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CERTARA®
*Accelerating Medicines, Together*

CASE STUDY

# USING PBPK FOR A FORMULATION CHANGE FOR PEDIATRIC PATIENTS (TABLET TO SUSPENSION)

Children are not small adults, and not all children are the same. Growth, maturation and environmental factors, along with factors around the disease and genetics, directly affects drug performance in children, especially in small children less than two years of age.

Physiological based pharmacokinetic modeling and simulation (PBPK) has been increasingly applied in pediatric drug development. This is encouraged by regulators. Medicines for children must be well explored and safe, while avoiding any unnecessary clinical testing. It is important to take advantage of all existing information to develop these drugs and these new formulations, while optimizing them for these different age groups.

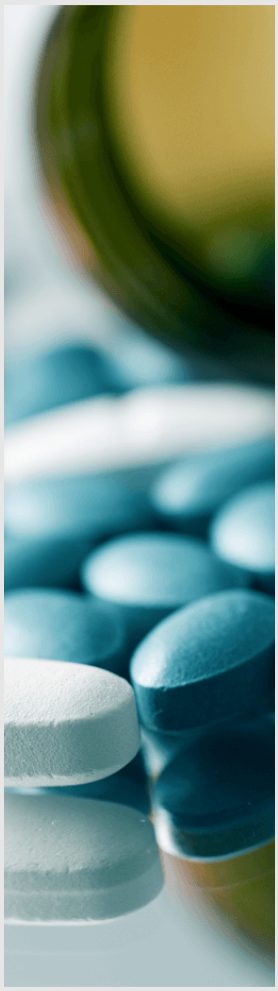
A suspension has several advantages, especially when it comes to the pediatric administration. It is easier to titrate the dose when compared to a tablet. In addition, there is no swallowing involved, so the suspensions are typically easier to administer. However, when you make these changes in the route of administration, the question is then how different it is going to be from the existing formulation.

In this case, the Certara team used modeling and simulation along with in vitro assessments. The PBPK model showed that the change in the formulation did not have a meaningful impact on the performance of the drug or the pharmacokinetic profile of the drug when it was changed from tablet to suspension because the tablet was again quite rapidly disintegrating. The primary particles used for manufacturing the tablet and the suspension were comparable.

A safe space assessment was also performed using the model, which looked at the critical formulation attributes, such as the tablet disintegration time, the particle size distribution and some of the manufacturing variables that we could capture in particularly wide distribution.

In addition, the simulator created a model to account for any viscosity effect and how much it would likely be. This was especially important when the drug was being liberated from the formulation in the stomach, and also effected the pH of the formulation.

Overall, the model provided additional evidence and exploration of the safe space of the formulation to support the biopharmaceutical risk assessment of the formulation change. Along with the suitable evidence and the in vitro data, the model was able to support this formulation change without a dedicated study.



**Certara used PBPK to change the formulation and gain regulatory approval for a suspension formulation of a drug, expanding its usage to children.**