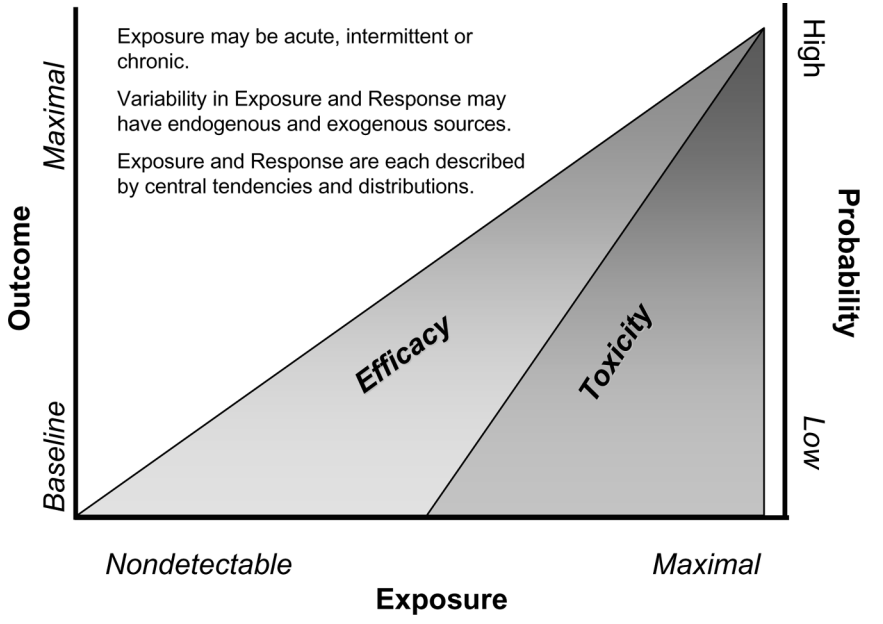

Figure 1 Exposure to drug product increases the likelihood of efficacy but also the potential for toxicity. For any given exposure, a probability distribution will exist for both efficacy and toxicity outcomes.

that receive pharmaceutical therapies. Phenotype, genotype, and lifestyle variability affect body composition and mass, drug transport and metabolism, and sensitivity to pharmacologic as well as toxic drug effects. Understanding sources of variability and the magnitude of that variability early in the development process permits clinical trial conduct that is most efficient and less likely to be encumbered with unanticipated events.

The realm of preclinical drug development can be compartmentalized into three disciplines that work in parallel from the stage of late research through clinical development. Two of these disciplines, pharmacokinetics and pharmacology/toxicology, are the subject of this text. The third discipline, bioanalytical research and development, is outside of the scope of this text and the reader will find many excellent publications elsewhere that are devoted to state of the art bioanalytical technology.

Before discussing the elements of a preclinical development program, some comments on the regulatory environment should be considered. The fundamental mandate of regulatory agencies is to ensure that clinical trials are conducted in a safe manner and that only drug candidates shown to be safe and effective are approved for commercial use. Early, scientifically rigorous interactions between a regulatory agency and industrial scientists will ensure that all concerns are addressed and that common objectives are determined.