

SRI International

Preclinical Development Plan

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SUMMARY

The general process for drug development is similar among most agents across a broad range of therapeutic uses. While specific differences between chemical structures exist, and results of preliminary testing may trigger additional testing for a given compound, it is useful to understand the general process for drug development. This Preclinical Development Plan is therefore provided as a “generic” document that applies, in general, to the development of a typical small molecule anti-infective agent.

Since most drug candidates are still in the research stage of the research and development process, the recommended strategy is to develop a Target Product Profile and to outline the key studies to enable submission of an Investigational New Drug (IND) application, indicating appropriate go/no-go decision points.

Minimum Requirements for Preclinical Development

- One gram of relatively pure (>95%) test article synthesized
- No intellectual property issues for synthesis, use and treatment
- Confirmed *in vitro* efficacy with more than one reproducible study.

In this report SRI recommends steps to bring this drug into human Phase I clinical trials. These recommendations include

- Performance of efficacy studies to confirm pharmacological activity
- Completion of pharmacokinetic (PK) and range-finding toxicity studies
- Completion of repeat-dose toxicity studies in two species, in compliance with U.S. Food and Drug Administration (FDA) Good Laboratory Practices (GLP)
- Performance of preformulation/formulation studies to identify a probable clinical formulation
- Synthesis of batches of bulk active pharmaceutical ingredient (API) under pilot and then FDA Good Manufacturing Practices (GMP) conditions
- Analytical chemistry method development and validation
- Clinical manufacturing of Phase I drug product
- Shelf stability studies of bulk API and drug product supplies to support ongoing clinical studies and to establish expiration dating
- Preparation and submission of pre-IND and IND documents to the FDA.
- SRI generally recommends that work proceed in three stages with a go/no-go decision at the end of each stage. The first stage is to demonstrate animal efficacy, the second stage is PK/range-finding studies, and the third stage is the full GLP and GMP studies required to move the product to a successful IND application.