The NCA Consortium: Standardizing Qualification of Noncompartmental Analysis

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Objectives: Methods for noncompartmental analysis (NCA) have long been described in many journal articles, textbooks, and regulations, and a nearly-standardized feature set has been identified. As a result, a multitude of software solutions are used for calculating NCA parameters: home-grown, open-sourced, and proprietary. However, every organization must generate its own requirements and validation specifications for NCA software. The objective of the NCA Consortium is to generate a standard, modular set of requirements documents to enable software developers and users to validate with a single standard ensuring interoperability and standardization of NCA calculations.

Methods: Using guidance documents, data standards, literature, and individual expertise and experience, a set of requirements, algorithms, and test cases for NCA parameter calculations were enumerated. The scope for the specifications include:

- Calculations
  - Single- and multiple-dose administration
  - For multiple-dose administration, prior to or at steady-state
  - Intravascular and extravascular administration
    - For intravascular, including bolus, short-duration infusion, and continuous infusion
  - Plasma and excretion-related (e.g. urine and feces) measurements
- Data cleaning
  - With or without unscheduled samples included
  - With multiple options for below limit of quantification (BLQ) rules
  - With interpolation, extrapolation, and corrections for time deviations from nominal times and concentration deviations

The scope of NCA parameters attempts to match commonly-used parameters from the SDTM PK Parameters controlled vocabulary.[1]

Results: A public draft specification will be available prior to ACoP 2016 incorporating each of the items defined in the Methods section.

Conclusions: By standardizing the methods of calculation, algorithmic choices, and validation tests across software and organizations, research will be more reproducible, teams in disparate organizations and working environments can work more closely together, and create more consistent NCA results.

References: