Covariate Model Building

Hands-On Session – Linearized XV SCM

Introduction: In this exercise we will evaluate an appropriate size of predictive covariate models using linearized stepwise covariate model building combined with cross-validation (linearized XV SCM) for the moxonidine dataset.

Files provided:

Data set:

   mx19.csv

Model files:

   run.mod = one compartment model parameterized in CL, V, Ka and lag time with inter-individual variability (IIV) and inter-occasion variability (IOV). The base model does not contain any covariate-parameter relations.

SCM configuration file:

   run_lin.scm

Other file:

   Relation_OFV.r, Relation_Inclusion.r = R script for plot

Tasks:

Seven covariates included in the dataset are AGE – age (yr), WT – weight (kg), CLCR – creatinine clearance (ml/min), DIG – concomitant medications digoxin (0=not taken; 1=taken), DIU - concomitant medications diuretic, ACE - concomitant medications ace inhibitors and SEX – gender (1=male; 2=female). You are to test covariate-parameter relations on CL and V.

1) Using the provided SCM configuration file (run_lin.scm), run linearized XV SCM. *xv_scm -config_file=run_lin.scm -dir=run_lin -groups=5 -splits=3 -max_steps=3*

2) Start R from the "files_provided" directory. To plot the mean XV_OFV and the XV_OFV for each split using xv_ofv_results.csv, run the commands in Relation_OFV.r. How many relations can be chosen as an appropriate model size?

3) To plot the inclusion rate of relations for each step in the linearized XV SCM using xv_percent_inclusion_by_level.csv, open the csv file, copy all, and transpose it in a new excel datasheet and save the datasheet as a csv file named "test.csv". Run the commands in Relation_Inclusion.r using R. Which relations are frequently included in the appropriate model size?