

URINE PARAMETERS

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Vanessa A. Rubano, Modesta Wiersema
Boehringer Ingelheim Pharmaceuticals Inc. USA, Boehringer Ingelheim Pharma GmbH & Co. KG Germany



Introduction: Clinical Pharmacology is an integral part of clinical trials and the approval of a new drug. To obtain regulatory approval for a New Drug Application (NDA), a sponsor is required to show the elimination of drug and metabolites within the human body's matrices, such as urine and feces, supported by plasma pharmacokinetic (PK) endpoints. The industry standard used for calculating PK endpoints is the application of clinical trial data to WinNonLin® (WNL), a software modeling package that is based on mathematical equations. The aim of this poster is to introduce a method, using SAS® programming, to derive PK urine endpoints for individual and cumulative amounts excreted (Ae), fractions of the administered dose excreted (fe) and renal clearance (CLR) of drug from the plasma matrix to urine for a complete profile of a subject or patient. A SAS® program was developed based on a standardize data file structure in which key variables were identified for the calculation of PK urine endpoints: analyte, matrix, visit, patient number, treatment information, AUC values, amounts excreted (urine volume * urine concentration), and planned urine start and stop times.

Method: The flowchart below illustrates the program. The initial step involves importing the plasma NCA results, generated from WNL, and the urine raw data files. Data steps filter through the plasma NCA results selecting observations that are required for renal CLR. After creating PK urine endpoint names the urine raw data is merged to the plasma data by analyte, treatment, visit number, patient number and planned time. The file now contains all necessary variables and the PK urine endpoints are derived. Missing data and observations that are excluded have rules applied to the derivations. Lastly, exclusion flags are assigned and the data is structured and formatted allowing for further processing with standardized tools.

Results: The program creates several files that can be consolidated and formatted in a final data file containing urine endpoints with exclusion criteria. Actual number of created data files is dependent on PK urine endpoints requested and sampling intervals provided in the raw data.

Conclusion: The methods described in this poster offer a new approach to calculate PK urine endpoints using SAS® programming.

