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Interspecies Differences in Physiology and Pharmacology: Extrapolating Preclinical Data to Human Populations

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1. OVERVIEW

Preclinical animal data are an integral component of the product development process, being used for predicting the potential for drug toxicity and for estimating first-time doses in humans. These extrapolations are based upon an assumption of a correlation between the exposure–response relationship in animals and man. Unfortunately, there is no single animal species that can serve as the "perfect" surrogate for human subjects, and the appropriate surrogate species needs to be evaluated for each situation (1).

Selection of the animal species to be used for toxicity testing should factor the potential interspecies differences that can influence systemic drug exposure and target cell sensitivity. These include potential differences in drug absorption, clearance, distribution, and metabolism. These factors can determine whether or not a species will exhibit toxicity or drug carcinogenicity (2).

In this chapter, the impact of study design, as well as interspecies differences in physiology and drug metabolism, will be explored from the perspective of the influence of these variables on the relationship between dose, drug exposure, and response.