Whole-Body Physiologically-Based Pharmacokinetic Modeling of Moxifloxacin to Support a Translational Approach in Pediatric Study Design

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Introduction
At present, many medicines are not developed for children or available in suitable dosage forms. Therefore, the FDA and the EMEA have launched initiatives that request pediatric assessment of new drugs. For antibiotics development strategies for dosing recommendations in order to maintain efficacy and safety in different age groups are required.

Objective
Since the ADME properties of moxifloxacin are fully investigated and age dependencies of the processes involved are available, a pediatric whole-body physiology based (WB-PBPK) model for moxifloxacin paying attention to developmental changes is applied to design clinical studies in children.

Methods
The Bayer standard workflow using PBPK modeling with the software PK-Sim® for extrapolation from adults to pediatric populations is used to describe moxifloxacin concentration-time profiles, as shown in Figure 1.²,³

Results
In an exemplary way, the simulated plasma concentration time profiles of 6 month old children following multiple administration of 50 mg moxifloxacin once daily are shown in Figure 3.

Conclusion
The evaluation of the relevant PK parameters, as shown in Figure 4, suggests that preschool children and infants require between 25 to 80% higher doses and/or shorter dosing intervals than those recommended in adults to achieve equivalent exposure. The results obtained from the pediatric PBPK model are used to plan first studies in pediatric patients.

References