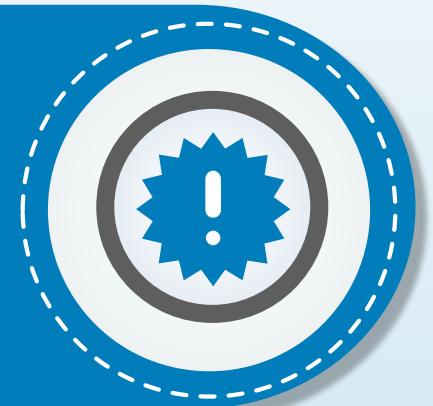


Population Pharmacokinetics Final Guidance

What is Recommended in this Guidance?

The final guidance entitled "Population Pharmacokinetics" describes the application of population PK in drug development and its role in informing therapeutic individualization. This guidance provides the FDA's current thinking on the data and model submissions to support regulatory decisions and recommendations on how to incorporate information from population PK analyses in labeling. The guidance also lays out the general expectations regarding the format and content for population PK reports submitted to the Agency.

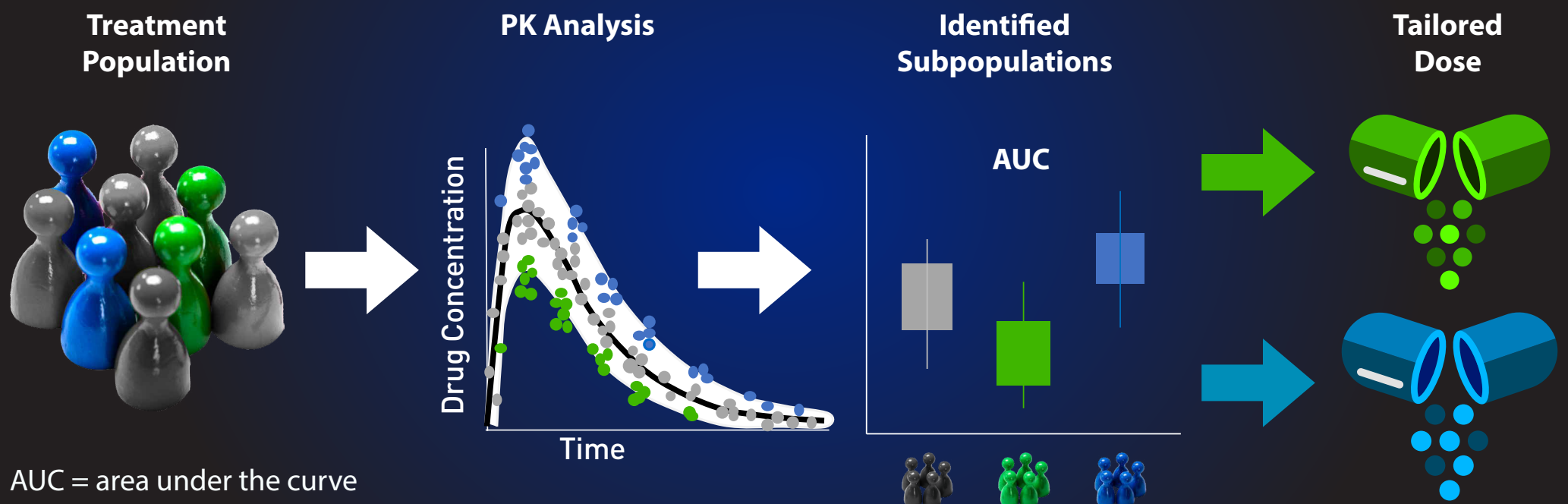


What is Population PK?

Population PK integrates all relevant PK information to identify factors that can affect a drug's exposure in an individual. A population PK analysis can be used to guide drug development and inform recommendations on therapeutic individualization (e.g., through tailored dosing).



Population PK Goal: Minimize Treatment Response Variability by Informing Dosing and Administration for Individuals or Subpopulations



Guidance Snapshots are a communication tool and are not a substitute for the guidance document.

To learn more about population PK, read the final guidance:

<https://www.fda.gov/regulatory-information/search-fda-guidance-documents/population-pharmacokinetics>

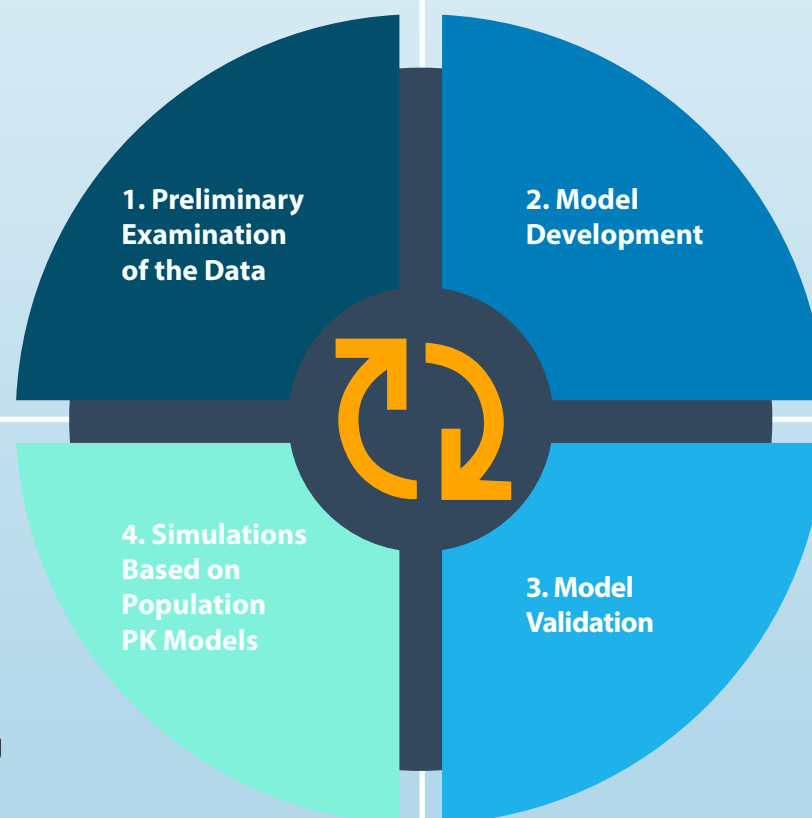
What are Potential Applications for Population PK?

- Selecting Dosing Regimens To Be Tested in Clinical Trials
- Informing Trial Design to Facilitate the Reliable Estimation of Covariate Effects
- Deriving Exposure Metrics for Conducting Exposure-Response Analysis
- Informing Pediatric Study Designs
- Selecting Dosing for Specific Populations



Analysis of Population PK Data

Sponsors should perform preliminary examination of the data using graphical and statistical techniques to reveal patterns and features in the population dataset.



Model development methods and best practice recommendations are constantly evolving. Sponsors should explicitly describe their model development procedures; some aspects include covariate identification, choice of the structural model, and distinguishing between outlying individuals and outlier data points.

When models are used for simulations, these models should be evaluated to address the specific question the simulation is trying to answer. Depending on the purpose of the model, various levels of uncertainty and variability should be incorporated into the simulations. Examples for evaluating various types of simulations are provided in the Population PK final guidance.

Model validation should be conducted to examine whether the developed model can sufficiently characterize the observed data to meet the needs of the analysis with an acceptable level of bias and an acceptable degree of precision. Basic goodness-of-fit (GOF) plots can illustrate how well the model describes the observed data. In general, several methods should be considered to adequately assess model performance and follow a fit-for-purpose approach.

How are Population PK Results Presented in the Labeling?

Results from population PK analysis may be presented in the CLINICAL PHARMACOLGY section and summarized in other sections of labeling, as appropriate, but the results don't need to explicitly state that the information is based on population PK analysis. Labeling recommendations are provided in the FDA guidance for industry entitled *Clinical Pharmacology Section of Labeling for Human Prescription Drug and Biological Products - Content and Format*.



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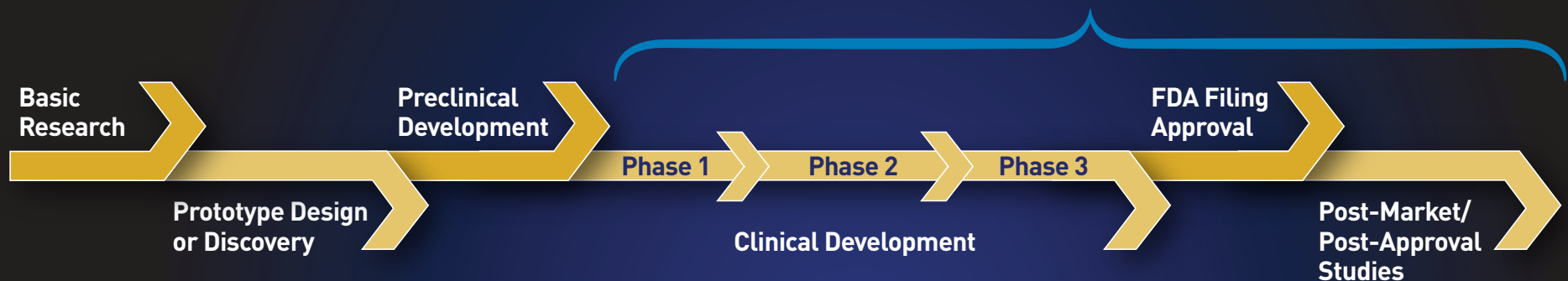
Why is This Guidance Important?

The population PK guidance includes common applications of population PK analyses to inform drug development and drug use. The guidance also provides FDA's current thinking on the population PK data and model submissions to support regulatory decisions, how to incorporate population PK analyses in the labeling, and the general expectations regarding the format and content for population PK reports submitted to the Agency. Population PK models are of great utility

in dose optimization as they can be used to simulate drug exposures that are expected to occur following doses or dosing regimens that have not been directly investigated in prior clinical studies. This guidance is timely and relevant, as it supports FDA's efforts and focus on model-informed drug development and the application of quantitative models for regulatory decision-making, including those derived through population PK approaches.

Drug Development Timeline

Apply Guidance Recommendations During and After Clinical Development



Seek Advice Prior to and During Clinical Studies

Sponsors seeking advice on the use of population PK analysis for drug development decisions or to answer regulatory questions are encouraged to do so at appropriate milestone meetings with the Agency. Confidence in a given population PK analysis is increased by the following:

- Understanding of the drug's PK properties
- Prespecified questions in the study protocol or analysis plan that will be addressed by a population PK analysis
- Sufficient PK data that represents the indicated population and relevant subpopulations of interest
- Good model performance (i.e., the model should describe the data with acceptable bias and precision) and valid for the intended purpose

Guidance Recap Podcast Hear Highlights Straight From FDA Staff

Speaker: Hao Zhu, Ph.D., Acting Director of the Division of Pharmacometrics in the Center for Drug Evaluation and Research's Office of Clinical Pharmacology



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Guidance Snapshots are a communication tool and are not a substitute for the guidance document.

To learn more about population PK, read the **final guidance**.

To see additional Guidance Snapshots, check out the **pilot program**.