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Preclinical Pharmacokinetic–Pharmacodynamic Modeling and Simulation in Drug Development

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1. INTRODUCTION

The pharmacokinetic literature is replete with examples of pharmacokinetic–pharmacodynamic models developed using animals. When those models can be extrapolated to the human condition, their value becomes significant. Otherwise, those models may still add to the (patho)physiology body of knowledge, but as far as the drug development process is concerned, they are simply exercises in modeling. Many books have been written on pharmacokinetic modeling, the most cited reference being Gibaldi and Perrier (1), and many excellent reviews have been written on pharmacodynamic models and modeling, including Derendorf and Meibohm (2) and Sheiner and Steimer (3). It would be redundant and add little to the scientific literature to re-present that material in a new format. Instead, the purpose of this chapter will be to review some interesting published case studies where the pharmacokinetic–pharmacodynamic models developed preclinically helped guide clinical drug development.