

# Dextromethorphan qualification report

esqLABS GmbH

2023-09-07 19:46:09

## Table of Content

<b>1</b>	<b>Introduction</b>	<b>3</b>
<b>2</b>	<b>Methods</b>	<b>3</b>
2.1	Software . . . . .	3
2.2	Drug-gene-interaction . . . . .	3
2.3	Qualification process . . . . .	3
2.4	Consolidation of expression profiles . . . . .	3
<b>3</b>	<b>Results</b>	<b>3</b>
<b>4</b>	<b>Conclusion</b>	<b>18</b>
	<b>References</b>	<b>18</b>

**i** Note

This report has been created with simulation results loaded from results folder 2023-07-21 12-59 .

# 1 Introduction

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

The PBPK model has been developed with OSPS version 9.1 and published by ([Rüdesheim et al. 2022](#)). Model snapshots have been downloaded on 16.06.2023 from the Open Systems Pharmacology (OSP) [repository](#). As of 16.06.2023, no model version qualified for OSP version 11.2 is publicly available.

## 2 Methods

### 2.1 Software

For recreating the original results from the publication, OSPS [version 9.1](#) was used. The qualification is done with OSPS [version 11.2.142](#).

### 2.2 Drug-gene-interaction

The model is intended to be used in drug-drug interactions (DDI) simulations with dextromethorphan as a CYP2D6 victim. Drug-gene interactions (DGI) to describe variabilities of CYP2D6 activity are modeled as variations of the catalytic rate constant  $k_{cat}$ . Following values are used in the project:

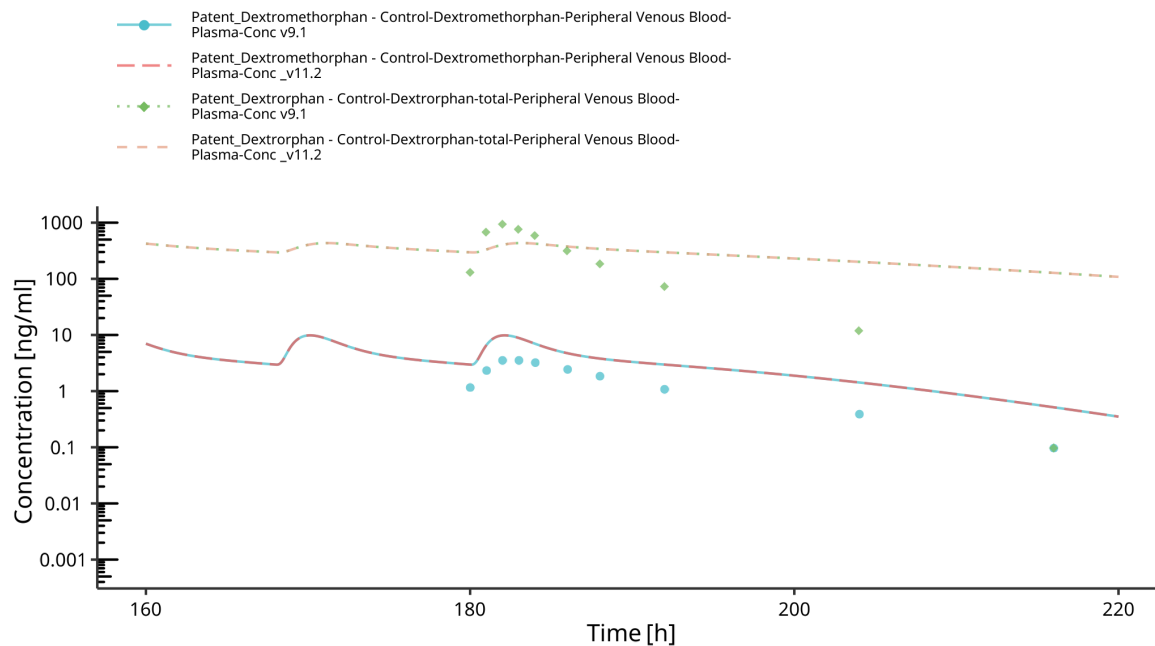
### 2.3 Qualification process

### 2.4 Consolidation of expression profiles

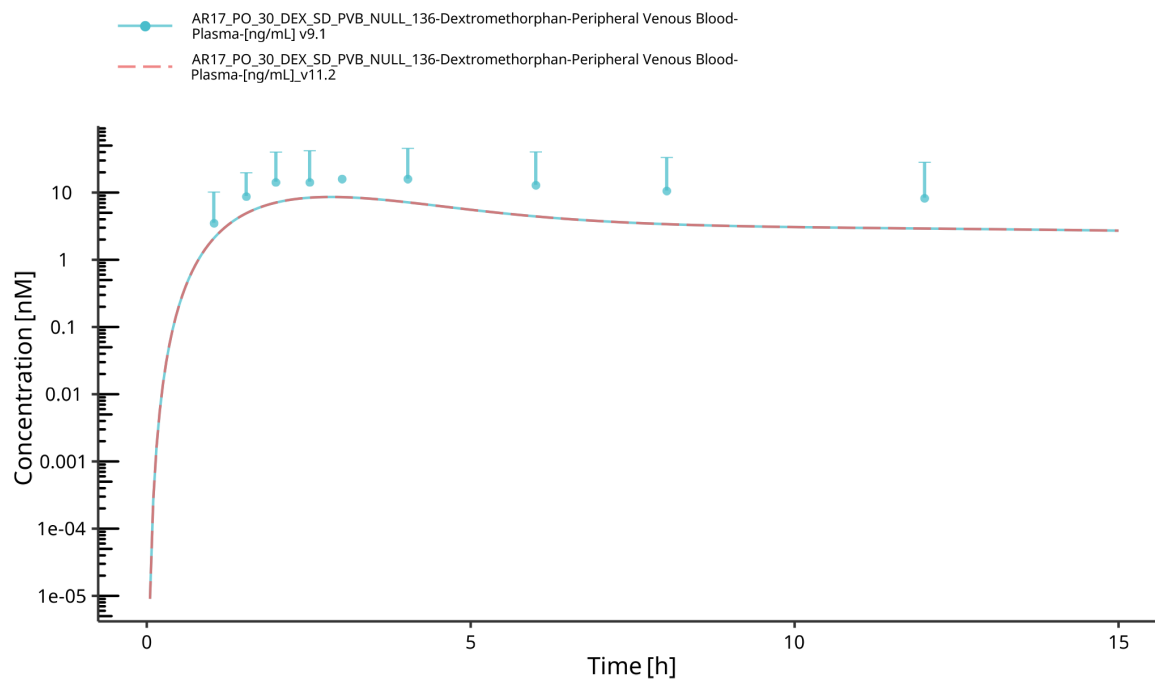
## 3 Results

Comparison of time-concentration profiles generated with the different software versions are presented in the following:

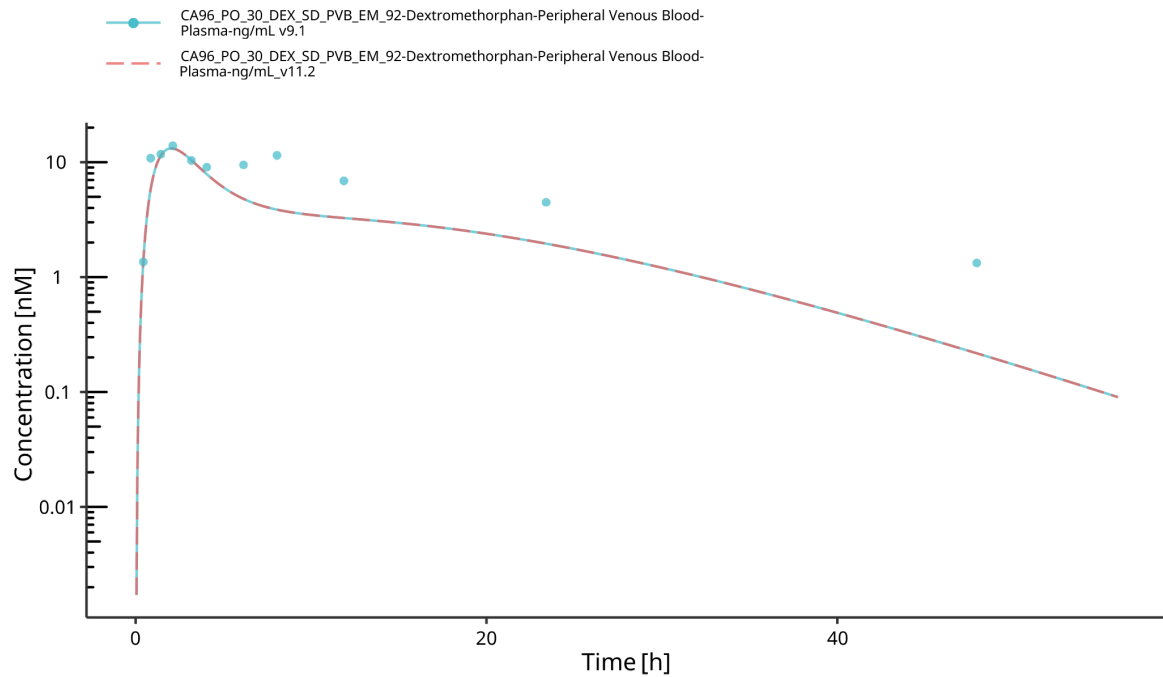
Antecip Bioventures EM, 60 mg dextromethorphan hydrobromide multiple dose (capsule/solution),  
n=10 - time profile



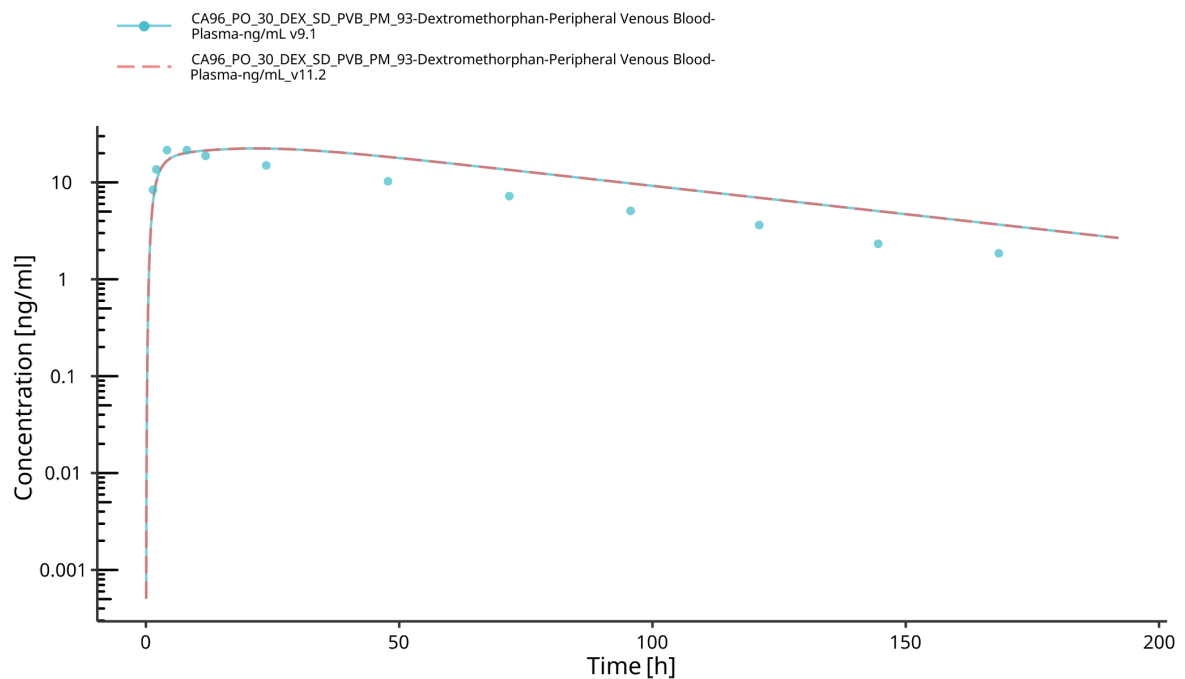
Armani 2017 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=20 - time profile



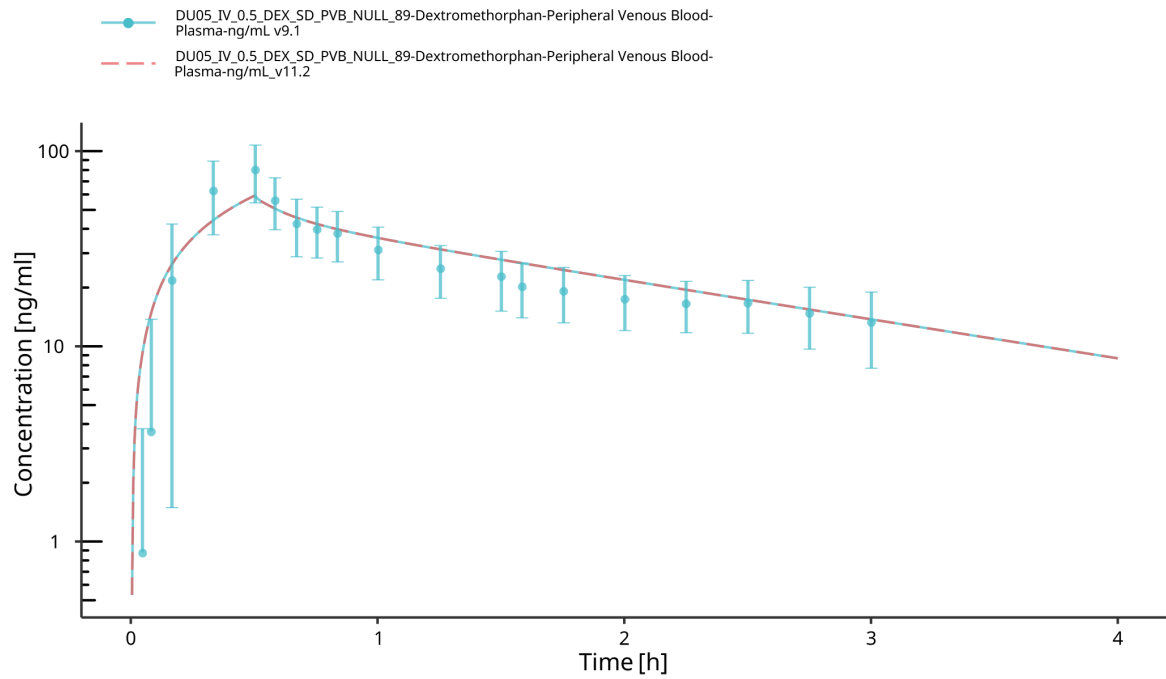
Capon 1996 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=6 - time profile



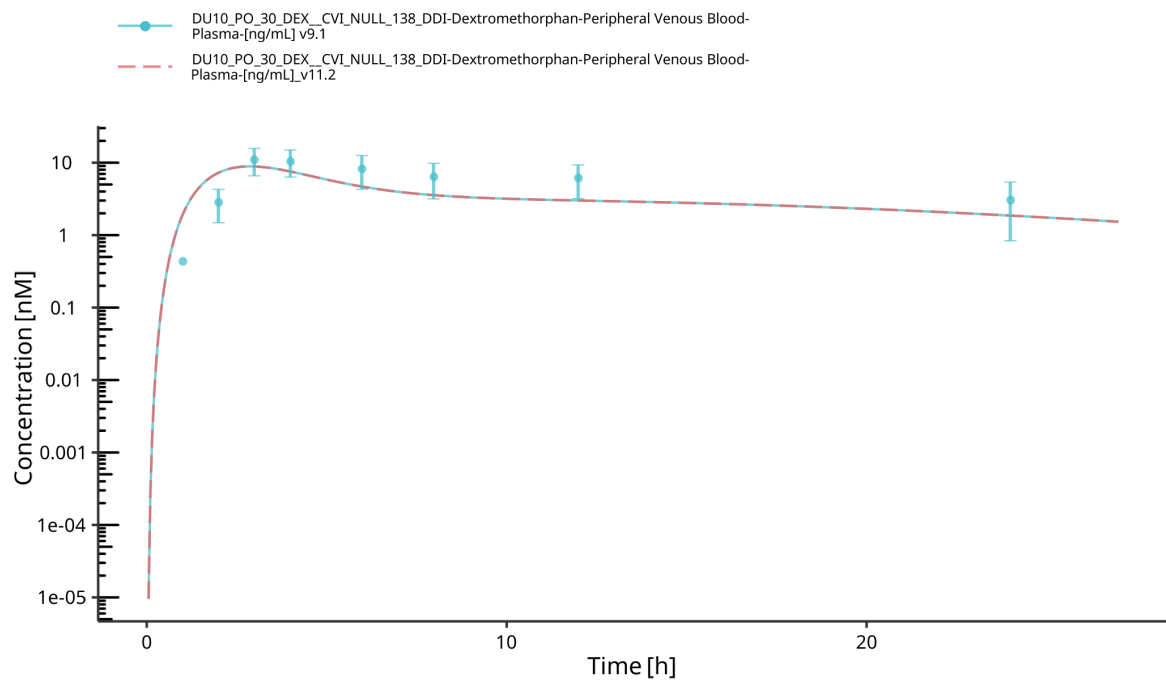
Capon 1996 PM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=6 - time profile



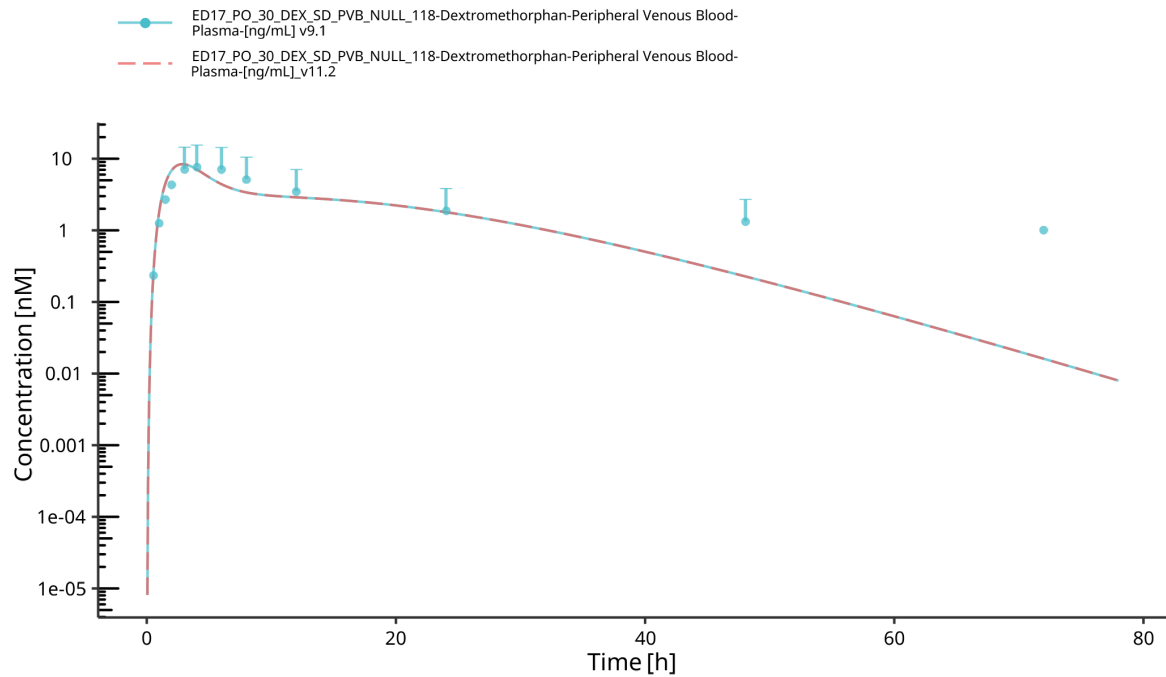
Duedahl 2005 EM, 0.5 mg/kg dextromethorphan base (infusion), n=24 - time profile



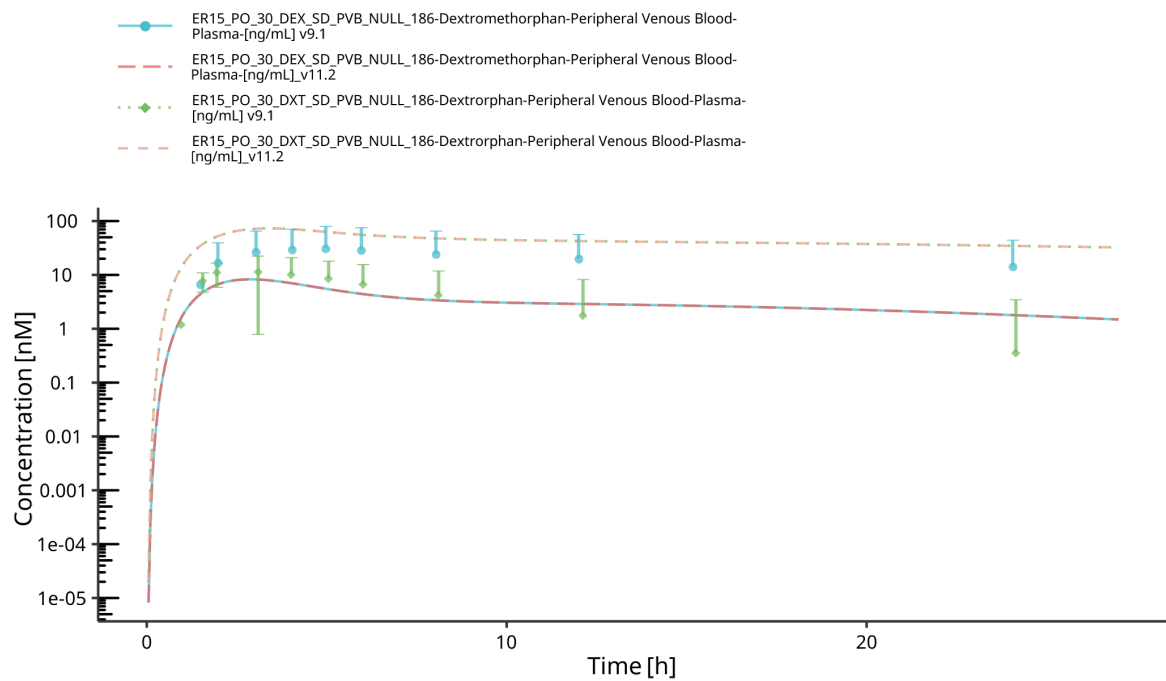
Dumond 2010 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=23 - time profile



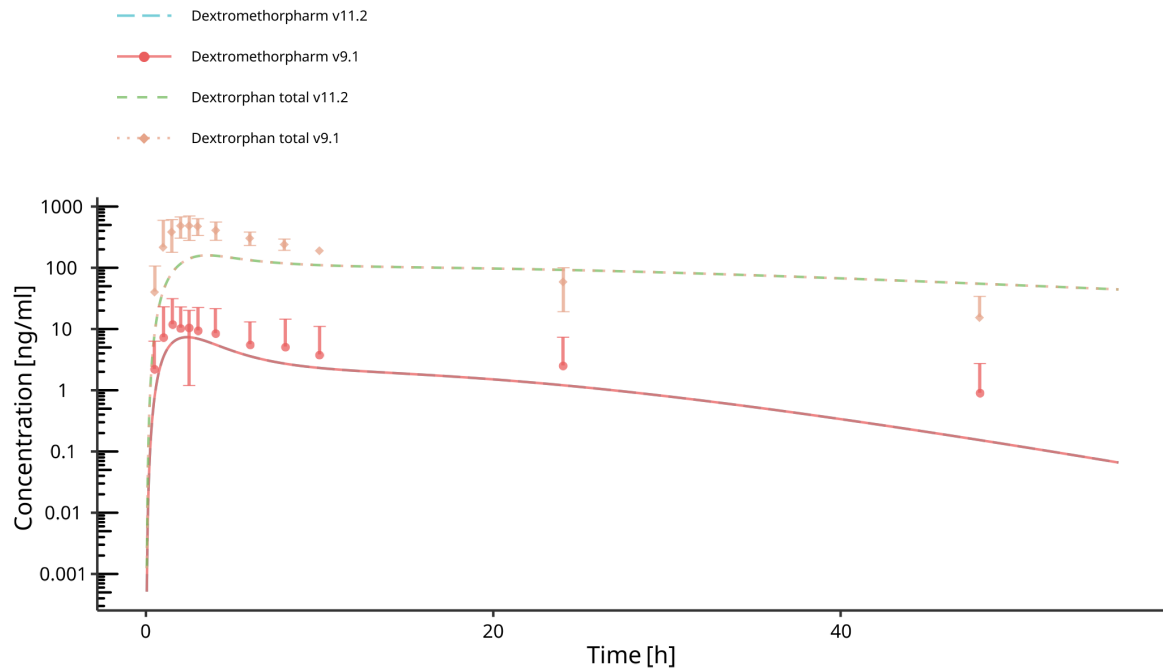
Edwards 2017 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=48 - time profile



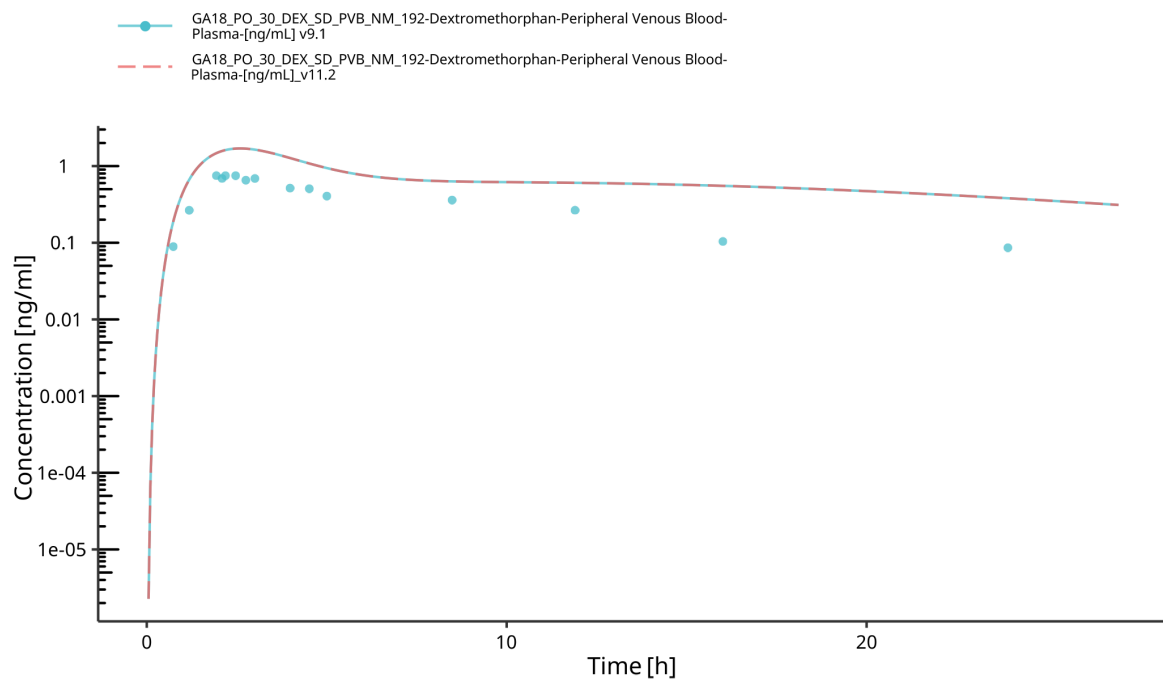
Ermer 2015 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=30 - time profile



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

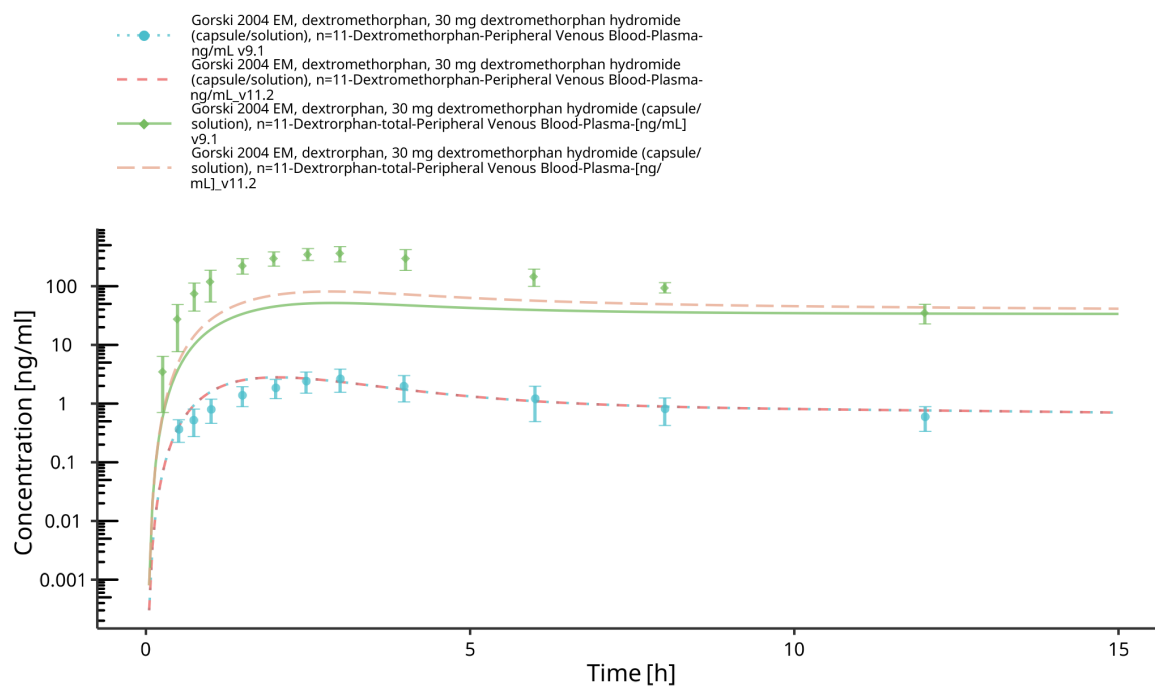


Gazzaz 2018 NM, 30 mg dextromethorphan hydrobromide (cocktail), n=30, AS=1.25 - time profile

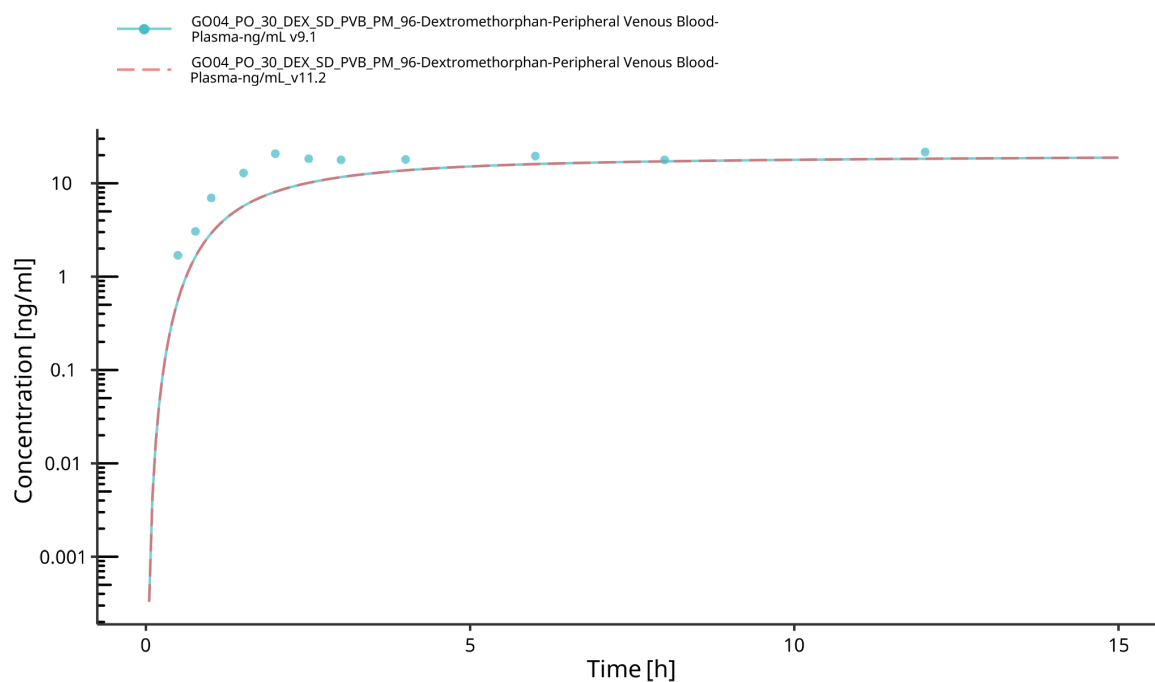




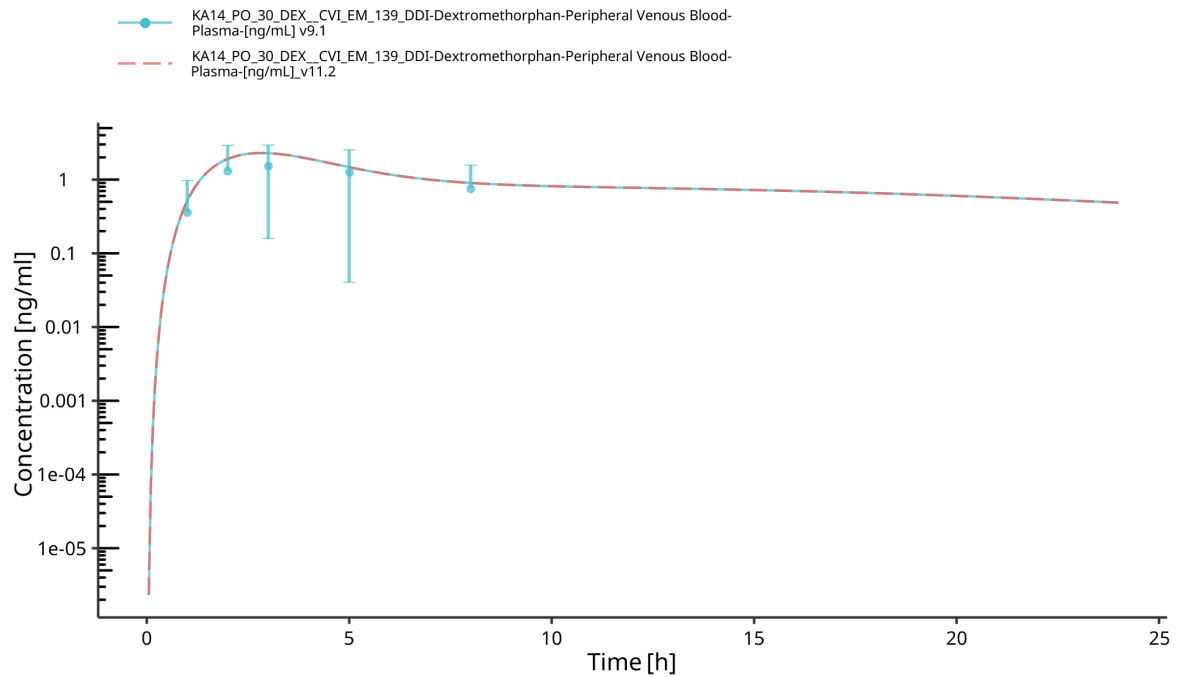
Gorski 2004 EM, 30 mg dextromethorphan hydromide (capsule/solution), n=11 - time profile



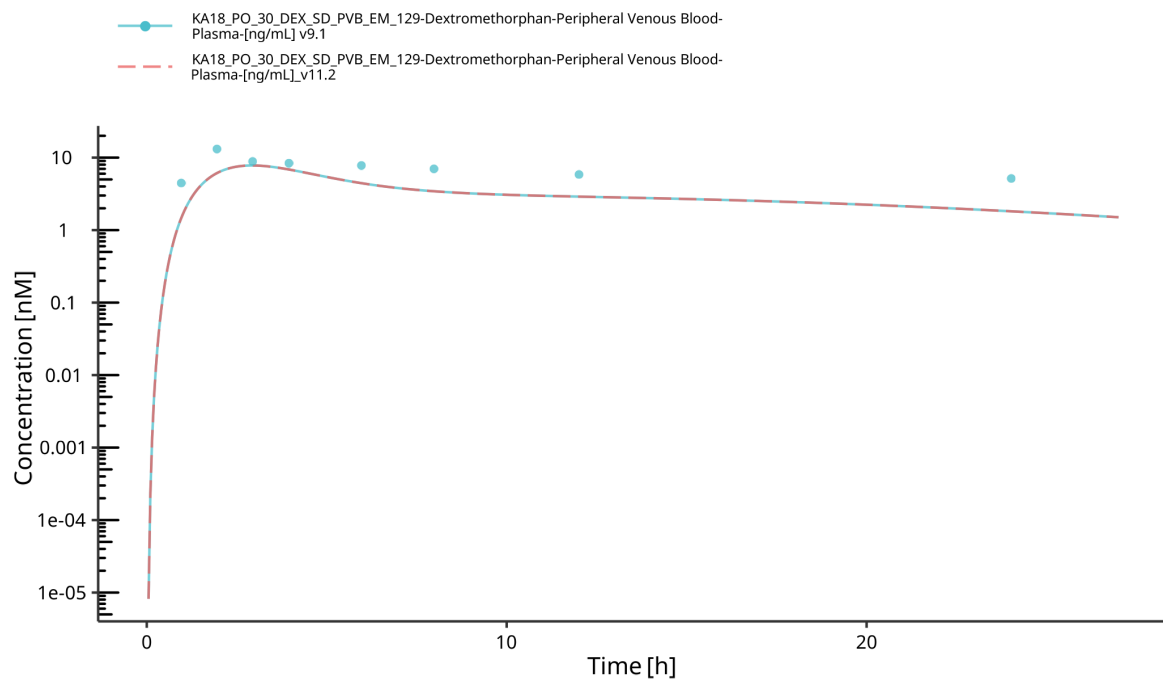
Gorski 2004 PM, 30 mg dextromethorphan hydromide (capsule/solution), n=1 - time profile



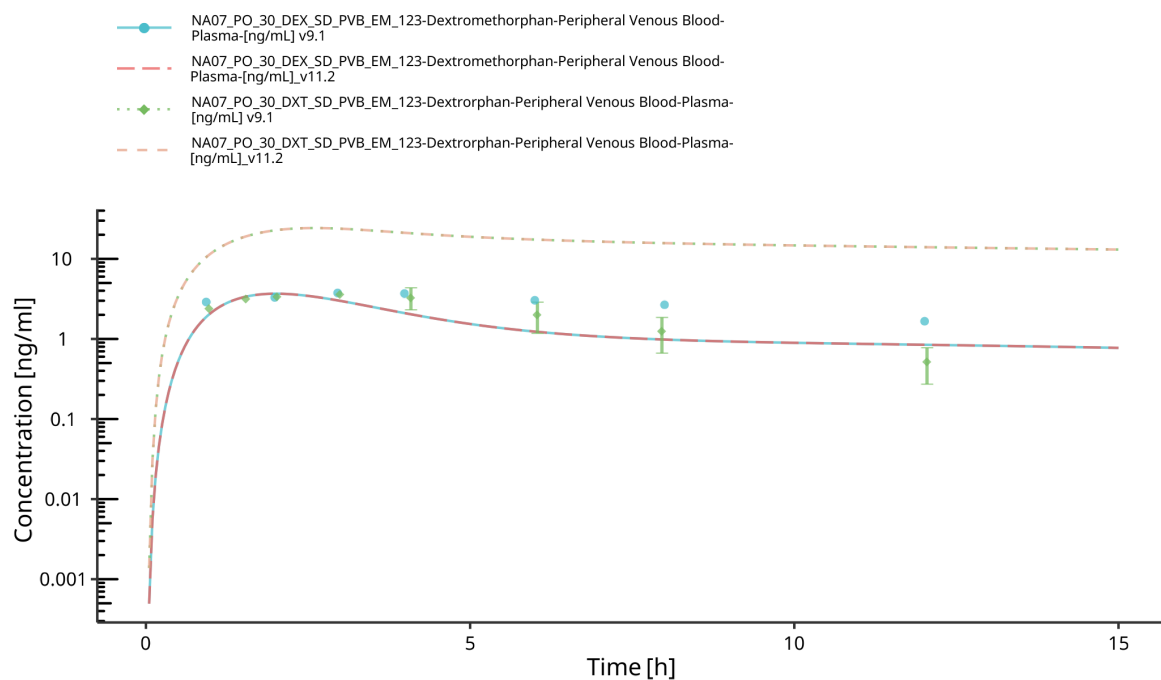
Kakuda 2014 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=14 - time profile



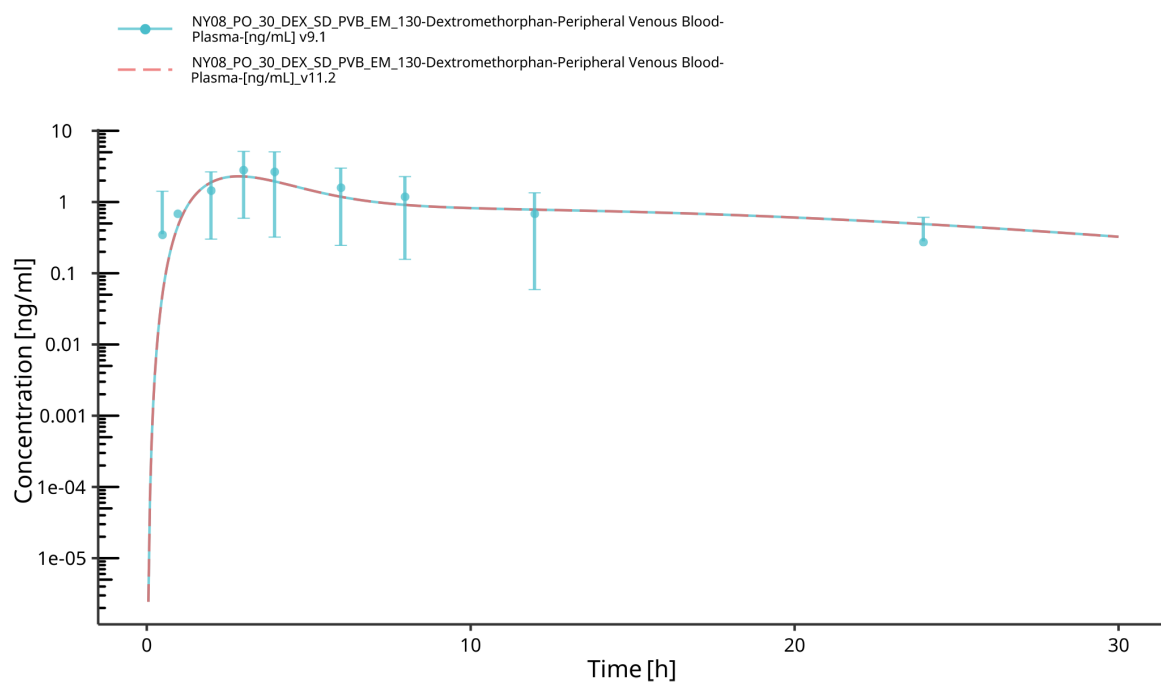
Khalilieh 2018 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=20 - time profile



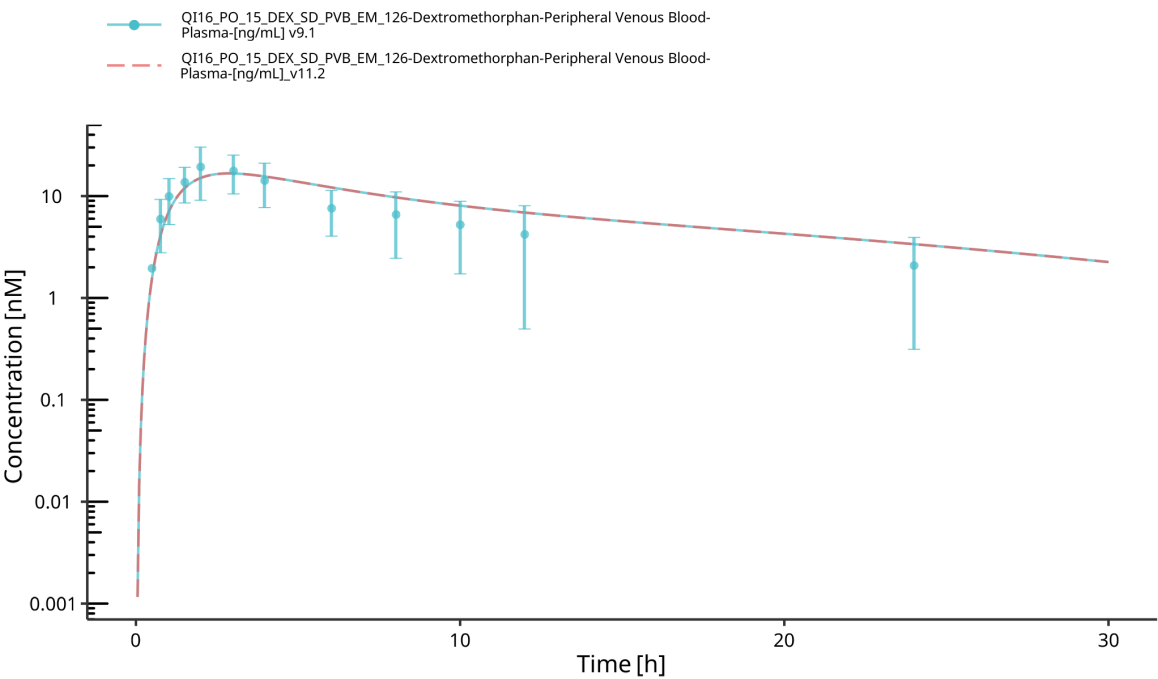
# Parasmina 2007 EM, 30 mg dextromethorphanhydrobromide (capsule), n=24 - time profile



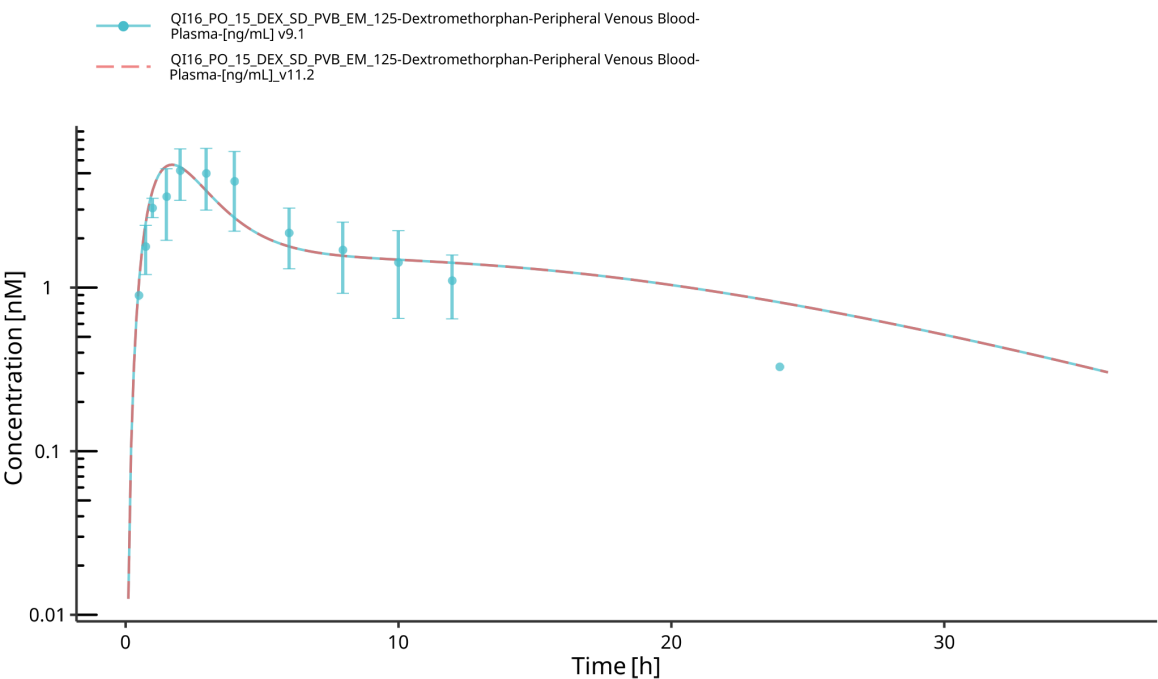
## Nyunt 2008 EM, 30 mg dextromethorphanhydrobromide (cocktail), n=12 - time profile



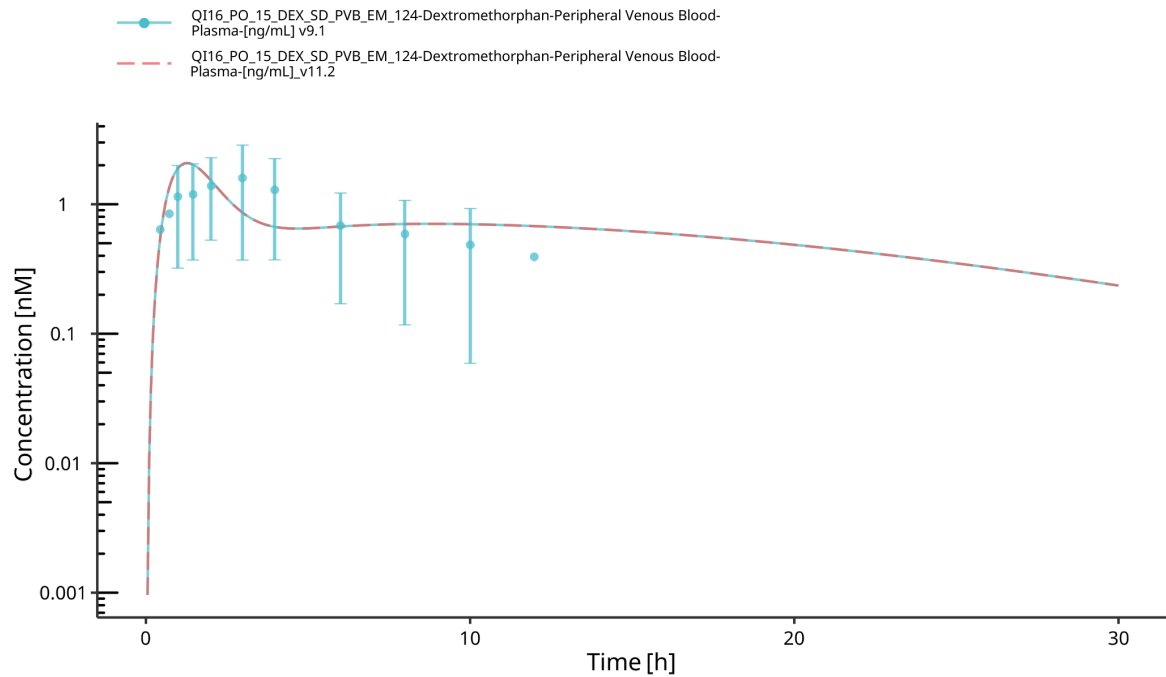
Qiu 2016 IM, 15 mg dextromethorphan hydrobromide (capsule/solution), n=6, AS=0.5 - time profile



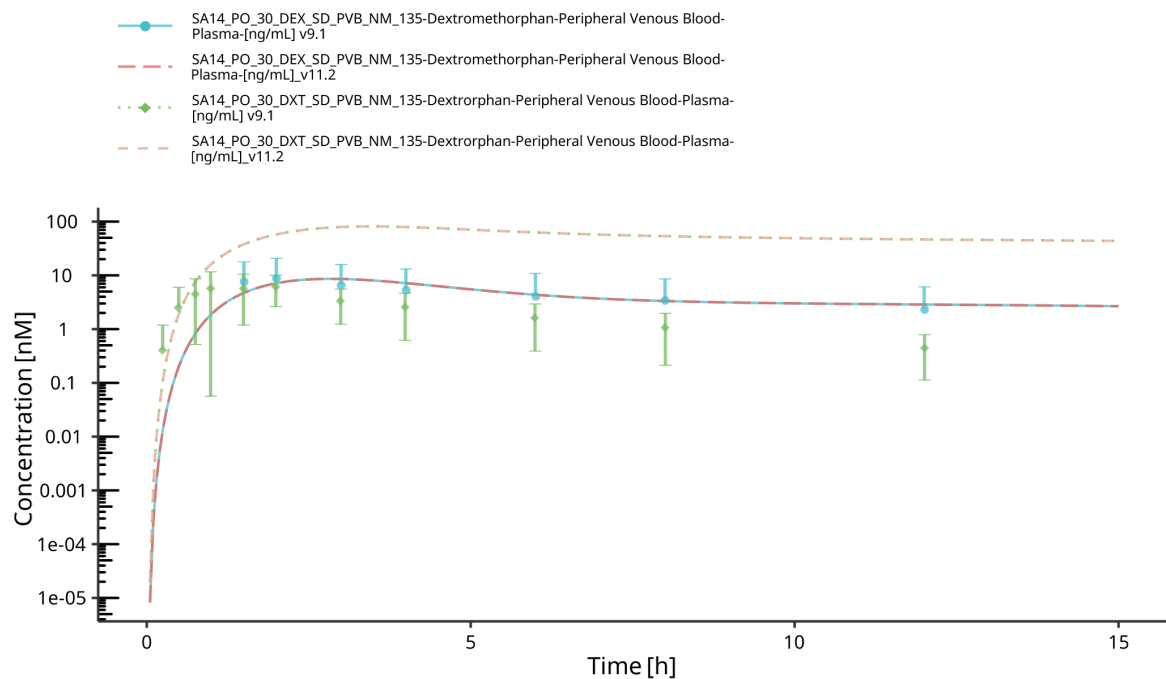
Qiu 2016 IM, 15 mg dextromethorphan hydrobromide (capsule/solution), n=6, AS=1.25 - time profile



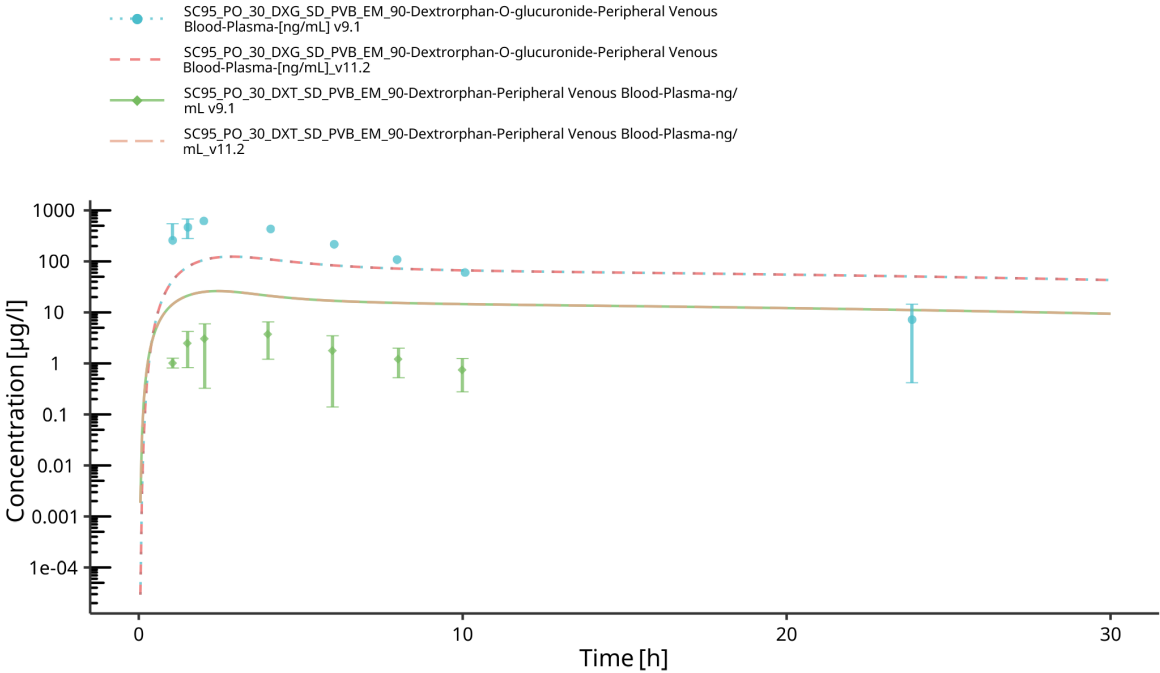
Qiu 2016 NM, 15 mg dextromethorphan hydrobromide (capsule/solution), n=6, AS=2 - time profile



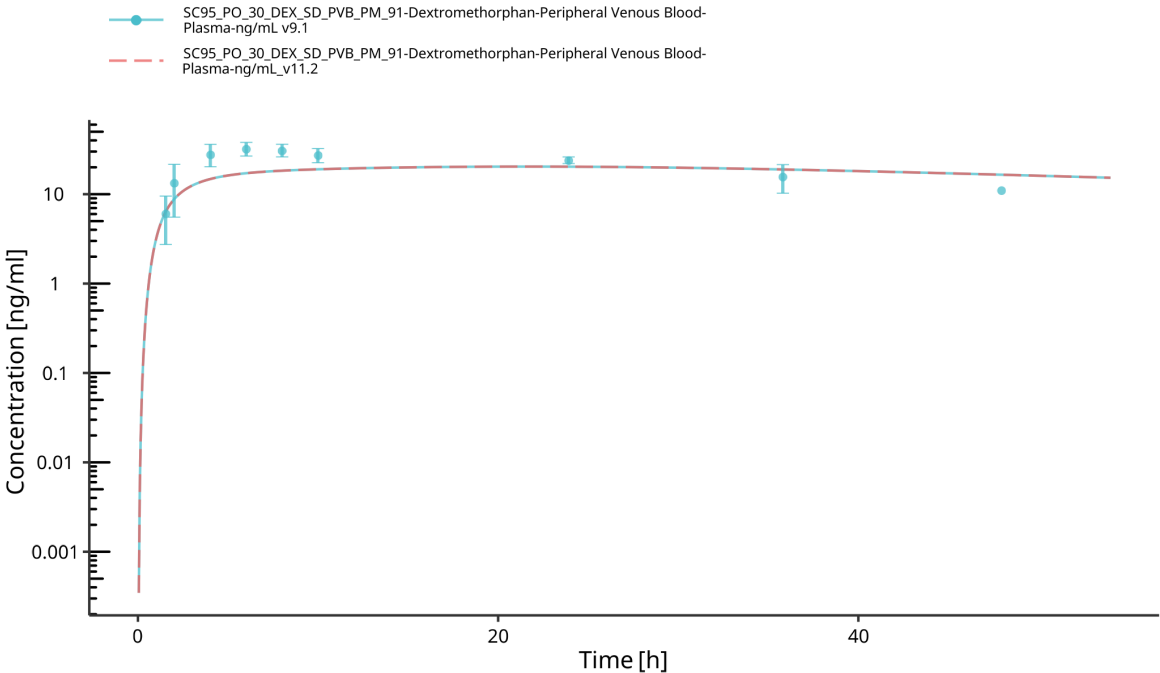
Sager 2014 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=10 - time profile



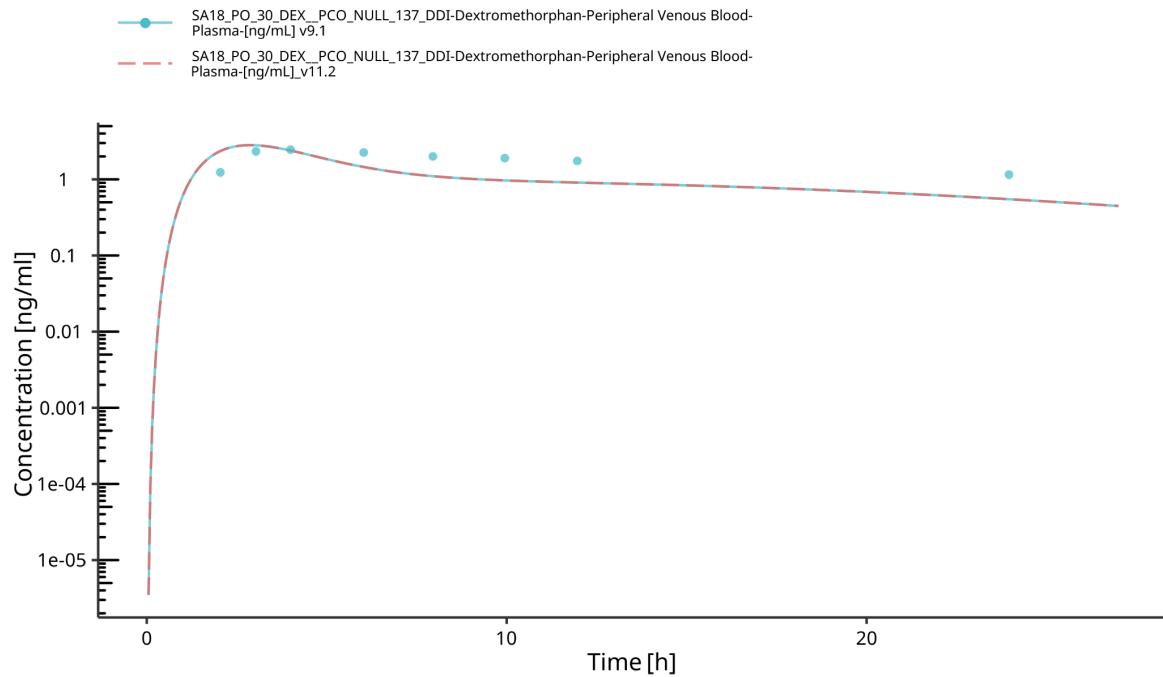
Schadel 1995 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=5 - time profile



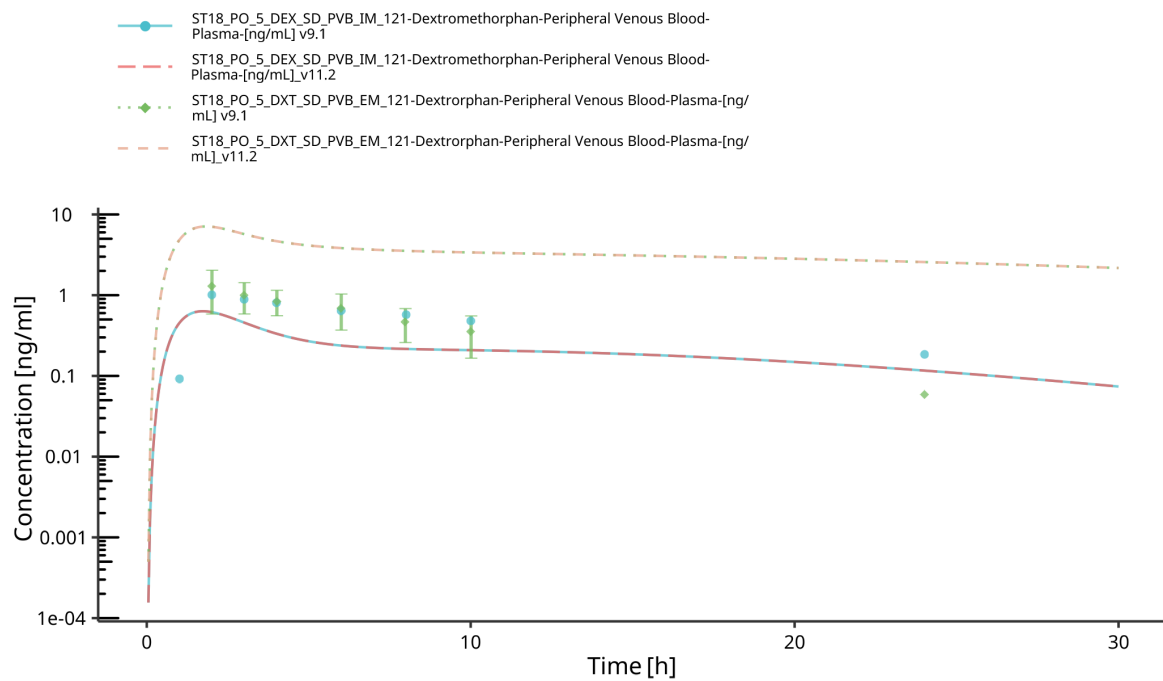
Schadel 1995 PM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=4 - time profile



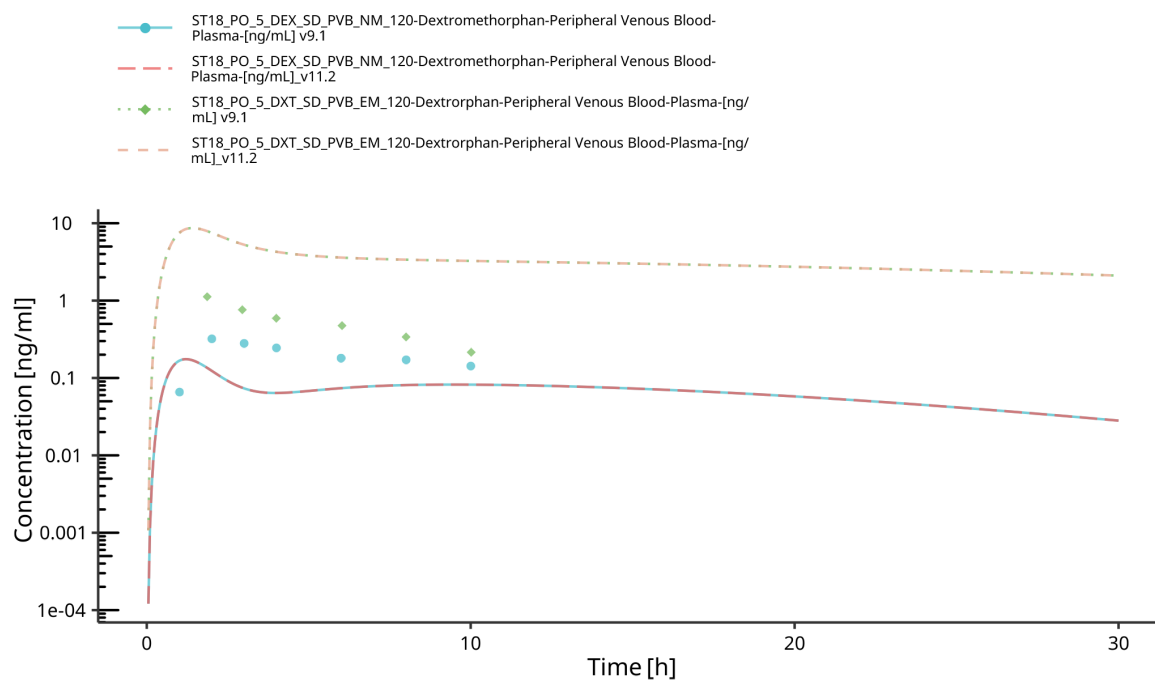
Stage 2018 EM, 30 mg dextromethorphan hydrobromide (cocktail), n=12 - time profile



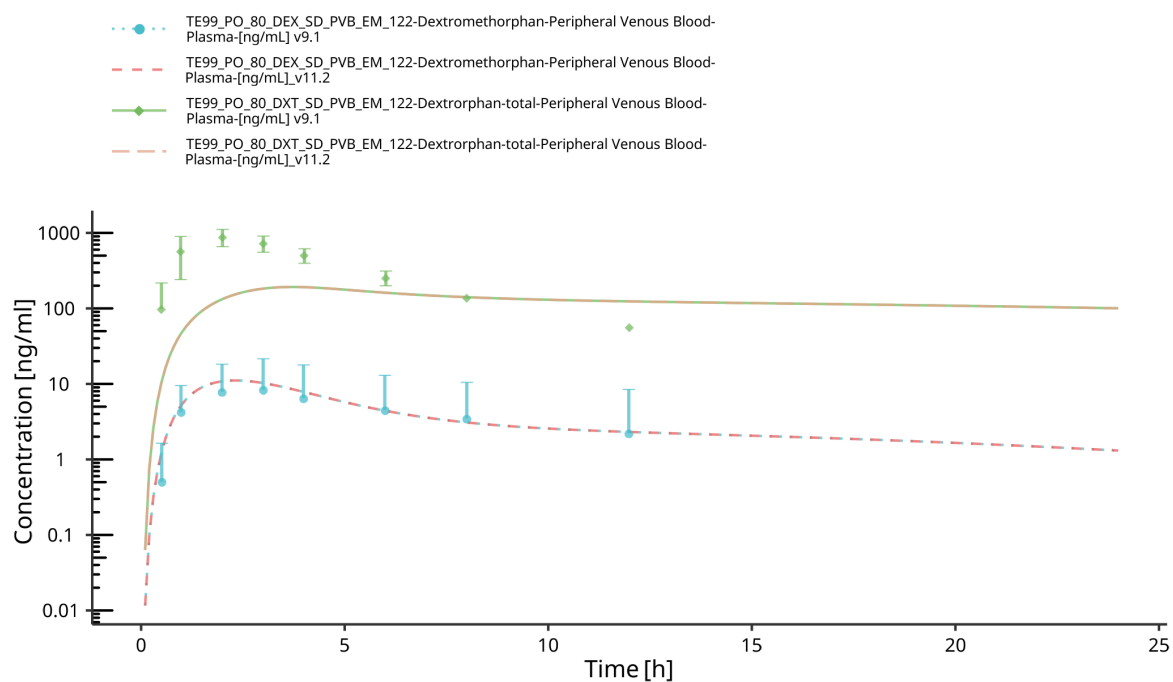
Storelli 2018 IM, 5 mg dextromethorphan base (capsule/solution), n=16 - time profile



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

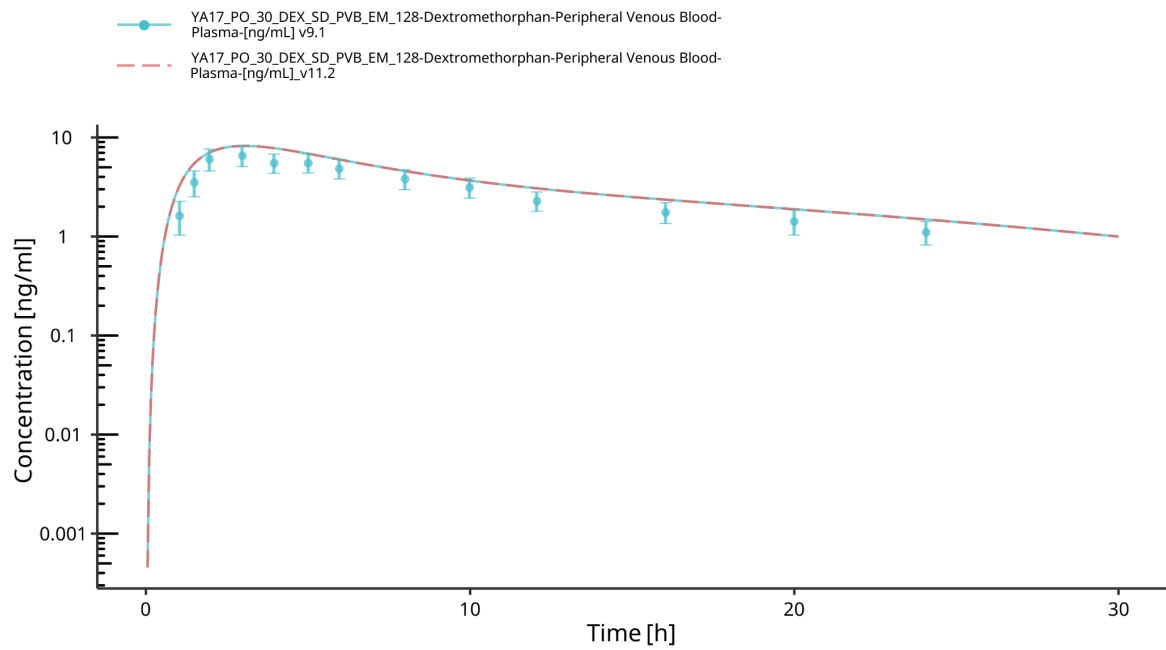


Tennez  1999 EM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=36 - time profile

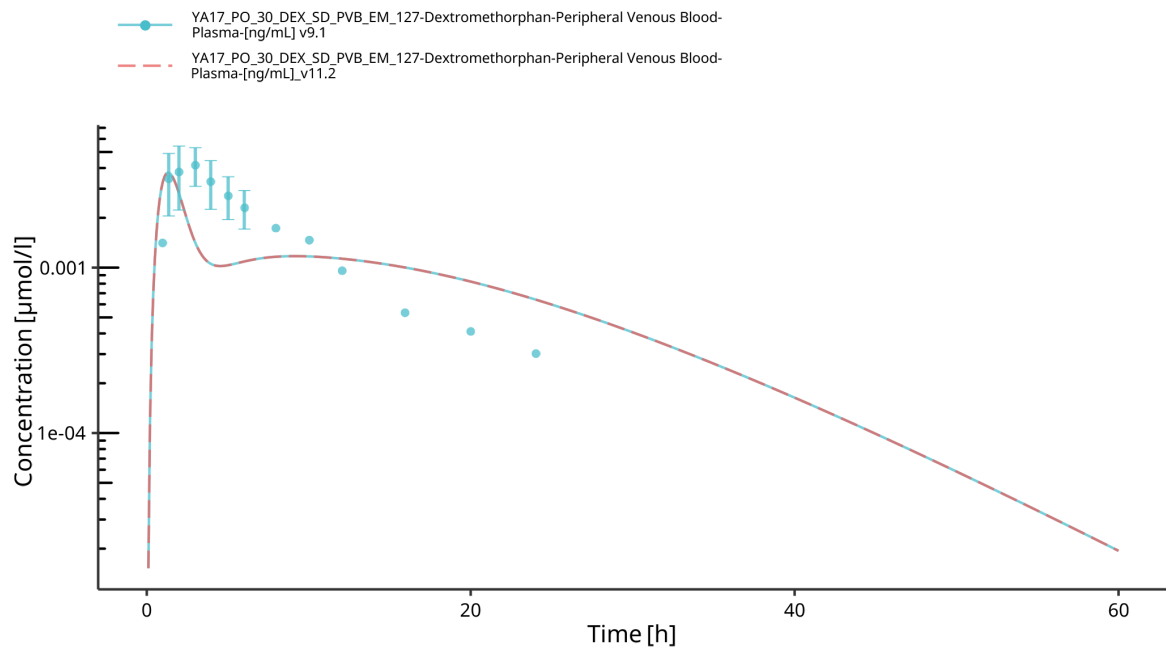




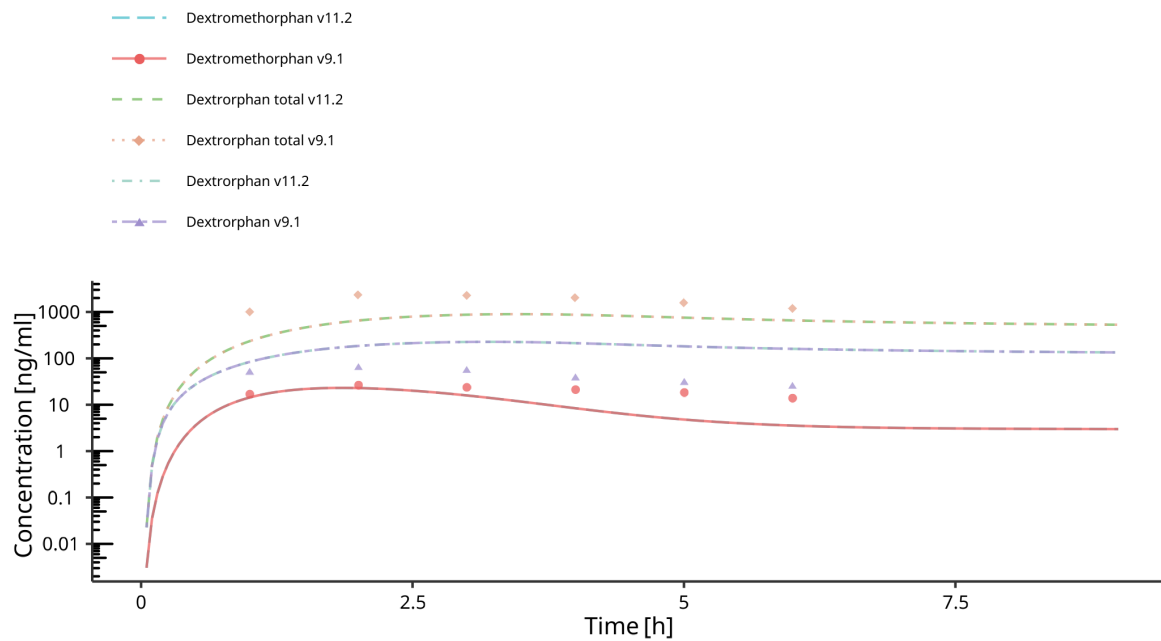
Yamazaki 2017 IM, 30 mg dextromethorphan hydrobromide (capsule/solution), n=12, AS=0.5 - time profile



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



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



## 4 Conclusion

## References

Rüdesheim, Simeon, Dominik Selzer, Uwe Fuhr, Matthias Schwab, and Thorsten Lehr. 2022. "Physiologically-Based Pharmacokinetic Modeling of Dextromethorphan to Investigate Interindividual Variability Within CYP2D6 Activity Score Groups." *CPT: Pharmacometrics & Systems Pharmacology* 11 (4): 494–511. <https://doi.org/10.1002/psp4.12776>.