Sandoz Clinical Development

An Industry Perspective on Successful Prediction of Food Effect and Fed BE Studies

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Disclaimer

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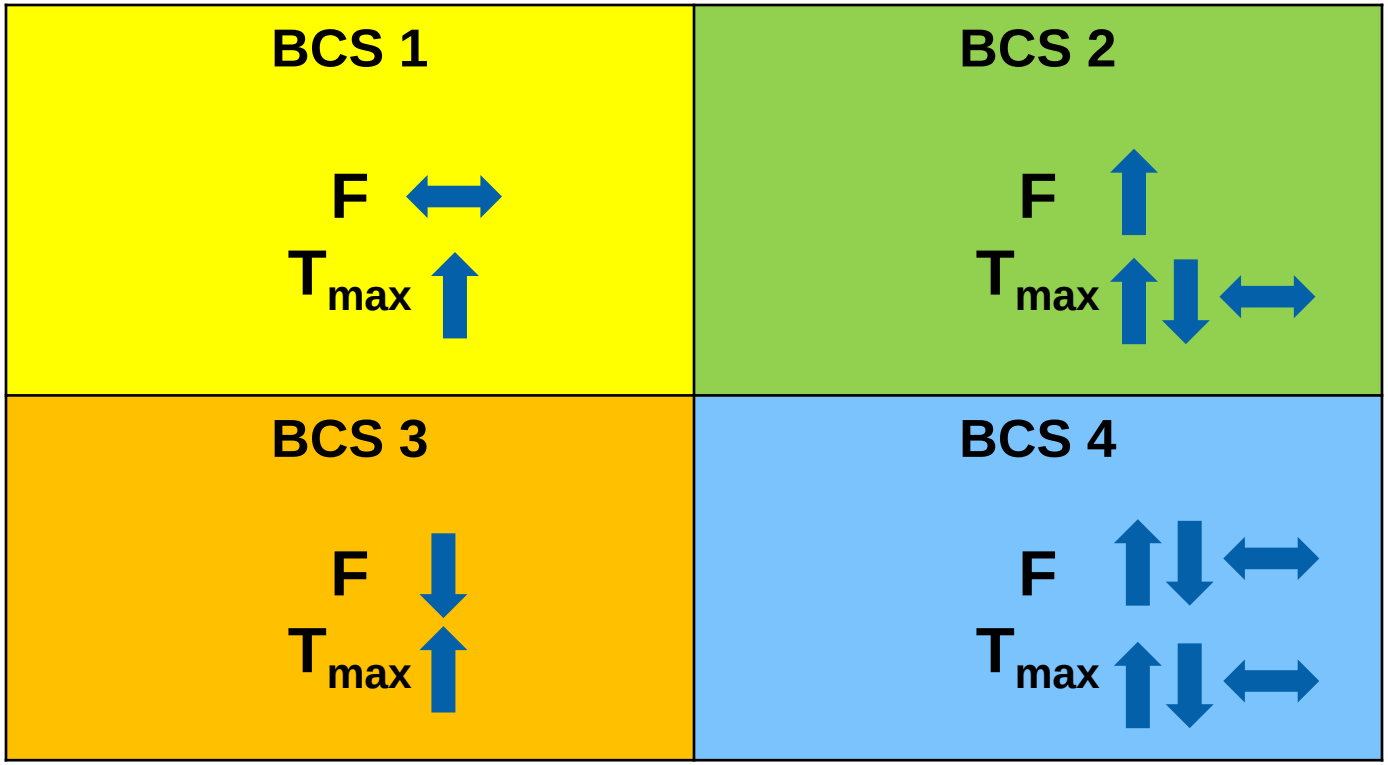
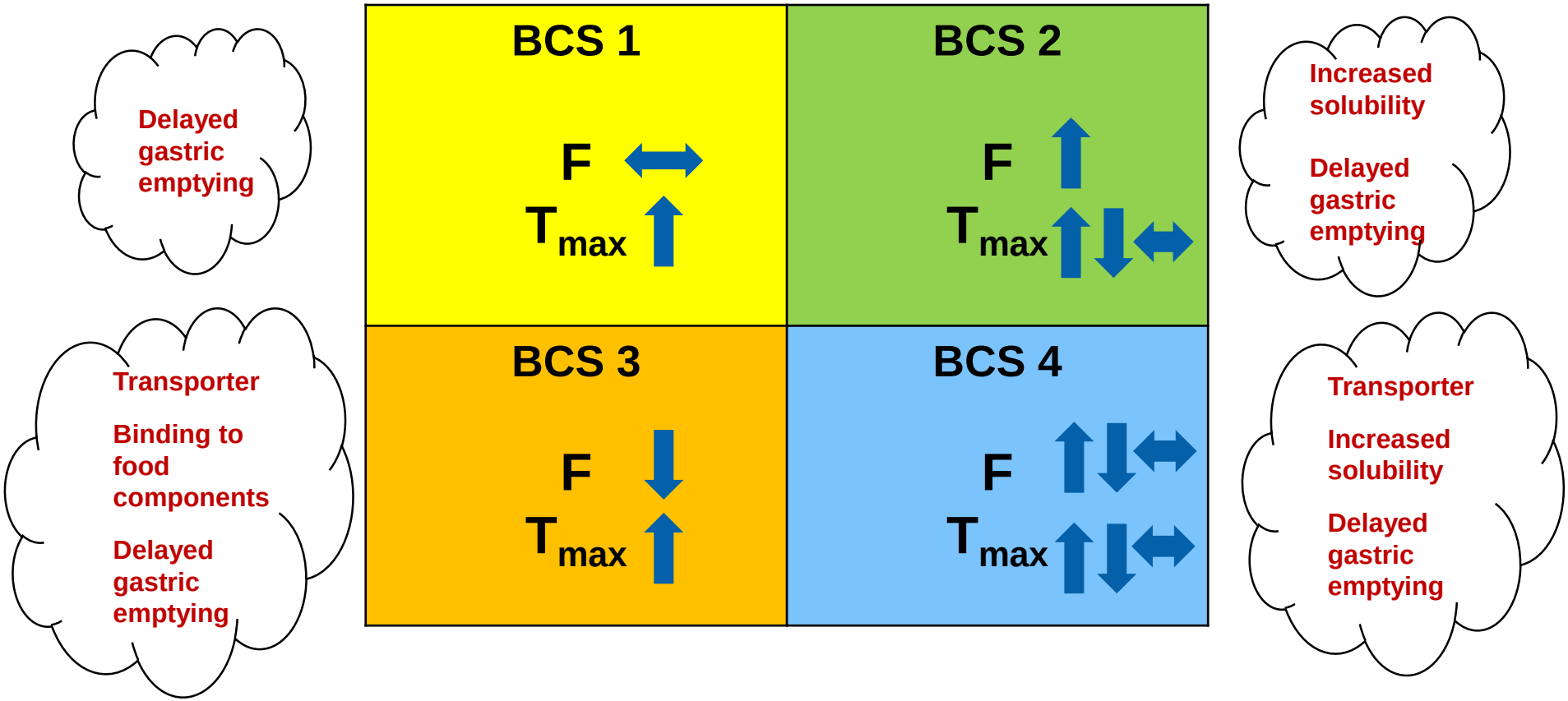
Effect of Food on Pharmacokinetics



Fleisher et al., Clinical Pharmacokinetics, 36, 233-254 (1999)

Primary Mechanism of Food Effect



Fleisher et al., Clinical Pharmacokinetics, 36, 233-254 (1999)

Where/How Can We Predict Effect of Food Reliably?

BCS 1 & 2 compounds with known food effect mechanism(s)

- Impact on gastric emptying
- Impact of fat & bile salts on solubility and dissolution

Linear PK or non-linearity due to saturation of absorption because of solubility limitation

- No known/obvious interaction of food with intestinal enzymes &/or transporters

Moderate to high bioavailability

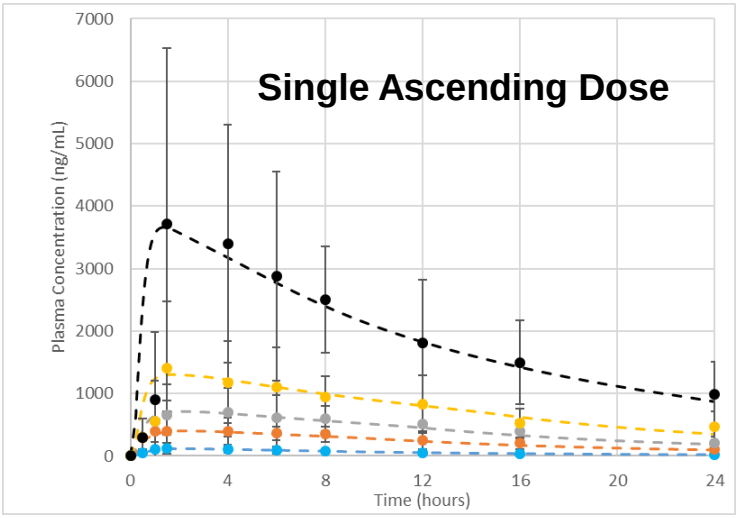
Reliable solubility and/or dissolution data

Reliable estimates of human PK parameters (either from single dose oral or IV data or pop-PK)

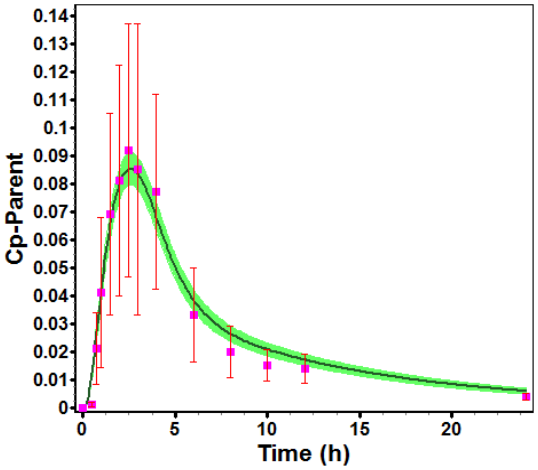
Clinical data are available in at least 1 prandial state for model verification

Estimates of intrasubject CVs on PK parameters from prior studies

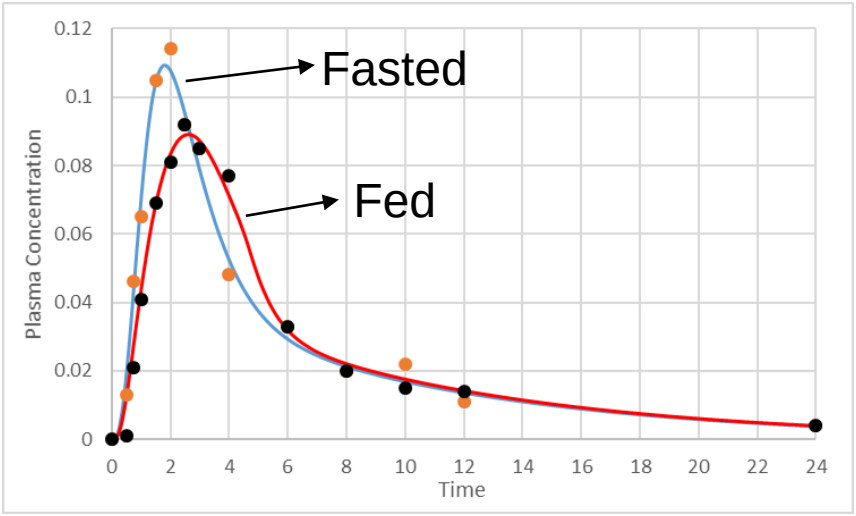
Typical Workflow for Prediction of Effect of Food

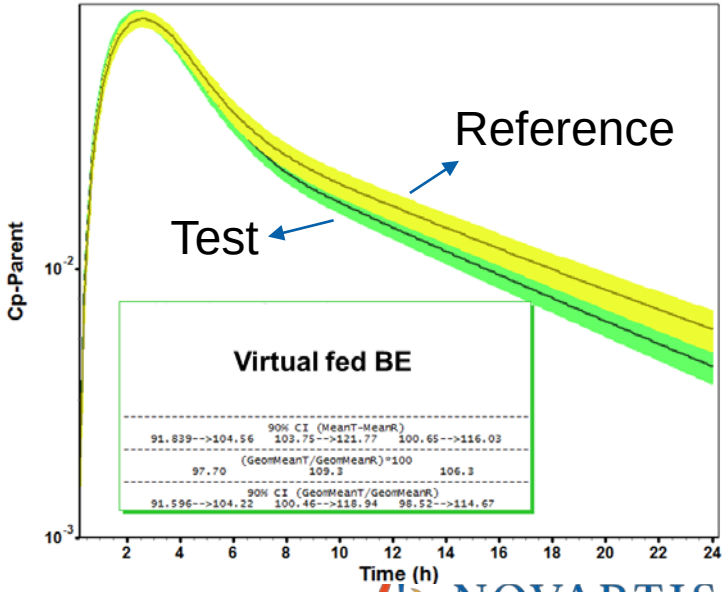


Population simulations by incorporating variability in PK parameters from pervious clinical studies



Crossover Population Simulations show BE





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Cross Industry Case Studies

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journal homepage: www.jpharmsci.org

Pharmacokinetics, Pharmacodynamics and Drug Transport and Metabolism

Food Effect Projections via Physiologically Based Pharmacokinetic Modeling: Predictive Case Studies

Check for updates

5 case studies from 4 Pharmaceutical companies demonstrating the successful prediction of food effect, using appropriately established and verified models

Summary

- Advances in PBPK modeling allow for waiver of food effect & fed BE studies, on a case-by-case basis
- Within constraints discussed here, there is good success in prediction of food effect & fed BE studies
- Regulatory research should focus on use of these models in waiver of food effect & fed BE studies
  - Fasted state is the most sensitive to assess formulation differences
  - Ethical considerations
  - Reduction in time & cost of development
- ANDA
  - BCS 1 IR product: if sponsor opts for in-vivo BE then only fasting BE should suffice
  - BCS 2 IR product: fed BE studies could be waived if molecules follow constraints discussed here

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Thank you

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