IND-ENBALING STUDIES COMPLETED

GLOBAL DRUG DEVELOPMENT

Goals/ Definition

Non clinical safety data and rationale for dose selection.

Preclinical drug candidate development activities to support clinical evaluation completed.

CRITERIA	SAMPLE CONTENT REQUIREMENT	GUIDELINES FOR LEVEL OF DETAIL NEEDED AT EACH GATE
▪ Initial nonclinical pharmacological studies completed	a) General pharmacology and mechanism(s) of action b) Dose formulation and regimen c) PK, PD, ADME (e.g., biomarker ID, *in vitro* vs. *in vivo* assessments, animal model selection, modeling strategies, etc.) d) Off-target screening e) Bioavailability (i.e., tissue, serum, spinal fluid, blood-brain distribution, etc.) f) Development and qualification of supporting bioanalytical and analytical methods (e.g., IR, HPLC, GC, GC/LC MS, etc.) for animal and human application	▪ Pre-IND briefing package, if available; or ▪ Summary of key data to substantiate conclusions ▪ Illustrative data tables or figures may be reported in an appendix
▪ Initial nonclinical efficacy studies completed	a) Desired outcome measurement criteria b) Demonstration of statistically significant response c) Dose-response relationships & formulation dependency d) Equal or superior efficacy data in comparative studies against licensed and alternative treatments e) Development and qualification of supporting bioanalytical and analytical methods for animal and human application (may overlap with pharmacological characterization)	▪ As above
▪ Initial nonclinical safety / toxicity studies completed	a) Acute and sub chronic animal toxicology studies, *in vitro* and *in vivo* assessments (e.g., genotoxicity screens, dose-response relationships, etc.) b) Establishment of NOAEL, ideally assessing equal or superior safety / toxicity data in comparative studies against licensed and alternative treatments c) Development and qualification of supporting bioanalytical and analytical methods for animal and human application (may overlap with pharmacological characterization)	▪ As above