Open Systems Pharmacology Suite - 10 Folder Comparison

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Chapter 1

Folder Comparison Results

Overall Comparison Result: Invalid Number of Compared Files: 146

1.1 Comparison Results

Overall Comparison Result Invalid

Old Folder

 $D:\Outputs_9.1$

New Folder

D:\Outputs_10.0

Using exclusions

- **|Interstitial|P-gp|**
- **|Intracellular|P-gp|**
- **|Plasma|OATP1B1|**
- **|Interstitial|OATP1B1|**
- **|Intracellular|OATP1B1|**
- **|Plasma|TRANS|**
- **|Interstitial|TRANS|**
- **|Intracellular|TRANS|**

Invalid Simulations (16/146)

 $Simulation: \ DDI_Multiple Combinations-05_MM_Mechanism based_Mechanism based$

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

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

Deviation for 'Organism|Liver|Periportal|Interstitial|Erythromycin|Concentration in container' is 45.33% and is

greater than the allowed max. tolerance of 3.00%

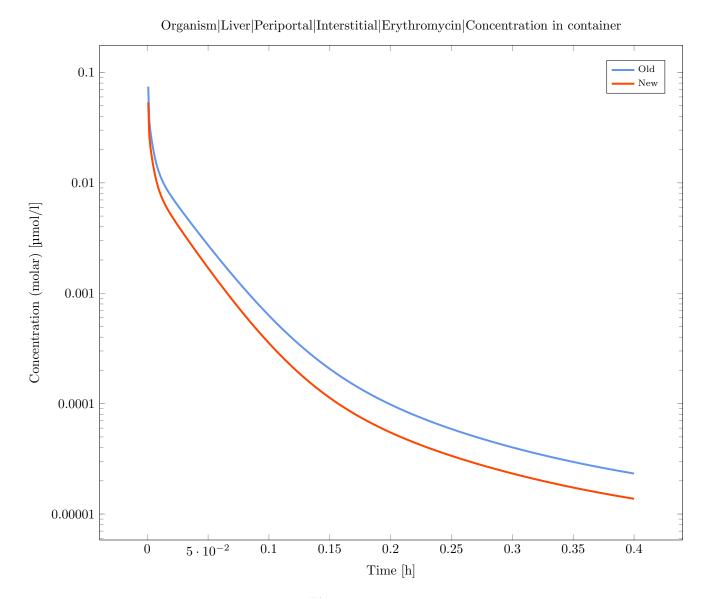
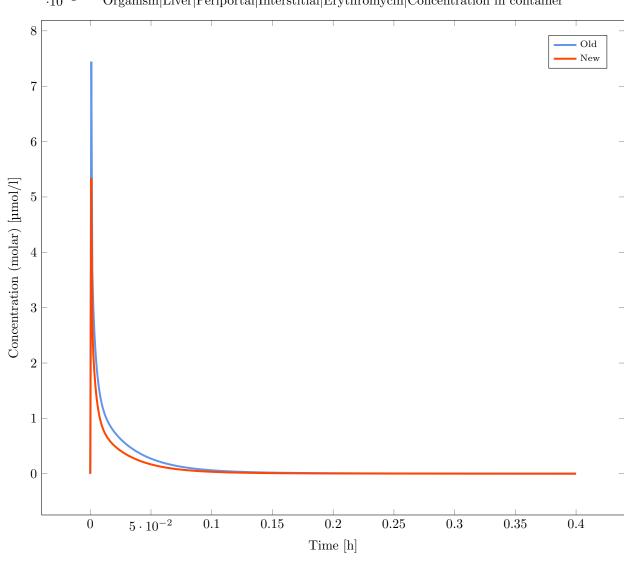


Figure 1.1



 $\cdot 10^{-2}$ Organism|Liver|Periportal|Interstitial|Erythromycin|Concentration in container

Figure 1.2

$Simulation: \ DDI_Multiple Combinations-06_MM_Induction_Induction$

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

Output Path: Organism|Lumen|ColonDescendens|Rifampicin|Fraction of oral drug mass absorbed into mucosa segment

Deviation for 'Organism|Lumen|ColonDescendens|Rifampicin|Fraction of oral drug mass absorbed into mucosa segment' is 1122.72% and is greater than the allowed max. tolerance of 3.00%

Deviation: 11.23

 $Organism | Lumen | Colon Descendens | Rifampicin | Fraction of oral drug \ mass \ absorbed \ into \ mucos a segment$

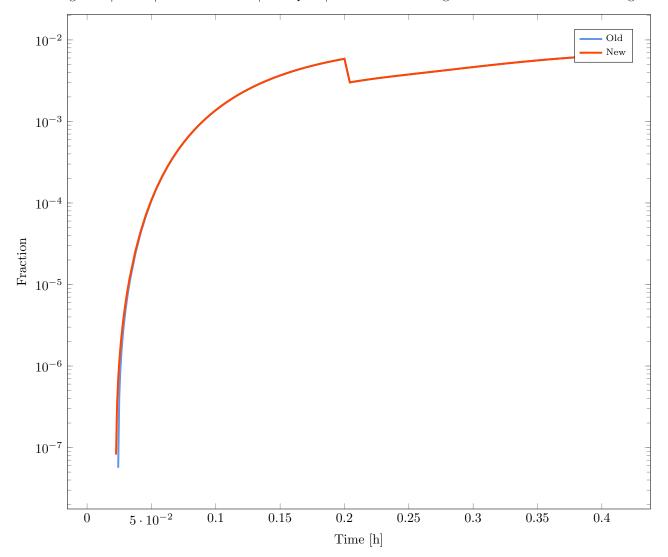


Figure 1.3

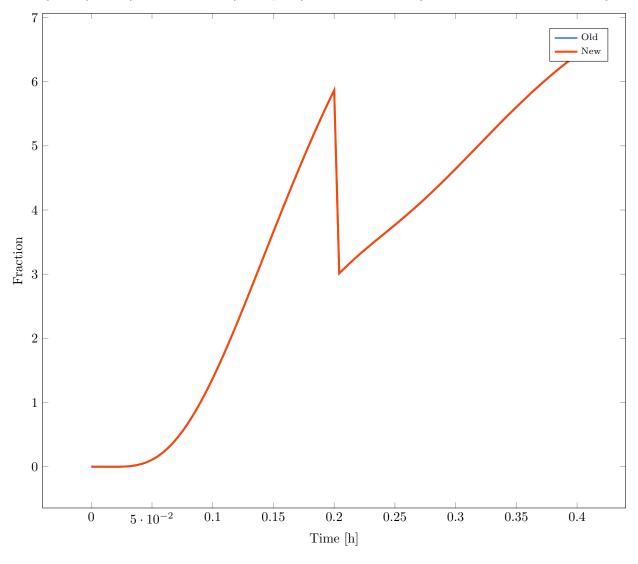


Figure 1.4

 $Simulation: DDI_MultipleCombinations-07_MM_Competitive_Competitive_Mechanism based_Mechanism based_Mechanism$

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

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

Deviation for 'Organism|Liver|Periportal|Interstitial|Erythromycin|Concentration in container' is 56.47% and is

greater than the allowed max. tolerance of 3.00%

$Organism|Liver|Periportal|Interstitial|Erythromycin|Concentration\ in\ container$

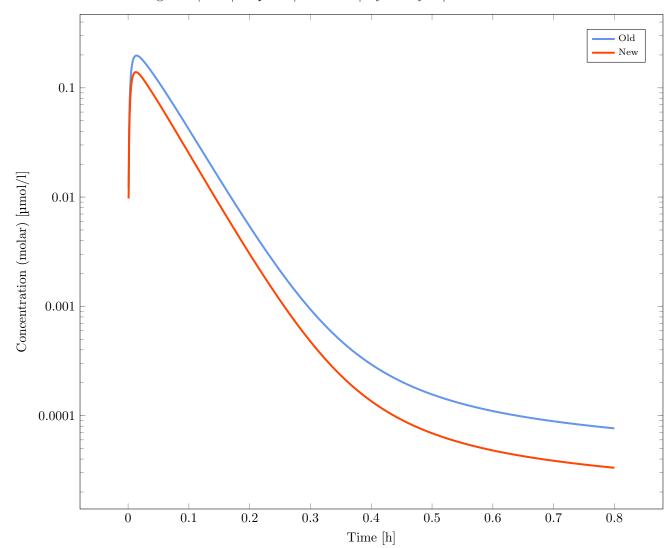
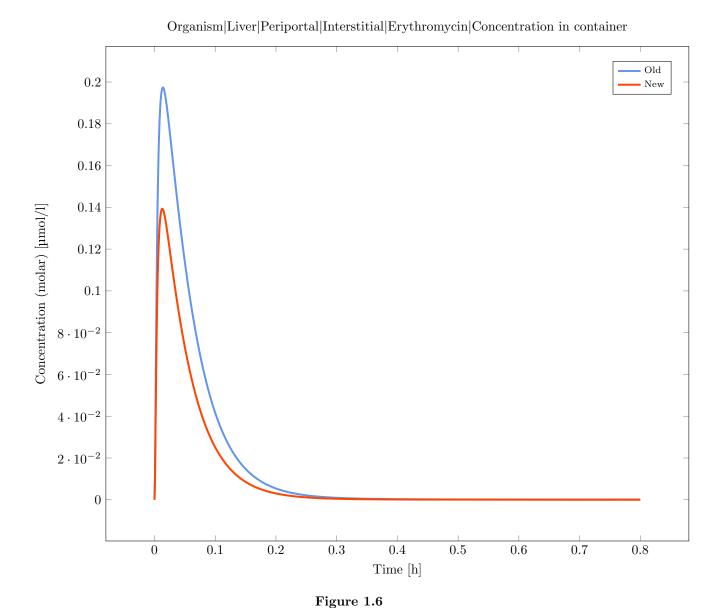


Figure 1.5



$Simulation: \ DDI_Multiple Combinations - 08_MM_Uncompetitive_Uncompetitive_Mechanism based_Mechanism based$

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

$Output\ Path:\ Organism|Liver|Periportal|Interstitial|MechanismBased_4|Concentration\ in\ container$

Deviation for 'Organism|Liver|Periportal|Interstitial|MechanismBased_4|Concentration in container' is 49.46% and is greater than the allowed max. tolerance of 3.00%

$Organism|Liver|Periportal|Interstitial|MechanismBased_4|Concentration\ in\ container$

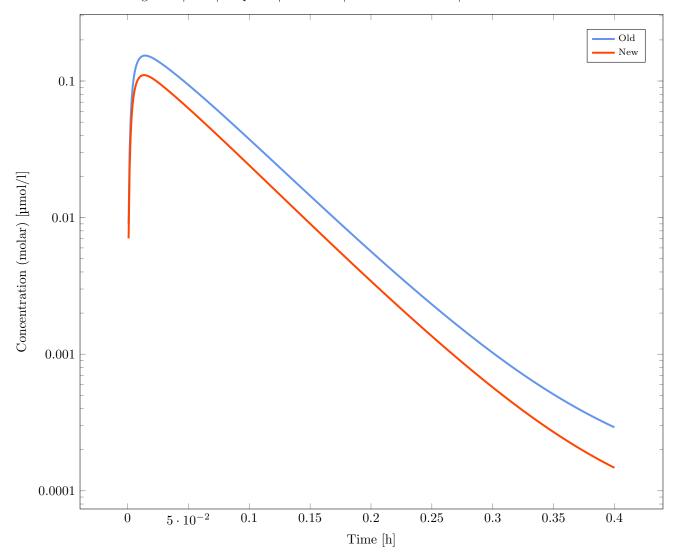
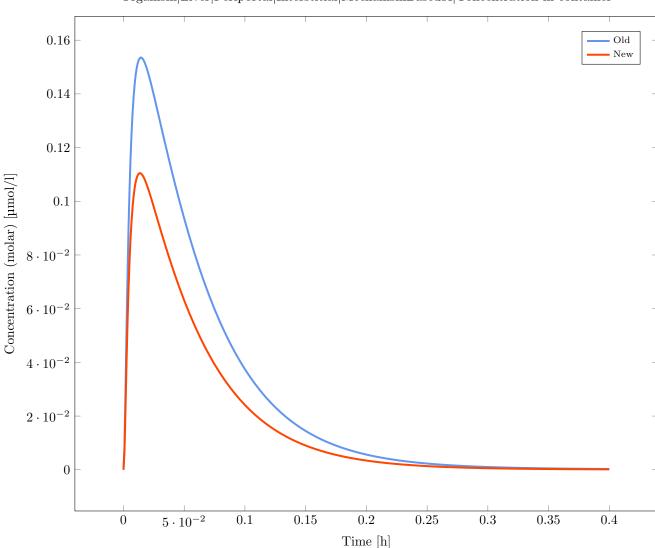


Figure 1.7



Organism|Liver|Periportal|Interstitial|MechanismBased_4|Concentration in container

Figure 1.8

$Simulation: \ DDI_Multiple Combinations - 09_MM_Noncompetitive_Noncompetitive_Mechanism based_-incompetitive_Noncompetitive_Mechanism based_-incompetitive_Noncompetitive$ Mechanismbased

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

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

 $Deviation \ for \ 'Organism | Liver | Periportal | Interstitial | Erythromycin | Concentration \ in \ container' \ is \ 39.95\% \ and \ is$ greater than the allowed max. tolerance of 3.00%

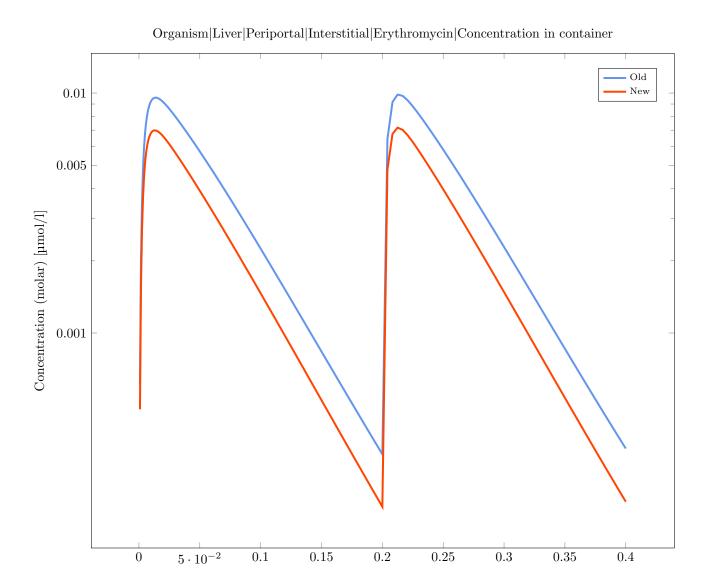
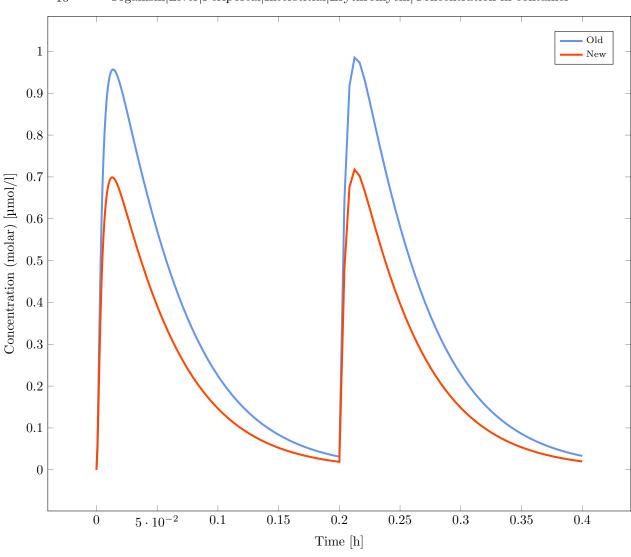


Figure 1.9

Time [h]



 $\cdot 10^{-2}$ Organism|Liver|Periportal|Interstitial|Erythromycin|Concentration in container

Figure 1.10

 $Simulation: DDI_Multiple Combinations - 10_MM_Mixed_Mechanism based_Mechanism based_Mechanis$

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

Output Path: Organism|Liver|Periportal|MechanismBased_3|Interstitial Unbound

 $Deviation for 'Organism | Liver | Periportal | Mechanism Based_3 | Interstitial \ Unbound' is 48.79\% \ and is greater \ than linear terms of the periportal of the periporta$

the allowed max. tolerance of 3.00%

$Organism | Liver | Periportal | Mechanism Based_3 | Interstitial \ Unbound$

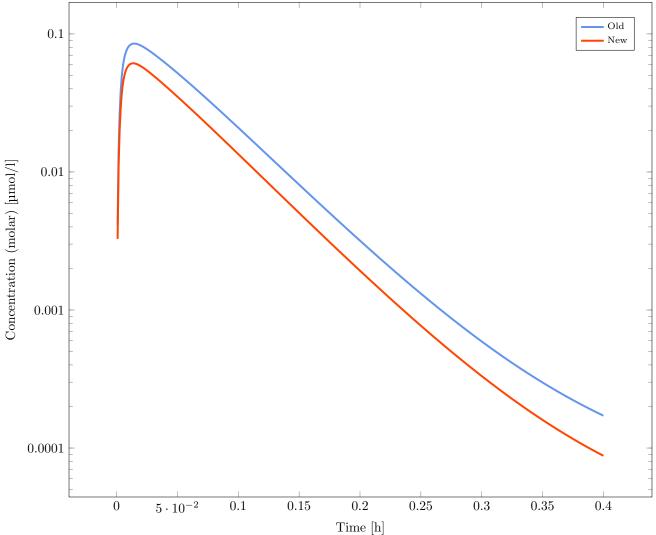


Figure 1.11

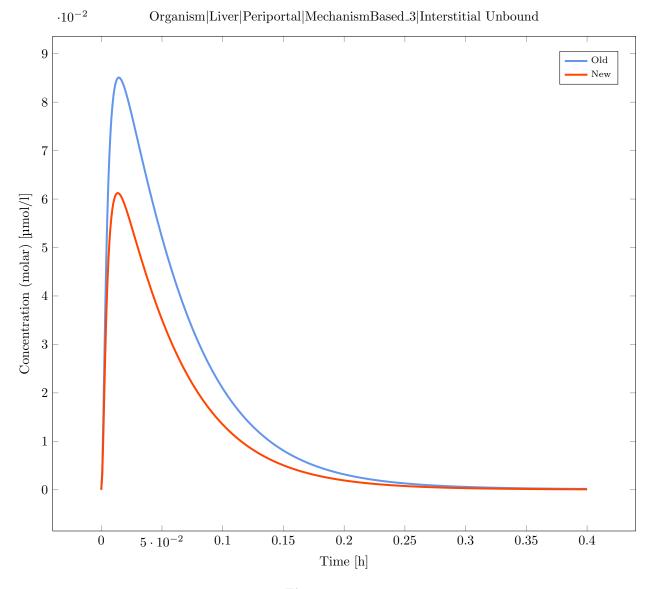


Figure 1.12

${\bf Simulation:} \ \ {\bf DDI_Multiple Combinations-11_MM_Mechanismbased_Mechanismbased_Induction$

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

Output Path: Organism |Lumen |ColonSigmoid |Rifampicin |Fraction of oral drug mass absorbed into mucosa segment

Deviation for 'Organism|Lumen|ColonSigmoid|Rifampicin|Fraction of oral drug mass absorbed into mucosa segment' is 1897.69% and is greater than the allowed max. tolerance of 3.00%

Deviation: 18.98

 $Organism | Lumen | Colon Sigmoid | Rifampicin | Fraction of oral drug \ mass \ absorbed \ into \ mucos a segment$

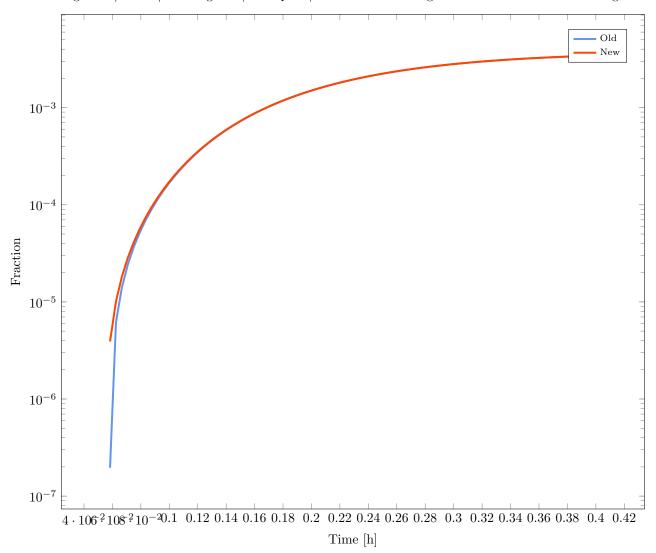
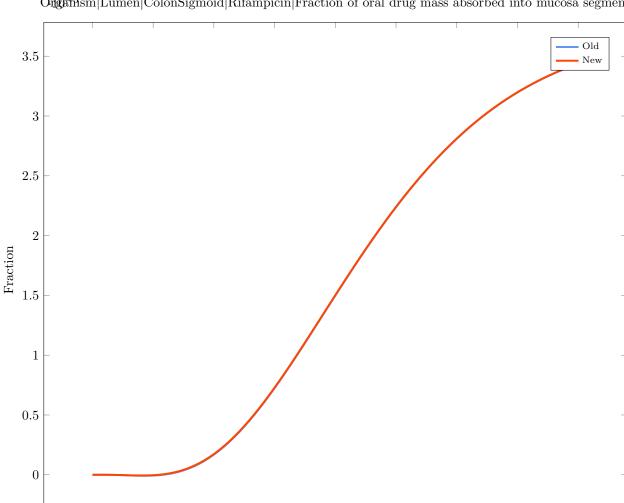


Figure 1.13



Onganism | Lumen | Colon Sigmoid | Rifampicin | Fraction of oral drug mass absorbed into mucosa segment

Figure 1.14

0.2

Time [h]

0.25

0.35

0.4

0.3

0.15

$Simulation: \ DDI_MultipleCombinations-12_MM_All_DDI_Types$

0.1

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

0

 $5\cdot 10^{-2}$

Output Path: Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration in con-

Deviation for 'Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration in container' is 48.14% and is greater than the allowed max. tolerance of 3.00%

$Organism | Liver | Periportal | Interstitial | Mechanism Based_3 | Concentration \ in \ container$

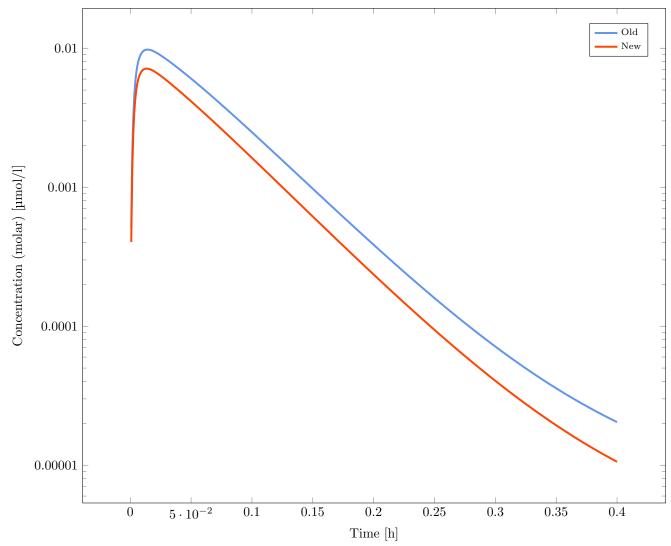
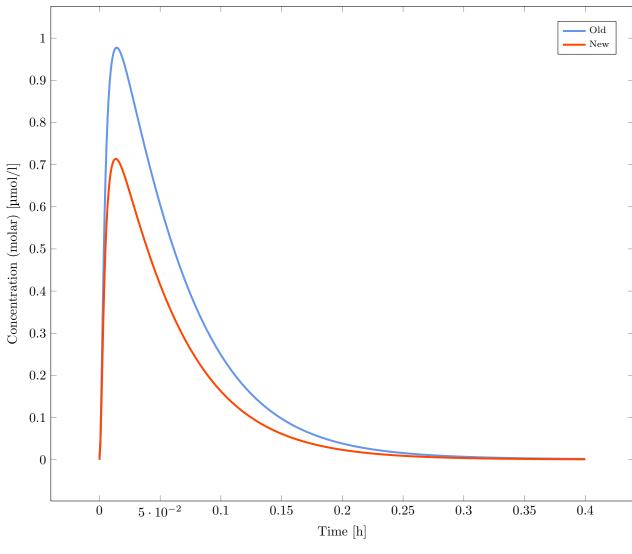


Figure 1.15



 $\cdot 10^{-2}$ Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration in container

Figure 1.16

$Simulation: \ DDI_Multiple Combinations \textbf{-} 25_1 st_Mechanism based_Mechanism based$

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

Output Path: Organism|Liver|Periportal|Erythromycin|Interstitial Unbound

 $Deviation \ for \ 'Organism | Liver | Periportal | Erythromycin | Interstitial \ Unbound' \ is \ 45.33\% \ and \ is \ greater \ than \ the$

allowed max. tolerance of 3.00%

${\bf Organism|Liver|Periportal|Erythromycin|Interstitial~Unbound}$

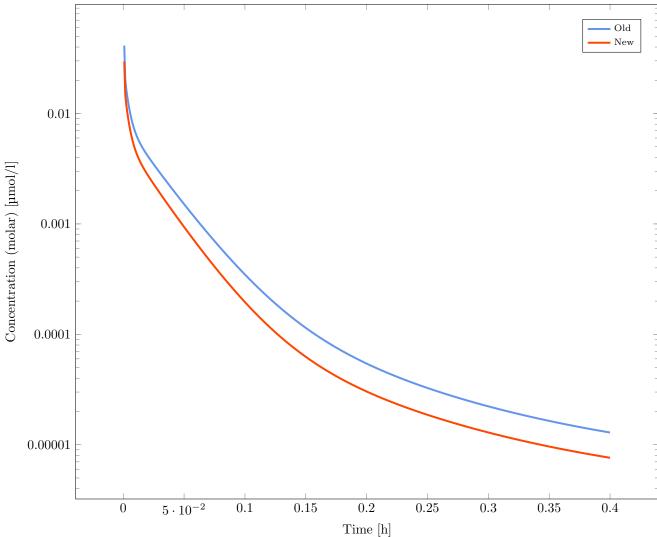


Figure 1.17

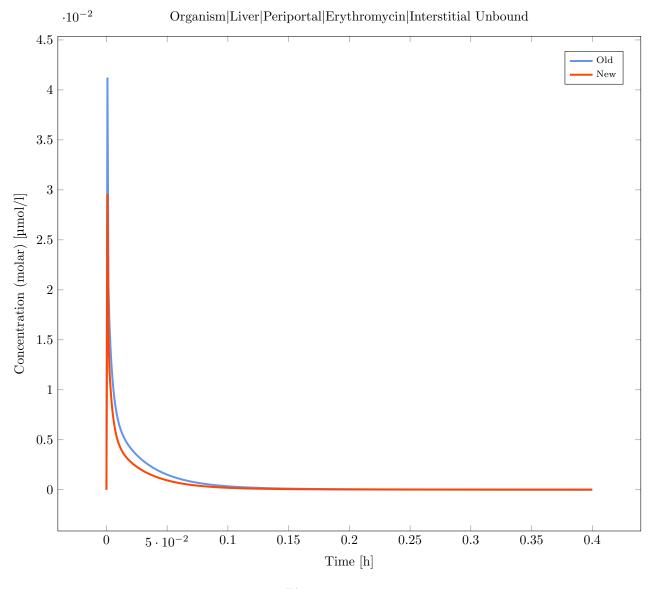


Figure 1.18

$Simulation: \ DDI_MultipleCombinations-26_1st_Induction_Induction$

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

$Output\ Path:\ Organism | Lumen | Colon Descendens | Rifampicin | Fraction\ of\ oral\ drug\ mass\ absorbed\ into\ mucosa\ segment$

Deviation for 'Organism | Lumen | Colon Descendens | Rifampicin | Fraction of oral drug mass absorbed into mucosa segment' is 1122.69% and is greater than the allowed max. tolerance of 3.00%

Deviation: 11.23

 $Organism | Lumen | Colon Descendens | Rifampicin | Fraction of oral drug \ mass \ absorbed \ into \ mucos a segment$

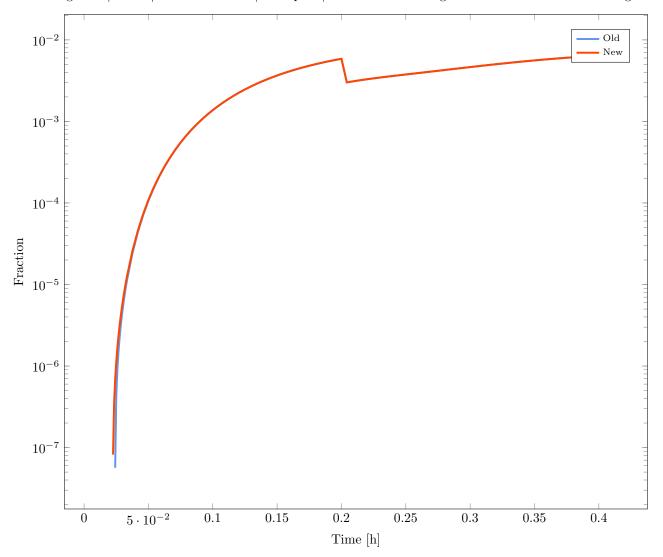
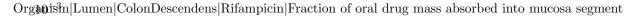


Figure 1.19



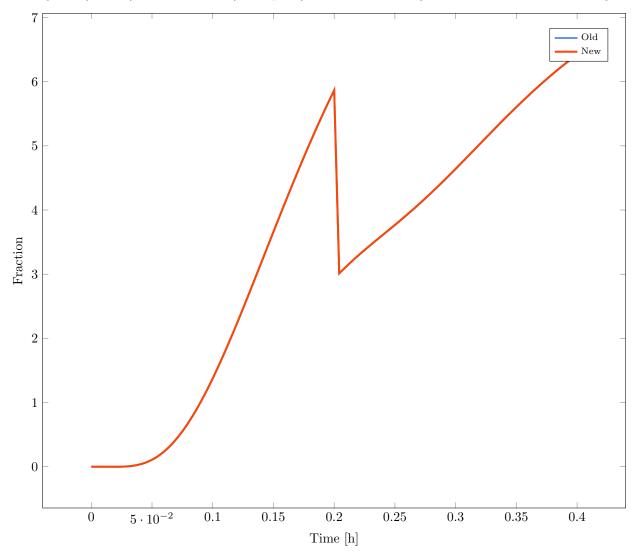


Figure 1.20

$Simulation: \ DDI_Multiple Combinations \textbf{-} 27_1 st_Competitive_Competitive_Mechanism based_Mechanism based$

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

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

Deviation for 'Organism|Liver|Periportal|Interstitial|Erythromycin|Concentration in container' is 56.47% and is greater than the allowed max. tolerance of 3.00%

greater than the anowed max. to

$Organism|Liver|Periportal|Interstitial|Erythromycin|Concentration\ in\ container$

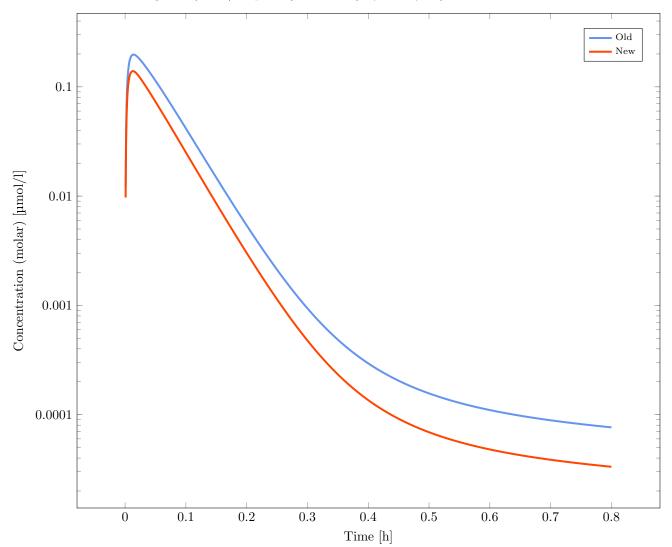
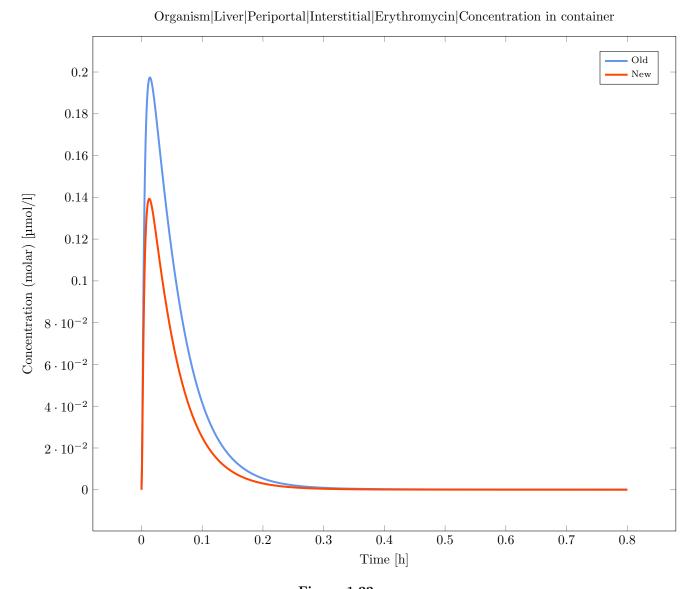


Figure 1.21



$\mathbf{Figure}\ \mathbf{1.22}$

$Simulation: \ DDI_Multiple Combinations - 28_1 st_Uncompetitive_Uncompetitive_Mechanism based_Mechanism based$

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

$Output\ Path:\ Organism|Liver|Periportal|Interstitial|MechanismBased_4|Concentration\ in\ container$

Deviation for 'Organism|Liver|Periportal|Interstitial|MechanismBased_4|Concentration in container' is 49.46% and is greater than the allowed max. tolerance of 3.00%

$Organism|Liver|Periportal|Interstitial|MechanismBased_4|Concentration\ in\ container$

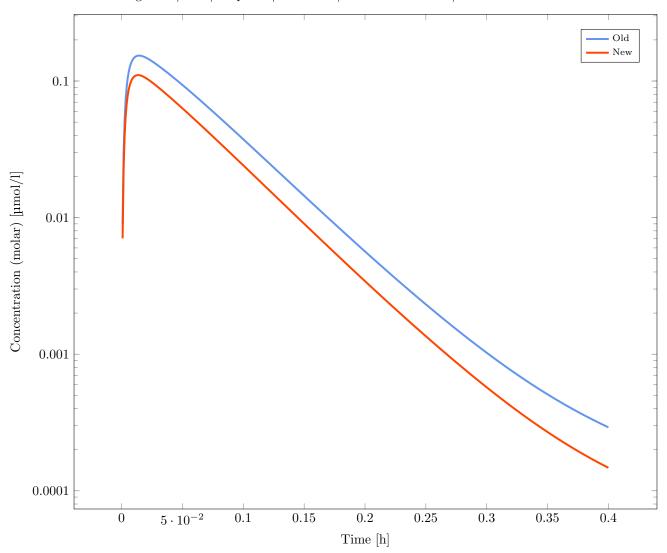
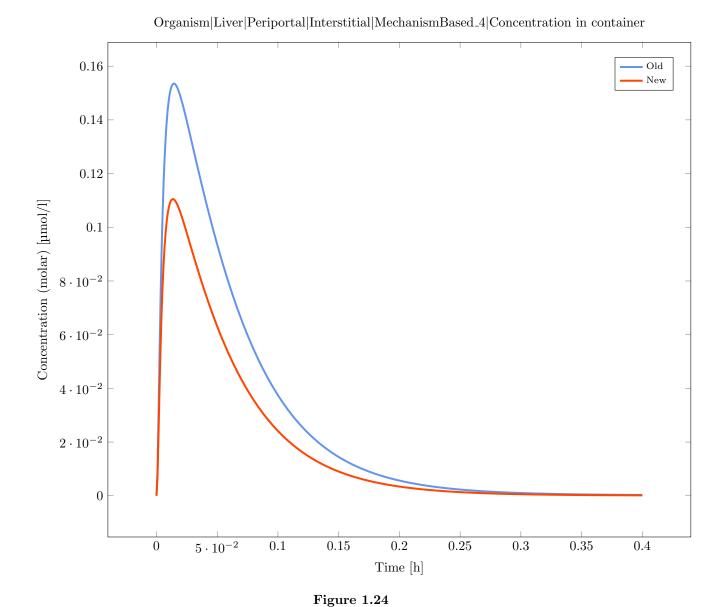


Figure 1.23



$Simulation: DDI_Multiple Combinations - 29_1st_Noncompetitive_Noncompetitive_Mechanism based_-1st_Noncompetitive_Noncompetit$ Mechanismbased

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

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

 $Deviation \ for \ 'Organism | Liver | Periportal | Interstitial | Erythromycin | Concentration \ in \ container' \ is \ 39.95\% \ and \ is$ greater than the allowed max. tolerance of 3.00%

Organism | Liver | Periportal | Interstitial | Erythromycin | Concentration in container 0.001 0.005 0.001 0.001

Figure 1.25

0.2

Time [h]

0.25

0.3

0.35

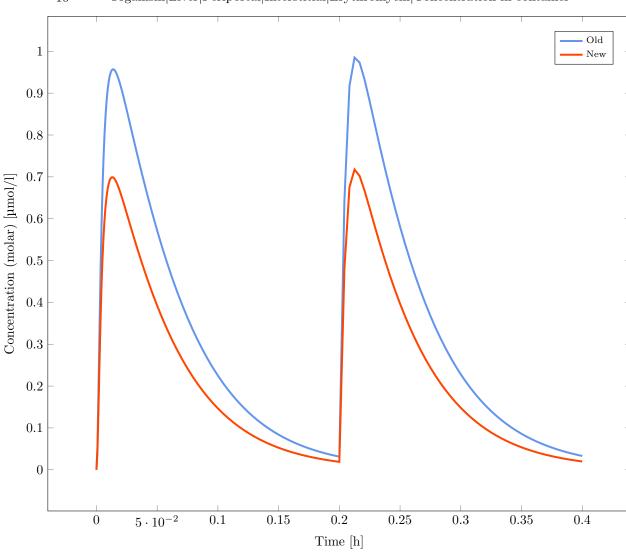
0.4

0.15

 $5 \cdot 10^{-2}$

0.1

0



 $\cdot 10^{-2}$ Organism|Liver|Periportal|Interstitial|Erythromycin|Concentration in container

Figure 1.26

 $Simulation: \ DDI_Multiple Combinations - 30_1st_Mixed_Mechanism based_Mechanism based$

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

$Output\ Path:\ Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration\ in\ container$

Deviation for 'Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration in container' is 48.80% and is greater than the allowed max. tolerance of 3.00%

$Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration\ in\ container$

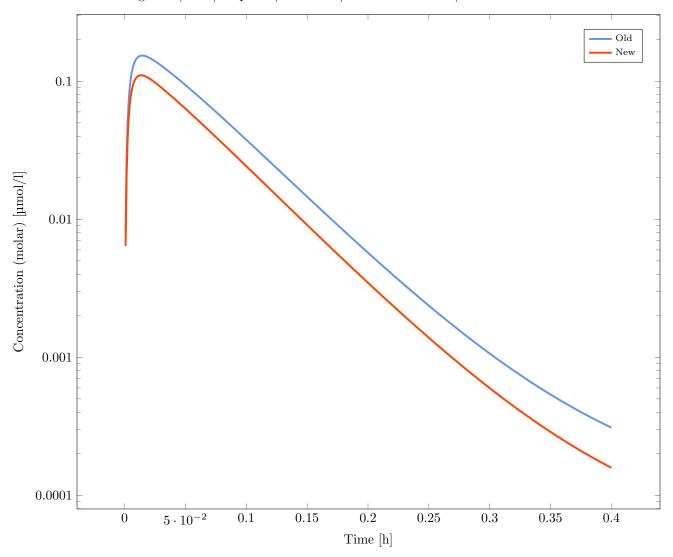
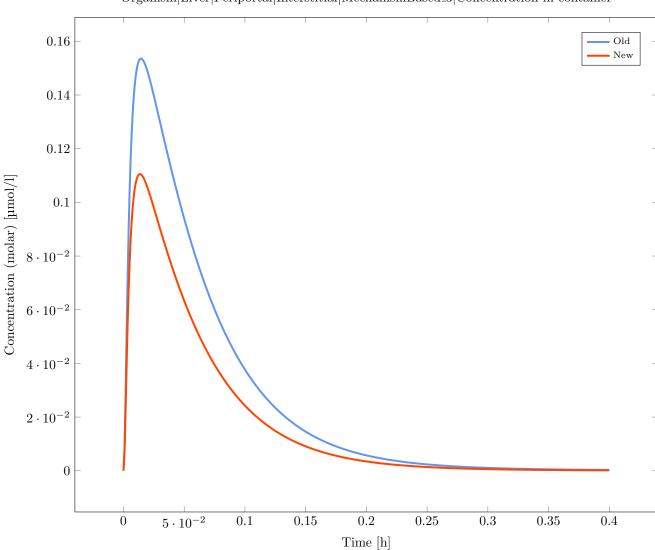


Figure 1.27



Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration in container

Figure 1.28

Simulation: DDI_MultipleCombinations-31_1st_Mechanismbased_Mechanismbased_Induction_Induction

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

$Output\ Path:\ Organism | Lumen | Colon Descendens | Rifampicin | Fraction\ of\ oral\ drug\ mass\ absorbed\ into\ mucosa\ segment$

Deviation for 'Organism|Lumen|ColonDescendens|Rifampicin|Fraction of oral drug mass absorbed into mucosa segment' is 825.21% and is greater than the allowed max. tolerance of 3.00%

 $Organism | Lumen | Colon Descendens | Rifampicin | Fraction of oral drug \ mass \ absorbed \ into \ mucos a segment$

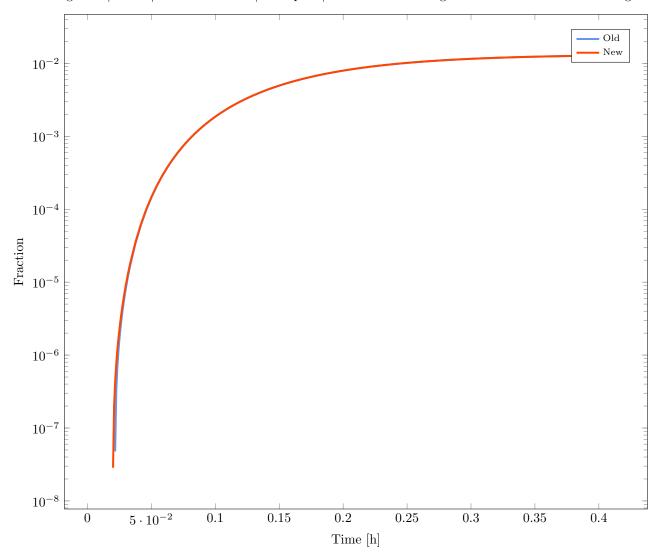
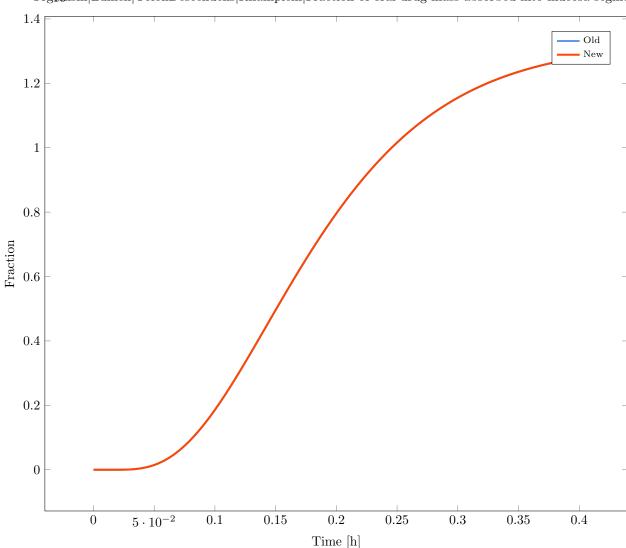


Figure 1.29



Organism | Lumen | ColonDescendens | Rifampicin | Fraction of oral drug mass absorbed into mucosa segment

Figure 1.30

$Simulation: \ DDI_MultipleCombinations - 32_1st_All_DDI_Types$

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

$Output\ Path:\ Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration\ in\ container$

Deviation for 'Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration in container' is 48.14% and is greater than the allowed max. tolerance of 3.00%

$Organism | Liver | Periportal | Interstitial | Mechanism Based_3 | Concentration \ in \ container$

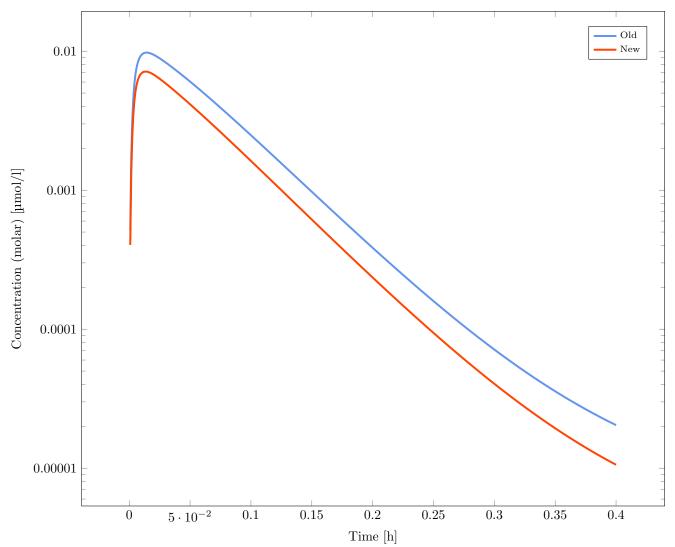
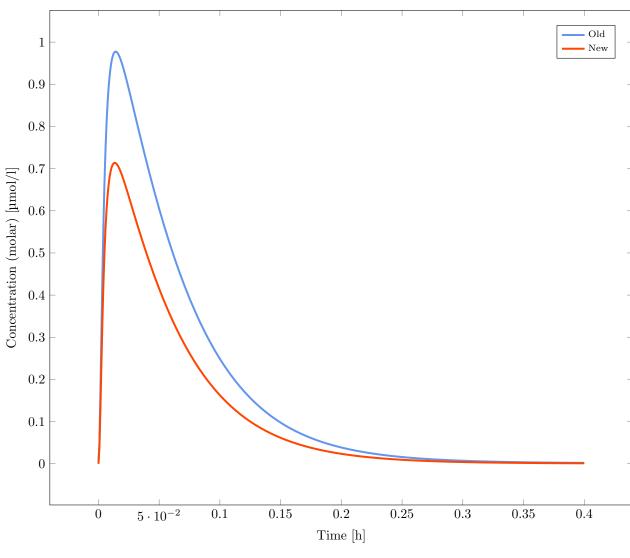


Figure 1.31



 $\cdot 10^{-2}$ Organism|Liver|Periportal|Interstitial|MechanismBased_3|Concentration in container

Figure 1.32

1.1.2 Valid Simulations (130/146)

 $Simulation: Beagle_SingleORAL_Dissolved-Beagle_SingleORAL_Dissolved$

Result of the validation: Valid

 $Simulation: Beagle_SingleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

 $Simulation: Beagle_SingleORAL_Dissolved_Beagle_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-$

 $Simulation: \ DDI_Multiple Combinations-01_MM_Competitive_Competitive$

Result of the validation: Valid

Simulation: DDI_MultipleCombinations-02_MM_Uncompetitive_Uncompetitive

Result of the validation: Valid

Simulation: DDI_MultipleCombinations-03_MM_Noncompetitive_Noncompetitive

Result of the validation: Valid

 $Simulation: \ DDI_MultipleCombinations-04_MM_Mixed_Mixed$

Result of the validation: Valid

Simulation: DDI_MultipleCombinations-21_1st_Competitive_Competitive

Result of the validation: Valid

Simulation: DDI_MultipleCombinations-23_1st_Noncompetitive_Noncompetitive

Result of the validation: Valid

 $Simulation: \ DDI_MultipleCombinations\hbox{-}24_1st_Mixed_Mixed$

Result of the validation: Valid

 $Simulation: \ Dog_MultiORAL_12_12_Dissolved-Dog_MultiORAL_12_12_Dissolved$

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

 $Simulation: \ Human_CompetitiveInhibition-Human_CompetitiveInhibition$

Simulation: Human_ICRP_AGP-01_ICRP_0y_Male

Result of the validation: Valid

 $Simulation: \ Human_ICRP_AGP-02_ICRP_0.05y_Female$

Result of the validation: Valid

Simulation: Human_ICRP_AGP-03_ICRP_0.18y_Male

Result of the validation: Valid

Simulation: Human_ICRP_AGP-04_ICRP_1y_Female

Result of the validation: Valid

 $Simulation: \ Human_ICRP_AGP-05_ICRP_12y_Male$

Result of the validation: Valid

Simulation: Human_ICRP_AGP-06_ICRP_30y_Female

Result of the validation: Valid

 $Simulation: \ Human_ICRP_AGP-07_ICRP_100y_Male$

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

 $Simulation: \ Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_13_13_Dissolved-Human_MultiORAL_6_13_Dissolved-Human_MultiORAL_6_13_Dissolved-Human_6_13_Disso$

Result of the validation: Valid

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_absorption_-tolder and the control of the co$

 $sink_conditions$

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
Result of the validation: Valid

 $Simulation: Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_EHC_continuous_fraction_1$

Result of the validation: Valid

 $Simulation: \ Human_MultiORAL_6_12_12_Dissolved-Human_MultiORAL_6_12_12_Dissolved_pKandle (AL-6-12-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-12-Dissolved-Human_MultiORAL-6-12-Dissolved-Human_MultiORAL-6-Dissolved-Human_MultiORA-6-Dissolved-Human_MultiORA-6-Dissolved-Human_MultiORA-6-Dissolved-Human_MultiOR$

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_Oral_BiDaily_TableFormulation-S1_suspension

Result of the validation: Valid

Simulation: Human_Oral_BiDaily_TableFormulation-S2_NoSuspension

Result of the validation: Valid

Simulation: Human_pH_SolubilityTable-S1_Table

Result of the validation: Valid

 $Simulation: \ Human_pH_SolubilityTable-S2_Measurement$

Result of the validation: Valid

Simulation: Human_pH_SolubilityTable-S3_Table_SolubilityChanged

Result of the validation: Valid

 $Simulation: \ Human_pH_SolubilityTable-S4_Table_SolubilityTableChanged$

Result of the validation: Valid

 $Simulation: Human_Single IV_Configuration-Human_Single IV_Configuration$

Result of the validation: Valid

Simulation: Human_SingleIV-Human_SingleIV

Result of the validation: Valid

 $Simulation: \ Human_SingleIV-Human_SingleIV_MW_200_fu_0.2_LogP_5$

Simulation: Human_SingleIV-Human_SingleIV_MW_800_fu_0.6_LogP_-5

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_SingleORAL-Dissolved_PlasmaClearance-Human_SingleORAL-Dissolved_PlasmaClearance-Human_SingleORAL-Dissolved_PlasmaClearance-Human_SingleORAL-Dissolved_PlasmaClearance-Human_Singl$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_Singl$

 $MW_200_fu_0.2_LogP_5$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Dissolved_PlasmaClearance-Human_Singl$

 $MW_800_fu__0.6_LogP_--5$

Result of the validation: Valid

Simulation: Human_SingleORAL_Dissolved-Human_SingleORAL_Dissolved

Result of the validation: Valid

 $Simulation: \ Human_SingleORAL_Dissolved_Human_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-INFIGURE AND SINGLE AND SINGLE$

5

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Dissolved_Human_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-RAL_Dissolved_MW_800_Fu_0.6_LogP_-RAL_Dissolved_MW_800_Fu_0.6_LogP_-RAL_Dissolved_MW_800$

-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

 $Simulation: Human_SingleORAL_MonoParticles_AsSuspention-Human_SingleORAL_MonoParticles_Assuspention-Human_Si$

AsSuspention

Result of the validation: Valid

 $Simulation: \ Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_AsSuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL_PolyParticlesLogNormal_Assuspention-Human_SingleORAL$

 $PolyParticlesLogNormal_AsSuspention$

Result of the validation: Valid

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

AsSuspention

 $Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNoAsSuspention_dissolved_radius$

Result of the validation: Valid

Simulation: Human_SingleORAL_PolyParticlesNormal_AsSuspention-Human_SingleORAL_PolyParticlesNo AsSuspention_treat_precipated_drug_as_soluble

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention$

Result of the validation: Valid

 $Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention_-Institute and the state of the$

MW_200_fu_0.2_LogP_5
Result of the validation: Valid

 $Simulation: Human_SingleORAL_Weibull_AsSuspention-Human_SingleORAL_Weibull_AsSuspention_-Include Simulation and SingleORAL_Weibull_AsSuspention_-Include SingleORAL_Weibull_-Include SingleORAL_Weibull_-Include SingleORAL_-Include SingleORAL_-Inclu$

MW_800_fu_0.6_LogP_-5
Result of the validation: Valid

 $Simulation: \ Human_SingleORAL_Weibull-Human_SingleORAL_Weibull$

Result of the validation: Valid

Simulation: Human_SingleORAL_Weibull-Human_SingleORAL_Weibull_MW_200_fu_0.2_LogP_5

Result of the validation: Valid

 $Simulation: \ Human_SingleORAL_Weibull-Human_SingleORAL_Weibull_MW_800_fu_0.6_LogP_-logP$

 $\mathbf{5}$

Result of the validation: Valid

Simulation: Human_UncompetitiveInhibition-Human_UncompetitiveInhibition

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_-

5

Result of the validation: Valid

 $Simulation: Minipig_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-fu_0.6_$

-5

 $Simulation: \ Monkey_SingleORAL_Dissolved-Monkey_SingleORAL_Dissolved$

Result of the validation: Valid

 $Simulation: Monkey_SingleORAL_Dissolved_Monkey_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-INFIGURE AND SIMULATION FOR SIMULATI$

 $\mathbf{5}$

Result of the validation: Valid

 $Simulation: Monkey_SingleORAL_Dissolved_MORAL_Dissolved_MW_800_fu_0.6_LogP_-fu_0.$

-5

Result of the validation: Valid

 $Simulation: \ Mouse_SingleORAL_Dissolved-Mouse_SingleORAL_Dissolved$

Result of the validation: Valid

 $Simulation: Mouse_SingleORAL_Dissolved_Mouse_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-fu_0.2_L$

 $\mathbf{5}$

Result of the validation: Valid

 $Simulation: Mouse_SingleORAL_Dissolved_Mouse_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-fu_0.6_L$

-5

Result of the validation: Valid

Simulation: Preterm_SingleIV_Age_0_GA_32_CYP3A4-Preterm_SingleIV_Age_0_GA_32_CYP3A4

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

 $Simulation: Rabbit_SingleORAL_Dissolved_Rabbit_SingleORAL_Dissolved_MW_200_fu_0.2_LogP_-Included to the control of the contr$

 $\mathbf{5}$

 $Simulation: Rabbit_SingleORAL_Dissolved_Rabbit_SingleORAL_Dissolved_MW_800_fu_0.6_LogP_-$

-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_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: SingleIV_2Pores_Human-SingleIV_2Pores_Human

Result of the validation: Valid

 $Simulation: Single IV_2 Pores_Human_Single IV_2 Pores_Human_Simulation C$

Result of the validation: Valid

Simulation: SingleIV_2Pores_Human_SingleIV_2Pores_Human_SimulationD

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

 $Simulation: Single IV_2 Pores_Monkey_Single IV_2 Pores_Monkey_Simulation G$

Result of the validation: Valid

Simulation: SingleIV_2Pores_Monkey_SingleIV_2Pores_Monkey_SimulationH

Result of the validation: Valid

Simulation: SingleIV_2Pores_Mouse-SingleIV_2Pores_Mouse

Result of the validation: Valid

 $Simulation: Single IV_2 Pores_Mouse_Single IV_2 Pores_Mouse_Simulation A$

 $Simulation: Single IV_2 Pores_Mouse_Simulation B$

Result of the validation: Valid

 $Simulation: Single IV_2 Pores_Mouse_Single IV_2 Pores_Mouse_Simulation E$

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: SingleIV_C2_4Comp_RR_standard_standa

Result of the validation: Valid

 $Simulation: Single IV_C2_4 Comp_standard_schmitt_standard_Single IV_C2_4 Comp_standard_schmitt_schmitt_standard_schmitts_schmitts_schmi$

 $\operatorname{standard}$

Result of the validation: Valid

Simulation: SingleIV_C3_4Comp_RR_schmitt_standard-SingleIV_C3_4Comp_RR_schmitt_standard

Result of the validation: Valid

 $Simulation: Single IV_C3_4 Comp_standard_schmittnorm lized_standard_Single IV_C3_4 Comp_standard_schmittnorm lized_standard_schmittnorm lized_schmittnorm lized_sch$

 $schmittnorm lized_standard$

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

 $Simulation: Single IV_C6_2 Pores_standard_stan$

Result of the validation: Valid

 $Simulation: Single IV_C7_2 Pores_standard_schmitt_standard-Single IV_C7_2 Pores_standard_schmitt_standard Single IV_C7_2 Pores_standard_schmitt_standard_schmitt_standard_schmitt$

Result of the validation: Valid

 $Simulation: Single IV_C7_4 Comp_schmitt_standard_standa$

Result of the validation: Valid

 $Simulation: Single IV_C8_2 Pores_standard_schmittnormalized_standard_Single IV_C8_2 Pores_standard_schmittnormalized_standard$

Result of the validation: Valid

 $Simulation: Single IV_C9_2 Pores_schmitt_standard_standard_Single IV_C9_2 Pores_schmitt_standard_sta$

Result of the validation: Valid

 $Simulation: Single ORAL_C10_4 Comp_PT_standard_standard-Single ORAL_C10_4 Comp_PT_standard-Single ORAL_C10_4 Comp_Single ORAL_C10_4 C00_4 C00_$

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

 $Simulation: Single ORAL_C13_2 Pores_schmitt_standard_st$

Result of the validation: Valid

 $Simulation: Single ORAL_C13_4 Comp_standard_schmittnormalized_schmittnormalized_sc$

 $Simulation: Single ORAL_C14_2 Pores_PT_standard_standard-Single ORAL_C14_2 Pores_PT_standard-Single ORAL_C14_2 Pores_SPT_standard-Single ORAL_C14_2 Pores_SPT_standard-SPT_standard-SPT_standard-SPT_sTandard-SPT_standard-SPT_sTandard-SPT_sTandard-SPT_sTandard-SPT_sTandard-SPT_sTandard-SPT_sTandard-SPT_sTandard-SPT_sTandard-SPT_sTandard-SPT_sTandard-SPT_sTa$

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

 $Simulation: Single ORAL_C4_2 Pores_standard_schmittnormalized_schmittnormalized_schmittnorm$

Result of the validation: Valid

 $Simulation: Single ORAL_C6_4 Comp_Ber_standard_standard_Single ORAL_C6_4 Comp_Ber_standard_$

Result of the validation: Valid

 $Simulation: Single ORAL_C6_4 Comp_RR_standard_standard-Single ORAL_C6_4 Comp_RR_standard-Single ORAL_C6_5 C$

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

 $Simulation: Single ORAL_C7_4 Comp_RR_schmitt_standard-Single ORAL_Schmitt_standard-Single O$

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

 $Simulation: Single ORAL_C9_2 Pores_RR_schmitt_standard-Single ORAL_C9_2 Pores_S_RR_schmitt_standard-Single ORAL_C9_2 Pores_S_RR_schmitt_standard-Single$

Result of the validation: Valid

Simulation: Test 18.1_I1_C1_A1_Config1-Test 18.1_I1_C1_A1_Config1

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

Result of the validation: Valid

 $Simulation: \ Test\ 18.1_I2_C3_A1_Config2-Test\ 18.1_I2_C3_A1_Config2$

Result of the validation: Valid

Simulation: Test $18.1_I3_C3_A3_Config2$ -Test $18.1_I3_C3_A3_Config2$