

SCIENTIFIC PERSPECTIVES ON THERAPEUTIC PROTEIN DRUG–DRUG INTERACTION ASSESSMENTS*

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10.1 INTRODUCTION

Many intrinsic and extrinsic factors can affect an individual patient's drug exposure and response.¹ The FDA has published a number of guidance documents that recommend how and when to evaluate these factors during drug development.² The most recent FDA draft guidance on drug interactions³ provides advice for *in vitro* and *in vivo* drug interaction studies, including suggestions for study design, dosing strategies, data analysis and interpretation, and the type of information that should be included in medical product labels; it updates the FDA's recommendations on the evaluation of important cytochrome P450 enzyme- and transporter-based drug interactions, and the use of physiologically based pharmacokinetic modeling approaches for drug interaction assessment; and it expands recommendations on therapeutic protein–drug interaction assessment. The recommendations are illustrated via a series of decision trees. This draft guidance and other FDA publications related to drug–drug interactions (DDIs),^{4–8} including the website *Drug Development and Drug Interactions*,⁹ provide recommendations on how to evaluate drug interaction potential for both small molecules (drugs or Ds) and therapeutic proteins (TPs).

Two review papers published in 2007 contain examples of drug interactions involving TPs.^{10,11} Several recent publications summarize the TP-DDI evaluation included in Biologics License Application (BLA) submissions and current strategies for the evaluation of TP-DDI potential during drug development.^{12–17}

*The views expressed in this book chapter are those of the authors and do not necessarily reflect the official views of the US Food and Drug Administration.