatory strategists as well as publishing and labeling teams. Like the resource pool, IQVIA's Centers of Excellence (CoEs) provide another valuable outsourcing asset. IQVIA maintains CoEs for specific therapeutic areas as well as verticals like regulatory. All the resources depicted below in Figure 1 have access to IQVIA's CoEs, including those specific to oncology, regulatory intelligence, and regulatory information management (RIM) — areas relevant to the customer. All team member locations are selected based on regulatory requirements and customer preferences. The RADDS team provides end-to-end process support for everything from early phase to lifecycle management; see Figure 2 for a detailed breakdown of our solutions.

Figure 1: IQVIA'S RADDS outsourcing team

Dedicated oversight & point of contact for ABC

IQVIA project team (drug dev., CMC, submissions, LCM +)

Global reg strategists, publishers, labeling +

Oncology, regulatory intelligence, RIM and IDMP +

Resource locations based on Regulatory requirements and ABC's preference

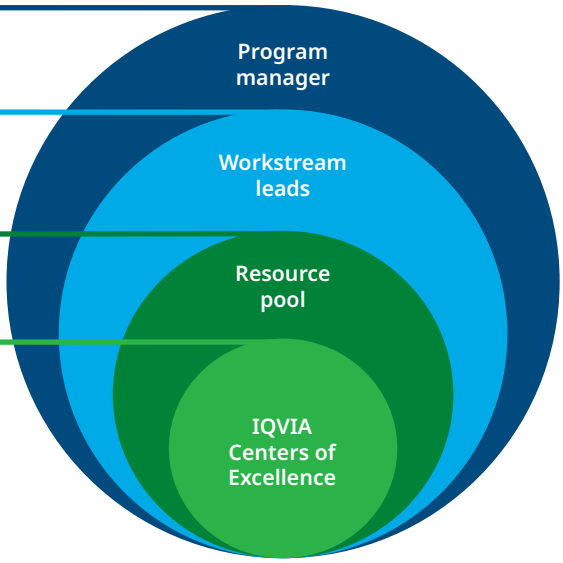


Figure 2: End-to end process support

Strategy, advice, consulting
- Indication prioritization
- Target product profiles
- Clinical development plans
- Study design and synopsis
- Due diligence (all phases)
- IND-enabling gap analyses

Pre-registration
- U.S./EU regulatory affairs services (e.g., U.S. agent, peds, orphan designation

Early phase
- Labeling and CMC
- Pre-IND and scientific advice meeting consultation and briefing packages

Ph2/3 consulting (filing package) and execution: differentiated products
- Exclusivity experts
- Orphan, QIDP, deuteration, expedited review, pediatric/PREA

Strategic submission planning
- NDA, MAA, DMF, 505b2
- Rx to OTC or NDA to OTC
- Speed-to-market expertise

Original/new market application
- Pre-submission meeting, document gathering and authoring
- HA query management and follow-up

Consulting
- Regulatory roadmap and gap analysis reports
- Regulatory intelligence

Lifecycle management
- New forms and dosages
- License renewals, withdrawals, MATs
- CMC and admin. variations
- Labeling updates
- DMF maintenance
- Tracking systems maintenance and administrative support

Post-registration PIPs market application expansion
- Pre-submission meeting, document gathering and local authoring
- HA query management and follow-up

Publishing management
- eCTD/NeeS/paper publishing
- Submission to HA via gateway
- Documents and submissions archiving

Labeling management
- SPL and SPM submission management
- Labeling artwork design

Regulatory intelligence and RIM
- Regulatory intelligence coordination and input data management
- Regulatory information management (RIM) — data maintenance

Regulatory innovation
- Automation (RPAs), system integration, process and framework

Early-stage project support

Typically, customers engage IQVIA towards the beginning of their preclinicals and often roughly 18 months before their first-in-human (FIH) trial. IQVIA helps its customers move through the early phases of product development with the following considerations top of mind:

- What assets and indications should we prioritize? How do we build our target product profile?
- What gaps exist in our nonclinical, CMC, and clinical plans that need to be addressed prior to our FIH? How do we create our clinical development plan and what will be the time, cost, and associated risk for our clinical trials to take us through registration? When should we file our IND? How do we prepare for interactions with the agency? What special accelerated approval designations might our product qualify for? What is our overarching regulatory strategy?
- What is the commercial worth of our asset? How will our asset value change at each milestone? Should we invest into a new asset we have identified? What is our probability of technical and regulatory success?
- How do we analyze the pharmacokinetic and pharmacodynamic data from our trial? How do we leverage biomarkers? Do we need a companion diagnostic?

Figure 3: Integrated asset strategy from discovery through marketing

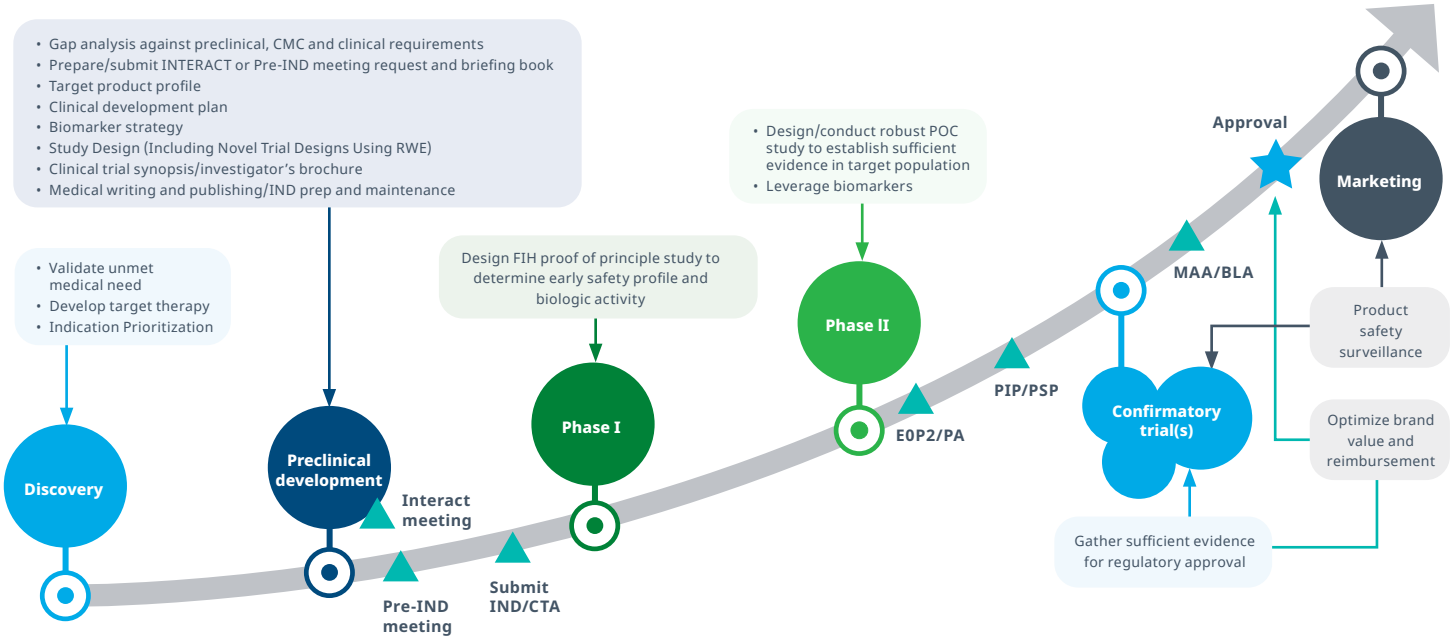


Figure 3 is an overview of what customers are looking to achieve at each milestone. In the discovery phase, IQVIA helps identify an ideal indication to prioritize based on three aspects: scientific, commercial, and operational. From a scientific perspective, we look at your candidate indications, the disease linkage based on your asset mechanism of action, preclinical evidence, and efficacy benchmarks. For each of those, we apply scores collaboratively. We also assess market attractiveness, commercial potential, and addressable patient population using global sales and longitudinal patient data, which includes electronic medical records, medical claims, hospital claims, hospital encounter data, and longitudinal prescription data. This helps determine a highly specific addressable patient population.

Next, our physicians look at the unmet medical need for each potential indication to determine if there are any sub-optimal therapeutic options or if you could be first in class. We'll also consider the market valuation and competitive landscape, including what's in line and promising in the pipeline. The last assessment is operational feasibility, which examines how expensive, time-consuming, and difficult it is to run a series of trials in one indication versus another. IQVIA will provide scores for each of these categories and determine recommended strategy. Once set, we'll populate an indication prioritization matrix and apply weights to the scores, providing a strong visual indication prioritization matrix to share with potential partners.

As you move into preclinical development, RADDS will determine a target product profile (TPP) to help set the strategy for the course of your development; the considerations for a TPP are outlined in Figure 4. We look at the attributes and build two cases: minimally acceptable (i.e., what your drug must do at a minimum to compete against the current standard of care) and the target case (i.e., what does your profile look like if you meet all of your endpoints).

Figure 4: Strategy for constructing a TPP

TPP ATTRIBUTES	ASSESSMENT APPROACH	IMPACTED DEVELOPMENT STRATEGY ATTRIBUTE
Indication	**Base case profile** **Optimal profile** **Competitor profile**	Target label indication
Patient population		Commercial value, clinical development population, regulatory acceptance
Dosage form/ regimen		Commercial value, cost of goods, clinical development, CMC planning
Clinical efficacy (approvable endpoint)		Commercial value, regulatory acceptance, pivotal study sizing. Needs to be specific: used as go/no-go criteria.
Biomarkers		
Safety		Reimbursement, regulatory acceptance
Quality of life		
Other aspects		Overall asset strategy: Out license? Partner?

Potential investors may request a TPP, which demonstrates your target goal (your future product label) and serves as a blueprint for a clinical development plan (CDP). The CDP charts time and cost of different development scenarios. Pipeline Architect, an IQVIA-designed tool, generates different clinical development scenarios with various levels of risk: aggressive, middle of the road, and conservative. For each option, we can generate an accurate estimate of time, cost, and risk, which is expressed in terms of probability of technical and regulatory success based on historical benchmarks for that therapy area and indication. As we approach agency engagement, we assemble a protocol synopsis written by a physician: 15-to-20 pages that illuminate primary/secondary objectives and endpoints, subject number, main inclusion/exclusion criteria, sequence of events, and basic statistical considerations. It is robust enough to give to a medical writer to make it into a full International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH) compliant protocol.

Next, RADDS assists sponsors as they begin to engage with the agency. With biologics, customers can try to take advantage of an Initial Targeted Engagement for Regulatory Advice on Center for Biologics Evaluation and Research (CBER) Products (INTERACT) meeting. A pre-IND meeting is another common deliverable with an IQVIA partnership, for which we put together a meeting information package with pharmacology, toxicology, CMC, and synopsis sections. For the meeting request letter, we craft thorough questions collaboratively with our sponsors to ensure maximum insight from the agency. Their answers will allow sponsors to make necessary fixes before an IND submission. Finally, the IND submission is generally over a thousand pages. It involves RADDS' publishing team, medical writers, and electronic common technical document (eCTD) leads putting everything into the eCTD format for submission.

Late-stage product support

RADDS supports our customer's strategic and operational aspects, from marketing authorization application and submission through to lifecycle management. With marketing authorizations, we leverage a five-stage approach focused on favorable consideration from health authorities. We begin with a gap analysis, data review, and assessment, including a detailed review of scientific content and documents being submitted.

Figure 5: IQVIA'S Health authority marketing authorization strategy

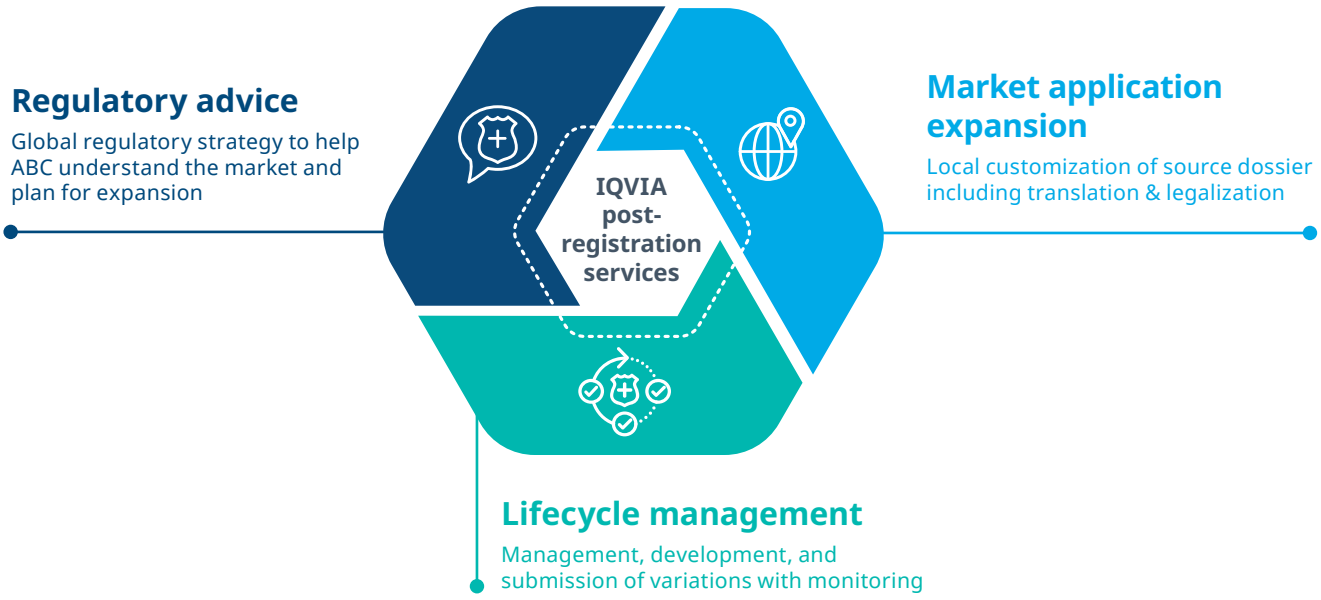
From assessment and data review, RADDS proposes strategies to present data to the health authority and prepare key questions to discuss in pre-submission meetings. The gap analysis identifies pitfalls and refines strategy. We serve as meeting concierges for our customers, liaising with the health authority, preparing meeting request letters and information packages, and attending follow-up meetings. Throughout dossier development, we prepare the submission, develop each module, draft labels, and any additional details required for assessment, i.e., the environmental impact statement (EIS). We provide full-service execution of the dossier, from putting them into submission-ready format to publishing and compiling the finalized submission packets for delivery to the health authorities. Finally, we provide support during the health authority assessment period where we respond to questions and handle any follow-up required. We follow along through the entire process to guide the new marketing authorization application to approval.

Once an authorization is on the market, it requires lifecycle management to stay on the market and safe for patient use. IQVIA provides three distinct, post-registration activities (Figure 6). First is regulatory advice and consulting, where we develop strategies and regulatory pathways for expansion to other global markets. Next, we perform the market application expansion and customize the local dossier based on local requirements, including any translations. We handle all aspects of legalization and local representation from a regulatory perspective. Finally, we track and manage the lifecycle by developing and submitting variations, including CMC and labeling changes. We also conduct a variety of other activities across lifecycle management, including license extensions for new indications, periodic reports, and market authorization transfers.

As part of application and variation submissions, publishing and regulatory operations play a critical role in efficiency gains. RADDS' goal in the publishing process is to utilize automation/robotic process automation (RPA) and innovative technology tools wherever possible to format, compile, deliver, and archive in the most streamlined manner. In terms of technology, we take different approaches depending on customer needs. We have the option of providing services on our customers' systems or using our own proprietary, validated RIM Smart system, which has integrated regulatory intelligence tools and automations. We can also utilize a hybrid solution that combines our customer's technology with our own. We co-develop process documentation and service-level agreements (SLAs) to work seamlessly in a cohesive environment.

RIM data maintenance and system support is a component of Regulatory Operations focused on keeping product registrations and key data up to date and accurate. We manage these systems as an extension of our customers, ensuring compliance and a single source of regulatory truth for all stakeholders.

Figure 6: IQVIA'S post-registration services



Case study: ABC Therapeutics' RADDS journey

ABC Therapeutics is a mid-size biopharma organization with specialties in oncology and immunology, assets in various phases, and several promising indications. Currently, they are primarily focused on the United States but are keen to expand to other global regions. They are facing subject matter expertise resource constraints in various therapeutic areas. Utilizing IQVIA's highly skilled resources, tailor-made outsourcing model, and collaborative technology, ABC Therapeutics was able to expedite their project.

ABC Therapeutics elected to use IQVIA RIM Smart as their primary system since they did not have a current system in place. IQVIA was able to provide the environment as part of regulatory services and gave them collaborative access. RADDS staff worked within the system to track product information, correspondence, and commitments to health authorities and publish submissions. ABC Therapeutics could access the system to track activity and pull their own reports. We connected seamlessly to their electronic document management system (EDMS), which meant there was no need for document and data migration. Since we own the system, we are able to build customized automation through RPA and no additional license costs were required from ABC Therapeutics. Once they are ready, they can assume ownership of the system and still utilize IQVIA services for zero interruptions.

ABC Therapeutics was initially hesitant about offshore to low-cost centers, so we designed the operating model with a mix of 60 percent offshore and 40 percent onshore. Once we ensured that

quality levels were maintained, based on SLAs and KPIs, and ABC Therapeutics gained confidence in our delivery, we recommended further offshoring in a phased approach. We moved to a 70/30 model at the end of year one and, eventually, a 90/10 model at the start of year three. Currently, 90 percent of the work is offshore and 10 percent of the work is managed in nearshore or onshore centers. The goal was ensuring maximum value in a comfortable, phased approach. RADDS utilized multiple offshore and low-cost centers to add additional layers of business continuity. Low-cost centers in Latin America (LATAM) and the Asia Pacific (APAC) region provided global coverage where ABC Therapeutics needed it most. Plus, dividing resource needs across multiple time zones provides better work-life balance for the project team. Often, when consolidating to a single offshore, staff must work night shifts to provide follow-the-sun coverage, resulting in attrition and turnover. It is not only bad for the staff; it poses a risk for the quality of project deliverables.

IQVIA calculated a 38 percent reduction in resource spend, a significant discount in the cost of what ABC Therapeutics would have spent on hiring and sub-contracting resources in global locations. By leveraging RADDS' subject matter expert pool and highly skilled resources, we were able to provide the exact amount they needed. Throughout the gap analysis, we defined clear program development pathways and created a foundation to develop new programs, particularly for global expansion. We were able to submit the application three months faster than ABC Therapeutics had anticipated and drive further efficiencies via strategic submission planning.

By partnering with IQVIA, ABC Therapeutics saw a 38% reduction in spending and an efficiency gain of 52%

RADDS collaboration on technology and infrastructure led to a 52 percent gain in time and efficiency utilizing automation and a shared system. We eliminated the need to migrate data and documents across two disparate systems. Ultimately, it resulted in a company-wide culture shift — the idea of working smarter gained traction and inspired innovation across ABC Therapeutics.

Conclusion

No two outsourcing models look the same but, with an experienced partner, your outsourcing strategy will incorporate techniques with proven track records to extract the most value from your program. IQVIA's RADDS group works with a customer to design a strategy that will bolster their existing organizational strengths and strive to ensure more efficient timelines from molecule to market. By partnering with IQVIA, ABC Therapeutics saw a 38 percent reduction in spending, an efficiency gain of 52 percent through automation and process improvements, and was able to submit their application three months faster than the initial projection.

About the authors

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Michel Denarié is a Senior Principal with IQVIA's Regulatory Affairs and Drug Development Solutions, a group that helps emerging biotech sponsors around the world with their early clinical development strategy and regulatory process. Denarié's experience in the pharmaceutical industry spans over three decades and encompasses roles in consulting, sales, marketing, market research, and offering development, both on the pharma and vendor side of the industry. He is also a member of IQVIA's Operating Committee for the Diversity & Inclusion Initiative in Clinical Trials.

A frequent author and speaker, Denarié's work has appeared in several trade publications. He has presented research findings and methodologies regarding the advanced application of real-world data at numerous industry conferences, including events sponsored by the DIA, the Pharmaceutical Management Science Association (PMSA), the Pharmaceutical Research Group (PRG), the International Society for Pharmacoeconomics and Outcomes Research (ISPOR), and the Association of Clinical Research Professionals (ACRP). Denarié earned an MBA from the Colgate Darden Graduate School of Business Administration at the University of Virginia and holds a BS in finance from the American University in Washington, DC.

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Michelle Gyzen is a Senior Director with IQVIA's Regulatory Affairs and Drug Development organization, designing strategic solutions for regulatory, focused on operational efficiency, scalability, and technology. She has over 20 years of experience in pharmaceuticals, biotech, and medical devices with particular expertise in designing large-scale regulatory outsourcing programs, offshore resource modeling, and regulatory tech integration and automation. She serves on industry panels and consortiums, providing expertise on Future-Fit Regulatory.

As part of IQVIA's Integrated Global Compliance organization, Gyzen supported cross-functional services and technology integration between Regulatory, Safety, Quality, and Commercial compliance. Prior to IQVIA, as the Global Head of Life Sciences Business Process Outsourcing (BPO) for a leading technology and services company, she led an organization providing regulatory consulting, regulatory operations, pharmacovigilance, medical writing, biostatistics, and business process transformation to many of the top 20 pharma companies.

Gyzen studied Business and Industrial Organization at both North Carolina State University and Southern New Hampshire University.

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