Size Matters: How Revised FDA Renal Impairment PK Study Guidance Will Impact Future Studies

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BACKGROUND

In September 2020, the FDA issued updated draft guidance for renal impairment (RI) pharmacokinetic (PK) studies which now recommends **sample size (n) calculation** to determine the number of patients per cohort. The guidance suggests to "*calculate the required n targeting 95% CI (60-140%) of the geometric mean estimate to achieve 80% power*". Previously, **6-8 patients/cohort** were enrolled. How will this new recommendation affect the number of patients to evaluate?

METHODS

- A convenience sample of 25 renal impairment PK studies managed by Celerion from 2011-2019 was selected.
- AUC_{0-t} and C_{max} **inter-subject CV%** results were reviewed to calculate sample size.
- **Concordance analysis** was determined if the calculated sample size was equal to the actual cohort size.

RESULTS

- Based on AUC_{0-t} and C_{max} variability, calculated n ranged from 4-19 and 4-26 subjects respectively.
- Concordance between the sample size required under the new guidance and actual n was only 8% and 14% using AUC_{0-t} and C_{max} variability respectively.

CONCLUSION

- Previous studies may have **underestimated** the required sample size to achieve 80% power. Moving forward, RI PK studies will likely require 9-11 patients per cohort.

Updated draft FDA **renal impairment PK guidance** now requires up to **50% more patients** than traditionally enrolled.

Take a picture to **download** our **white paper** summarizing **updates** to the guidance

Table 1. Summary of Inter-Subject CV% data from 25 RI PK studies

Parameter	Average	Min - Max
AUC_{0-t}	36.3%	15.9% - 67.0%
C_{max}	39.7%	9.9% - 85.0%

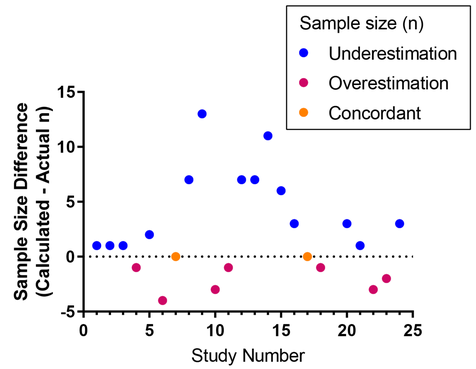
AUC_{0-t} variability data available from 24 studies; C_{max} available from 22 studies.

Table 2. Calculated sample size based on variability from 25 RI PK studies

Parameter	Average	Min - Max
AUC_{0-t}	9	4 – 19
C_{max}	11	4 - 26

AUC_{0-t} variability data available from 24 studies; C_{max} available from 22 studies.

Figure 1. Difference between calculated and actual study cohort size based, on AUC_{0-t} variability



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