Drug Development Using the College of Veterinary Medicine at Virginia Tech: Incorporating Quality into Early Preclinical Safety Assessment

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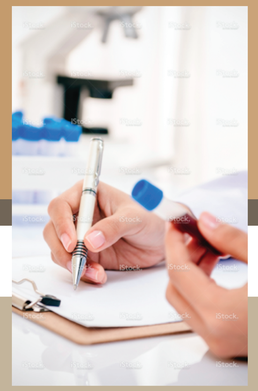

INTRODUCTION

- FDA quality regulations assure data integrity for preclinical safety studies in animals and clinical trials in humans
- Adopting quality system practices during drug discovery and early preclinical assessments can benefit future product development
- Virginia-Maryland College of Veterinary Medicine (VMCVM) has developed a data integrity model for exploratory safety and toxicology in rodents based on the Good Laboratory Practice regulations

QUALITY REGULATIONS IN THE DRUG DEVELOPMENT PATHWAY

UNREGULATED

Research & Discovery
- Synthesis
- Screening
- ID active compounds
- Lead optimization

Early Preclinical
- Preclinical efficacy
- Exploratory toxicology/ pharmacology/pathology

REGULATED

Preclinical Safety
- Safety pharmacology
- Repeated dose toxicity
- Genetic toxicology

Investigational New Drug (IND) Application

Clinical Phases I, II, III
- Healthy volunteers (I)
- 100-300 Patients (II)
- 3000-10,000 Patients (III)

New Drug Application (NDA)

Approval
- Post-marketing safety
- Large-scale manufacturing
- Distribution

Good Laboratory Practice (GLP)

Good Clinical Practice (GCP)

Good Manufacturing Practice (GMP)

GOOD LABORATORY PRACTICE REGULATIONS
21 CFR Part 58, final rule 1978

- Establish minimum standards for the conduct and reporting of studies to assure the quality and integrity of safety data submitted to the FDA
- Describe the organization, process and conditions under which laboratory studies are planned, performed, monitored, recorded and reported

VMCVM EARLY PRECLINICAL ASSESSMENT TEAM

Toxicologist /Pharmacologist Analytical Chemist
- Board-certified faculty
- Safety toxicology study design (dose response, single and repeat dose)
- Pharmacokinetics study design
- Dose formulation analysis
- Bioanalytical analysis for drug concentration

Rodent In-Life Study Staff
- Expertise in dosing, observations, behavior, necropsy, blood/tissue collection
- AAALAC-accredited facility
- AALAS-certified husbandry staff

Veterinary Pathologist
- Board-certified faculty
- Histopathology evaluation
- Neuropathology expertise
- GLP-compliant transmission electron microscopy service

Clinical Pathologist
- Board-certified faculty
- Hematology, clinical chemistry, urinalysis

Statistician
- On-site
- Experimental design/proposed statistics
- Specialized statistical analysis

ADVANTAGE

Research and Diagnostic Expertise

Voluntary GLP-Like Quality System Standards

Produces accurate, reliable, transparent and reproducible data

Provides confidence in the data-based decision to move a product from academia to industry for commercial development

VMCVM GOOD LABORATORY PRACTICE PROGRAM

- Mature GLP quality system infrastructure
- Over 20 years of support for faculty conducting GLP-compliant work for industry
- In-house GLP regulatory knowledge for GLP and GLP-like quality system training in an academic setting
- Experience navigating industry contracts, timelines and expectations