

EXAMPLES OF PRECLINICAL MODELS AND CLINICAL FAILURES

Examples of Predictive Models of Efficacy

In vivo preclinical & clinical models
Translational medicine
Disease process models
Modeling and simulations
In silico models

Examples of Efficacy Failures

Low compound potency
Compound ineffective for indication
Impractical PK/PD relationship
Trial design inappropriate
Low fraction of patients responding

Examples of Predictive Models of Safety

General safety/toxicology
Safety pharmacology
Genotoxicity
Reproductive toxicology
Carcinogenicity

Examples of Safety/Toxicology Failures

Poor safety/tolerability profile
Narrow clinical safety margin
Specific organ toxicities
Geno/reprotoxicity or carcinogenicity
Rare or unexpected SAE's

Examples of Predictive Models of Compound Properties

Absorption & bioavailability
Human pharmacokinetics
Food effect
Drug metabolism
Drug interactions

Examples of Compound Properties Failures

Poor absorption
Unacceptable PK profile
Unacceptable food effect
Toxic metabolites
Unacceptable drug interactions