

# CONSULTING

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# CONSULTING: OVERVIEW

## OVERVIEW

Changing pharmaceutical development regulations represent a complex environment in which to develop new therapeutics. To assist you in addressing these requirements, PharmaNet has assembled an exceptional team of international regulatory and pharmaceutical experts, including former senior-level FDA and EMA officials, physicians, regulatory experts, and biostatisticians.

Whether you have a product in preclinical or clinical development, PharmaNet's in-house experts are proficient in the planning and execution of clinical trials and regulatory processes and submissions from pre-IND/CTA to marketing applications on five continents. We can provide detailed advice to clients on regulatory challenges and opportunities, prepare and submit regulatory dossiers, resolve issues and expedite the regulatory review process, and assist in overall clinical development planning and execution.

PharmaNet's expertise includes direct experience with regulatory agencies on five continents, covering every stage of development and type of therapeutic, including:

- Biosimilars/follow-on biologic proteins
- Cell, gene, and tissue therapies
- Combination products
- Drug delivery systems
- Small molecules
- Therapeutic proteins, including monoclonal antibodies
- Vaccines

# CONSULTING: OVERVIEW

Strategic planning during the earliest stages of development optimizes project efficiencies. PharmaNet professionals begin by understanding your objectives and goals, and then build a cohesive strategic plan to meet your specific needs. By preparing early in your development program, PharmaNet can help anticipate potential issues and regulatory risks and build contingencies into the plan. Global clinical development programs can be developed to avoid duplicative steps for new market introductions and to comply with local regulations and international standards.

PharmaNet can also help you better understand risks and formulate a proactive strategy for assessing and minimizing uncertainty associated with your program. An important aspect of risk management is gap analysis; a critical component of your regulatory submissions and marketing applications.

PharmaNet professionals can review your product development plan, evaluate your study design, identify potential regulatory risks, suggest corrective measures, and assess your chances for first-pass approval.

Expert advice backed by direct experience — it's just one more reason why PharmaNet regulatory and pharmaceutical consulting *works for you*.

Consulting Services Through All Phases of Development					
Preclinical	I	II	III	IV	Submissions
Assessment	Program Development/ Execution				NDA
	Risk Management/Safety/ Pharmacovigilance				
Strategic Planning and Study Design	Chemistry/Manufacturing/ Controls				ANDA
	Regulatory Affairs				BLA*
	FDA/EMA/International Agency Meetings				
	Comparability Exercise/ Quality Dossier				
	Bioequivalence				
Post-marketing					
<b>Global Reach:</b> North America, South America, Europe, Asia, and Australia					

*\*Biologics License Application*

# CONSULTING: SERVICES

## EARLY PRODUCT DEVELOPMENT

PharmaNet offers the integrated preclinical, regulatory, medical/scientific, and pharmaceutical expertise you need to efficiently advance a product from R&D to early-stage clinical studies. Our consultants can assist you in the top-level strategic planning and evaluations that will maximize the chances of a successful new drug/product development program.

In addition to the identification of development candidates emerging from discovery, we can assist with the review of products and portfolios to support sponsors' licensing in/out strategies. To bridge the gap from bench to the clinic, we can prepare nonclinical plans to support clinical trials. We'll help you consider options such as an exploratory IND with tailored toxicology programs, design/execute Proof of Principle/Concept studies, or evaluate the impact of adverse findings in nonclinical plans for products intended for women of childbearing potential and children.

PharmaNet also provides valuable guidance to companies with new biosimilars or generic drug products, including performing due diligence, selecting the best drug candidate, and determining the optimal formulation for the intended route of administration.



# CONSULTING: SERVICES

## PHASE II - III PRODUCT DEVELOPMENT

Backed by years of practical experience, PharmaNet will help you prepare comprehensive Phase II through Phase III clinical development plans, including designing your studies and developing your protocols.

From developing a comprehensive strategic plan to implementing a sound regulatory and clinical strategy, PharmaNet professionals can provide objective advice for clinical development. In addition to most aspects of clinical development, we can review your products and portfolios to support licensing strategies, assess regulatory issues around potential new product acquisitions, and help identify development candidates emerging from discovery.

Our worldwide regulatory resources allow us to develop local and global regulatory strategies that are tailored to your product development strategy. PharmaNet can assist you in devising a strategy to collect the data needed to support your endpoints, while enabling you to meet both your business objectives and your obligation to the safety of study participants.

## 505(B)(2)

PharmaNet provides expertise and support services to help clients navigate the challenging 505(b)(2) NDA regulatory pathway. Utilizing the 505(b)(2) pathway can help you leverage existing product assets and save you valuable time and money. Look to PharmaNet for a partner who understands the regulatory guidelines and intricacies of the regulatory process.

If you are considering brand extensions or new indications, formulations, or dosages, PharmaNet has experienced professionals that can help you develop strategies to compete with newly introduced products and reinvigorate your brands.

### Our services for 505(b)(2) applications include:

- Assist sponsors in crafting their CMC and nonclinical program
- Coordinate with regulatory agency for pre- and post-IND meeting
- Customized consulting and feasibility assessment
- IND, NDA, and 505(b)(2) NDA preparation and submission
- Interaction with regulatory agency
- Preparation and writing of pre-IND and IND package
- Provide strategic considerations and key development steps before embarking on a 505(b)(2) approval route
- Regulatory support for clinical program development (study design, biostatistics, etc.)

# CONSULTING: SERVICES

## CHEMISTRY, MANUFACTURING, AND CONTROLS (CMC)

PharmaNet regulatory and pharmaceutical experts can guide you on formulations and manufacturing controls and specifications for both new chemical entities and new formulations of approved products based on provided data.

Through experience and practical knowledge of the drug development process, PharmaNet provides strategic regulatory insights and important recommendations on selecting the optimum formulation, identifying and managing capable vendors, validating a bioanalytical assay method, and setting product shelf life and product specifications.

## PharmaNet can help you:

- Consult on GMP training and feasibility audits
- Develop stability studies and programs
- Identify qualified vendors for cGMP manufacturing
- Meet with regulatory authorities on CMC issues
- Prepare CMC summaries for regulatory submissions
- Select a formulation for the intended route of administration
- Select compatible excipients
- Select the best API candidates
- Write standard operating procedures

# CONSULTING: SERVICES

## NONCLINICAL PHARMACOLOGY AND TOXICOLOGY

With scientific and regulatory expertise in pharmacology and toxicology, PharmaNet can support the development of tailored preclinical plans. Responding directly to client needs, we offer consulting services and solutions *a la carte*, or as a part of an integrated program to:

- Support the intended dose, phase of development, and route and duration of treatment in the clinic, including nonclinical strategies for inclusion of women of childbearing potential and children, and tailored toxicology programs to support INDs
- Identify and address toxicology issues unique to the compound, indication, or patient population, and the impact of the toxicological findings in relation to planned clinical trials
- Review and prepare the preclinical pharmacology and toxicology sections of regulatory submission and meeting packages
- Provide integrated and expanded services throughout the development program by working with your clinical and regulatory functions.

## PHARMACOLOGY, TOXICOKINETICS, AND CLINICAL PHARMACODYNAMICS

PharmaNet offers expertise on designing quantitative toxicokinetic and PK/PD models and interpreting results obtained from these studies. In a nonclinical setting, allometric scaling can be used to model human exposure, adverse events, and clinical response for different doses or dosing regimens to help prepare your design of first-in-man studies.

In a clinical setting, knowledge gained from well-designed PK/PD (dose linearity, impact of demographic variables, effect of food, and drug drug interactions) and PD (adverse events profiles, biomarkers, QT prolongation, and early clinical efficacy) studies can help you optimize treatment regimens, improve the productivity and efficiency of your development program, increase confidence in strategic decisions, and maximize the commercial value of your product.

In Phase IIb and III studies, PharmaNet pharmacometrics experts can utilize more advanced techniques for population PK analysis through medical and biostatistical modeling and biomarker and clinical outcomes simulations. We can provide assistance with PK/PD models of clinical studies for both branded and generic products.

# CONSULTING: SERVICES

## BIostatISTICS

PharmaNet's world-class biostatisticians have a broad knowledge in all aspects of clinical trials, which can help facilitate smooth regulatory submissions. Our biostatistics team can work with you to plan the analyses you'll need before the study begins, then provide prompt, accurate reports, statistical summaries, and efficacy and safety analyses as the study progresses.

### Biostatistics services include:

- Clinical outcomes modeling to evaluate study designs in order to assess the impact of dosing strategies, patient selection, and clinical endpoint selection
- Database integration (ISS/ISE preparation)
- Interim analysis and DMC support
- Interpretation and reporting of data for clinical trial reports and publications
- Medical and biostatistical modeling and biomarker and clinical outcomes simulations
- Randomization schedules
- Regulatory representation
- Statistical analyses using current methodologies
- Statistical analysis plans
- Statistical programming in SAS®
- Therapeutic monitoring and population response models

# CONSULTING: SERVICES

## REGULATORY SERVICES

PharmaNet can answer your questions regarding regulatory channels to help achieve the most efficient path to market for new drugs and biological products. You can avoid frustrating and costly delays by relying on our experts for pre-submission quality reviews to ensure completeness, adequate strategic approach, scientific accuracy, and ease of agency review. With regional offices in the Asia Pacific, Canada, Europe, Latin America, and the United States, PharmaNet helps you adhere to the complex array of regulatory requirements in all the major regions of the world where clinical research is taking place. A well-designed regulatory submission meets the information needs of all relevant stakeholders.

In Europe, the Voluntary Harmonization Procedure (VHP) is the new alternative to obtain clinical trial approval. In comparison to the traditional standard national submissions, which must be completed in parallel and submitted to each of the different European agencies, the VHP consolidates these activities into a single submission. As compared to the national approval procedures, the VHP provides

clinical trial approval of all the technical documentation in every country/agency involved and can save up to two months to get a study approved.

The VHP procedure has been in place in Europe for approximately two years with more than fifty successful applications. PharmaNet has successfully experienced this new centralized approval procedure and recommends it to expedite the start of your study.



# CONSULTING: SERVICES

## REGULATORY SERVICES (cont.)

### Services include:

- Clinical trial supply management for Phase II-III
  - Facilitate delivery of investigational drug to investigative sites
  - Facilitate packaging/labeling of investigational supplies
- Electronic submission services
  - Automation of quality-control procedures
  - Documents formatted for you to make the electronic submission
  - Electronic publication of regulatory submissions with state-of-the-art software tools (e.g., Documentum®, Lipient Insight Publisher®)
  - Facilitation of review process
  - IND/CTA in eCTD format
  - Marketing applications produced in eCTD format
- Global safety and pharmacovigilance
  - Post-marketing pharmacovigilance
  - Risk minimization plans
  - Safety reporting for clinical trials
- Medical writing
  - Clinical study reports
  - Investigator brochures
  - Protocols
  - Summary documents for CTDs/MAAs/NDAs
- Preparation and submission of regulatory documents and marketing applications
  - Clinical Trial Applications (CTAs)
  - Investigational New Drug (IND) applications
  - Investigational Medicinal Product Dossier (IMPD)
  - Marketing Authorization Applications (MAA), New Drug Applications (NDA), Common Technical Document (CTD)
  - Observational studies
  - Orphan Drug Application (ODA)
  - Paediatric Investigational Plan (PIP)
  - Reformatting of dossiers
  - Supplements/variations and renewals
- Regulatory strategy and drug development planning

# CONSULTING: SERVICES

## REGULATORY LIAISON

The ideal person to serve as liaison between your internal regulatory affairs department and a regulatory agency is someone who has experience on both sides of the table. PharmaNet offers the services of former senior-level FDA officials from these FDA human therapeutic centers: Center for Drug Evaluation and Research (CDER) and Center for Biologics Evaluation and Research (CBER). In addition, PharmaNet professionals also offer experience with the Canadian HPFB, European MHRA, as well as other international agencies, and can assist you with meetings, briefing documents, warning letters, and hearings.

We can liaise with regulatory authorities worldwide for:

- End of Phase II/pre-NDA meetings
- Pre-IND and EMA pre-submission meetings
- Protocol assistance meetings
- Scientific advice meetings

## SAFETY AND PHARMACOVIGILANCE

In today's environment, more and more drug development teams are adding post-approval activities as part of their risk management planning. PharmaNet professionals can help you develop a program to monitor and manage product utilization and safety, mitigate risk, establish your product's risk-benefit profile, and ensure understanding of its market value.

Services include:

- Clinical endpoint studies
- Epidemiological assessments
- Post-approval safety studies
- Risk Evaluation & Mitigation Strategy (REMS)
- Risk management programs
- Signal detection/database analyses

## LIFE SCIENCES INVESTMENTS

If you are considering an investment in a company with an exciting new therapeutic in development, PharmaNet can assist you with assessing the medical, regulatory, and technical risks and issues associated with their product or products.

Once you have made your investment decision, we can help define strategies for benchmarks, compliance, and regulatory submission. PharmaNet professionals offer proven expertise in medicine, science, and international pharmaceutical regulations to life science investors.





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