Open Systems Pharmacology Suite - 7.3.0 Folder Comparison

ztsoj

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Chapter 1

Folder Comparison Results

Overall Comparison Result: Invalid Number of Compared Files: 112

1.1 Comparison Results

Overall Comparison Result

Invalid

Old Folder

M:\0000_7.3\BatchComparison\Outputs 7.2.2

New Folder

M:\0000_7.3\BatchComparison\Outputs 7.3.0

1.1.1 Invalid Simulations (4/112)

$Simulation: \ Human_MultipleIV_AllActive Processes-Human_MultipleIV_AllActive Processes$

Result of the validation: Invalid Absolute Tolerance: 1.00E-10 Relative Tolerance: 1.00E-5

Output Path: Organism|Bone|Intracellular|TRANS|Concentration in container

Output 'Organism|Bone|Intracellular|TRANS|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_AllActiveProcesses'

Deviation: 0

Output Path: Organism|Brain|Interstitial|TRANS|Concentration in container

 $Output \ 'Organism|Brain|Interstitial|TRANS|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_MultipleIV_AllActiveProcesses'$

Deviation: 0

Output Path: Organism|Fat|Intracellular|TRANS|Concentration in container

 $Output \ 'Organism|Fat|Intracellular|TRANS|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined in \ 'Human_Multiple IV_All Active Processes'$

Output Path: Organism|Gonads|Intracellular|TRANS|Concentration in container

Output 'Organism|Gonads|Intracellular|TRANS|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_AllActiveProcesses'

Deviation: 0

Output Path: Organism|Heart|Intracellular|TRANS|Concentration in container

 $Output \ 'Organism|Heart|Intracellular|TRANS|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_Multiple IV_All Active Processes'$

Deviation: 0

Output Path: Organism|Kidney|Intracellular|TRANS|Concentration in container

 $Output \ 'Organism|Kidney|Intracellular|TRANS|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined in 'Human_MultipleIV_AllActiveProcesses'$

Deviation: 0

$Output\ Path:\ Organism|Stomach|Intracellular|TRANS|Concentration\ in\ container$

Output 'Organism|Stomach|Intracellular|TRANS|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_AllActiveProcesses'

Deviation: 0

Output Path: Organism|SmallIntestine|Intracellular|TRANS|Concentration in container

Output 'Organism|SmallIntestine|Intracellular|TRANS|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_AllActiveProcesses'

Deviation: 0

Output Path: Organism|LargeIntestine|Intracellular|TRANS|Concentration in container

 $Output \ 'Organism|LargeIntestine|Intracellular|TRANS|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_MultipleIV_AllActiveProcesses'$

Deviation: 0

Output Path: Organism|Liver|Periportal|Intracellular|TRANS|Concentration in container

Output 'Organism|Liver|Periportal|Intracellular|TRANS|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_AllActiveProcesses'

Deviation: 0

Output Path: Organism|Liver|Pericentral|Intracellular|TRANS|Concentration in container

Output 'Organism|Liver|Pericentral|Intracellular|TRANS|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_AllActiveProcesses'

Deviation: 0

Output Path: Organism|Lung|Intracellular|TRANS|Concentration in container

 $Output \ 'Organism | Lung | Intracellular | TRANS | Concentration in container' is missing from simulation 'Sim' defined in 'Human_Multiple IV_All Active Processes'$

Output Path: Organism|Muscle|Intracellular|TRANS|Concentration in container

 $Output \ 'Organism|Muscle|Intracellular|TRANS|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined in 'Human_Multiple IV_All Active Processes'$

Deviation: 0

Output Path: Organism|Pancreas|Intracellular|TRANS|Concentration in container

 $Output \ 'Organism|Pancreas|Intracellular|TRANS|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_Multiple IV_All Active Processes'$

Deviation: 0

Output Path: Organism|Skin|Intracellular|TRANS|Concentration in container

 $Output \ 'Organism | Skin | Intracellular | TRANS | Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_Multiple IV_All Active Processes'$

Deviation: 0

$Output\ Path:\ Organism | Spleen | Intracellular | TRANS | Concentration\ in\ container$

 $Output \ 'Organism|Spleen|Intracellular|TRANS|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_AllActiveProcesses'$

Deviation: 0

Output Path: Organism|Bone|Interstitial|TRANS|Concentration in container

Output 'Organism|Bone|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|Brain|Plasma|TRANS|Concentration in container

Output 'Organism|Brain|Plasma|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_-AllActiveProcesses' defined in 'Sim'

Deviation: 0

$Output\ Path:\ Organism|Fat|Interstitial|TRANS|Concentration\ in\ container$

 $\label{lem:container} Output \ 'Organism|Fat|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_-MultipleIV_AllActiveProcesses' defined in 'Sim'$

Deviation: 0

Output Path: Organism|Gonads|Interstitial|TRANS|Concentration in container

Output 'Organism|Gonads|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

$Output\ Path:\ Organism | Heart | Interstitial | TRANS | Concentration\ in\ container$

 $\label{lem:container} Output \ 'Organism|Heart|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_-MultipleIV_AllActiveProcesses' defined in 'Sim' \\$

Output Path: Organism|Kidney|Interstitial|TRANS|Concentration in container

Output 'Organism|Kidney|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_-MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|Stomach|Interstitial|TRANS|Concentration in container

Output 'Organism|Stomach|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|SmallIntestine|Interstitial|TRANS|Concentration in container

Output 'Organism|SmallIntestine|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|LargeIntestine|Interstitial|TRANS|Concentration in container

Output 'Organism|LargeIntestine|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|Liver|Periportal|Interstitial|TRANS|Concentration in container

Output 'Organism|Liver|Periportal|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|Liver|Pericentral|Interstitial|TRANS|Concentration in container

Output 'Organism|Liver|Pericentral|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|Lung|Interstitial|TRANS|Concentration in container

Output 'Organism|Lung|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_- ${\bf Multiple IV_All Active Processes'\ defined\ in\ 'Sim'}$

Deviation: 0

Output Path: Organism|Muscle|Interstitial|TRANS|Concentration in container

Output 'Organism|Muscle|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_-MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|Pancreas|Interstitial|TRANS|Concentration in container

Output 'Organism|Pancreas|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_MultipleIV_AllActiveProcesses' defined in 'Sim'

$Output\ Path:\ Organism|Skin|Interstitial|TRANS|Concentration\ in\ container$

Output 'Organism|Skin|Interstitial|TRANS|Concentration in container' is missing from simulation 'Human_-MultipleIV_AllActiveProcesses' defined in 'Sim'

Deviation: 0

Output Path: Organism|Spleen|Interstitial|TRANS|Concentration in container

 $Output \ 'Organism | Spleen | Interstitial | TRANS | Concentration in container' is missing from simulation 'Human_-Multiple IV_All Active Processes' defined in 'Sim' \\$

Deviation: 0

Output Path: Organism|Brain|Interstitial|drug|Concentration in container

Deviation for 'Organism|Brain|Interstitial|drug|Concentration in container' is 2.83E+6% and is greater than the allowed max. tolerance of 2.00%

Deviation: 28285.35

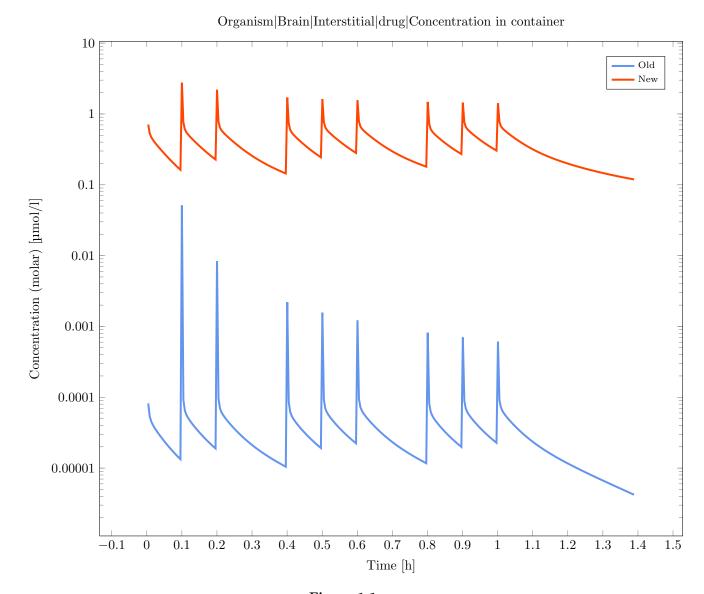


Figure 1.1

Organism|Brain|Interstitial|drug|Concentration in container 3 Old 2.8 New 2.6 2.4 2.2 2 Concentration (molar) [µmol/1] 1.8 1.6 1.4 1.2 1 0.8 0.6 0.40.2 0 -0.20.1 0.20.3 0.4 0.50.60.7 0.8 0.9 1.1 1.2 1.3 -0.10 1.5 Time [h]

Figure 1.2

Simulation: Human_MultipleIV_transporters-Human_MultipleIV_transporters

Result of the validation: Invalid Absolute Tolerance: 1.00E-10 Relative Tolerance: 1.00E-5

Output Path: Organism|Bone|Intracellular|TRANS1|Concentration in container

Output 'Organism|Bone|Intracellular|TRANS1|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_transporters'

Deviation: 0

Output Path: Organism|Fat|Intracellular|TRANS1|Concentration in container

Output 'Organism|Fat|Intracellular|TRANS1|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_transporters'

Output Path: Organism|Gonads|Intracellular|TRANS1|Concentration in container

 $Output \ 'Organism|Gonads|Intracellular|TRANS1|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_Multiple IV_transporters'$

Deviation: 0

Output Path: Organism|Heart|Intracellular|TRANS1|Concentration in container

 $Output \ 'Organism|Heart|Intracellular|TRANS1|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined in 'Human_Multiple IV_transporters'$

Deviation: 0

$Output\ Path:\ Organism | Kidney | Intracellular | TRANS1 | Concentration\ in\ container$

 $Output \ 'Organism|Kidney|Intracellular|TRANS1|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_Multiple IV_transporters'$

Deviation: 0

$Output\ Path:\ Organism | Stomach | Intracellular | TRANS1 | Concentration\ in\ container$

Output 'Organism|Stomach|Intracellular|TRANS1|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_transporters'

Deviation: 0

Output Path: Organism|SmallIntestine|Intracellular|TRANS1|Concentration in container

Output 'Organism|SmallIntestine|Intracellular|TRANS1|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_transporters'

Deviation: 0

Output Path: Organism|LargeIntestine|Intracellular|TRANS1|Concentration in container

 $Output \ 'Organism | Large Intestine | Intracellular | TRANS1 | Concentration in container' is missing from simulation 'Sim' defined in 'Human_Multiple IV_transporters'$

Deviation: 0

Output Path: Organism|Liver|Periportal|Intracellular|TRANS1|Concentration in container

 $Output \ 'Organism|Liver|Periportal|Intracellular|TRANS1|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_MultipleIV_transporters'$

Deviation: 0

Output Path: Organism|Liver|Pericentral|Intracellular|TRANS1|Concentration in container

Output 'Organism|Liver|Pericentral|Intracellular|TRANS1|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_transporters'

Deviation: 0

Output Path: Organism|Lung|Intracellular|TRANS1|Concentration in container

 $Output \ 'Organism | Lung| Intracellular | TRANS1| Concentration in container' is missing from simulation 'Sim' defined in 'Human_Multiple IV_transporters'$

$Output\ Path:\ Organism | Muscle | Intracellular | TRANS1 | Concentration\ in\ container$

 $Output \ 'Organism|Muscle|Intracellular|TRANS1|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_Multiple IV_transporters'$

Deviation: 0

Output Path: Organism|Pancreas|Intracellular|TRANS1|Concentration in container

 $Output \ 'Organism|Pancreas|Intracellular|TRANS1|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Sim' \ defined \ in \ 'Human_Multiple IV_transporters'$

Deviation: 0

$Output\ Path:\ Organism | Skin | Intracellular | TRANS1 | Concentration\ in\ container$

 $Output \ 'Organism | Skin | Intracellular | TRANS1 | Concentration in container' is missing from simulation 'Sim' defined in 'Human_Multiple IV_transporters'$

Deviation: 0

$Output\ Path:\ Organism | Spleen | Intracellular | TRANS1 | Concentration\ in\ container$

Output 'Organism|Spleen|Intracellular|TRANS1|Concentration in container' is missing from simulation 'Sim' defined in 'Human_MultipleIV_transporters'

Deviation: 0

Output Path: Organism|Bone|Interstitial|TRANS1|Concentration in container

Output 'Organism|Bone|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human_MultipleIV_transporters' defined in 'Sim'

Deviation: 0

Output Path: Organism|Fat|Interstitial|TRANS1|Concentration in container

Output 'Organism|Fat|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human-Multiple IV_transporters' defined in 'Sim'

Deviation: 0

Output Path: Organism|Gonads|Interstitial|TRANS1|Concentration in container

 $Output \ 'Organism|Gonads|Interstitial|TRANS1|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Human_Multiple IV_transporters' \ defined \ in \ 'Sim'$

Deviation: 0

Output Path: Organism|Heart|Interstitial|TRANS1|Concentration in container

Output 'Organism|Heart|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human_MultipleIV_transporters' defined in 'Sim'

Deviation: 0

Output Path: Organism|Kidney|Interstitial|TRANS1|Concentration in container

 $Output \ 'Organism|Kidney|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human-Multiple IV_transporters' defined in 'Sim'$

$Output\ Path:\ Organism | Stomach | Interstitial | TRANS1 | Concentration\ in\ container$

 $Output \ 'Organism|Stomach|Interstitial|TRANS1|Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Human_Multiple IV_transporters' \ defined \ in \ 'Sim'$

Deviation: 0

Output Path: Organism|SmallIntestine|Interstitial|TRANS1|Concentration in container

 $Output \ 'Organism | Small Interstitial | TRANS1 | Concentration \ in \ container' \ is \ missing \ from \ simulation \ 'Human_Multiple IV_transporters' \ defined \ in \ 'Sim'$

Deviation: 0

Output Path: Organism|LargeIntestine|Interstitial|TRANS1|Concentration in container

Output 'Organism|LargeIntestine|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human_MultipleIV_transporters' defined in 'Sim'

Deviation: 0

$Output\ Path:\ Organism | Liver | Periportal | Interstitial | TRANS1 | Concentration\ in\ container$

 $Output \ 'Organism | Liver | Periportal | Interstitial | TRANS1 | Concentration in container' is missing from simulation 'Human_Multiple IV_transporters' defined in 'Sim' \\$

Deviation: 0

Output Path: Organism|Liver|Pericentral|Interstitial|TRANS1|Concentration in container

Output 'Organism|Liver|Pericentral|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human_MultipleIV_transporters' defined in 'Sim'

Deviation: 0

Output Path: Organism|Lung|Interstitial|TRANS1|Concentration in container

Output 'Organism|Lung|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human-Multiple IV_transporters' defined in 'Sim'

Deviation: 0

Output Path: Organism|Muscle|Interstitial|TRANS1|Concentration in container

 $Output \ 'Organism | Muscle | Interstitial | TRANS1 | Concentration in container' is missing from simulation 'Human_-Multiple IV_transporters' defined in 'Sim' \\$

Deviation: 0

Output Path: Organism|Pancreas|Interstitial|TRANS1|Concentration in container

Output 'Organism|Pancreas|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human_MultipleIV_transporters' defined in 'Sim'

Deviation: 0

Output Path: Organism|Skin|Interstitial|TRANS1|Concentration in container

Output 'Organism|Skin|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human_Multiple IV_transporters' defined in 'Sim'

$Output\ Path:\ Organism | Spleen | Interstitial | TRANS1 | Concentration\ in\ container$

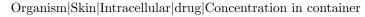
Output 'Organism $|Spleen|Interstitial|TRANS1|Concentration in container' is missing from simulation 'Human_Multiple IV_transporters' defined in 'Sim'$

Deviation: 0

Output Path: Organism|Skin|Intracellular|drug|Concentration in container

Deviation for 'Organism|Skin|Intracellular|drug|Concentration in container' is 589.08% and is greater than the allowed max. tolerance of 2.00%

Deviation: 5.89



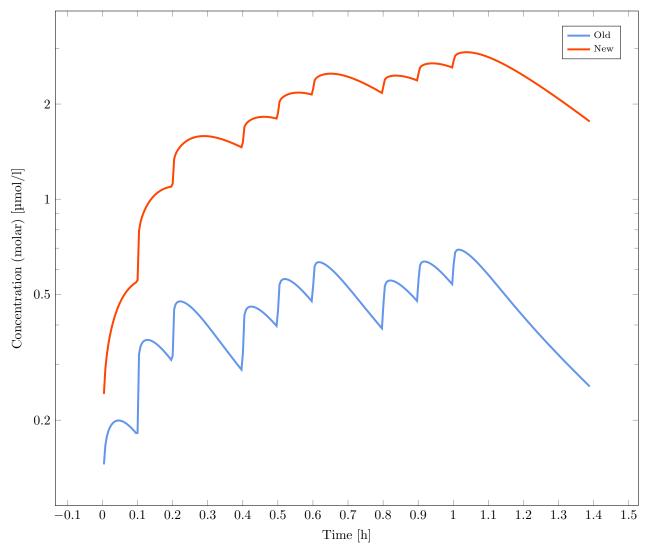


Figure 1.3

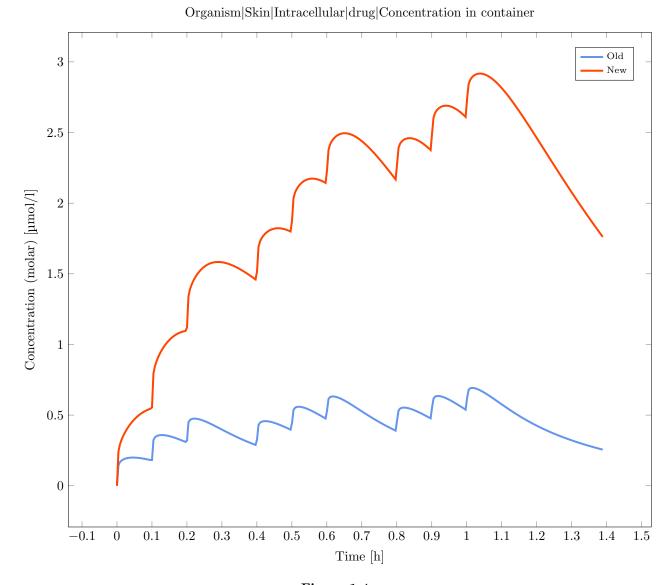


Figure 1.4

Simulation: Test 18.1_I2_C3_A1_Config2-Test 18.1_I2_C3_A1_Config2

Result of the validation: Invalid Absolute Tolerance: 1.00E-12 Relative Tolerance: 1.00E-7

Output Path: Organism|Kidney|Plasma|C3|Concentration in container

 $Deviation \ for \ 'Organism|Kidney|Plasma|C3|Concentration \ in \ container' \ is \ 3.12E+9\% \ and \ is \ greater \ than \ the$

allowed max. tolerance of 2.00%

Deviation: 3.12E+7

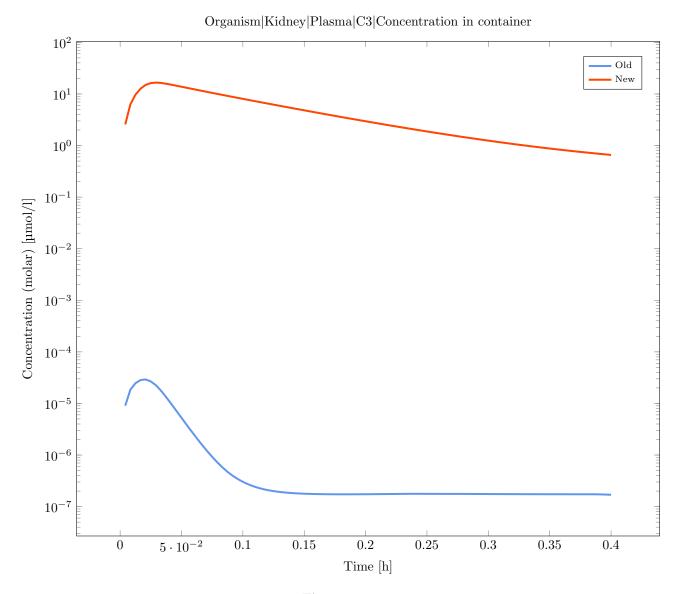


Figure 1.5

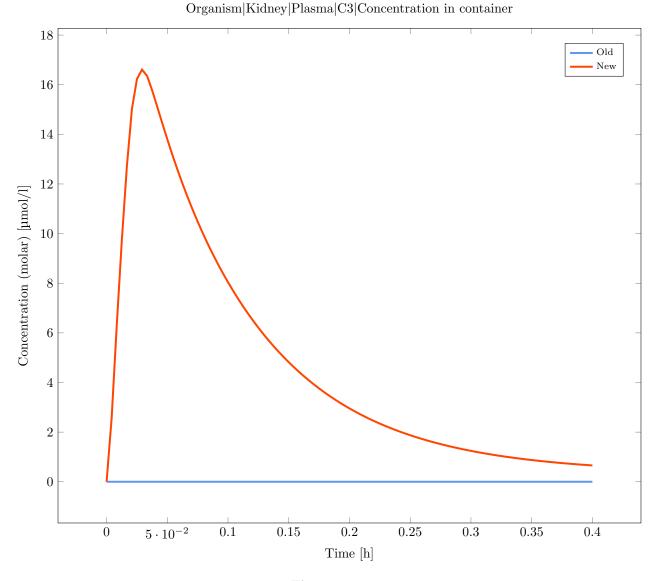


Figure 1.6

Simulation: Test 18.1_I3_C3_A3_Config2-Test 18.1_I3_C3_A3_Config2

Result of the validation: Invalid Absolute Tolerance: 1.00E-10 Relative Tolerance: 1.00E-5

Output Path: Organism|Kidney|Plasma|C3|Concentration in container

Deviation for 'Organism|Kidney|Plasma|C3|Concentration in container' is 1.86E+9% and is greater than the

allowed max. tolerance of 2.00%

Deviation: 1.86E+7

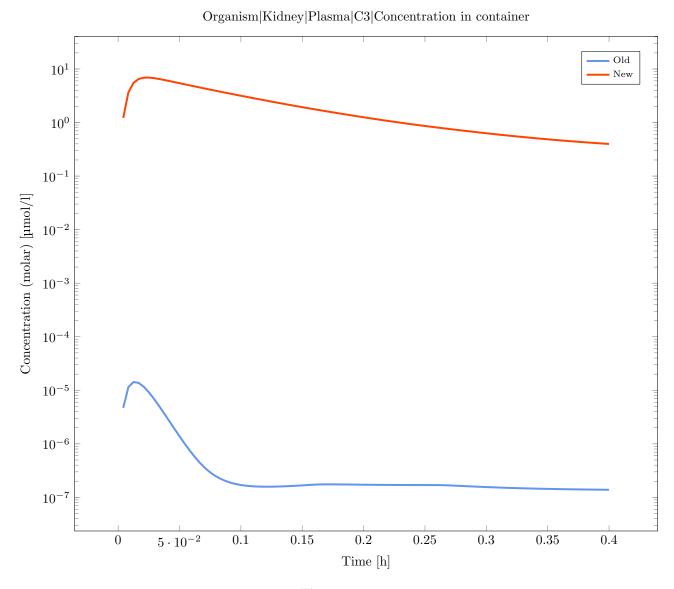


Figure 1.7

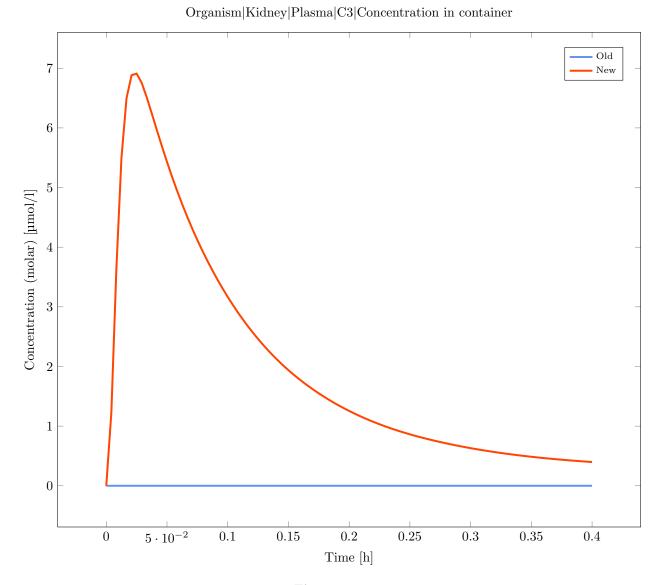


Figure 1.8

1.1.2 Valid Simulations (108/112)

 $Simulation: Beagle_SingleORAL_Dissolved-Beagle_SingleORAL_Dissolved$

Result of the validation: Valid

 $Simulation: Beagle_SingleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

 $Simulation: Beagle_SingleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-$

Simulation: Dog_MultiORAL_12_12_Dissolved-Dog_MultiORAL_12_12_Dissolved

Result of the validation: Valid

 $Simulation: \ Dog_MultiORAL_24_Dissolved-Dog_MultiORAL_24_Dissolved$

Result of the validation: Valid

Simulation: European_SingleORAL_Age_0_CYP3A4-European_SingleORAL_Age_0_CYP3A4

Result of the validation: Valid

Simulation: European_SingleORAL_Age_0_GFR-European_SingleORAL_Age_0_GFR

Result of the validation: Valid

Simulation: European_SingleORAL_Age_1_CYP3A4-European_SingleORAL_Age_1_CYP3A4

Result of the validation: Valid

 $Simulation: European_SingleORAL_Age_1_GFR-European_SingleORAL_Age_1_GFR$

Result of the validation: Valid

Simulation: Human_CompetitiveInhibition-Human_CompetitiveInhibition

Result of the validation: Valid

 ${\bf Simulation: \ Human_Irreversible Inhibition-Human_Irreversible Inhibition}$

Result of the validation: Valid

Simulation: Human_MixedInhibition-Human_MixedInhibition

Result of the validation: Valid

 $Simulation: \ Human_MultiIV_6_6_12-Human_MultiIV_6_6_12$

Result of the validation: Valid

Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved

Result of the validation: Valid

Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_absorption_-

sink_conditions

Result of the validation: Valid

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-$

continuous_fraction_0.5

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_12_Dissolved_EHC_-12_Dissolved_EHC_$ continuous_fraction_1

Result of the validation: Valid

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKa-12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKa-12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKa-12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKa-12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKa-12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_12_Dissolved_pKa-12_D$

dependent penalty factor Result of the validation: Valid

Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_solubility

Result of the validation: Valid

 $Simulation: \ Human_NonCompetitiveInhibition-Human_NonCompetitiveInhibition$

Result of the validation: Valid

Simulation: Human_SingleIV_Configuration-Human_SingleIV_Configuration

Result of the validation: Valid

Simulation: Human_SingleIV-Human_SingleIV

Result of the validation: Valid

Simulation: Human_SingleIV-Human_SingleIV_MW_200_fu_0.2_LogP_5

Result of the validation: Valid

 $Simulation: \ Human_SingleIV-Human_SingleIV_MW_800_fu_0.6_LogP_-5$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance-Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance-Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverPlasmaClearance_KidneyPlasmaClearance_Human_SingleORAL_Dissolved_LiverSingleOR$

 $Single ORAL_Dissolved_Liver Plasma Clearance_Kidney Plasma Clearance$

Result of the validation: Valid

 $Simulation: Human_Single ORAL_Dissolved_Liver Plasma Clearance_Kidney Plasma Clearance-Human_Single ORAL_Dissolved_Liver Plasma Clearance_Kidney Plasma Clearance-Human_Single ORAL_Dissolved_Liver Plasma Clearance_Kidney Plasma Clearance-Human_Single ORAL_Dissolved_Liver Plasma Clearance_Kidney Plasma Clearance_Human_Single ORAL_Dissolved_Liver Plasma Clearance_ManaGar$ $Single ORAL_D is solved_Liver Plasma Clearance_Kidney Plasma Clearance_MW_200_fu_0.2_Log P_5$

Result of the validation: Valid

 $Simulation: Human_Single ORAL_Dissolved_Liver Plasma Clearance_Kidney Plasma Clearance-Human_single ORAL_Dissolved_Liver Plasma Clearance_Kidney Plasma Clearance_Kidn$

 $Single ORAL_Dissolved_Liver Plasma Clearance_Kidney Plasma Clearance_MW_800_fu_0.6_Log P_-5$

Result of the validation: Valid

Simulation: Human_SingleORAL_Dissolved-Human_SingleORAL_Dissolved

 $Simulation: Human_SingleORAL_Dissolved_Human_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-Lo$

 $\mathbf{5}$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Dissolved_Human_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-RAL_Dissolved_MW_800$

-5

Result of the validation: Valid

Simulation: Human_SingleORAL_Lint80_AsSuspention-Human_SingleORAL_Lint80_AsSuspention

Result of the validation: Valid

Simulation: Human_SingleORAL_Lint80-Human_SingleORAL_Lint80

Result of the validation: Valid

 $Simulation: Human_SingleORAL_MonoParticles_AsSuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_Si$

AsSuspention

Result of the validation: Valid

Simulation: Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_-

 $PolyParticlesLogNormal_AsSuspention$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNo$

AsSuspention

Result of the validation: Valid

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNo$

 ${\bf As Suspention_dissolved_radius}$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_Assuspention-Human_SingleORAL_PolyParticlesNormal_SingleORAL_PolyParticlesNormal_SingleORAL_Pol$

 $As Suspention_treat_precipated_drug_as_soluble$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention_-Incomplete the state of the sta$

 $MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention_-Included and the property of the pr$

 $MW_800_fu_0.6_LogP_-5$

 $Simulation: \ Human_SingleORAL_Weibull-Human_SingleORAL_Weibull$

Result of the validation: Valid

Simulation: Human_SingleORAL_Weibull-Human_SingleORAL_Weibull_MW_200_fu_0.2_LogP_5

Result of the validation: Valid

Simulation: Human_SingleORAL_Weibull-Human_SingleORAL_Weibull_MW_800_fu_0.6_LogP_-

 $\mathbf{5}$

Result of the validation: Valid

 ${\bf Simulation: Human_Uncompetitive Inhibition-Human_Uncompetitive Inhibition}$

Result of the validation: Valid

 $Simulation: \ Minipig_SingleORAL_Dissolved-Minipig_SingleORAL_Dissolved$

Result of the validation: Valid

Simulation: Minipig_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-

 $\mathbf{5}$

Result of the validation: Valid

Simulation: Minipig_SingleORAL_Dissolved-Minipig_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-

-5

Result of the validation: Valid

 $Simulation: Monkey_SingleORAL_Dissolved-Monkey_SingleORAL_Dissolved$

Result of the validation: Valid

 $Simulation: Monkey_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-logP$

5

Result of the validation: Valid

 $Simulation: Monkey_SingleORAL_Dissolved_MOnkey_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-Incomplete the control of the contro$

-5

Result of the validation: Valid

 $Simulation: \ Mouse_SingleORAL_Dissolved-Mouse_SingleORAL_Dissolved$

Result of the validation: Valid

 $Simulation: Mouse_SingleORAL_Dissolved_Mouse_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-Incomplete SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-Incomplete SingleORAL_Dissolved_MW_200_Dissolved_MW_200_Dissolved_MW_200_Dissolved_MW_$

5

 $Simulation: Mouse_SingleORAL_Dissolved_Mouse_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-_gradering to the control of the contr$

Result of the validation: Valid

Result of the validation: Valid

Result of the validation: Valid

 $Simulation: Preterm_SingleIV_Age_15_GA_32_CYP3A4-Preterm_SingleIV_Age_15_CYP3A4-Prete$

Result of the validation: Valid

 $Simulation: \ Preterm_SingleIV_Age_15_GA_32_GFR-Preterm_SingleIV_Age_15_GA_32_GFR$

Result of the validation: Valid

 $Simulation: Rabbit_SingleORAL_Dissolved-Rabbit_SingleORAL_Dissolved$

Result of the validation: Valid

 $Simulation: Rabbit_SingleORAL_Dissolved_Rabbit_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-Rabbit_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-Rabbit_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-Rabbit_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-Rabbit_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-Rabbit_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-Rabbit_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-Rabbit_SingleORAL_Dissolved_MW_200_Fu_0.2_LogP_-Rabbit_SingleORAL_Dissolved_MW_200_F$

5

Result of the validation: Valid

 $Simulation: Rabbit_SingleORAL_Dissolved_Rabbit_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-Income Simulation: Rabbit_SingleORAL_Dissolved_Rabbi$

-5

Result of the validation: Valid

 $Simulation: Rat_MultiORAL_6_6_12_Dissolved-Rat_MultiORAL_6_6_12_Dissolved$

Result of the validation: Valid

Simulation: Rat_MultiORAL_6_6_6_6_Dissolved-Rat_MultiORAL_6_6_6_6_Dissolved

Result of the validation: Valid

Simulation: Rat_MultiORAL_8_8_8_Dissolved-Rat_MultiORAL_8_8_8_Dissolved

Result of the validation: Valid

 $Simulation: Single IV_2 Pores_Human-Single IV_2 Pores_Human$

Result of the validation: Valid

Simulation: SingleIV_2Pores_Human_SingleIV_2Pores_Human_SimulationC

 $Simulation: Single IV_2 Pores_Human_Single IV_2 Pores_Human_Simulation D$

Result of the validation: Valid

 $Simulation: Single IV_2 Pores_Human_Single IV_2 Pores_Human_Simulation F$

Result of the validation: Valid

Simulation: SingleIV_2Pores_Monkey-SingleIV_2Pores_Monkey

Result of the validation: Valid

Simulation: SingleIV_2Pores_Monkey_SingleIV_2Pores_Monkey_SimulationG

Result of the validation: Valid

Simulation: SingleIV_2Pores_Monkey_SingleIV_2Pores_Monkey_SimulationH

Result of the validation: Valid

 $Simulation: Single IV_2 Pores_Mouse-Single IV_2 Pores_Mouse$

Result of the validation: Valid

 $Simulation: Single IV_2 Pores_Mouse_Single IV_2 Pores_Mouse_Simulation A$

Result of the validation: Valid

 $Simulation: Single IV_2 Pores_Mouse_Single IV_2 Pores_Mouse_Simulation B$

Result of the validation: Valid

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse_SimulationE

Result of the validation: Valid

 $Simulation: Single IV_C1_4 Comp_standard_stand$

standard

Result of the validation: Valid

 $Simulation: Single IV_C2_4 Comp_PT_standard_st$

Result of the validation: Valid

 $Simulation: Single IV_C2_4 Comp_RR_standard_st$

Result of the validation: Valid

 $Simulation: Single IV_C2_4 Comp_standard_schmitt_standard_Single IV_C2_4 Comp_standard_schmitt_schmittschmitt_schmitt$

standard

 $Simulation: Single IV_C3_4 Comp_RR_schmitt_standard-Single IV_C3_schmitt_standard-Single IV_C3_schmitt$

 $Simulation: Single IV_C3_4 Comp_standard_schmittnorm lized_standard-Single IV_C3_4 Comp_standard_schmittnorm lized_standard$

Result of the validation: Valid

 $Simulation: Single IV_C4_2 Pores_RR_standard_s$

Result of the validation: Valid

 $Simulation: Single IV_C4_4 Comp_Ber_standard_s$

Result of the validation: Valid

 $Simulation: Single IV_C5_2 Pores_Ber_standard_$

Result of the validation: Valid

 $Simulation: Single IV_C5_2 Pores_PT_standard_s$

Result of the validation: Valid

 $Simulation: Single IV_C5_2 Pores_RR_schmitt_standard-Single IV_C5_2 Pores_schmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_standard-Single IV_SChmitt_Schmit$

Result of the validation: Valid

 $Simulation: Single IV_C6_2 Pores_standard_stan$

standard

Result of the validation: Valid

 $Simulation: Single IV_C7_2 Pores_standard_schmitt_standard_Single IV_C7_2 Pores_standard_schmitt_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_schmitts_sc$

standard

Result of the validation: Valid

 $Simulation: Single IV_C7_4 Comp_schmitt_standard_standa$

standard

Result of the validation: Valid

 $Simulation: Single IV_C8_2 Pores_standard_schmittnormalized_standard_Single IV_C8_2 Pores_standard_schmittnormalized_standard_Single IV_C8_2 Pores_standard_schmittnormalized_standard_schmittnormalized_standard_schmittnormalized_standard_schmittnormalized_standard_schmittnormalized_standard_schmittnormalized_standard_schmittnormalized_standard_schmittnormalized_standard_schmittnormalize$

 $schmittnormalized_standard$

Result of the validation: Valid

 $Simulation: Single IV_C9_2 Pores_schmitt_standard_standard_Single IV_C9_2 Pores_schmitt_standard_sta$

standard

 $Simulation: Single ORAL_C10_4 Comp_PT_standard_standard-Single ORAL_C10_4 Comp_PT_standard-Single ORAL_C10_4 Comp_PT_standard-Single ORAL_C10_4 Comp_Single ORAL_C10_4 C00_4 C0$

Result of the validation: Valid

 $Simulation: Single ORAL_C11_4 Comp_schmitt_standard_sta$

Result of the validation: Valid

 $Simulation: Single ORAL_C11_4 Comp_standard_st$

Result of the validation: Valid

 $Simulation: Single ORAL_C12_4 Comp_standard_schmitt_standard-Single ORAL_C12_4 Comp_standard_schmitt_standard\\$

Result of the validation: Valid

 $Simulation: Single ORAL_C13_2 Pores_schmitt_standard_standard_Single ORAL_C13_2 Pores_schmitt_standard_standa$

Result of the validation: Valid

 $Simulation: Single ORAL_C13_4 Comp_standard_schmittnormalized_schmittnormalized_schmittnorm$

Result of the validation: Valid

 $Simulation: Single ORAL_C14_2 Pores_PT_standard_standard_Single ORAL_C14_2 Pores_PT_standard_standar$

Result of the validation: Valid

 $Simulation: Single ORAL_C2_2 Pores_standard_st$

Result of the validation: Valid

 $Simulation: Single ORAL_C3_2 Pores_standard_schmitt_standard-Single ORAL_C3_2 Pores_standard_schmitt_standard$

Result of the validation: Valid

 $Simulation: Single ORAL_C4_2 Pores_standard_schmittnormalized_standard_Single ORAL_C4_2 Pores_standard_schmittnormalized_schmittnormalized_schmittnormaliz$

Result of the validation: Valid

 $Simulation: Single ORAL_C6_4 Comp_Ber_standard_standard_Single ORAL_C6_4 Comp_Ber_standard_$

 $Simulation: Single ORAL_C6_4 Comp_RR_standard_standard_Single ORAL_C6_4 Comp_RR_standard_st$

Result of the validation: Valid

 $Simulation: Single ORAL_C7_2 Pores_Ber_standard_standard_Single ORAL_C7_2 Pores_Ber_standard_standar$

Result of the validation: Valid

 $Simulation: Single ORAL_C7_4 Comp_RR_schmitt_standard-Single ORAL_C7_5 Comp_RR_schmitt_standard-Single ORAL_C7_5$

Result of the validation: Valid

 $Simulation: Single ORAL_C8_2 Pores_RR_standard_standard_Single ORAL_C8_2 Pores_RR_standard_$

Result of the validation: Valid

 $Simulation: Single ORAL_C9_2 Pores_RR_schmitt_standard-Single ORAL_C9_2 Pores_schmitt_standard-Single ORAL_c9_2 Pores_schmitt_schmitt_standard-Single ORAL_c9_2 Pores_schmitt_sc$

Result of the validation: Valid

Simulation: Test 18.1_I1_C1_A1_Config1-Test 18.1_I1_C1_A1_Config1

Result of the validation: Valid

Simulation: Test $18.1_I2_C1_A1_Config2$ -Test $18.1_I2_C1_A1_Config2$