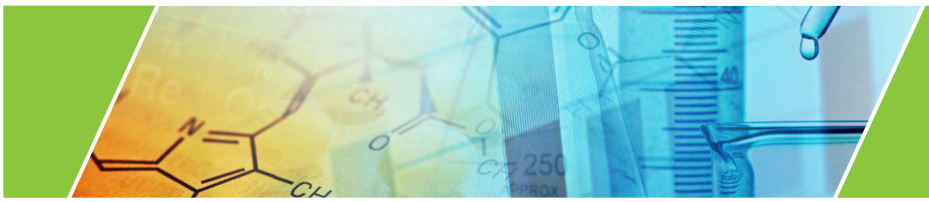
Biopharmaceutical/Pharmaceutical Safety Qualifications

ToxStrategies



ToxStrategies is a multidisciplinary scientific consulting firm that strives to develop innovative solutions to address the scientific, technical, and regulatory challenges confronting our clients. We are recognized for applying sound science and novel approaches tailored to meet the specific needs of our clients, whether a rapid response or a comprehensive analysis is required.

ToxStrategies scientists provide a comprehensive range of consulting services in nonclinical toxicology for the clinical development of biopharmaceutical (innovator and biosimilars) and pharmaceutical drug candidates. Our extensive experience with regulatory authorities, such as FDA, EMA, and Health Canada, enables us to successfully address scientific and regulatory hurdles throughout the drug approval process. We employ a product-specific approach to design nonclinical safety programs that are aligned with current regulatory expectations. Our overall strategy is to efficiently execute nonclinical studies that minimize costs and accelerate timelines for optimal success in clinical trials.

Selected examples of our experience include:

Clinical Development Support
- Early discovery phase
- First-in-human Phase 1 clinical trials
- Phase 2/3
- Biologics Licensing Application (BLA), New Drug Application (NDA), Marketing Authorization Application (MAA)
- Registration and Post-marketing

Biological Products
- Monoclonal antibodies
- Recombinant and fusion proteins
- Antibody/protein drug conjugates
- Bi-specific antibodies
- Biosimilars
- Enzyme replacement therapies
- Vaccines

Pharmaceutical Products
- Small molecules
- Botanicals
- Peptides
- Oligonucleotides

Disease Areas/Indications
- Oncology
- Pulmonary/allergy
- Metabolic
- Immunology
- Rheumatology
- Neurology
- Ophthalmology
- Anti-infectives
- Pediatric diseases
- Animal rule indications
- Orphan and rare diseases

Biopharmaceutical Expertise
- Selection of relevant animal species
- Immunogenicity or anti-drug antibodies
- Immunogenicity-mediated toxicity
- Cytokine-mediated toxicity
- Infusion reactions

Pharmacology/Toxicology Study Design and Protocol Development
- Species: mouse, rat, rabbit, dog, minipig, and non-human primate
- Optimal study design for best science while minimizing cost
- General and mechanistic toxicology (*in vitro* and *in vivo*)
- Safety pharmacology
- Reproductive and developmental toxicology
- Carcinogenicity studies
- Tissue cross-reactivity

Management of GLP and Non-GLP Toxicology Studies
- Identify CROs and evaluate price bids
- Protocol development
- Monitor study
- Manage day-to-day activities and issues
- Review/write study reports
- Address protocol deviations and study management issues

Comparability Studies
- Nonclinical studies to support manufacturing changes
- Risk-based strategy to support use of new material in clinical trials
- Biosimilars
- Changes in formulation or route of administration

Target Liability and Risk Assessment
- Evaluation of off-target or unexpected toxicity
- Metabolite safety qualification and assessment
- Generation of expert reports/white papers and toxicology monographs
- Risk mitigation/management of toxicity

Regulatory Document Writing/ Preparation and Review
- PreIND
- IND, IMPD, and CTA
- EMA scientific advisory packages
- BLAs, NDAs, MAAs
- Investigator Brochures and clinical protocols
- Nonclinical expert reports (e.g., carcinogenicity risk assessment, waivers)
- Critical review and second opinions

Toxicology Representation
- Project Teams
- Board and venture capital (VC) funding meetings
- Regulatory authority meetings
  - PreIND, EOP2, pre-BLA, pre-NDA,
  - Advisory Committee meetings
  - Type A, B, and C meetings (FDA)
  - Biosimilar meetings
  - EMA scientific advisory meetings

Regulatory Guidance and Strategy
- Provide current regulatory perspective
- Respond to regulatory authority and clinical investigator questions
- Address clinical holds associated with nonclinical toxicity
- Identify and mitigate nonclinical regulatory risks

Due Diligence Activities (In-licensing and Out-licensing)
- Data gap and target liability analyses
- Critical review of nonclinical programs for in-licensing
- Prepare summary of nonclinical package for out-licensing