# Step-by-step guide for case study “Oral drug absorption modeling in PK-Sim”

In this walkthrough guide basic operations and usage of PK-Sim are not show explicitly as there are excellent YouTube videos from scientist of [Clinical Pharmacy Saarland University](https://www.youtube.com/channel/UCrjhCoM0g5C5wtQQ4JQYpJg/featured) and detailed documentations on [Open Systems Pharmacology](https://docs.open-systems-pharmacology.org/working-with-pk-sim/pk-sim-documentation)

In this content overview links are pointing to these YouTube videos.

* Generate Healthy [individual](https://youtu.be/8kd1RfK_ms4?list=PLpeorG4ZXRzYWLQEj124yHUlzahrrwwMp)
* Generate [compounds](https://www.youtube.com/watch?v=HAY2jK5D_6w&list=PLpeorG4ZXRzYWLQEj124yHUlzahrrwwMp&index=4) (from template DB)
* Set up [administration](https://www.youtube.com/watch?v=xLYYr0U_O2E) scenarios
* Import [observed data](https://www.youtube.com/watch?v=eo2uiHJD79E)
* Build population and run [simulations](https://www.youtube.com/watch?v=JndcMlv47sY) and compare to observed data
* Compare Simulations

## Detailed Step-by-Step

| **File (Session #2-HandsOn.pksim5)** | **Step** | **action** | **comment** | image |
| --- | --- | --- | --- | --- |
| **(1) Establish oral absorption model** | | | | |
|  |  |  |  |  |
|  | **1.a** | ***Clone compound*** | Clone simulation “IV\_100mg”, name “ORAL\_100mg”  Select Administration protocol “ORAL\_100mg” and formulation “Solution” |  |
|  | **1.b** | ***Observe data*** | Remove “IVdata” and add “ORALdata” |  |
|  | **2.a** | ***Add GI enzyme in individual*** | Add “ENZ\_GI” for individual Man30 |  |
|  | **2.a** | ***Add GI enzyme in individual*** | Add relative expression = 1 in small intestine mucosa and keep other inputs as default |  |
|  | 2.b | ***Add enzyme in compound*** | Add “Metabolizing enzyme” for ENZ\_GI in compound Drug |  |
|  | 2.b | ***Add enzyme in compound*** | Fill in, ENZ\_GI, in vitro, CL-first other, Enzyme concentration and specific clearance 1 μmol |  |
|  | **2.b** | ***Add enzyme in compound*** | Create new “specific intestinal permeability value” (PI) set to calculate value (3.11E-6 cm/min) |  |
|  | **3.a** | ***Simulate oral model performance*** | Update “Man30” and “Drug” from Building Block and Select the “Drug” in automatically opened configuration window |  |
|  | **3.b** | ***Simulate oral model performance*** | 1. Use new permeability value (PI) form drop-down |  |
|  | **3.b** | ***Simulate oral model performance*** | Exclude absorption from colon ascendens –rectum e.g. by setting intestinal solubility (visible in “Advanced” view-mode) to 0 in these compartments |  |
|  | 4a | ***Parameter Identification*** | Create a parameter Identification and include “ORAL\_100mg” |  |
|  | 4a | ***Parameter Identification*** | Delete IV data |  |
|  | 4a | ***Parameter Identification*** | Select “Specific intestinal permeability (transcellular)” and “CLspec/[Enzyme]” for (only!) ENZ\_GI and Run |  |
|  | 4b | ***Transfer Parameter Identification*** | Transfer to Simulations from “Results” and “Commit to building block” |  |
|  | **5.a** | ***Look at results*** |  |  |
| **(4) Formulation performance in virtual populations** | | | | |
|  | **6.a** | ***Set up simulations for different formulations for typical individual*** | Clone simulation “ORAL\_100mg” and name “Tablet\_Reference” and select formulation “Tablet\_Reference. Remove ORALdata observations. |  |
|  | **6.b** | ***Set up simulations for different formulations for typical individual*** | Clone simulation “Tablet\_Reference” to create simulations “Tablet\_Test1”, “Tablet\_Test2” and “Tablet\_Test3” and run each simulation. |  |
|  | **7.a** | ***Create a virtual population*** | Create virtual population based on ”Man30”, e.g., age 25-40 , 100% men, n=100 |  |
|  | **7.b** | ***Add variability*** | Add under “User Defined Variability” ENZ\_GI and define variability with a SD of 0.3. |  |
|  | **8** | ***Clone tablet simulations*** | Clone tablet simulations, add suffix “\_POP”, and replace “Man30” with created virtual population for all tablet forms |  |
|  | **9** | ***Run simulations*** | Run all formulations and add the 95% quantile and add AUC\_inf and C\_max for PK-parameters check. |  |
|  | **10.a** | ***Visualize results*** | Make a simulation comparison of all Tablet forms under “Run & Analyze” and then “Compare Results”. Select all pop tablet formulations. Select the 95% quantile under output and add AUC\_inf and C\_max under PK-Parameters. |  |
|  | **10.a** | ***Visualize results*** | Time Profile comparison |  |
|  | **10.b** | ***Visualize results*** | Make a Box Whisker comparison for AUC\_inf by clicking on Box Whisker under analyze. Add AUC\_inf and drag Simulation name to X-grouping under Box Whisker Analysis. |  |
|  | **10.b** | ***Visualize results*** | Repeat for C\_max |  |