Background Current dosage regimen of aminophylline is similar in both Appropriate for Gestational Age (AGA) and Small for Gestational Age (SGA) preterm neonates. In contrast with AGA babies, SGA babies handle drugs in a different way. However, developing countries like India has significant proportion of Growth Restricted/SGA babies. Hence, there is a need to develop an appropriate dosage regimen in this population. Objective of the current study was to develop and qualify the Population-Pharmacokinetic (PPK) model for aminophylline in premature neonates in Indian population.

Methods Aminophylline-treated neonates with IV loading dose of 5 mg/kg followed by maintenance dose of 1.5 or 2 mg/kg 8th hourly for Apnoea of Prematurity (AOP) were included. Any other conditions for secondary causes were excluded. Blood samples were collected by adopting sparse sample scheme and estimated by LCMS-MS. PPK model was developed with appropriate covariates. Data was analysed by NONMEM version 7.3. Non-parametric bootstrap procedure and Visual Predictive Check (VPC) was used to qualify the developed model.

Results One compartment, first-order structured model was fitted to the dataset containing 454 observations from 107 neonates. PPK parameters were represented as model estimated values and variability was depicted as% Co-efficient of variation (%CV). Typical population value of CL was 0.011 L/hour with inter-individual variability (IIV) of 59% and V was 0.332 (L/kg) with 31% IV. Residual error was found to be 19%. Only postnatal age (PNA) had significant effect on V which was assessed by forward addition and backward elimination regression model.

Conclusion AGA and SGA had no influence on PK parameters. However, PNA showed to have significant influence on V. Developed nomogram based on the qualified model may be effective and safe for aminophylline therapy in preterm neonates with apnoea.

REFERENCES
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to ensure high quality research. Specifications for the validation process, but also for the assessment of data, acquired in a study setting, are given by the EMA and FDA to ensure highest quality of the data.

**Methods** A multi-level analytical quality system was established. Data of the validation standards (CSs), quality control samples (QCs), and incurred sample reanalysis (ISR) were evaluated according to the specifications given by the EMA and FDA guidelines. For a run to be considered valid or 75% of the CSs and 67% of the QCs (≥50% per level) had to vary ±20% (LLOQ ±25%) from their nominal concentration. For the ISR analysis at least 67% of the ISR samples have to lay in ±30% to the nominal concentration of the mean of the original and reanalyzed value.

**Results** Seventy analytical runs were conducted, applying the quality measures, 79% runs were classified as valid and were used to determine unknown samples in a paediatric study. The high quality of the acquired data is reflected in the high conformity of the CSs and QCs to the EMA and FDA guidelines, 99% of the CSs and 95% of the QCs were accepted. Further underlining the high quality of the acquired data, 85% of the IRS have also been accepted. The assay was successfully used over a time period of 29 months.

**Conclusion** The results of the quality assessment confirmed the robustness of the aldosterone assay throughout the whole study duration. Thus, the samples measured by this assay are reliable and facilitate the high quality research in the paediatric population.

**REFERENCES**

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