

Dextromethorphan qualification report

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1 Notes

Note

This report has been created with simulation results loaded from results folder .

2 Introduction

This document describes the qualification of a published paroxetine physiologically-based pharmacokinetics (PBPK) model for use with the Open Systems Pharmacology Software (OSPS) Version 11.2.

The PBPK model has been developed with OSPS version 10 and published by [[@rudesheimPhysiologicallyBasedPharmacokinetic2022](#)]. Model snapshot was downloaded on 21.07.2023 from the model [repository](#). As of 21.07.2023, no model version qualified for OSP version 11.2 is publicly available.

3 Methods

3.1 Software

The qualification is performed with OSPS [version 11.2.142](#).

3.2 Qualification process

1. Import project snapshot “Dextromethorphan-model.json” in PK-Sim v11.2.
2. The snapshot contains 33 simulations. All simulations were exported to *.pkml for simulation in R.
3. All observed data from the project created with version 11.2 were exported *.pkml for loading in R.
4. Simulations were simulated in R and the results visually compared to the results reported in the original publication.

3.3 Data

3.4 Model consolidation

During conversion of projects created with versions before 11, a separate expression profile is created for each individual. To ensure that all individuals are using the same expression, expression profiles of the same protein were compared. All expression profiles for the same protein were equal. Therefore, the same expression profile was set in every individual, and the remaining profiles were removed.

4 Results

Comparison of time-concentration profiles with observed data are presented in the following:

Antecip Bioventures EM, 60 mg dextromethorphan hydrobromide multiple dose (capsule/solution),
n=10 - time profile

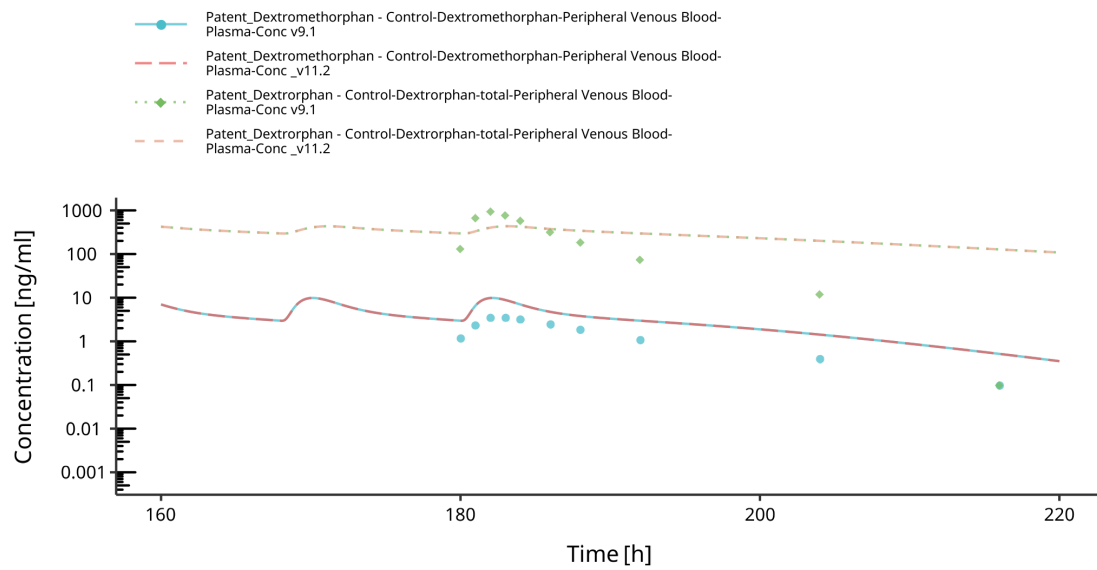


Figure 1: Antecip Bioventures EM, 60 mg dextromethorphan hydrobromide multiple dose (capsule_solution), n=10

Armani 2017 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=20 - time profile

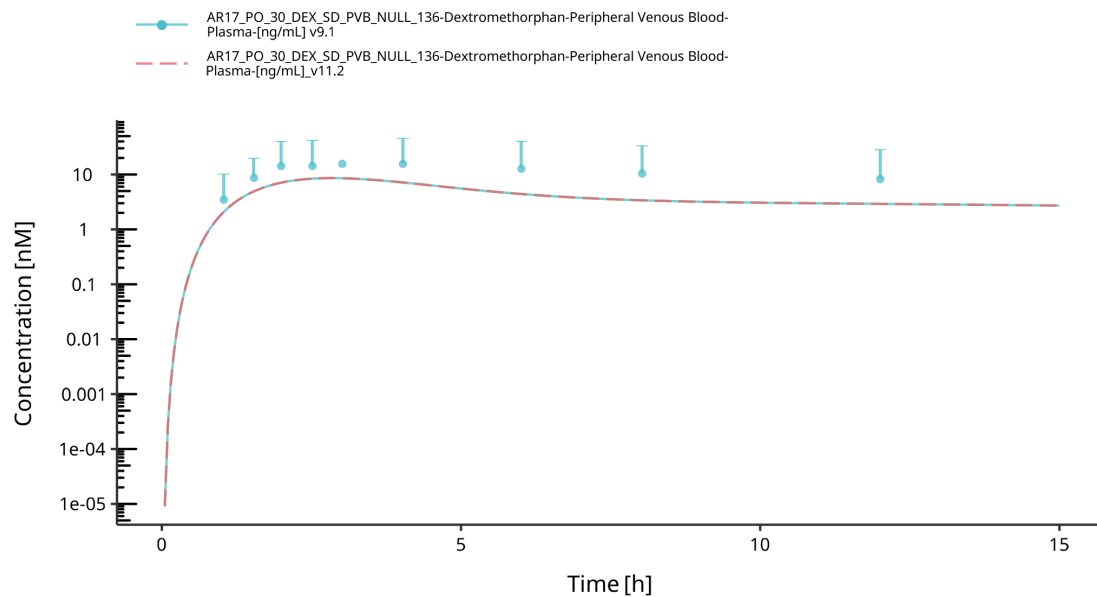


Figure 2: Armani 2017 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=20

Capon 1996 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=6 - time profile

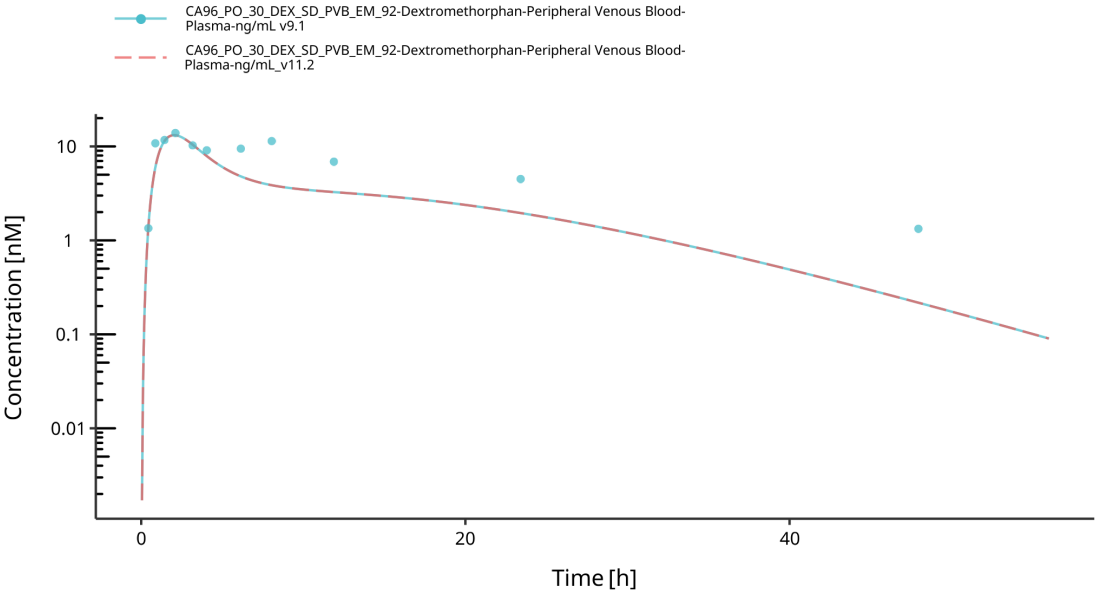


Figure 3: Capon 1996 EM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=6

Capon 1996 PM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=6 - time profile

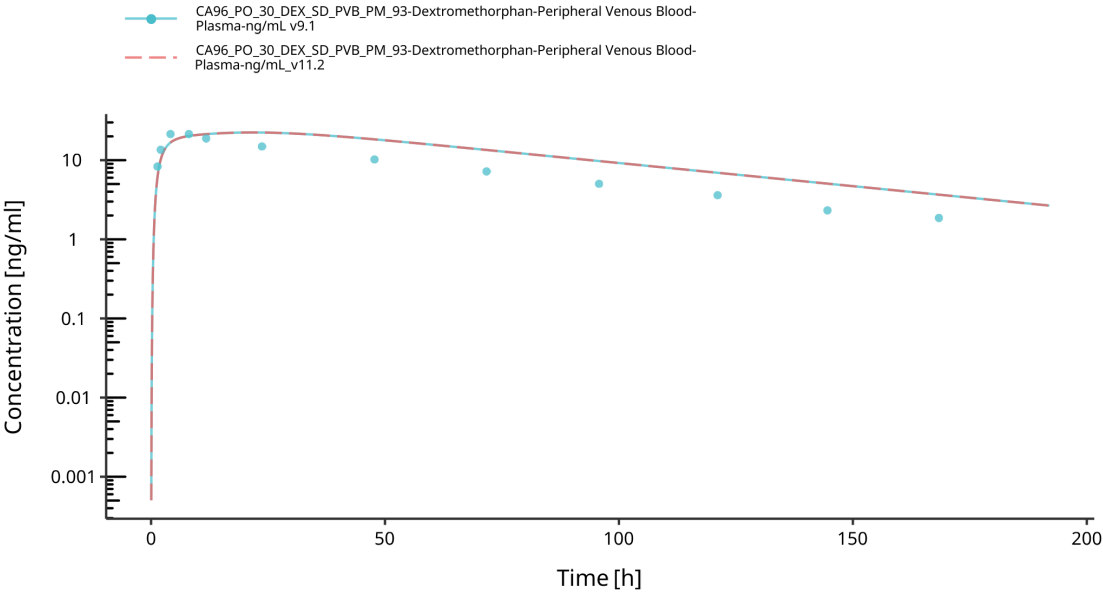


Figure 4: Capon 1996 PM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=6

Duedahl 2005 EM, 0.5 mg/kg dextromethorphan base (infusion), n=24 - time profile

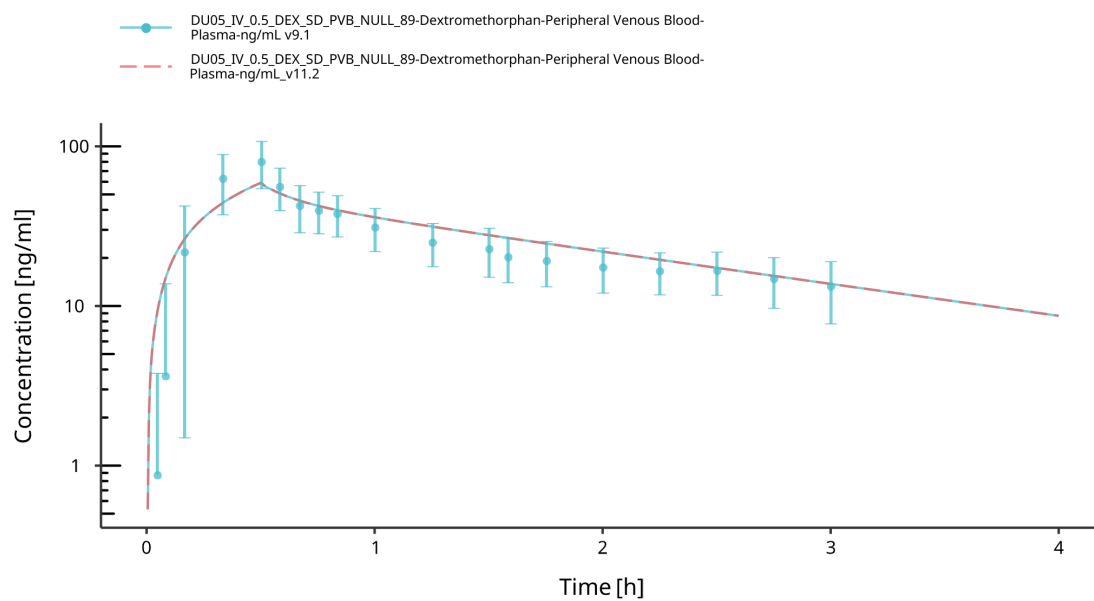


Figure 5: Duedahl 2005 EM, 0.5 mg/kg dextromethorphan base (infusion), n=24

Dumond 2010 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=23 - time profile

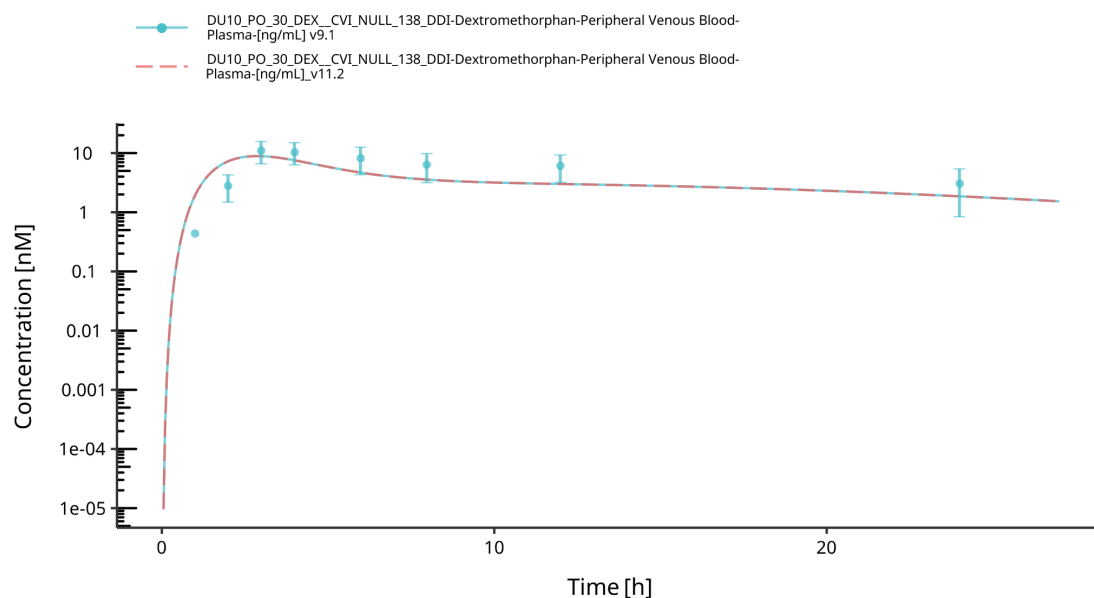


Figure 6: Dumond 2010 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=23

Edwards 2017 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=48 - time profile

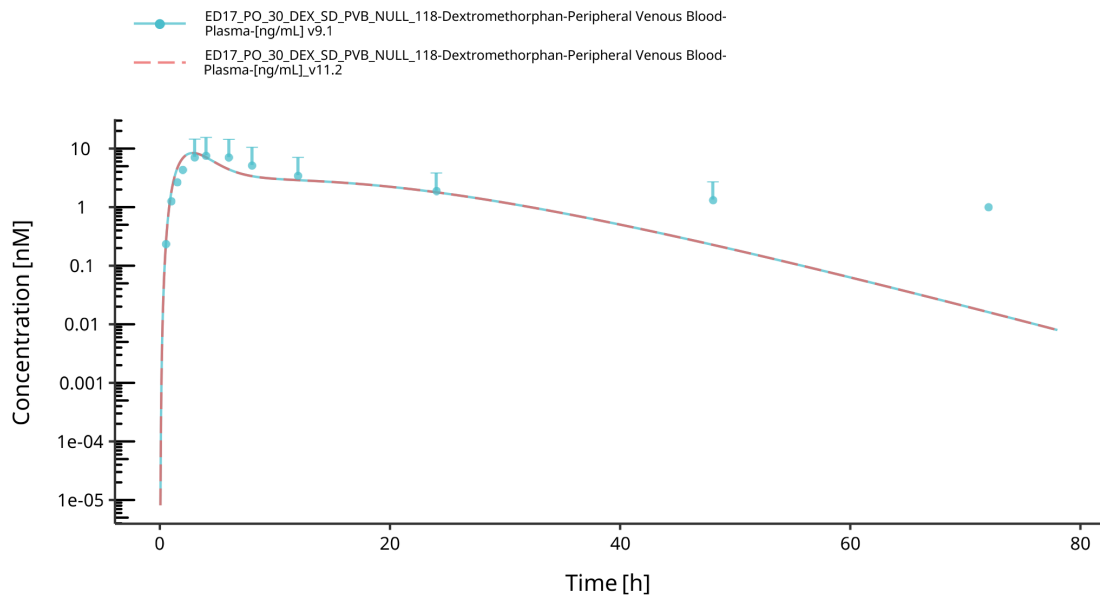


Figure 7: Edwards 2017 EM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=48

Ermer 2015 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=30 - time profile

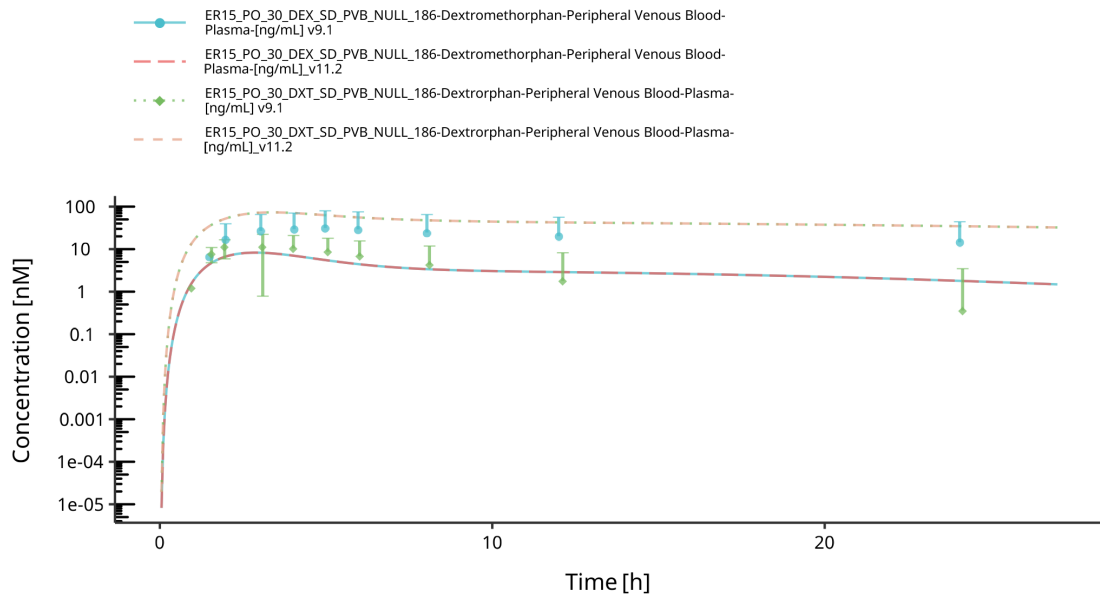


Figure 8: Ermer 2015 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=30

Feld 2013 EM, 60 mg dextromethorphan hydrobromide (capsule/solution), n=17 - time profile

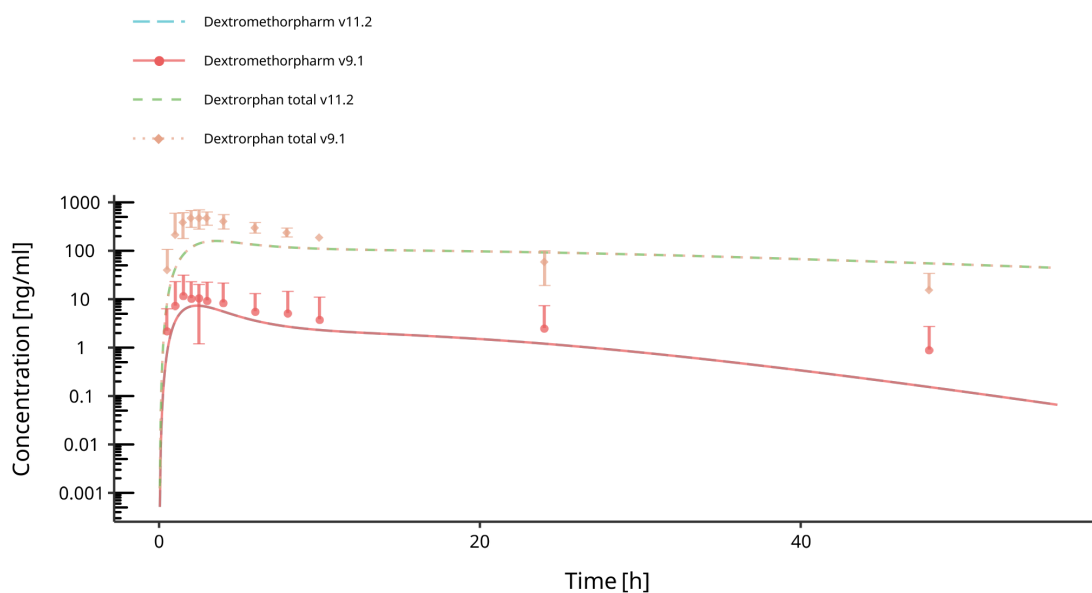


Figure 9: Feld 2013 EM, 60 mg dextromethorphan hydrobromide (capsule_solution), n=17

Gazzaz 2018 NM, 30 mg dextromethorphan hydrobromide (cocktail), n=30, AS=1.25 - time profile

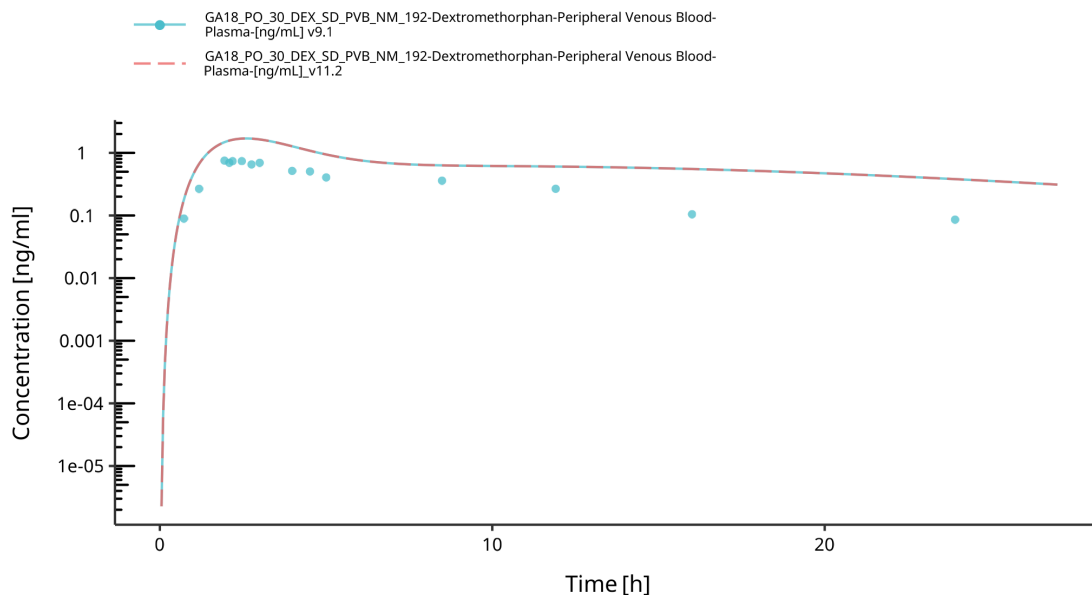


Figure 10: Gazzaz 2018 NM, 30 mg dextromethorphan hydrobromide (cocktail), n=30, AS=1.25

Gorski 2004 EM, 30 mg dextromethorphan hydromide (capsule/solution), n=11 - time profile

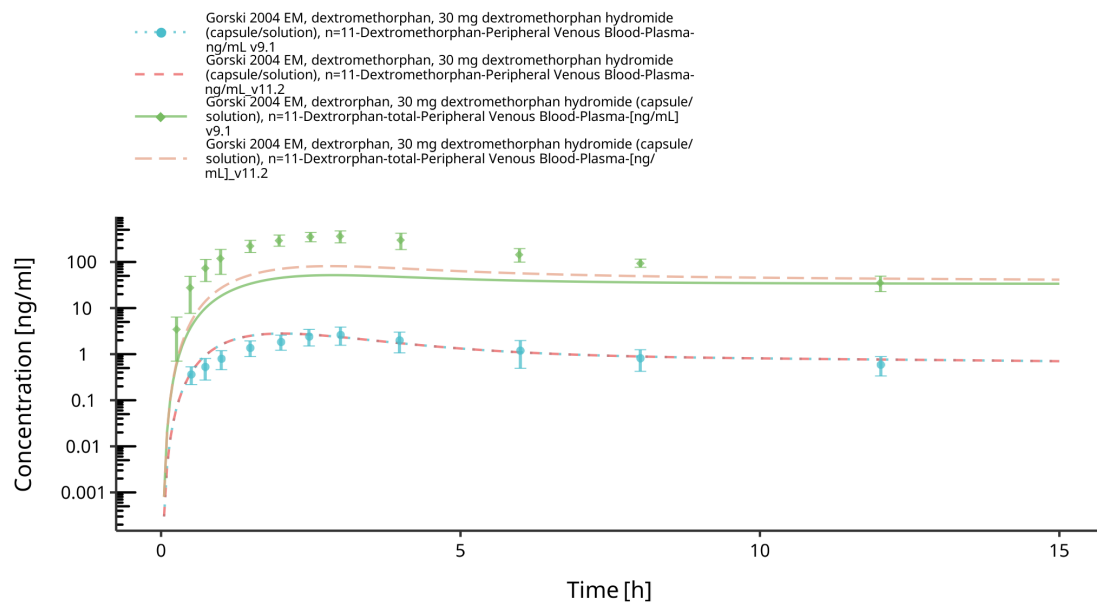


Figure 11: Gorski 2004 EM, 30 mg dextromethorphan hydromide (capsule_solution), n=11

Gorski 2004 PM, 30 mg dextromethorphan hydromide (capsule/solution), n=1 - time profile

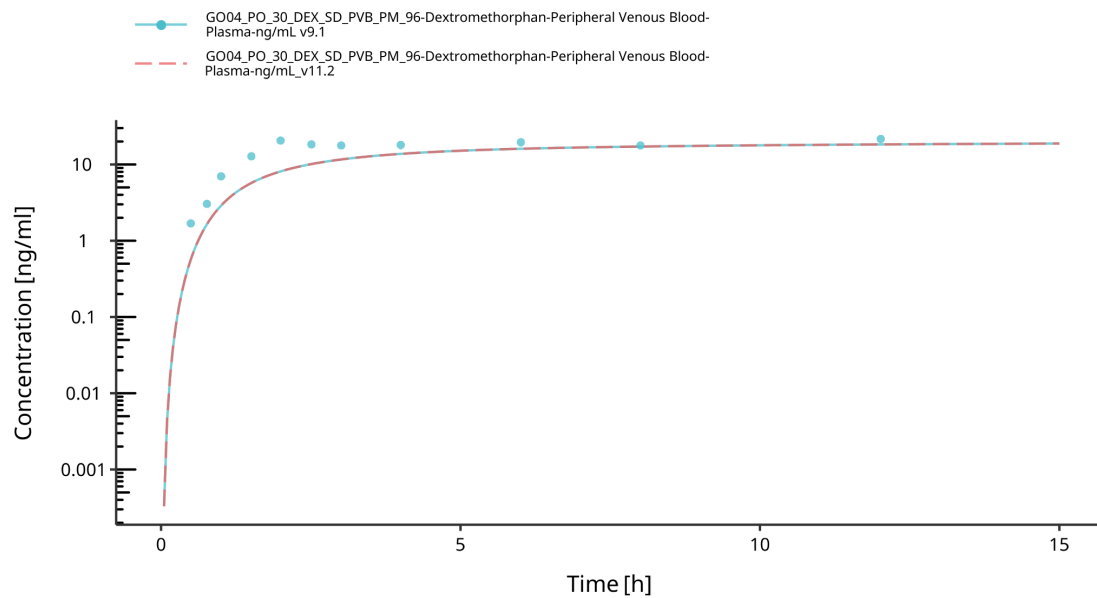


Figure 12: Gorski 2004 PM, 30 mg dextromethorphan hydromide (capsule_solution), n=1

Kakuda 2014 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=14 - time profile

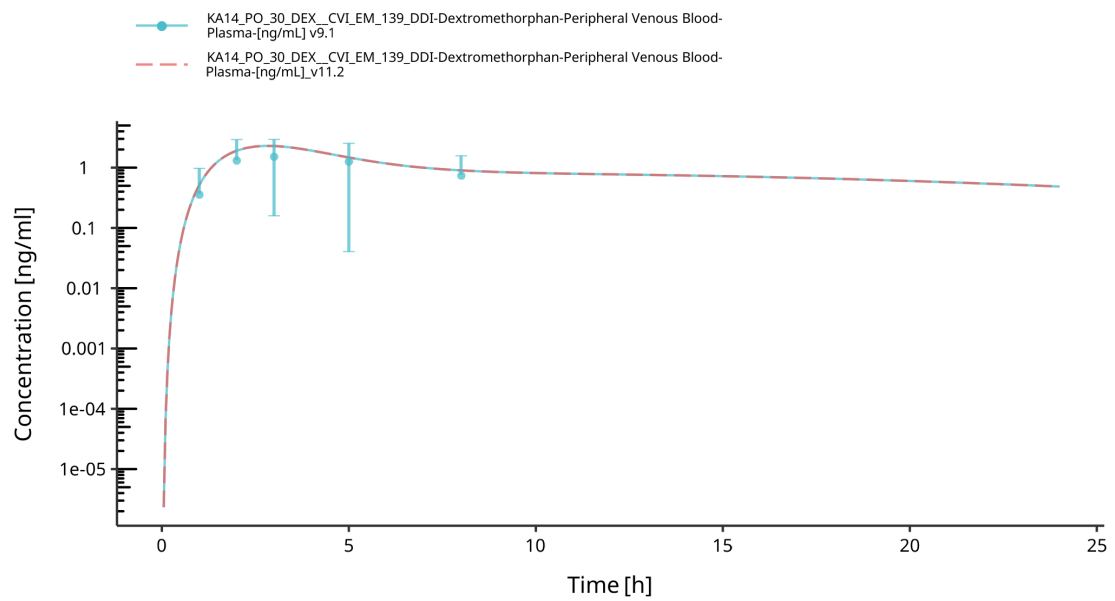


Figure 13: Kakuda 2014 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=14

Khalilieh 2018 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=20 - time profile

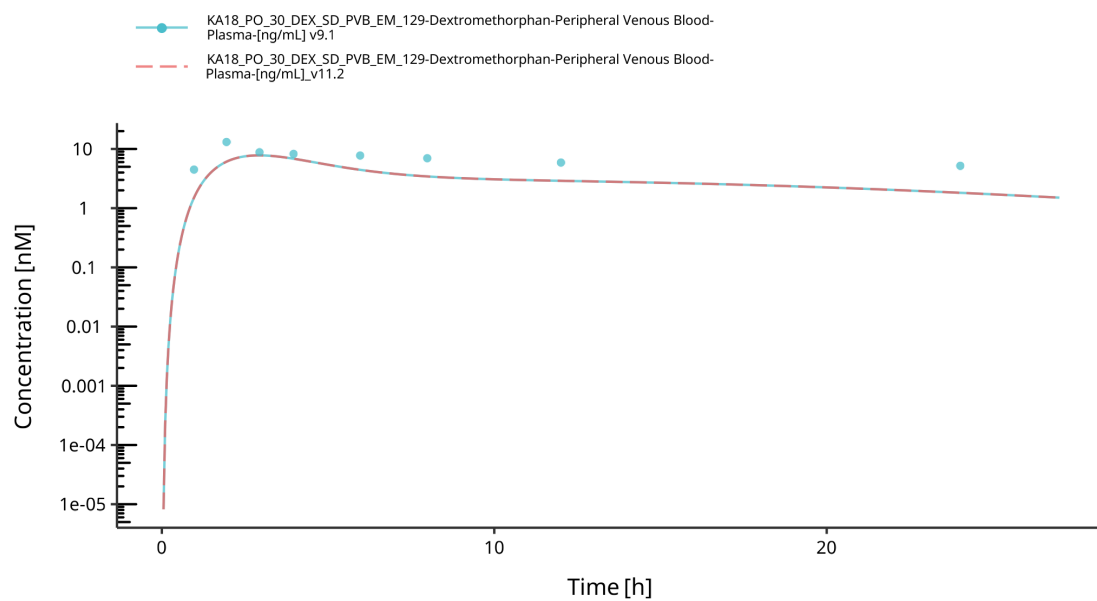


Figure 14: Khalilieh 2018 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=20

Nakashima 2007 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=24 - time profile

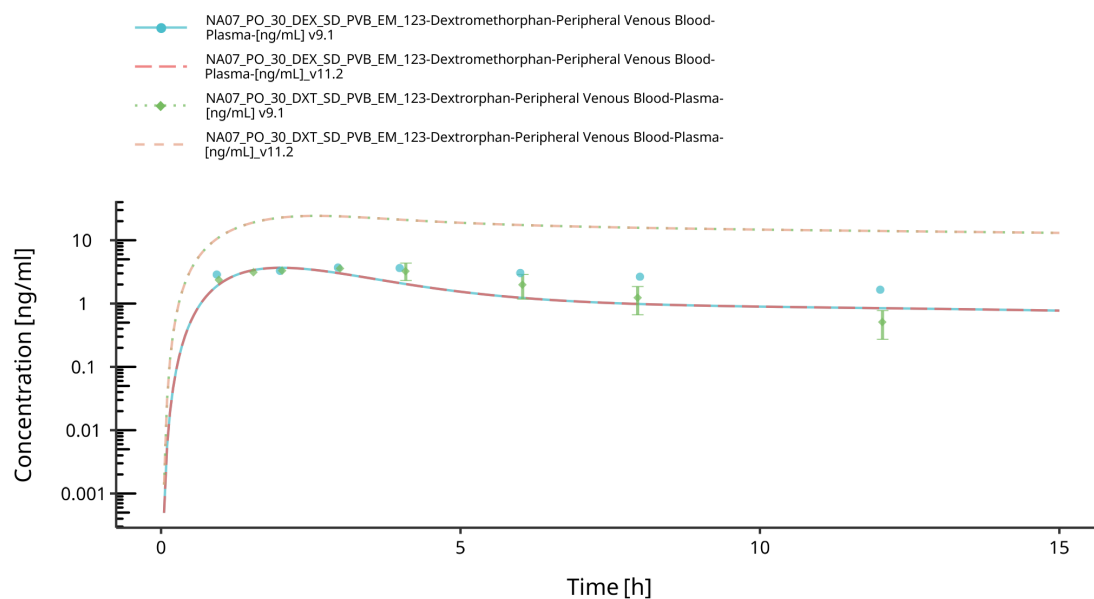


Figure 15: Nakashima 2007 EM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=24

Nyunt 2008 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=12 - time profile

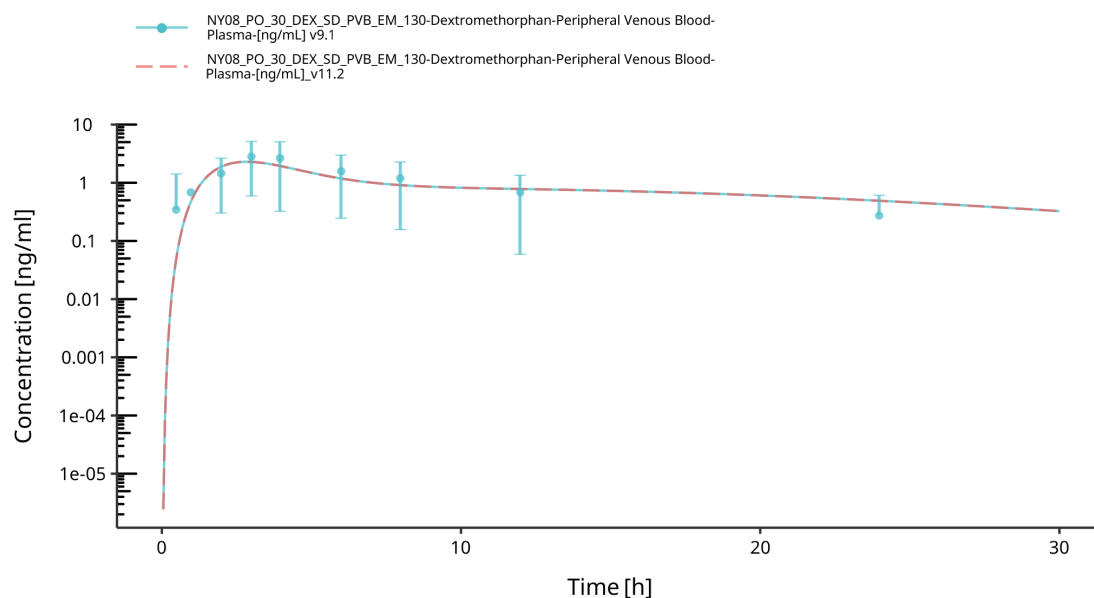


Figure 16: Nyunt 2008 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=12

Qiu 2016 IM, 15 mg dextromethorphan hydrobromide (capsule/solution), n=6, AS=0.5 - time profile

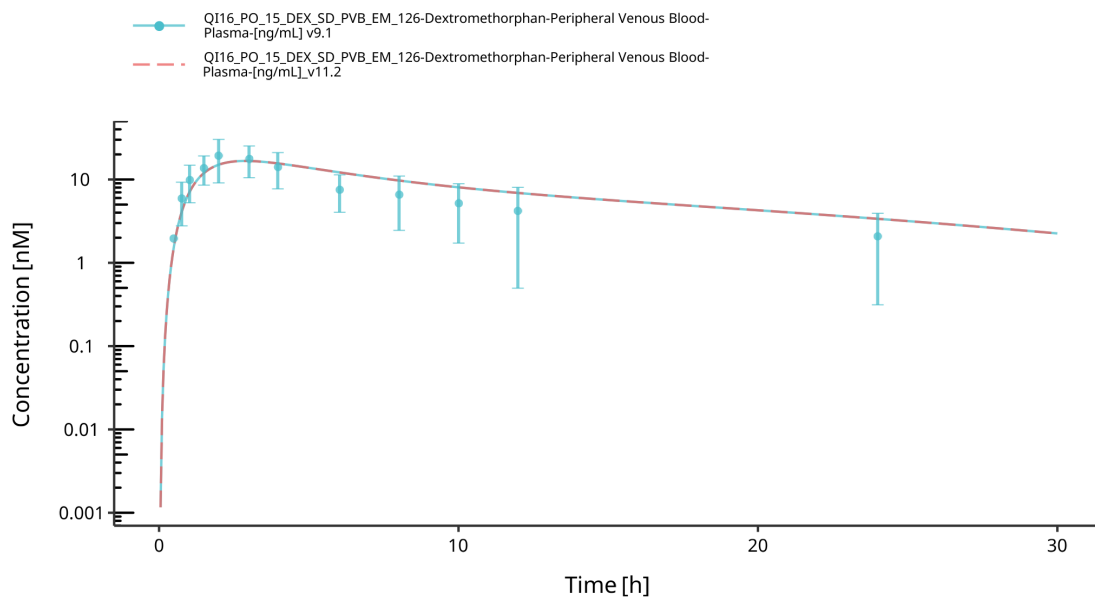


Figure 17: Qiu 2016 IM, 15 mg dextromethorphan hydrobromide (capsule_solution), n=6, AS=0.5

Qiu 2016 NM, 15 mg dextromethorphan hydrobromide (capsule/solution), n=6, AS=1.25 - time profile

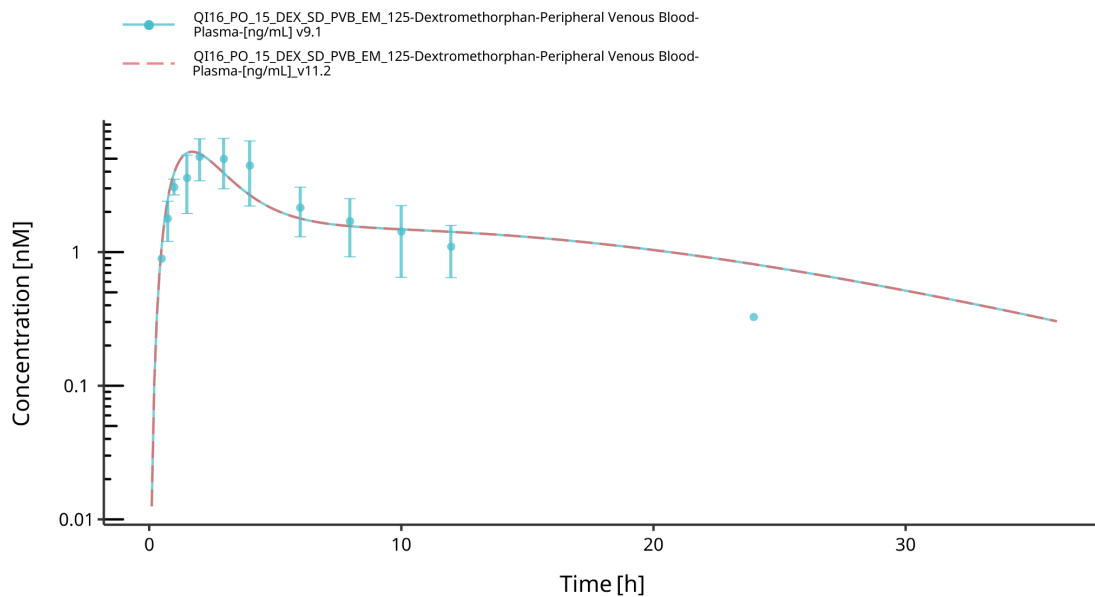


Figure 18: Qiu 2016 NM, 15 mg dextromethorphan hydrobromide (capsule_solution), n=6, AS=1.25

Qiu 2016 NM, 15 mg dextromethorphan hydrobromide (capsule/solution), n=6, AS=2 - time profile

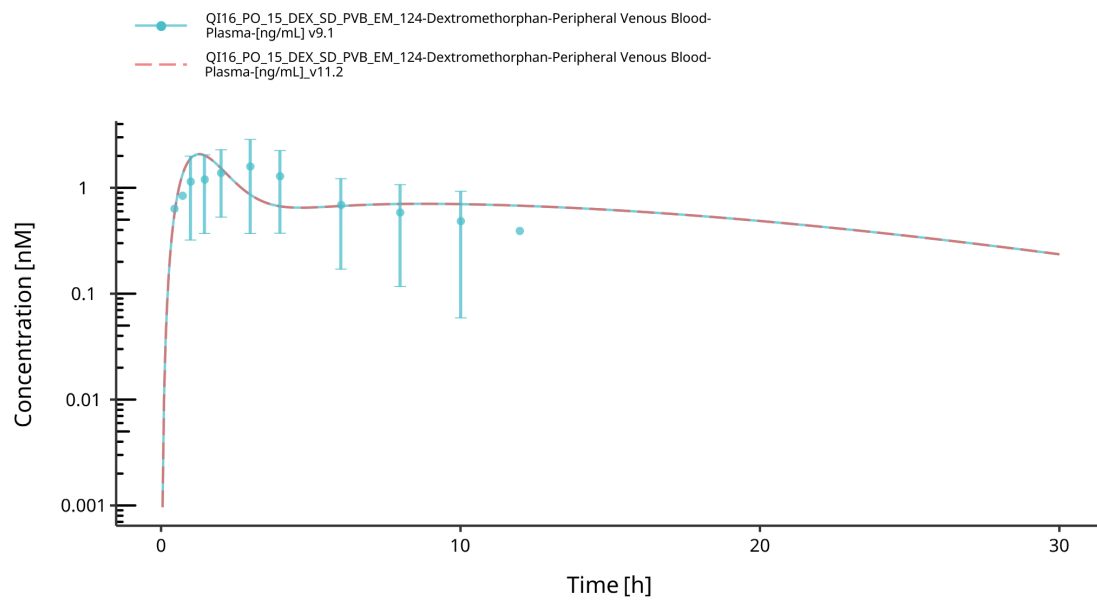


Figure 19: Qiu 2016 NM, 15 mg dextromethorphan hydrobromide (capsule_solution), n=6, AS=2

Sager 2014 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=10 - time profile

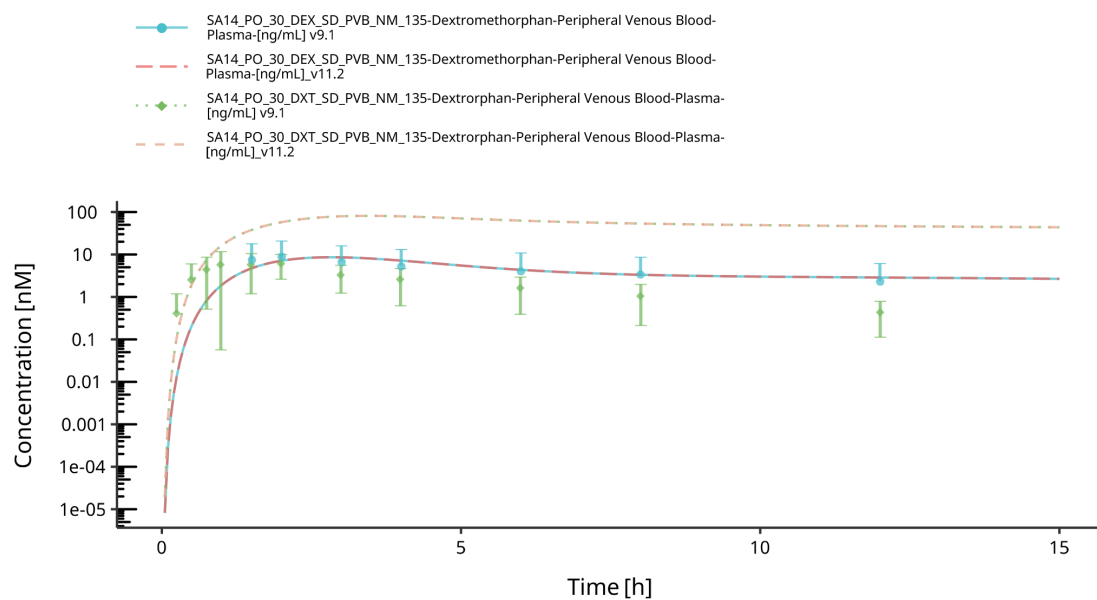


Figure 20: Sager 2014 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=10

Schadel 1995 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=5 - time profile

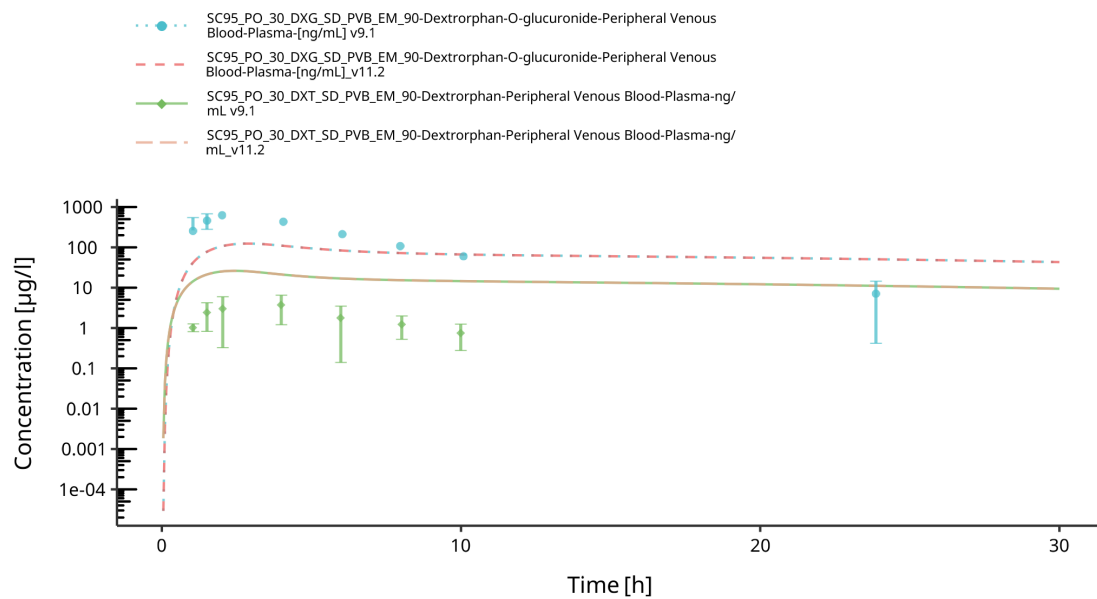


Figure 21: Schadel 1995 EM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=5

Schadel 1995 PM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=4 - time profile

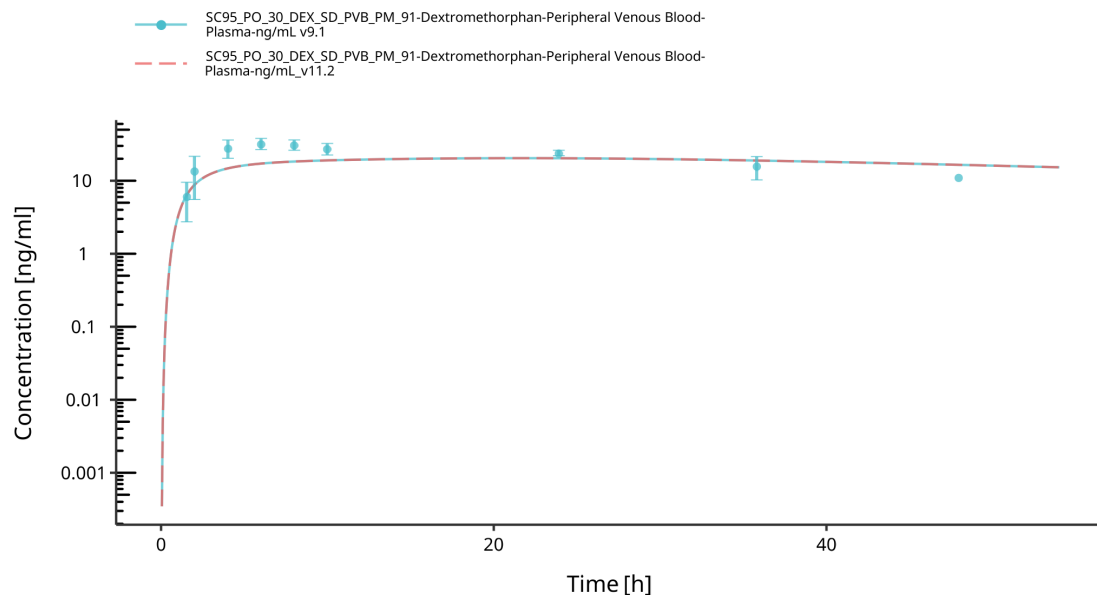


Figure 22: Schadel 1995 PM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=4

Stage 2018 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=12 - time profile

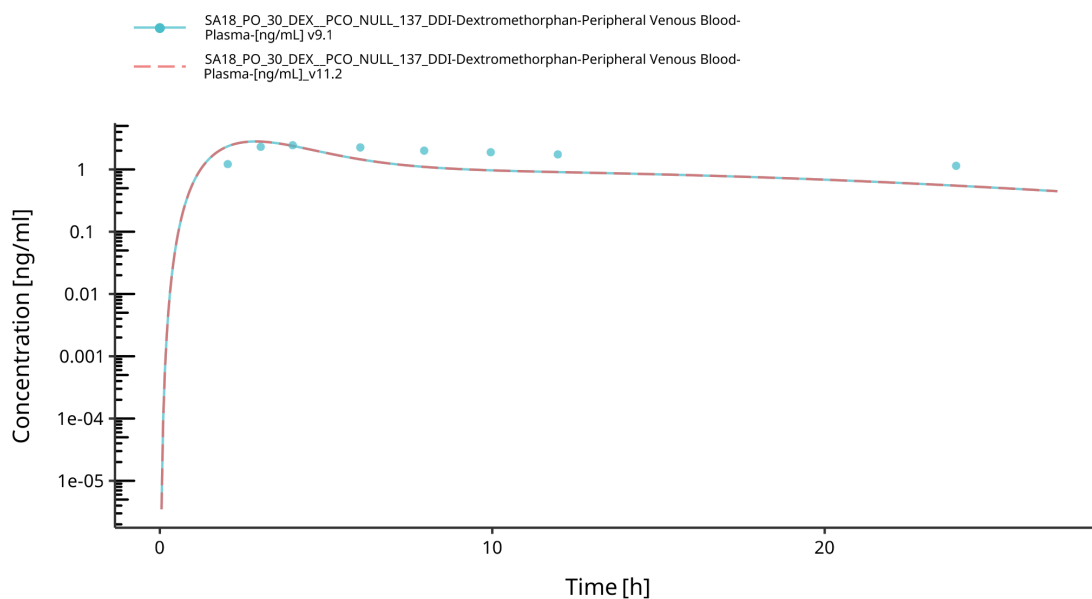


Figure 23: Stage 2018 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=12

Storelli 2018 IM, 5 mg dextromethorphan base (capsule/solution), n=16 - time profile

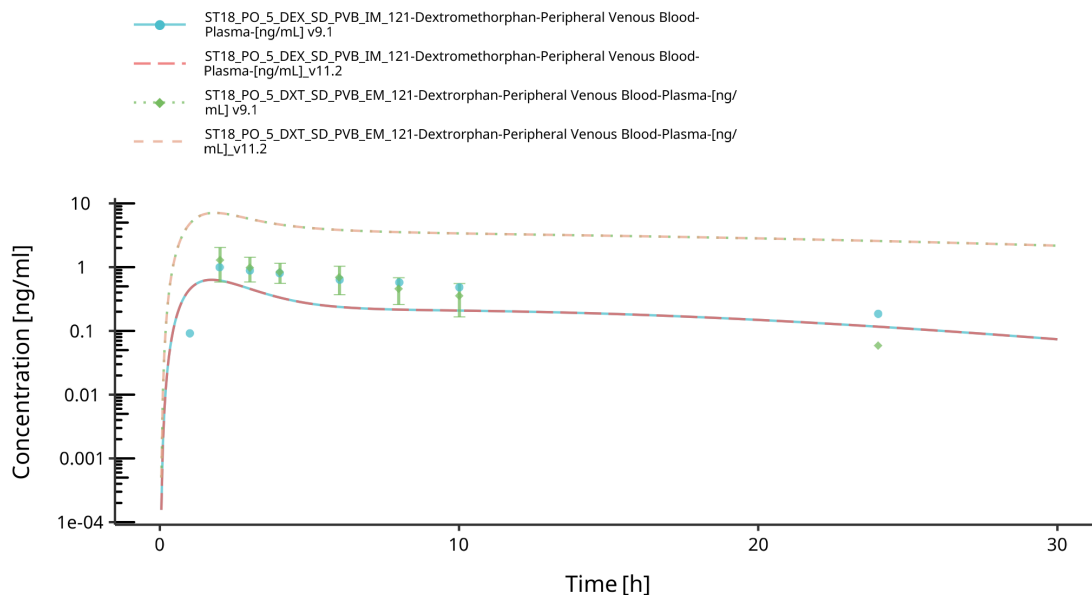


Figure 24: Storelli 2018 IM, 5 mg dextromethorphan base (capsule_solution), n=16

Storelli 2018 NM, 5 mg dextromethorphan base (capsule/solution), n=17, AS=2 - time profile

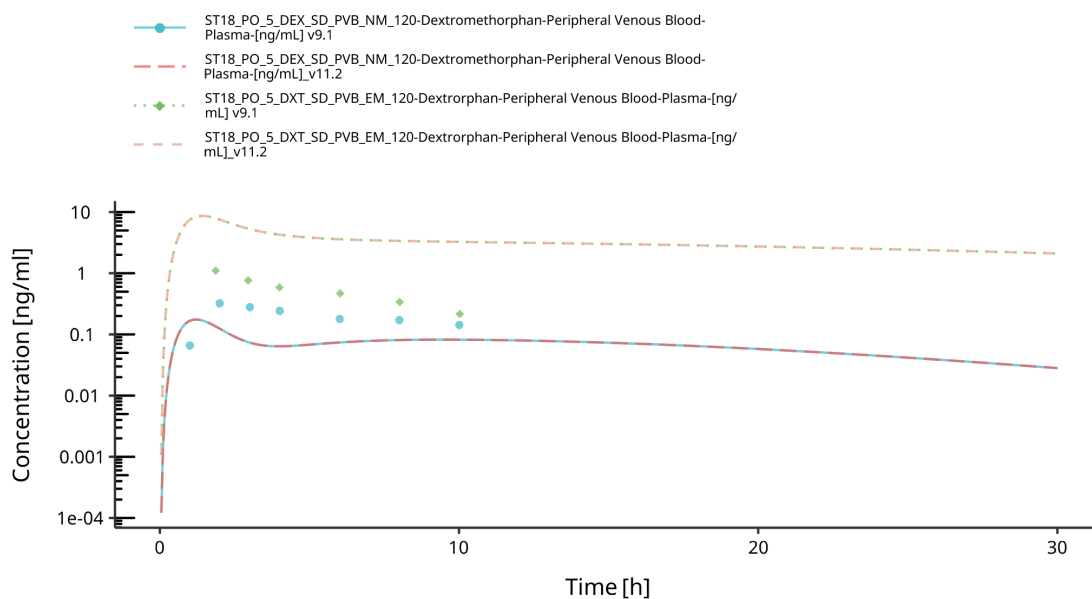


Figure 25: Storelli 2018 NM, 5 mg dextromethorphan base (capsule_solution), n=17, AS=2

Tennezé 1999 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=36 - time profile

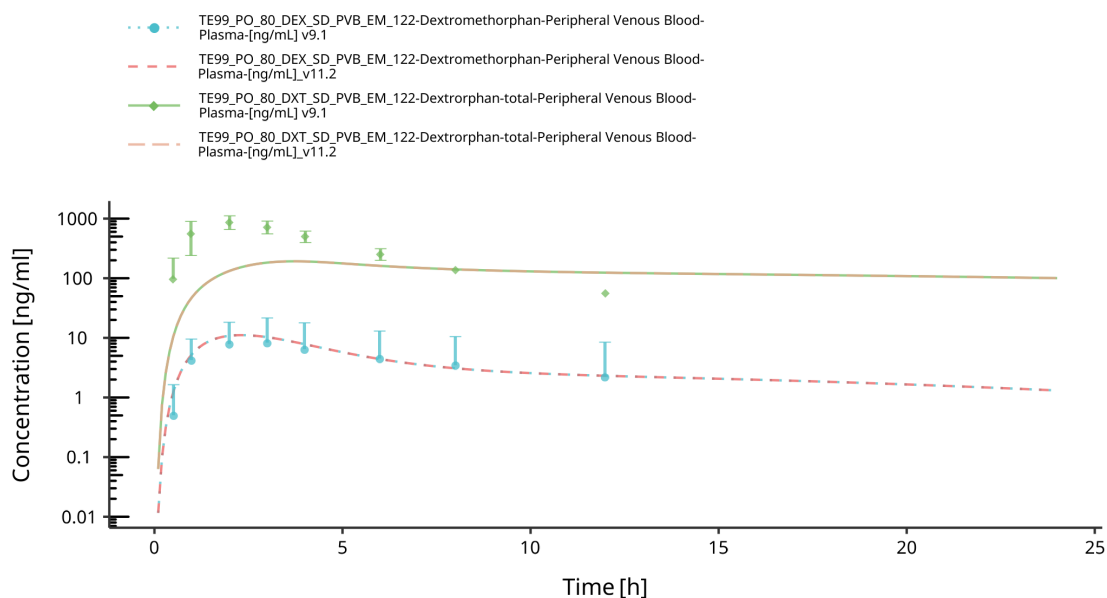


Figure 26: Tennezé 1999 EM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=36

Yamazaki 2017 IM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=12, AS=0.5 - time profile

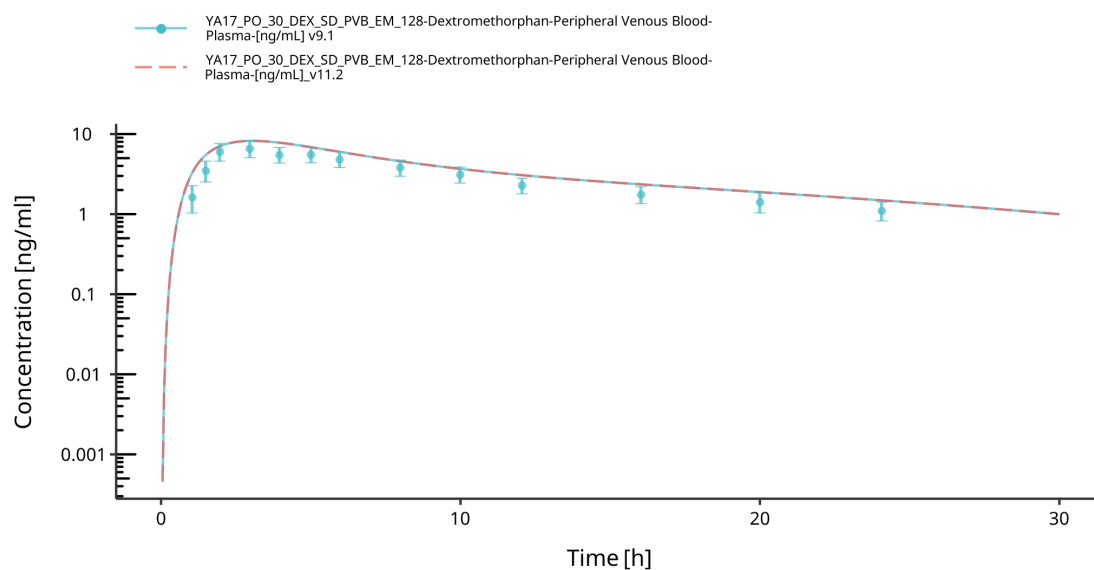


Figure 27: Yamazaki 2017 IM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=12, AS=0.5

Yamazaki 2017 NM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=11, AS=2 - time profile

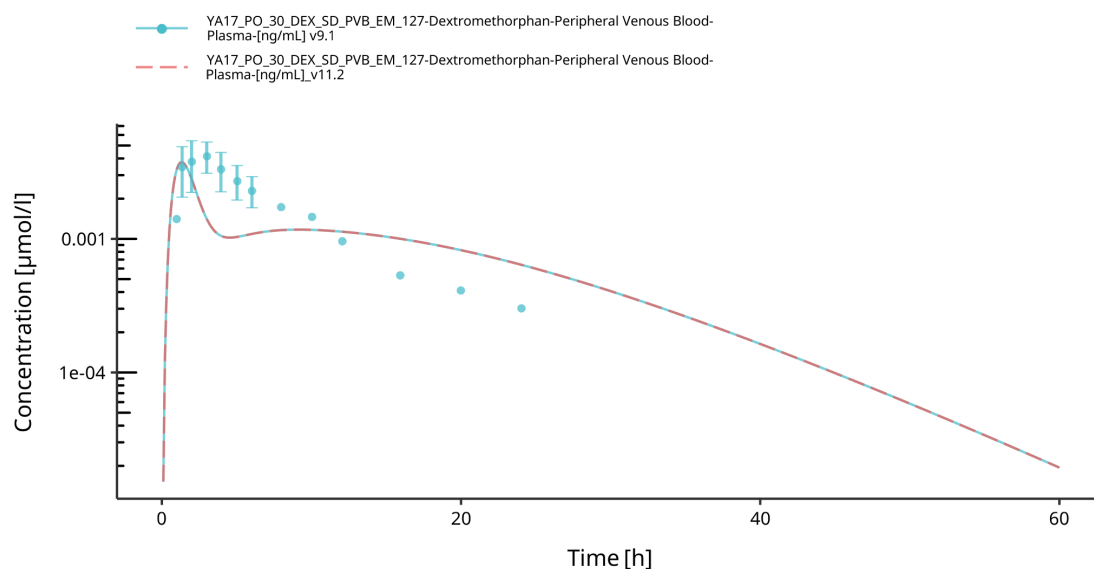


Figure 28: Yamazaki 2017 NM, 30 mg dextromethorphan hydrobromide (capsule_solution), n=11, AS=2

Zawertailo 2009 NM, 3 mg/kg dextromethorphan hydrobromide (capsule/solution), n=6, AS=2 -
time profile

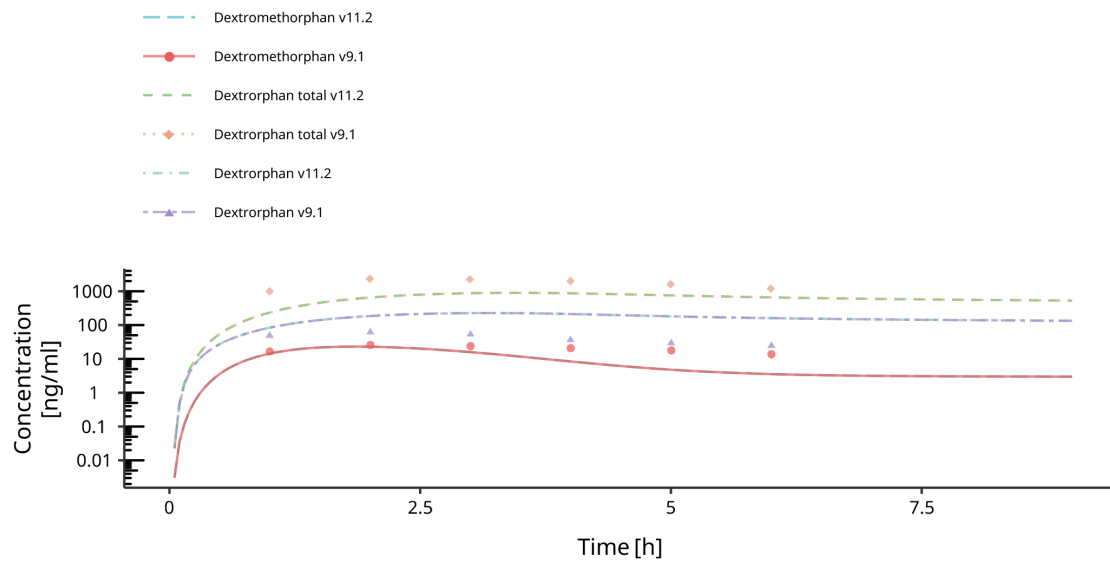


Figure 29: Zawertailo 2009 NM, 3 mg/kg dextromethorphan hydrobromide (capsule_solution), n=6, AS=2

5 Conclusion

All simulations that are available in the snapshot produced the same results as in the original publication (by visual comparison). Not all reported simulations are implemented in the snapshot, their comparison was not possible. It is, however, assumed that the model behaves exactly as described in the original publication.