MEDIWARE

Project MwPharm

FREQUENTLY ASKED QUESTIONS

Name
Frequently Asked Questions

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1.0	05.09.2016	Jan Kraus	First Revision
1.1	25.01.2017	Jan Kraus	Second Revision
1.2	29.03.2017	Jan Kraus	Third Revision
1.3	28.11.2017	Jan Kraus	Fourth Revision
1.4	15.02.2018	Marek Kordík	Fifth Revision
1.5	07.08.2018	Aleš Hrudička	Sixth Revision
1.6	01.11.2019	Matouš Kasal	Seventh Revision
1.7	30.01.2020	Matouš Kasal	Eight Revision
1.8	18.10.2022	George Douša	Ninth Revision
1.9	01.09.2023	Zdislava Matušková	Tenth Revision
1.10	01.10.2024	Marina Radić	Eleventh Revision

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Content

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1 General Information

1.1 About application

1.1.1 What is MwPharm++?

MwPharm is clinical pharmacokinetic program used primarily to establish proper dosing regimen which is determined by both the population pharmacokinetic parameters from a drug database being a part of MwPharm and individual patient physiological parameters.

1.1.2 What are the benefits from using this software?

The program was designed to:

- Improve the drug prescription quality
- Prevent patient intoxication
- Prevent patient underdosage
- Reduce the number of measurements of plasma drug concentration
- Shorten the time spent in the hospital for the patient
- Simplify the communication among doctors

1.1.3 What is the difference between MWpharm++ and MwPharm 4.0?

MwPharm++ is a new version of MwPharm 4.0. It is now based on Edsim++ software for PKPD modelling, so it is possible to create and add new drugs to the MwPharm++ database easily. The ++ version is very similar to our DOS version.

MwPharm 4.0 vs. MwPharm++: both versions are quite different. The ++ version was designed to make the switching from DOS easy. There are same computational results, same hot keys, possibility to control the app from keyboard, etc. There is also larger drug database (you can find the list here) and it is possible to add new drugs easily. There will also be adjustable output reports. We are also working on some extensions, for example app for noncompartmental analysis, genetic module, etc. Cystatin C levels can be entered in the future.

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1.1.4 What is the difference between MwPharm++ and MwPharm Online?

MwPharm++ is an older, stand-alone version of our product. Switching to online version makes it easier for customer to access and work with the software from anywhere in the world.

There is a significant difference between MwPharm++ and the DOS version regarding the effect the GammaSD. That is because MwPharm++ uses double precisions matrix and DOS uses single precision. So MwPharm++ should perform better. The usual range of GammaSD should be between 1 and 4.

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1.2 Registration

1.2.1 How long is the trial version valid for use?

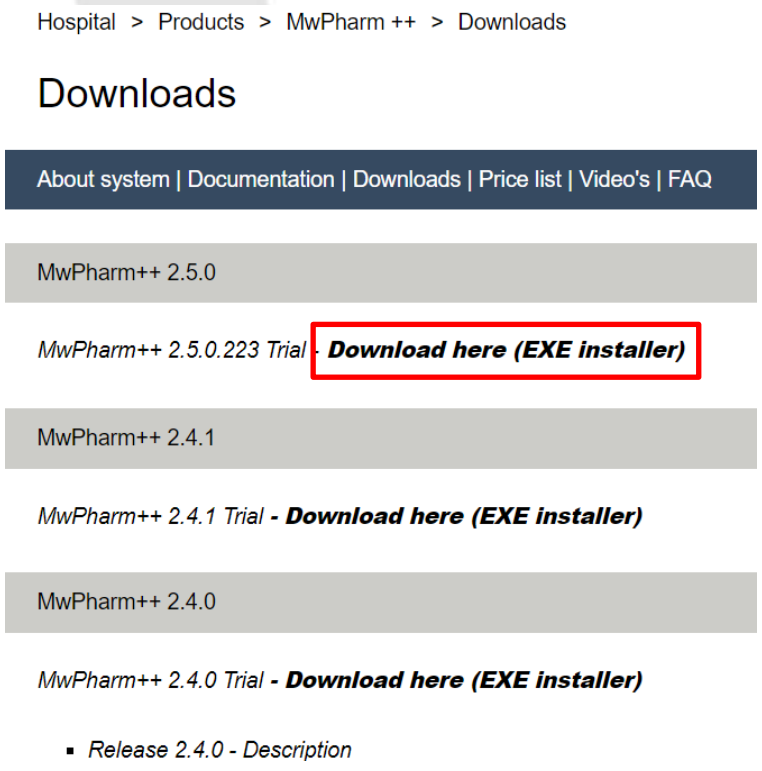
Trial version license works for **30 days**. You have all components of our software unlocked to truly test out our software. After this time period, it is necessary to buy a license in order to be able to use the application.

1.2.2 How to get a licence?

If you decided that you want a license for our software, feel free to email us: **info@mediware.cz** where you will obtain a pricelist with specification on the price and period of usage for our software.

1.2.3 How to register to the application?

You can register to the application by downloading latest version of the software on this link https://www.mediware.cz/en/mwpharm-plus-plus-downloads. Use your e-mail to access the software features and automatically start your 30 day trial period.



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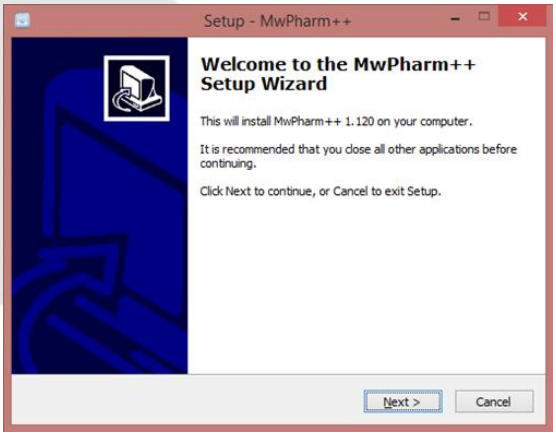
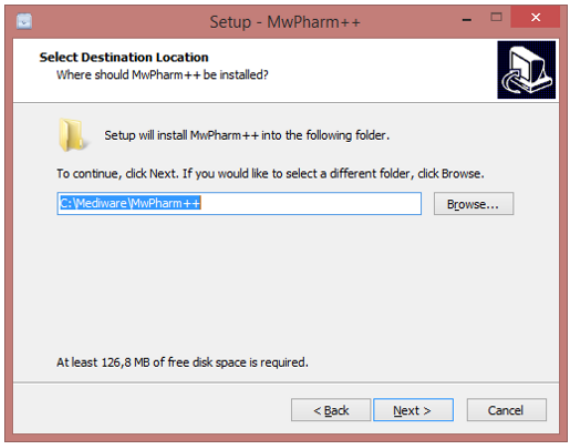
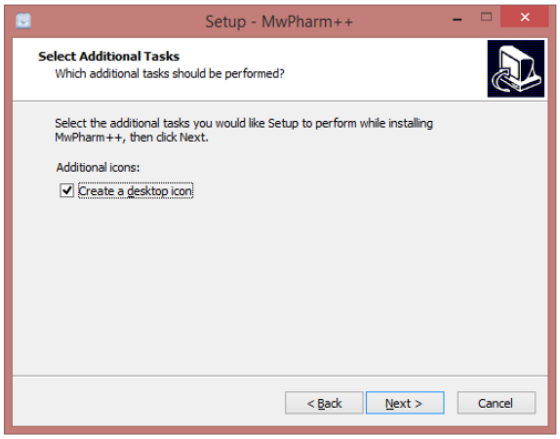
1.2.4 How to install the software?

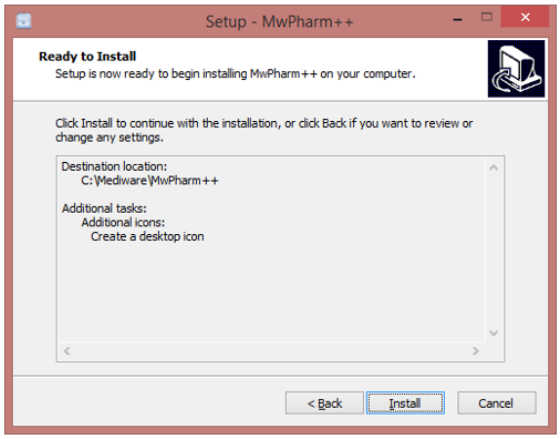
After downloading the file, run it. If you have an old version of MwPharm already installed, the installation will do a complete reinstall. If you want to maintain your current database, backup your database file, that is in

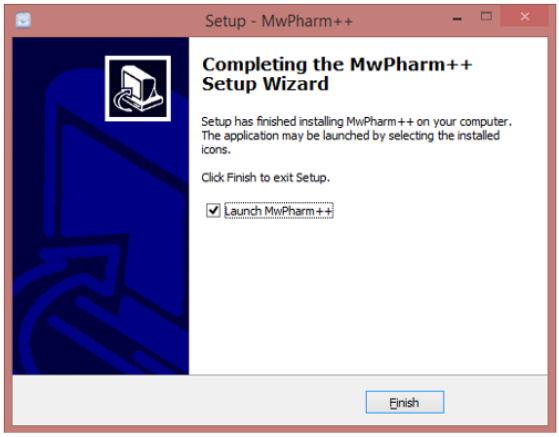
For the installation, proceed as shown in the pictures below.











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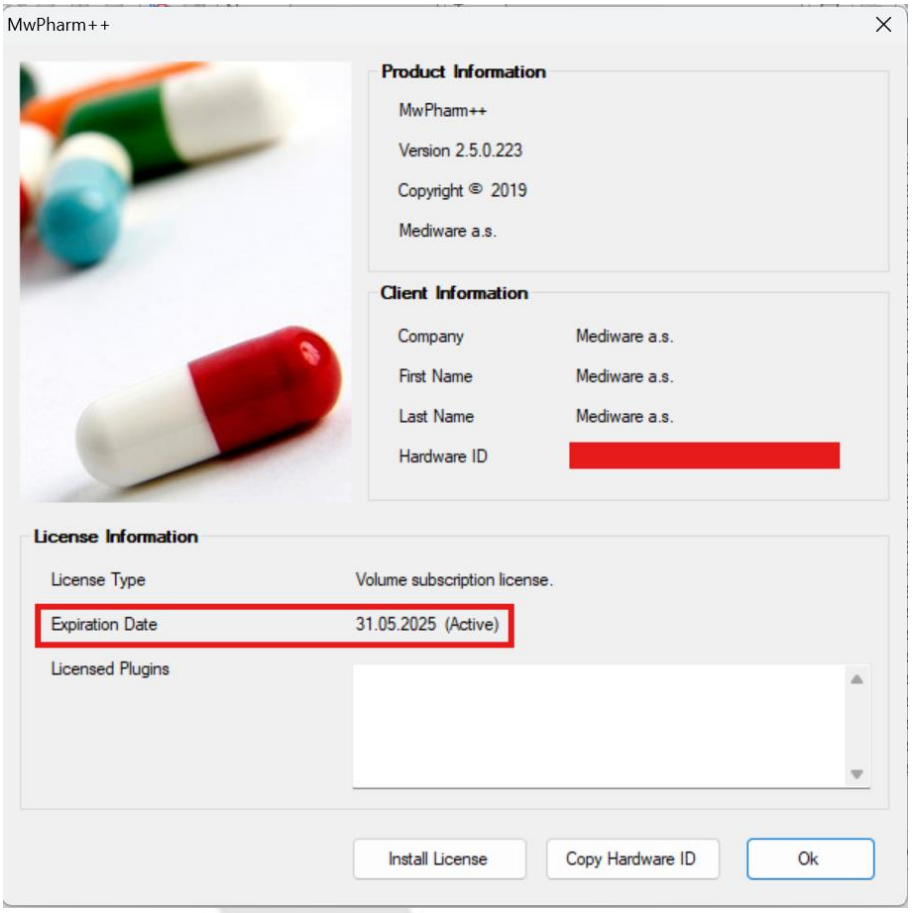
1.2.5 How to check the expiration date of a license?

After logging in to the application, choose **Help – About MwPharm++** and new window containing license information will open as in image below.



1.2.6 What is Hardware ID?

Hardware ID is a unique set of characters and numbers to identify your device. We issue license to one unique device, so that is why we need to get this information from you. Our software allows you to seek this information in no time.

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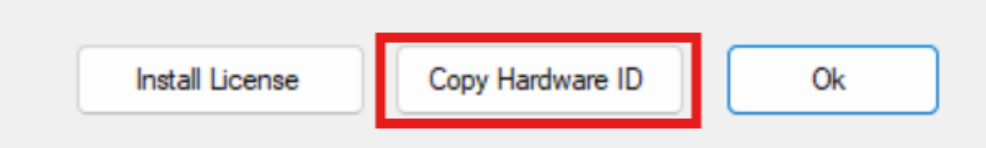
1.2.7 Where do I find Hardware ID?

Open the same window as in 1.2.4 and choose the button **Copy Hardware ID**.



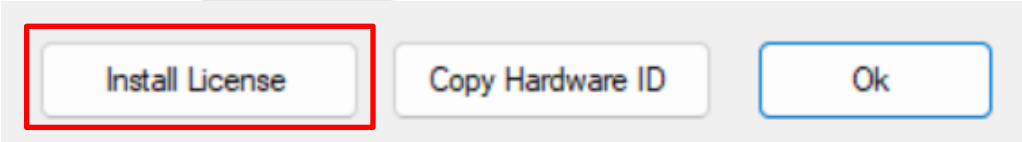
By following the instructions, you now copied the Hardware ID. Now just paste this to an email for us, and we will create a license file for you.

1.2.8 How to install the license?

Download the license file after receiving a response email from us with the file. Move the license file (it has a suffix *.license) into the "**C:\Mediware\MwPharm++"** folder. Make sure you removed the old license files. Now open the MwPharm++ again and do as shown in the pictures below.

Open the window from 1.2.4.

Choose **Install License**.



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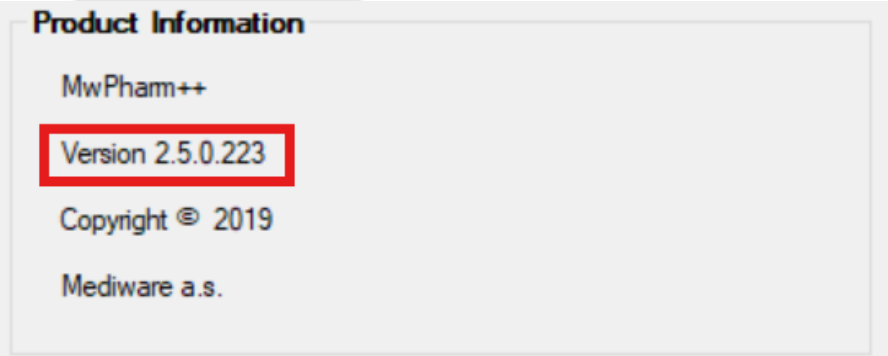
1.3 Updates and Maintenance

1.3.1 Where can I see application version?

You can find information about current application version in the same window as in 1.2.4, where product information is listed. You can compare current version with the latest version released on web page https://www.mediware.cz/en/mwpharm-plus-plus-downloads.



1.3.2 How often is application updated?

The application is updated 4 times a year. You can see list of all main realeases at the web page https://www.mediware.cz/en/mwpharm-plus-plus-downloads.

1.3.3 Will my database be saved after installing latest update of the software?

If you want to maintain your current database, backup your database file, that is located in "**C:\Mediware\MwPharm++\PlugIns\MwPharm\MwPharm.db3**" (if the user did not change the location where the application is installed).

1.3.4 Do I need to install all the updates?

You should update your software as soon as possible when a new one is released for the best user experience. Every update improves the last version by adding some new features or by getting rid of some bugs. You don't have to uninstall the software, just backup your database and run the update.

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1.3.5 When to do the Back up?

It is always good to back up your MWpharm++ data before every update, change of database or before eventual hotfixes.

In order to do that, back up the whole folder “C:\Mediware” and also database file “C:\Mediware\MwPharm++\PlugIns\MwPharm\mwpharm.db3”.

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1.4 Support and Contact Information

1.4.1 How do I contact customer support?

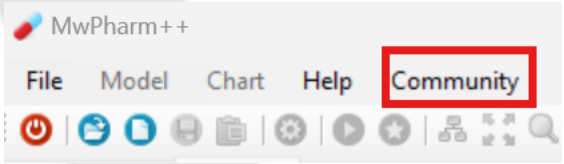
Directly send comment or question to our client support team **support@mediware.cz** or register on our service desk to get access to help faster https://mediware.atlassian.net/servicedesk/customer/portal/3.

1.4.2 What support resources are available?

We provide customer support via e-mail, telephone, forum and service desk. Register on our service desk via e-mail and get the support as soon as possible https://mediware.atlassian.net/servicedesk/customer/portal/3.

1.4.3 Are there user forums or community support options?

Yes, access our MwPharm Forum using Community button as in the image below. MwPharm Forum is designed specifically for our users to share valuable insights in software and discuss important topics regarding pharmaceutical field. You can also easily access it via this link: https://forum.mwpharm.online/.



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1.5 Training and Onboarding

1.5.1 Will I be trained to use the software?

Yes, we provide our customers with training via Workshops. Workshops are usually held online and they are defined by the level.

1.5.2 What types of Workshop there are?

First level Workshop

First level Workshop is held for beginner users that are getting to know the software.

Second level Workshop

Second level Workshop is held for users that need furher, more detailed explanation of software use.

Technical Workshop

Technical Workshop is set for users that have trouble installing to software, where we provide help to the IT team.

Questions & Answers Workshop

This type of Workshop is set for users that have defined use area of the software that they would like to further discuss.

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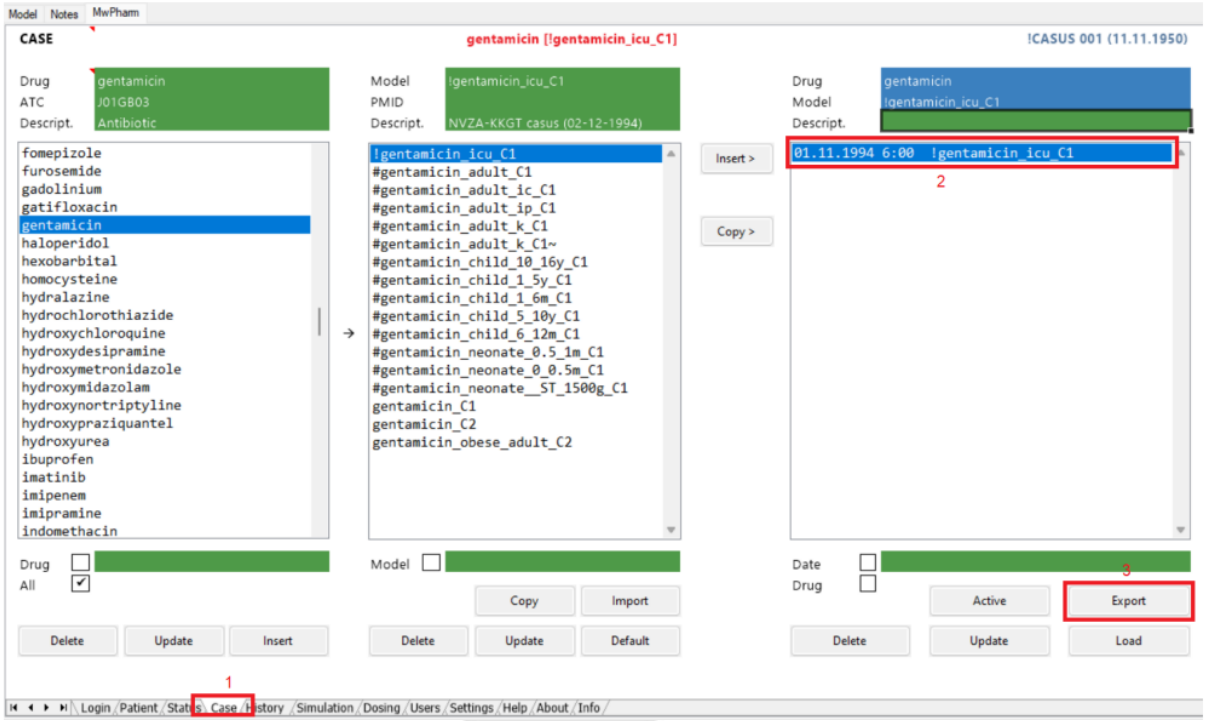
1.6 Troubleshooting

1.6.1 Bug Report

If you come across a bug or a fault in our software, please, send us the description of the bug, some printscreens of the bugs, the *.edx file of the case the bug appeared in (there are instructions for exporting the .edx file below) and most importantly the version of MwPharm++ you are currently running. Send the information to support@mediware.cz. All these information will help us to solve the bug as quickly as possible.

Exporting .edx file:

- Load the patient and go to the Case tab. In the Case tab, choose the case you want to export and click the Export button as shown in the picture.



A popup window will appear. In this window, choose the location you want to save the case to. Default path is "C:\Mediware\MwPharm++\PlugIns\MwPharm\Cases". Now that you have exported the case, you can attach it to the email.

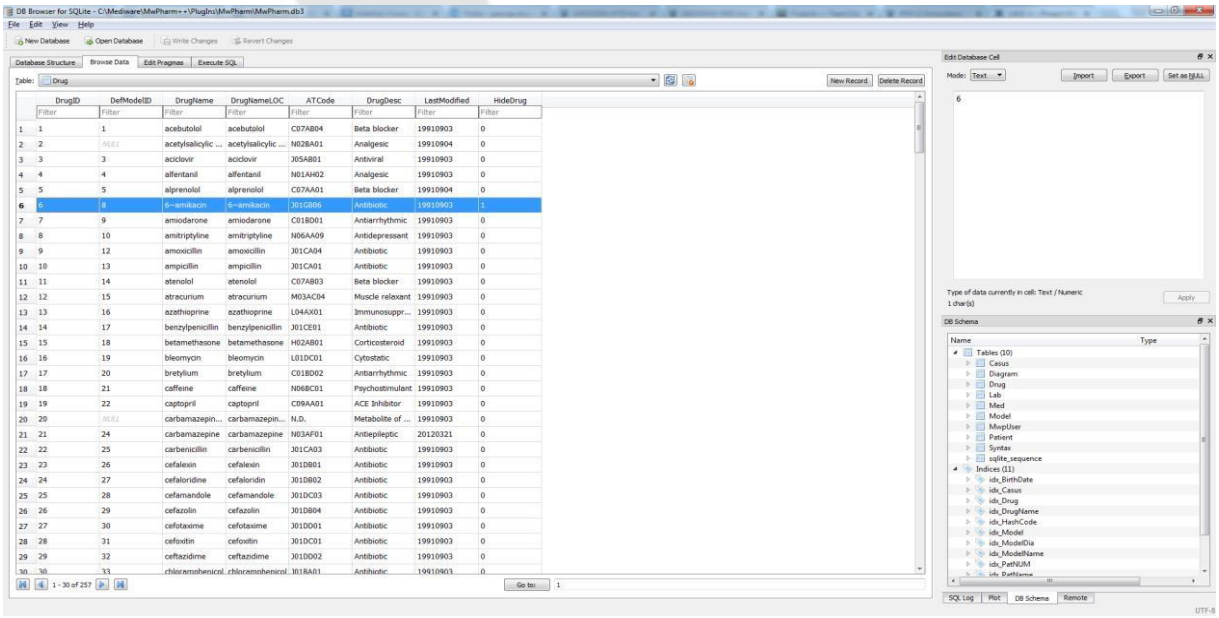
1.6.2 How to fix problems with .NET Framework

There could be a problem happening when windows install new actualizations. To repair this problem, first backup your database file. Then use this link that goes to Microsoft Support site to a Repair tool, that should help with your problem. If you don't have .NET Framework installed, use this link to install it.

1.6.3 How to recover deleted records?

The instructions listed below are applicable from version 1.4.0.

1) Back up the whole app file C:\Mediware
2) Download app SQLite DB Browser from https://sqlitebrowser.org/
3) Open file "C:\Mediware\MwPharm++\PlugIns\MwPharm\Mwpharm.db3" in SQLite DB Browser
4) Select table Drug
5) Rewrite values 1 to value 0 in column HideDrug (1=deleted, 0=active record) for drugs for recovery
6) Remove number and curvy mark from beginning of the name of the drug (6~amikacin to amikacin)
7) Check table Model and column HideModel (no record should have value 1=deleted). If there is such, change the value to 0 (=active record).



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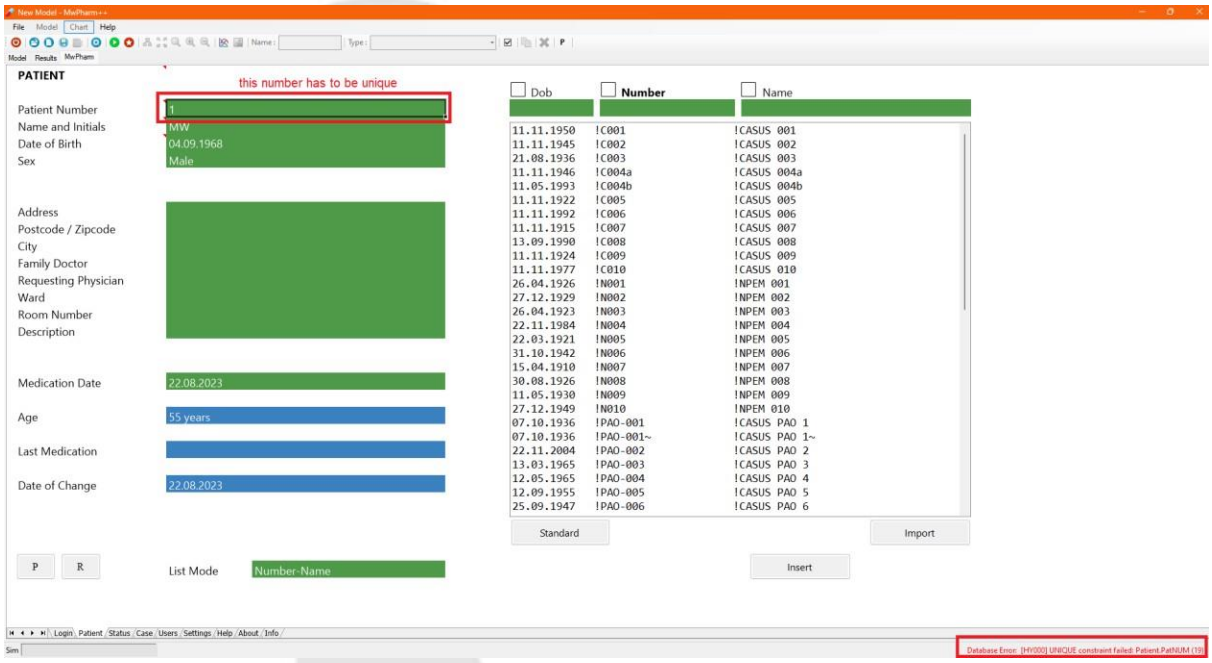
1.6.4 Errors in Patient tab

If this error, shown on the photo below, occurs, you didn't fill in unique patient number correctly. The number you filled in is already assigned to another patient.



There is also a similar error, that occurs, even though you filled in the unique ID. This error means, that you, as a user, don't have access to write in the database (create a new patient). To get access to this, contact your IT department.

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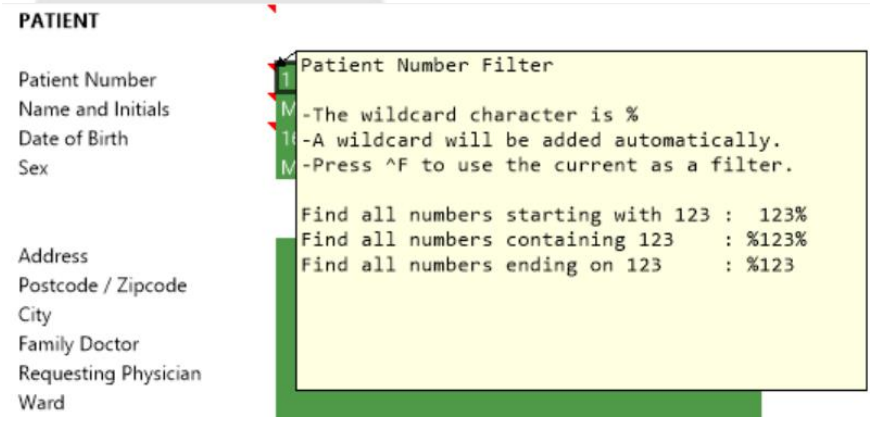
2 Features and Functionality

2.1 Understanding Key Parameters

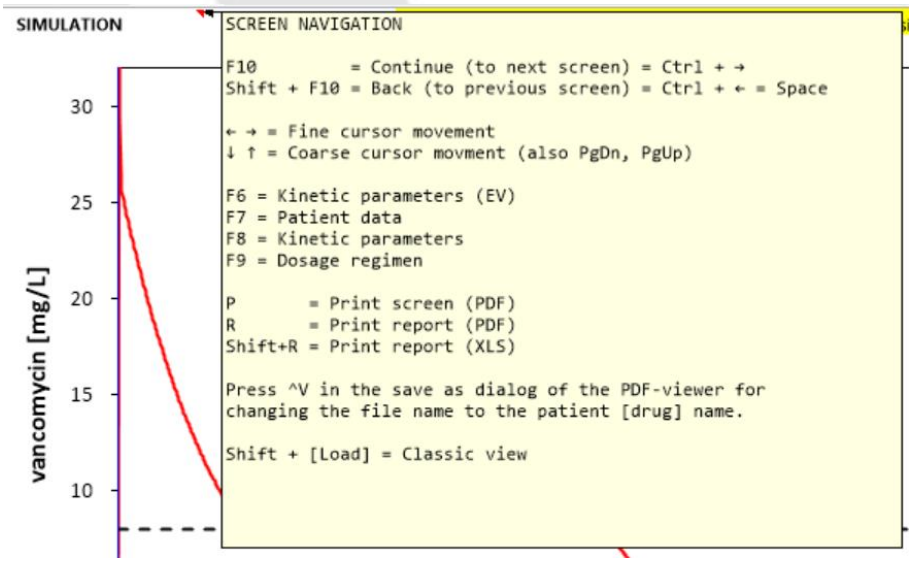
2.1.1 What does the red mark by the items mean?

Moving your mouse to the red mark will show you detailed explanation of the parameter mentioned or detailes of the possible choices to choose from.



2.1.2 How can I navigate specific tabs?

By clickin on tab name is specific tabs, you will find detailed instructions on how to navigate the unique tab.



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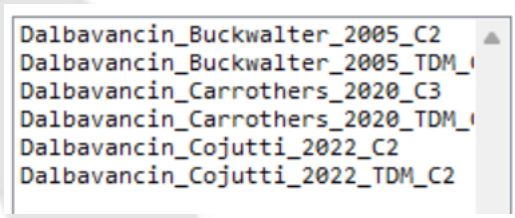
2.1.3 What do the prefixes and suffixes mean?

The following table shows the meaning of these suffixes and prefixes.

Prefix / Suffix	**Meaning**
C1, C2, C3	number of compartments in the model
child, adult, neonate	specifies the use of the model for the age of the patient
0-0.5m,0.5-1m,1-6m, 6-12m, 1-5y, 5-10y, 10-16y	specifies the use and range of the model for the age of the patient (m – months, y – years)
prefixes like !, # etc.	these models have different studies backing them up then our base models
cf	cystic fibrosis
ic	intensive care
k	elimination rate constant
capd	continuous ambulatory peritoneal dialysis

2.1.4 What does C1, C2 and C3 mean?

The C stands for compartment and the number by the letter stands for the number of compartments that are included in the model.



2.1.5 How to create a new user?

To create a new user, log in as an **Administrator**. Visit section Users and fill in the green boxes and select Level of the user. Then you click **Insert to insert a new user** and **Update** in order to update the database. You can also use **Update** if you are only updating user information. You can also delete any user you want, except the last administrator account.

Beware, that we can't restore your password. If you forget the password to your only administrator account, you would have to reinstall your software.

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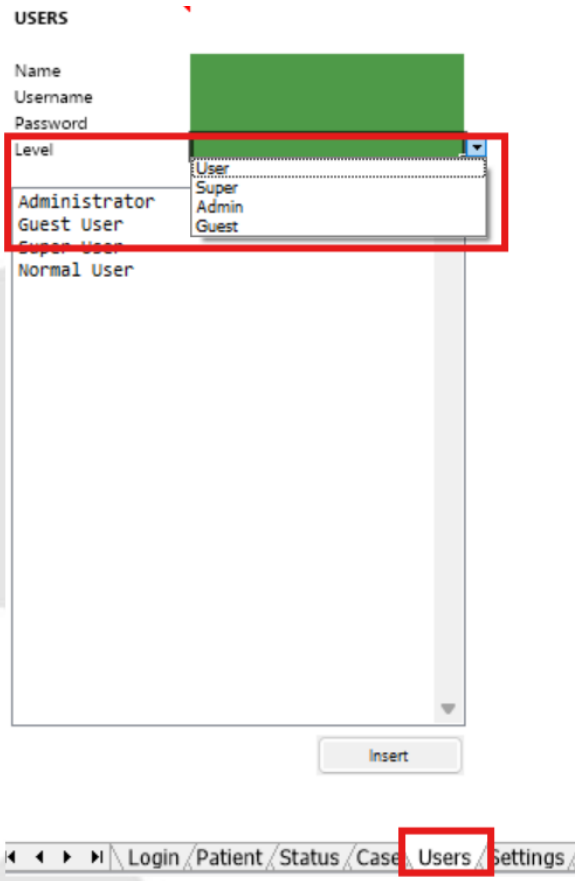

2.1.6 What is the difference between different User Levels?

Our program has 4 default types of users: Administrator, Super user, Normal user and Guest. The differences between these are shown in the table below.

Screen	Feature	Admin	Super	User	Guest
Edsim	All (params)	+	+	-	-
Settings	All	+	+	-	-
Users	All	+	-	-	-
Case	Edit drugs	+	-	-	-
	Edit models	+	+	-	-
	Edit cases	+	+	+	-
Other	See personal information	+	+	+	-
	Other	+	+	+	+

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The account logins are as follow:

Level	Username	Password
Administrator	admin	admin
Super user	super	super
Normal user	user	user
Guest	guest	guest

2.1.7 How to change User password?

In order to perform such actions, you must log in as the admin and open section **Users**. You can delete users in the same tab or change their password simply by highlighting and typing a new password for the selected user and afterwards updating the database by clicking on "**Update**".

We recommend that, before altering the user, you **back up** the whole application folder (C:\Mediware) - if something goes wrong, you can than restore whole version to the state before the change.

The same actions can also be performed by SQL database browsers, such as DB browser for SQLite.

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2.2 Settings

2.2.1 How can I change the basic default units?

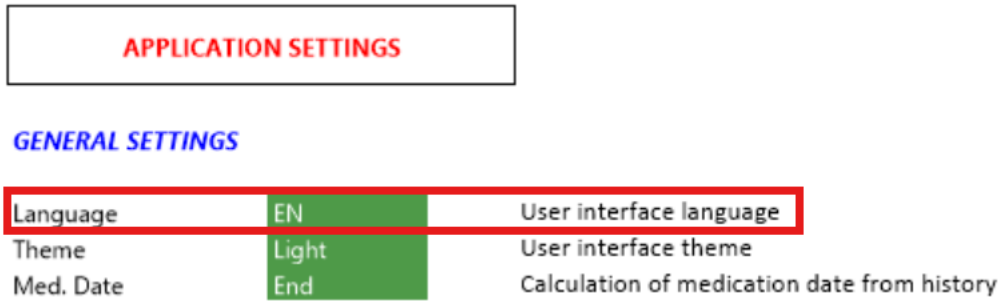
Go to **Settings – Application Settings** and there you can decide which units you prefere to use as default for each of the parameters.

2.2.2 How can I change the basic default unit of concentration for chosen model?

Unit of concentration can be changed in Application settings, as mentioned in 2.1.2.

2.2.3 How to change the localization?

To change the localization of our software, you need to go to Setting and to the section General settings and there you can see an option, to change the language. Choose the language you want.



A LocalizationKit (http://www.mediware.cz/LocKit++1.37.664.zip) can be used for translation of other parts.

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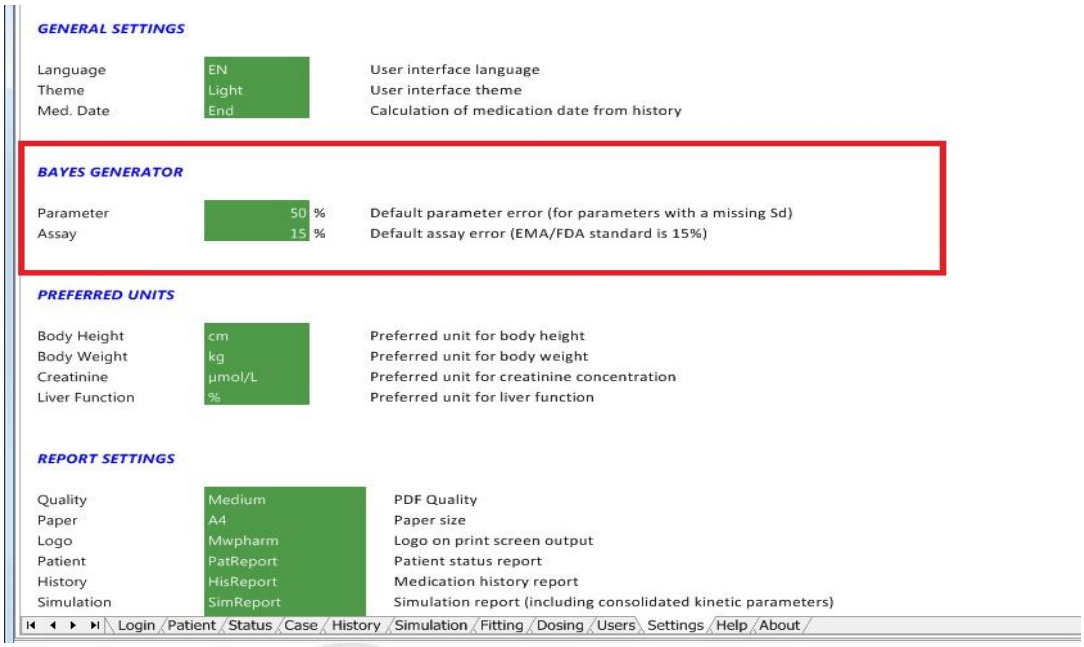
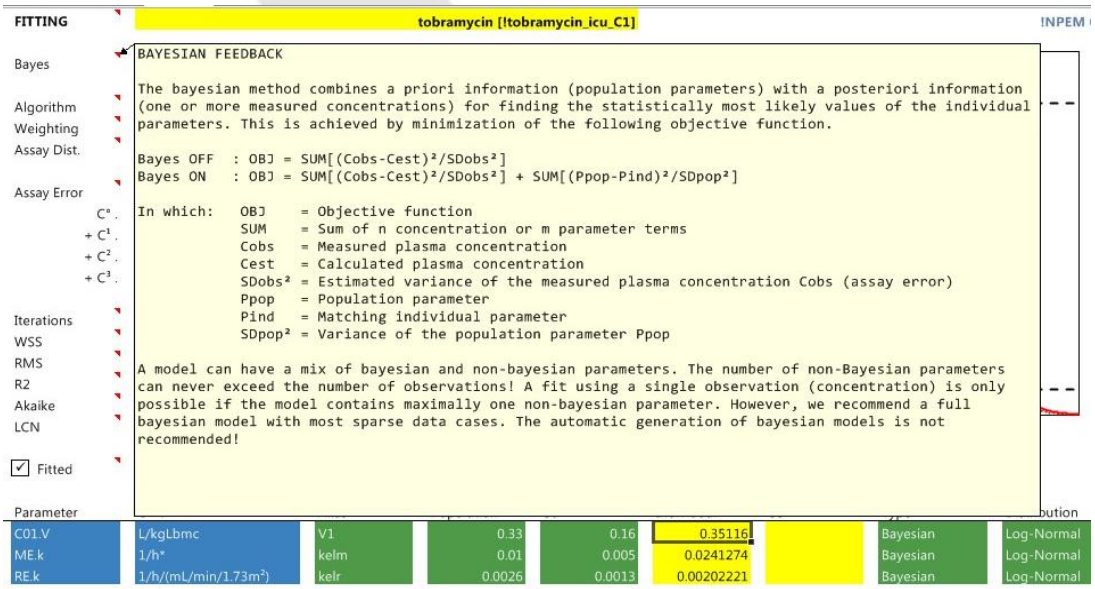
2.2.4 How to change Bayes settings?

To change Bayes settings, go to the Settings tab and scroll down to the Bayes Generator area. There you can change both parameters for Bayes.



If you want to know more information about Bayes, go to the **Fitting** tab and move your cursor to the red arrow next to the Fitting title.



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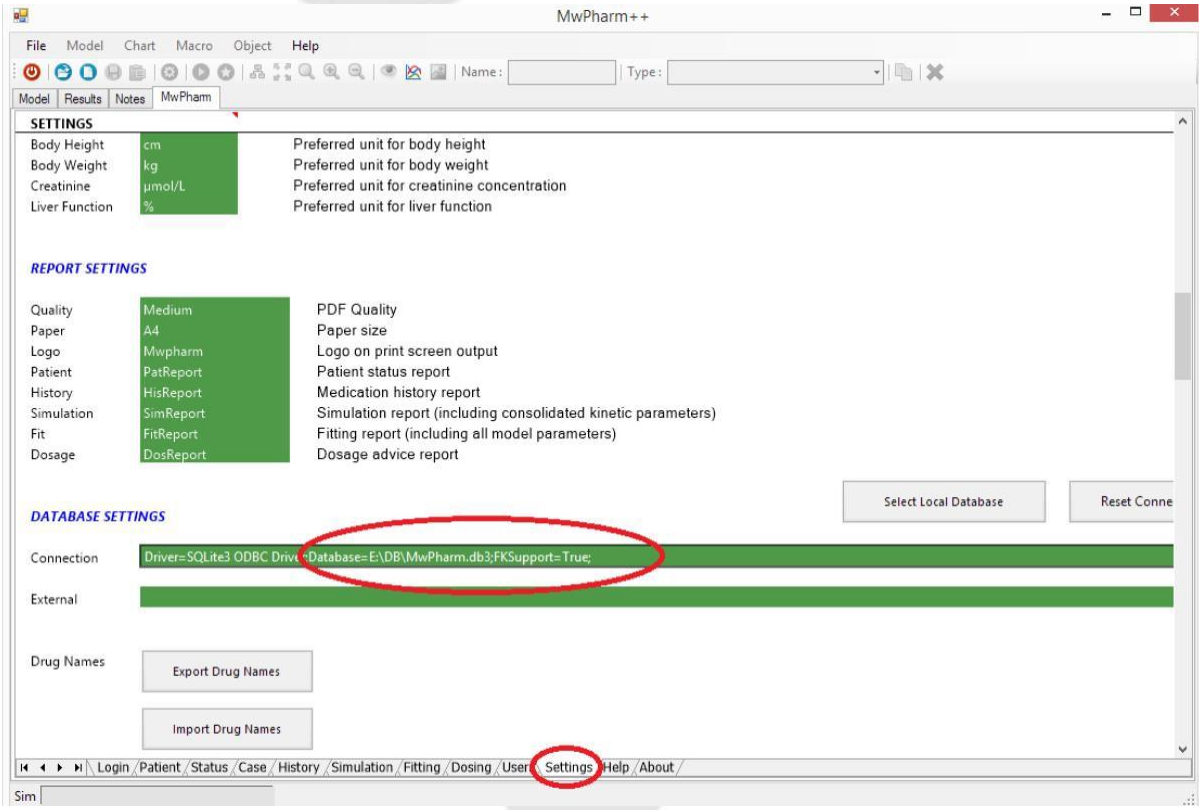
2.3 Database

2.3.1 How to use a shared database?

First, you need to install a client of MwPharm++ on each device. Now, find the database, you want to use. The default route to the database is "**c:\Mediware\MwPharm++\PlugIns\MwPharm\".** The database file name is "**MwPharm.db3**".

Now you need to copy the database filed to the shared drive or server and enable read and write rights for the users and applications, that will be using this shared database.

Now you need to set the connection string in the Settings tab of MwPharm++. Change the location or even access rights.



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2.3.2 Database missing or invalid connection string

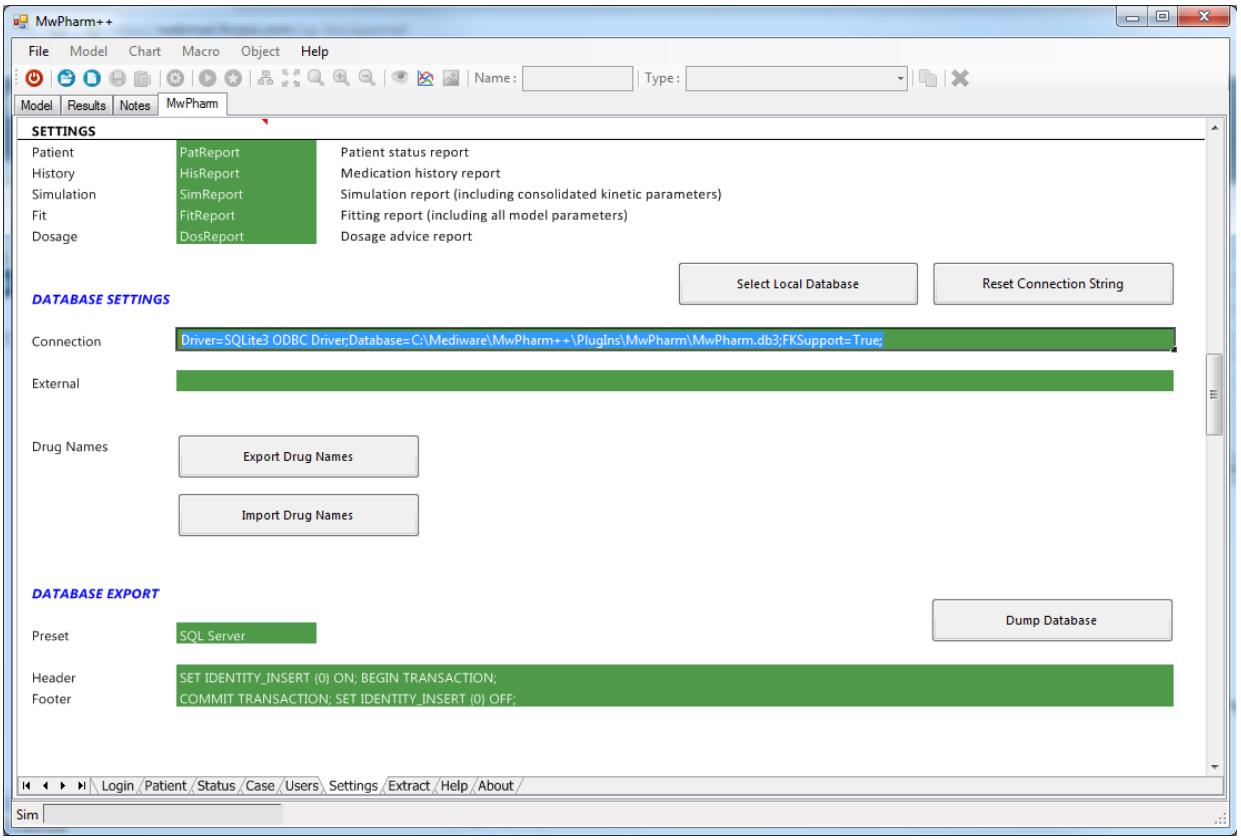
This could possibly occur after upgrading the software version. Follow the procedure below.

1) Settings >> Database settings
2) Connection string should be as following: **Driver=SQLite3 ODBC Driver;Database=C:\Mediware\MwPharm++\PlugIns\MwPharm\MwPharm.db3;FKSupport=True;**

If access to Database settings is not possible, do the following:

1) Back up file "c:\Mediware\MwPharm++\PlugIns\MwPharm\MwPharm.cfg" and delete that file
2) This file contains settings for connecting to database and if deleted, the app will automaticaly create a new default one

Do not forget to back up your database before each upgrade.



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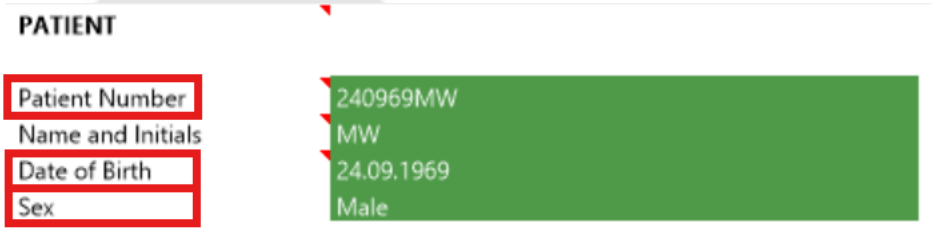
2.4 Patient

2.4.1 How to add a new patient?

To create a new patient, you need to go to the **Patient** tab and fill out the rows. In order to successfully create a new patient, it is mandatory to fill following information: **Patient Number**, **Date of Birth** and **Sex**.

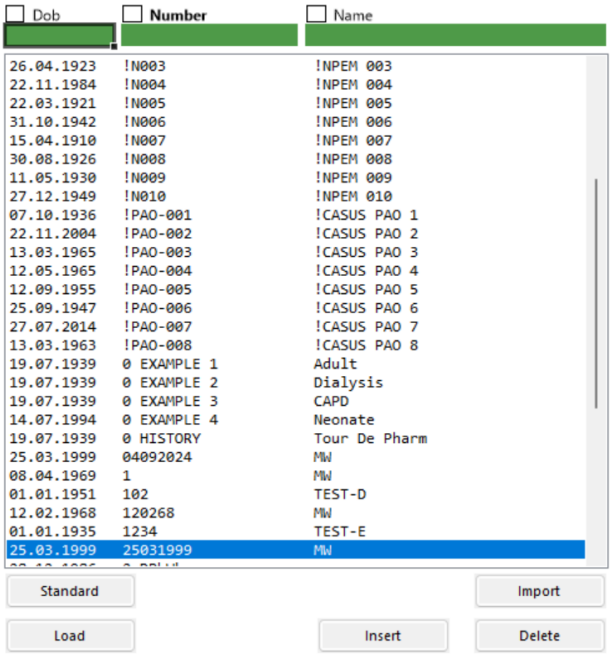


After you fill out these rows click **Insert** to create a new patient in your database.

Now you can go to the tab **Status**. Here you can change other attributes of your patient. To save your progress go back to the tab Patient and click **Update**.

2.4.2 How do I access the patient I have been working with before?

In section **Patient** you can see the list of all your patients and choose the one that you would like to continue to work with. Click **Load** to load the selected patient.



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2.4.3 Do I have to fill in personal patient information?

While entering patient data, user can also fill in personal and sensitive information, but this is not required for the application calculations. Personal information such as first name, last name, e-mail, phone number, and address can be filled.

2.4.4 What do buttons under Patient List mean?

STANDARD: it will create a standard patient (male, 55 years old, 70 kg, 175 cm) BUT you still need to click insert to add him to the database

LOAD: will load your chosen patient

ACTIVE: if you loaded a patient and unmarked him in the database, you can mark him back by clicking this button

DELETE: will delete your chosen patient

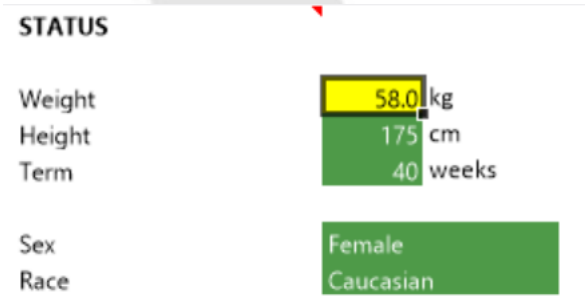
UPDATE: will update your patient information e. g. address, physician, status, case etc.

IMPORT: enables to import cases that are not in your database yet

2.4.5 How to define patients' medical condition?

Defining patients' medical condition is necessary for the software to make individual calculations and it is done using the tab **Status** after creating a new patient. Weight and height are mandatory fields, you can also specify other patient parameters such as body constitution, sex and race which will help in specification of the dosing.

Don't forget to insert patients' creatinine clearance in the tab Status too.



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2.4.6 What does Renal function field serve for?

Organ function is very important field since its purpose is to define the value of creatinine clearance. This parameter is calculated from the inserted serum creatinine value based on the renale function that the user chooses. User can decide between 14 offered renal functions, as well as the option user-estimated creatinine clearance.

2.4.7 What is the difference between Jelliffe "renal functions" in Status card + Schwartz children formula?

Jelliffe Ⅰ and Jelliffe Ⅱ are two methods published by Dr. Jelliffe. The equations are following:

Jelliffe 1 *(Ann. Int. Med. 79: 604, 1973)*

$$CL_{cr} = F_{sex} \cdot \frac{98 - 0.8 \cdot (Y - 20)}{Cr} \cdot 88.5$$

F_{male} = 1.00

F_{female} = 0.90

Jelliffe 2 *(Math. Biosc. 14: 17-24, 1972)*

$$F_1 = (29.305 - 0.203 \cdot Y) \cdot LBM \cdot \frac{(1344.3 - 43.76 \cdot \frac{\Delta Cr}{2})}{(1344.3 - 43.76 \cdot 1.1)} \cdot 0.85 \cdot F_{sex}$$

$$F_2 = 4 \cdot LBM \cdot \frac{\Delta Cr}{\Delta t} \qquad F_3 = \frac{\Delta Cr}{2} \cdot 1440 \qquad \Delta Cr = \frac{(Cr_1 - Cr_2)}{88.5}$$

$$CL_{cr} = \frac{F_1 - F_2}{F_3} \cdot 100 \cdot \frac{1.73}{BSA}$$

F_{male} = 1.00

F_{female} = 0.90

Δt is the time (`days`) between two successive creatinine level measurements Cr_1 and Cr_2 ($\mu mol/L$).

Schwartz *(Pediatrics 58: 259-263, 1976)*

$$CL_{cr} = \frac{0.55 \cdot BH}{Cr} \cdot 88.5$$

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The Jelliffe Ⅱ-2 serum creatinine levels method is suitable for calculating the creatinine clearance in case of an instable kidney function. It is the only method that takes the non-renal creatinine clearance into account with patients suffering from a chronic kidney disease.

The net creatinine production is only dependent on Ccr levels in case of Jelliffe 2.

The Schwartz children formula is only available if the subject is younger than 20.

Schwartz *(Pediatrics 58: 259-263, 1976)*

$$CL_{cr} = \frac{0.55 \cdot BH}{Cr} \cdot 88.5$$

2.4.8 What is the difference between Simplex and Marquardt method?

The Simplex method calculates without standard deviation. The Marquardt calculates with standard deviation.

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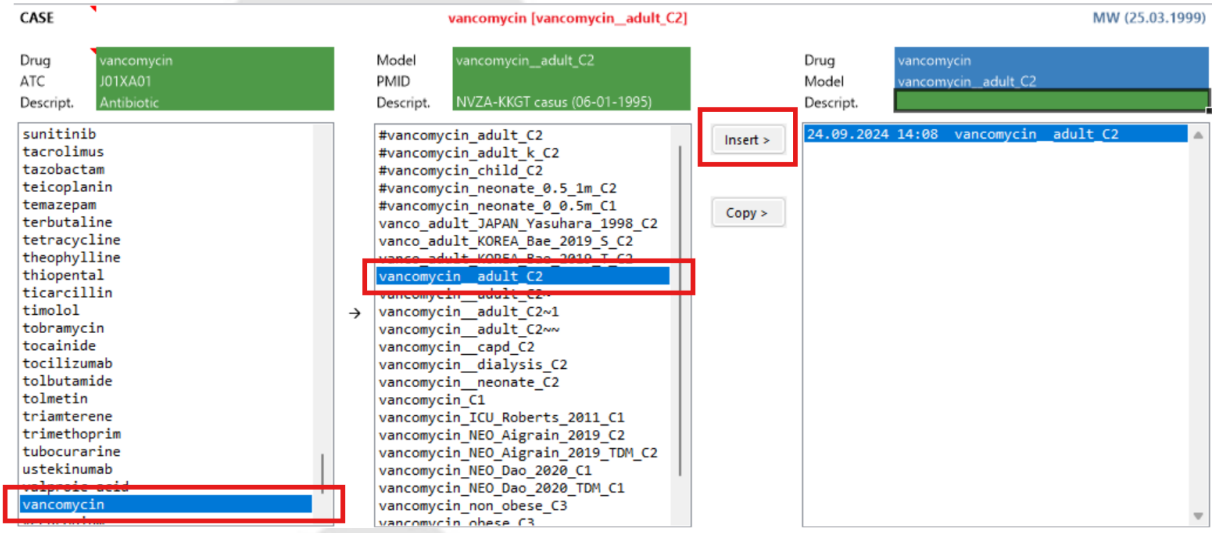
2.5 Case

2.5.1 How do I create a new case?

Once you have created a new patient or opened details of the old one, go to the section **Case**. First, choose the drug substance you want to work with and later on choose the specific drug model. Once you have made your choise click **Insert** in order to create a new case.

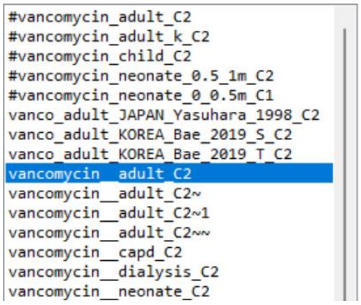


2.5.2 How do I decide which drug model to use?

While creating a new case, you can choose the medicine that you would like to apply to your actual patient. You can choose the medicine from Drug model list, which contains about 180 different drugs, and around 300 models altogether.

You can choose the model based on the characteristics of your patient or on the litareture that the model was created by.

For example, vancomycin for adult, neonate or dialysis patient.



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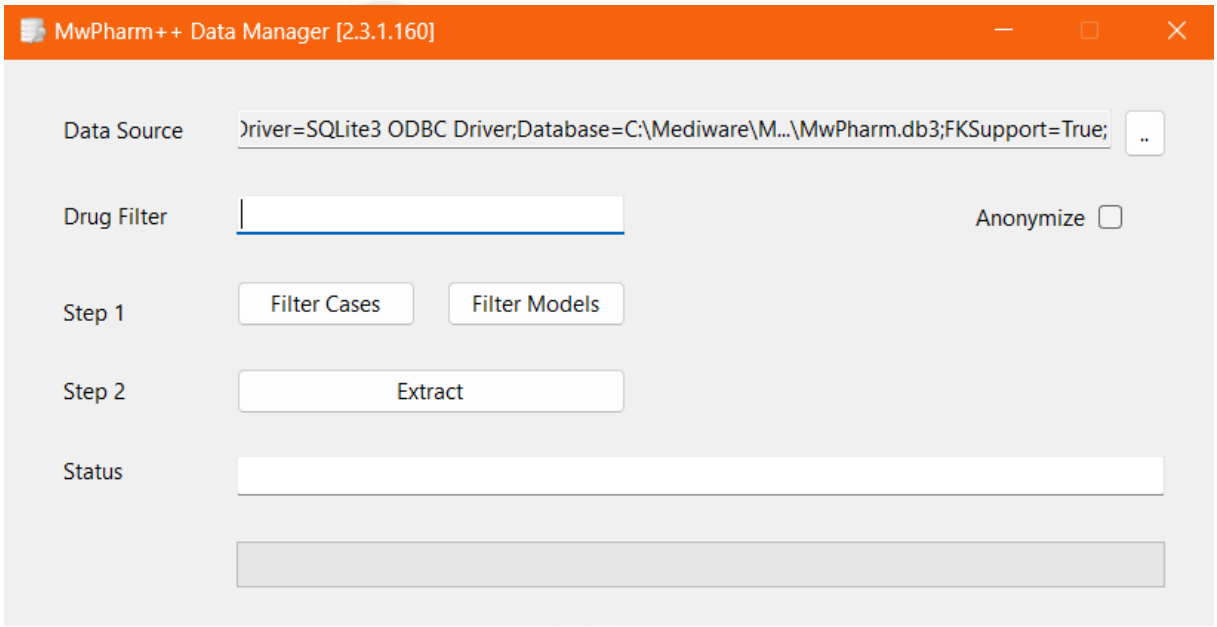
2.5.3 How to extract several cases or models at once?

You can extract cases using our **DatMan** application. You can find the application following the path: "**C:\Mediware\MwPharm++\DatMan\DatMan.exe**".

If you open DatMan, the following window will show up:



In the row **Data Source**, you can choose the database. The default setting is: "Driver=SQLite3 ODBC Driver;Database=C:\Mediware\MwPharm++\PlugIns\MwPharm\MwPharm.db3;FKSupport=True;".

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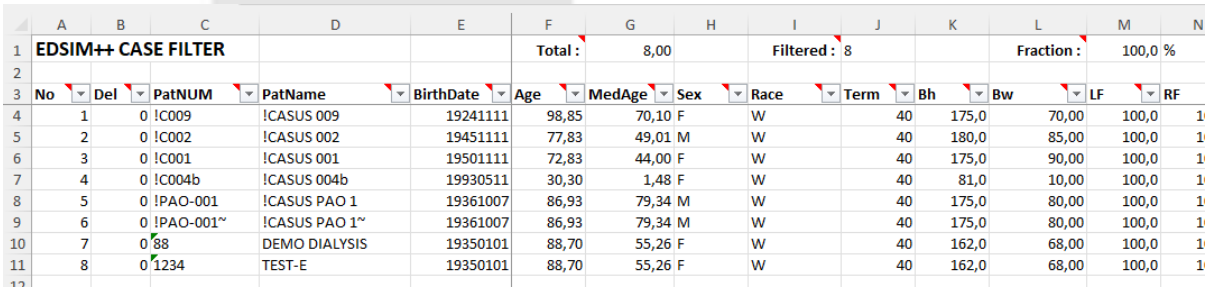
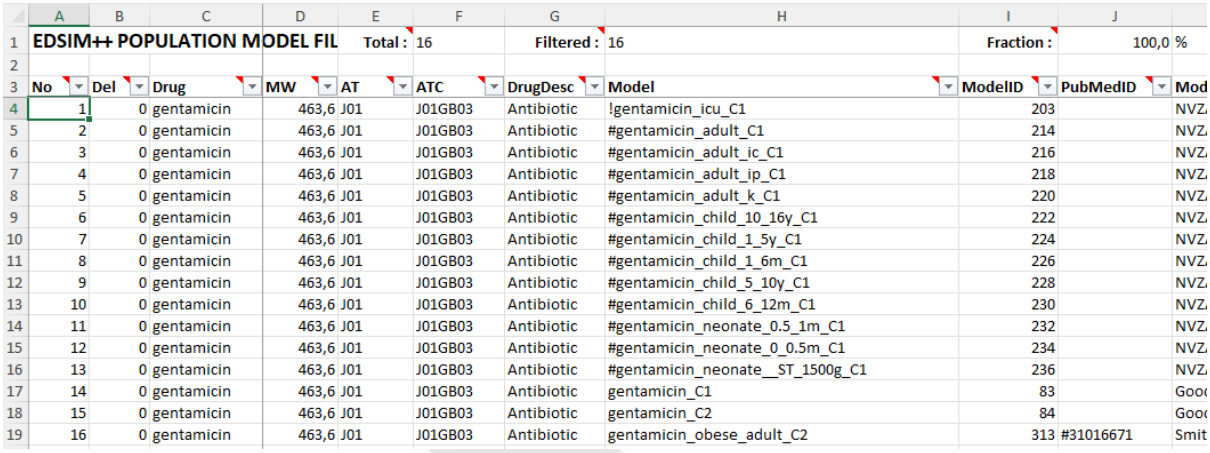
You can also choose the file manually by clicking on the button with dots on the same row.

The row **Drug Filter** is for specifying the name of the drug used in the cases or models you want to export. The wildcard character is **%**. For example, phrase "genta%" gives you all types of models which name starts with the phrase "genta".

If you then hit the button **Filter Cases**, an Excel sheet will open. In this sheet, there is list of all cases in which the selected drug participates. If you hit the button **Filter Models**, the list of models with the selected name will be created. For example, for the data source "genta%" the list can look as in the following pictures:



	A	B	C	D	E	F	G	H	I	J	K	L	M	N
1	EDSIM++ CASE FILTER					Total :	8,00		Filtered :	8		Fraction :	100,0	%
2														
3	No	Del	PatNUM	PatName	BirthDate	Age	MedAge	Sex	Race	Term	Bh	Bw	LF	RF
4	1	0	!C009	!CASUS 009	19241111	98,85	70,10	F	W	40	175,0	70,00	100,0	1
5	2	0	!C002	!CASUS 002	19451111	77,83	49,01	M	W	40	180,0	85,00	100,0	1
6	3	0	!C001	!CASUS 001	19501111	72,83	44,00	F	W	40	175,0	90,00	100,0	1
7	4	0	!C004b	!CASUS 004b	19930511	30,30	1,48	F	W	40	81,0	10,00	100,0	1
8	5	0	!PAO-001	!CASUS PAO 1	19361007	86,93	79,34	M	W	40	175,0	80,00	100,0	1
9	6	0	!PAO-001~	!CASUS PAO 1~	19361007	86,93	79,34	M	W	40	175,0	80,00	100,0	1
10	7	0	88	DEMO DIALYSIS	19350101	88,70	55,26	F	W	40	162,0	68,00	100,0	1
11	8	0	1234	TEST-E	19350101	88,70	55,26	F	W	40	162,0	68,00	100,0	1



	A	B	C	D	E	F	G	H	I	J	
1	EDSIM++ POPULATION MODEL FIL			Total :	16		Filtered :	16		Fraction :	100,0 %
2											
3	No	Del	Drug	MW	AT	ATC	DrugDesc	Model	ModelID	PubMedID	Mod
4	1	0	gentamicin	463,6	J01	J01GB03	Antibiotic	!gentamicin_icu_C1	203		NVZ
5	2	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_adult_C1	214		NVZ
6	3	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_adult_ic_C1	216		NVZ
7	4	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_adult_ip_C1	218		NVZ
8	5	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_adult_k_C1	220		NVZ
9	6	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_child_10_16y_C1	222		NVZ
10	7	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_child_1_5y_C1	224		NVZ
11	8	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_child_1_6m_C1	226		NVZ
12	9	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_child_5_10y_C1	228		NVZ
13	10	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_child_6_12m_C1	230		NVZ
14	11	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_neonate_0.5_1m_C1	232		NVZ
15	12	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_neonate_0_0.5m_C1	234		NVZ
16	13	0	gentamicin	463,6	J01	J01GB03	Antibiotic	#gentamicin_neonate__ST_1500g_C1	236		NVZ
17	14	0	gentamicin	463,6	J01	J01GB03	Antibiotic	gentamicin_C1	83		Gooc
18	15	0	gentamicin	463,6	J01	J01GB03	Antibiotic	gentamicin_C2	84		Gooc
19	16	0	gentamicin	463,6	J01	J01GB03	Antibiotic	gentamicin_obese_adult_C2	313	#31016671	Smit

You can edit the list of cases or models before extracting, just don't forget to save the changes.

Now, if you hit the **Extract** button, a window will pop-up. In this window, choose the created file **Cases.xlsx** or **Models.xlsx**. After that, a new folder containing selected cases or models will be created. You can find it in the same folder as the selected *.xlsx file.

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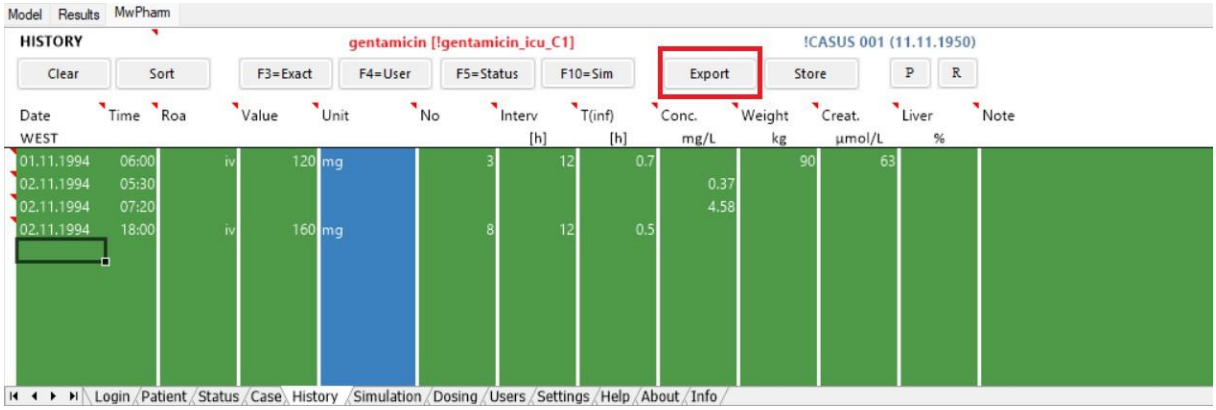
2.5.4 How to export / import patient case?

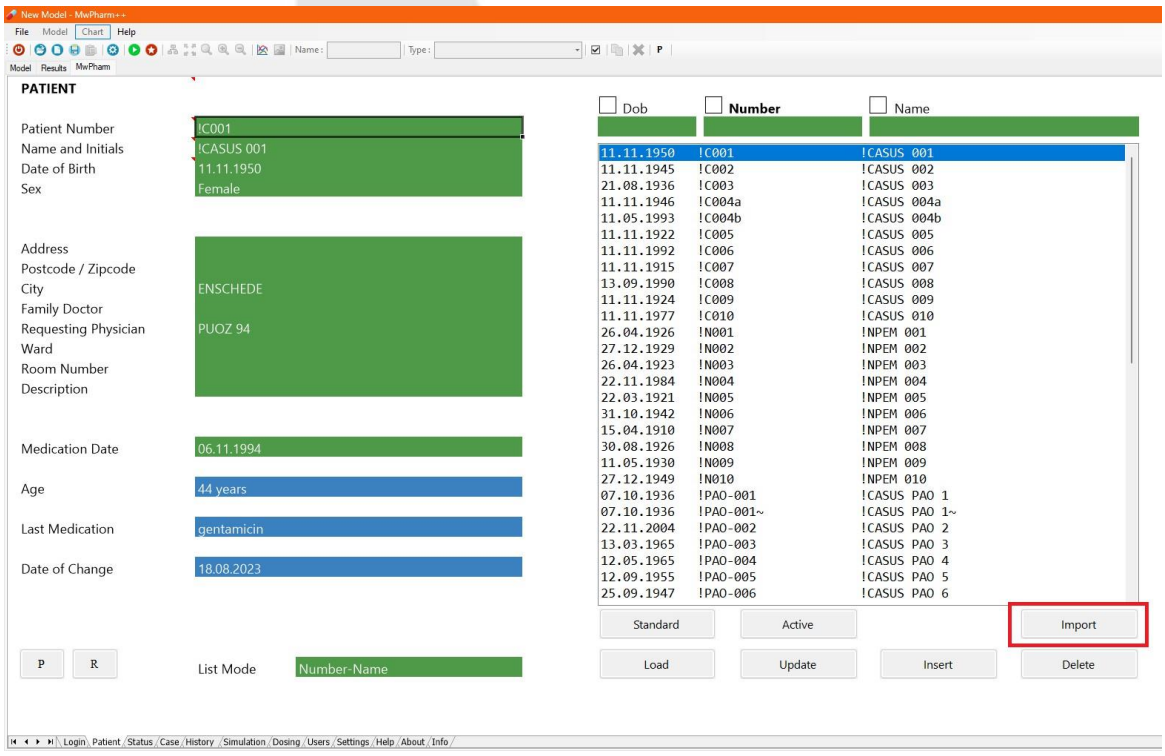
In order to share an information about a certain MwPharm++ case with other user, device or lab you can **export** the case from the history tab. Load the patient which should be exported, go to **History** tab of the case and use **EXPORT** button as shown below.



Save the case into the desired folder in your computer.

Default folder: **C://Mediware/MwPharm++/PlugIns/MwPharm/Cases**

You can import a case by clicking **IMPORT** button in the **Patient** tab of MwPharm++. Click Import and choose the case which should be imported from the appropriate folder.



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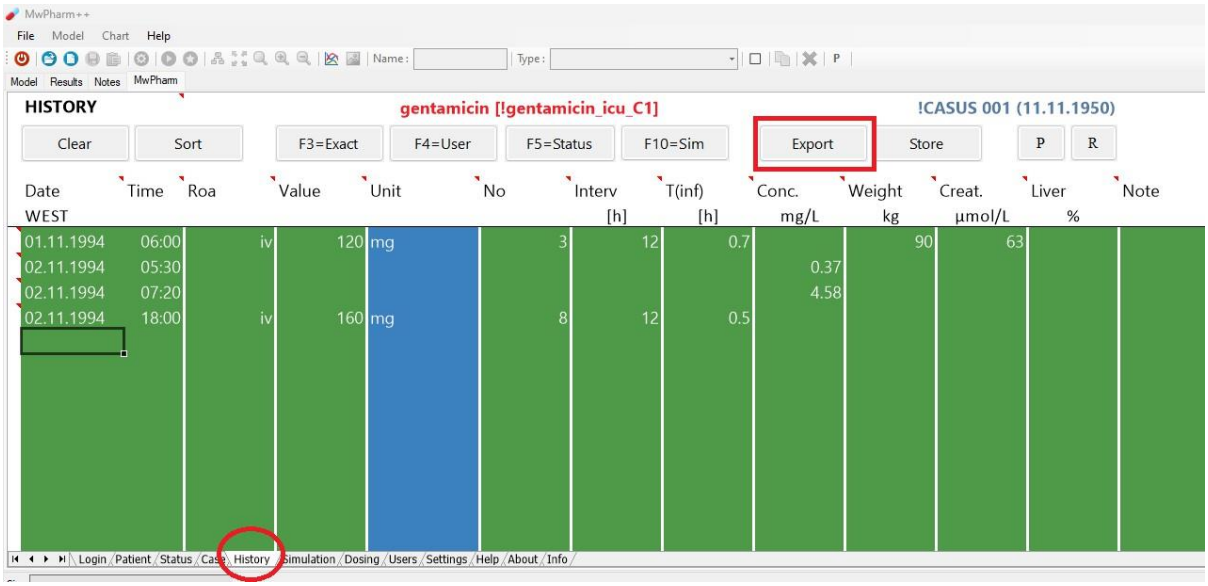
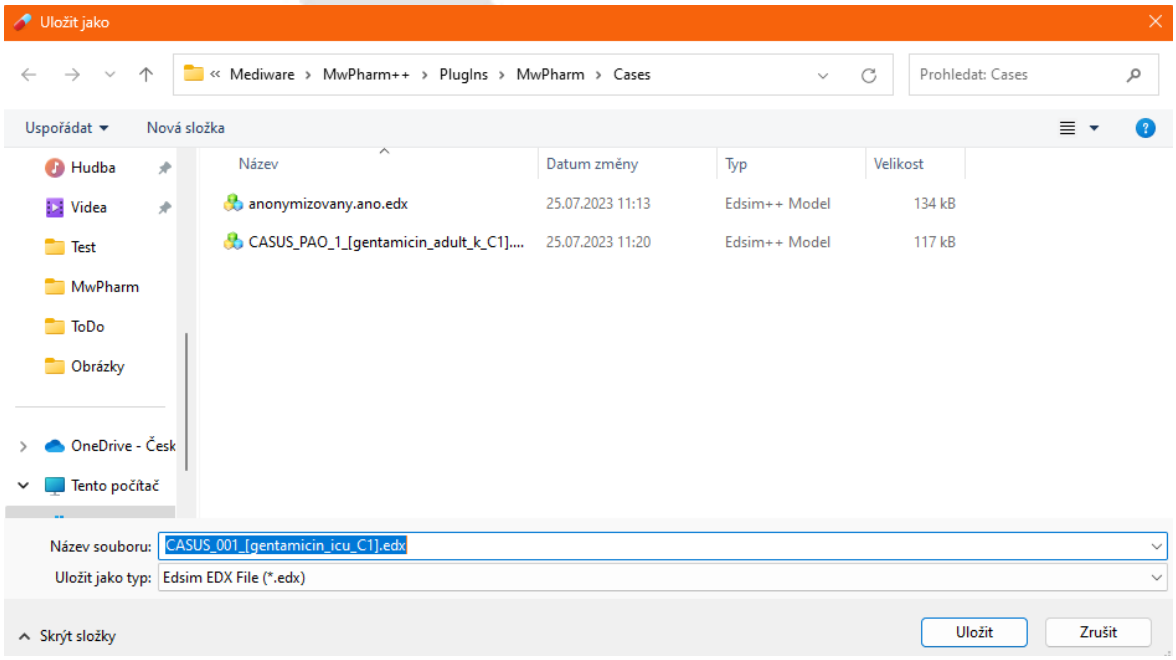
2.5.5 How to move case from MwPharm++ to MwPharm Online?

Go to the **Patient** tab and load the case you want to move. Then go to the **History** tab and click the button **Export** as shown in the picture.



Now, a "Save as" window will pop-up. In this window, choose a name of the exported file and a location you want to save it to and hit the **Save** button. The default path is "C:\Mediware\MwPharm++\PlugIns\MwPharm\Cases".



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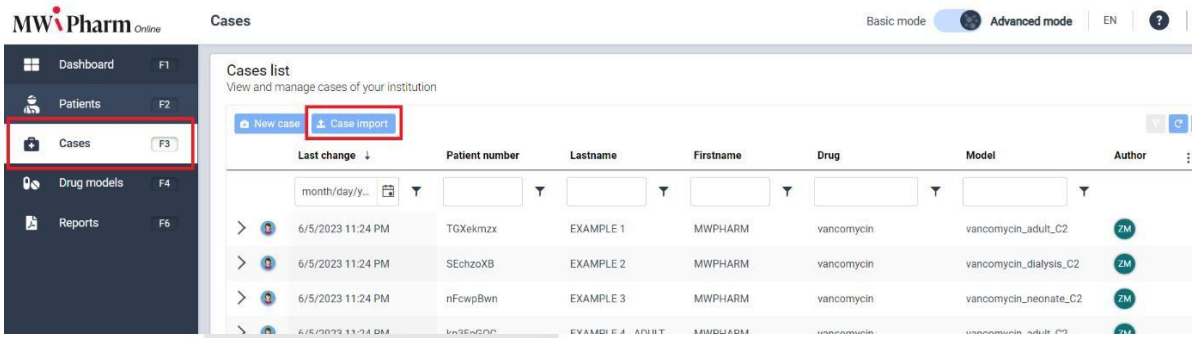
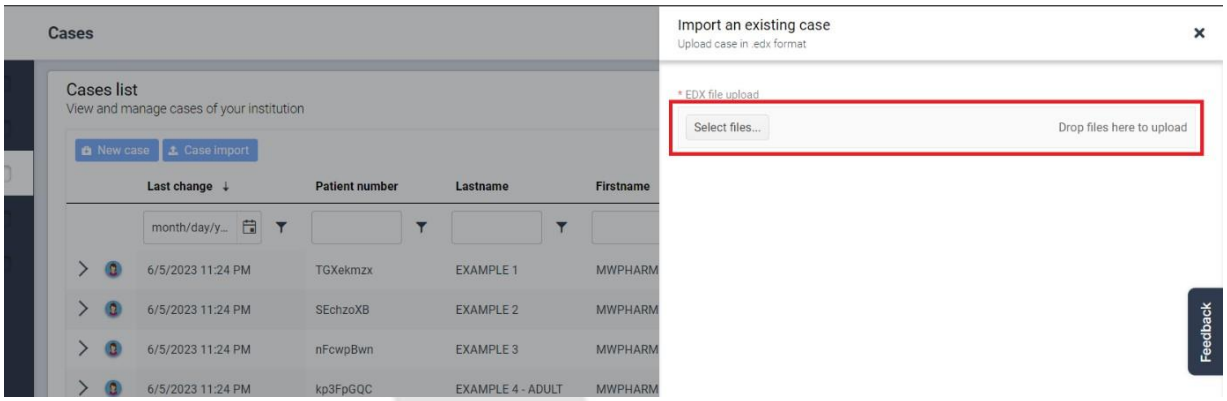
Log into MwPharm Online and go to the **Cases** tab on the left. Now, click the button **Case import** in the upper part of the page.



A new panel will appear in the right part of the page. In this panel, either drag the case you exported in the 2nd step into the gray field, or hit the button **Select files…** and choose the desired case manually.



After selecting the desired file, the file is uploaded. There should appear the name of the case together with a confirmation that the upload of the file was successful. The last step is to hit the button **Import case** below in this panel. Now, the case should appear in your MwPharm Online database.

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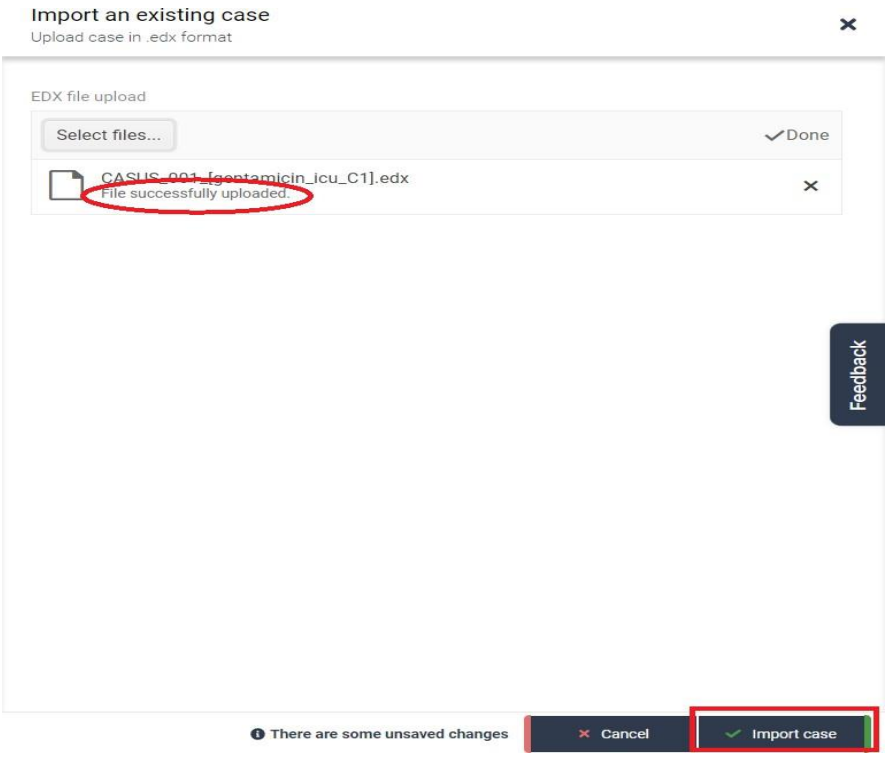

2.5.6 How to move the case from MwPharm Online to Mwpharm++?

Log into you MwPharm Online account and go to the tab **Cases**. Choose the case you want to move and go to the **Simulation** tab. Hit the button Export in the right upper corner.

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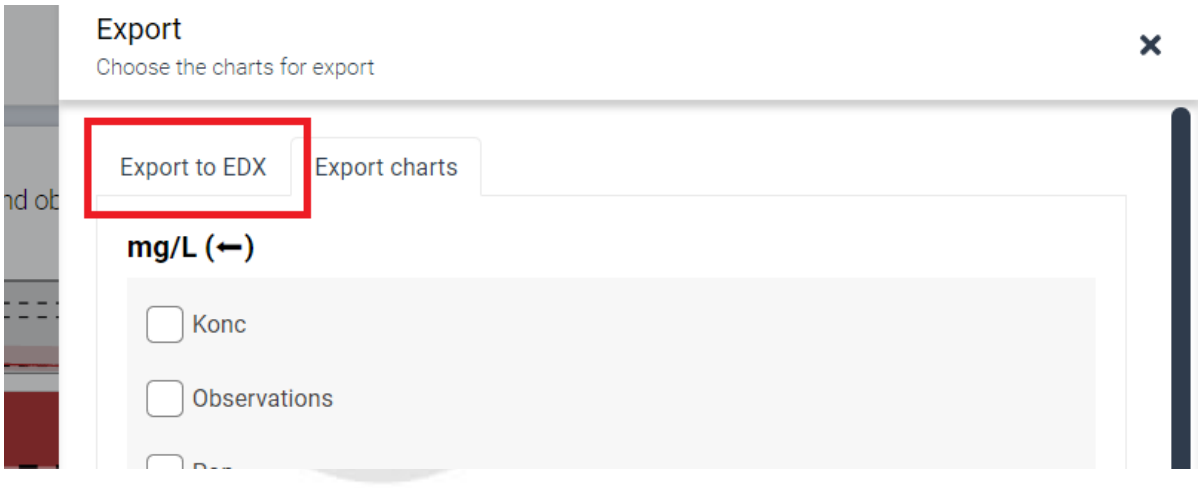
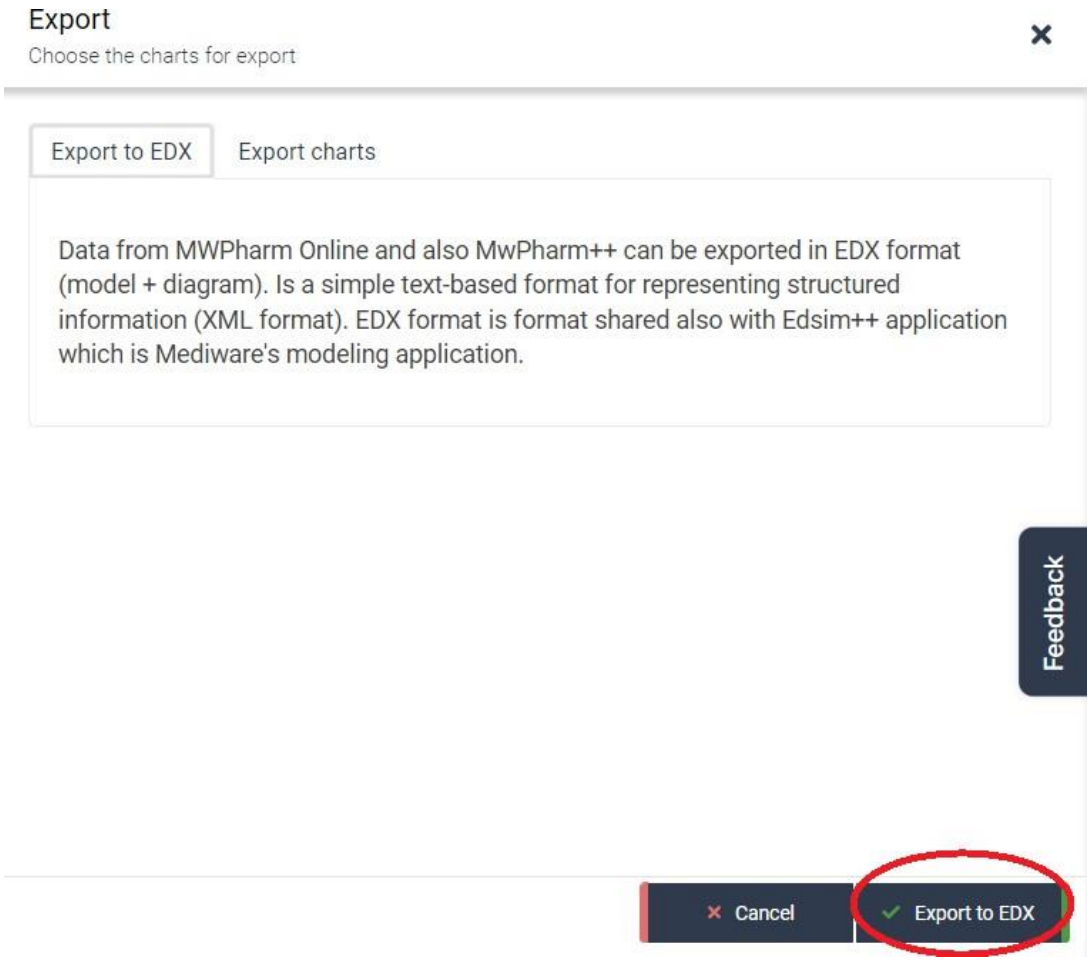
In the right side of the page, a panel called **Export** will appear. In this panel, switch to the **Export to EDX** tab.



Hit the button **Export to EDX** below in the panel. The chosen case will be downloaded automatically.



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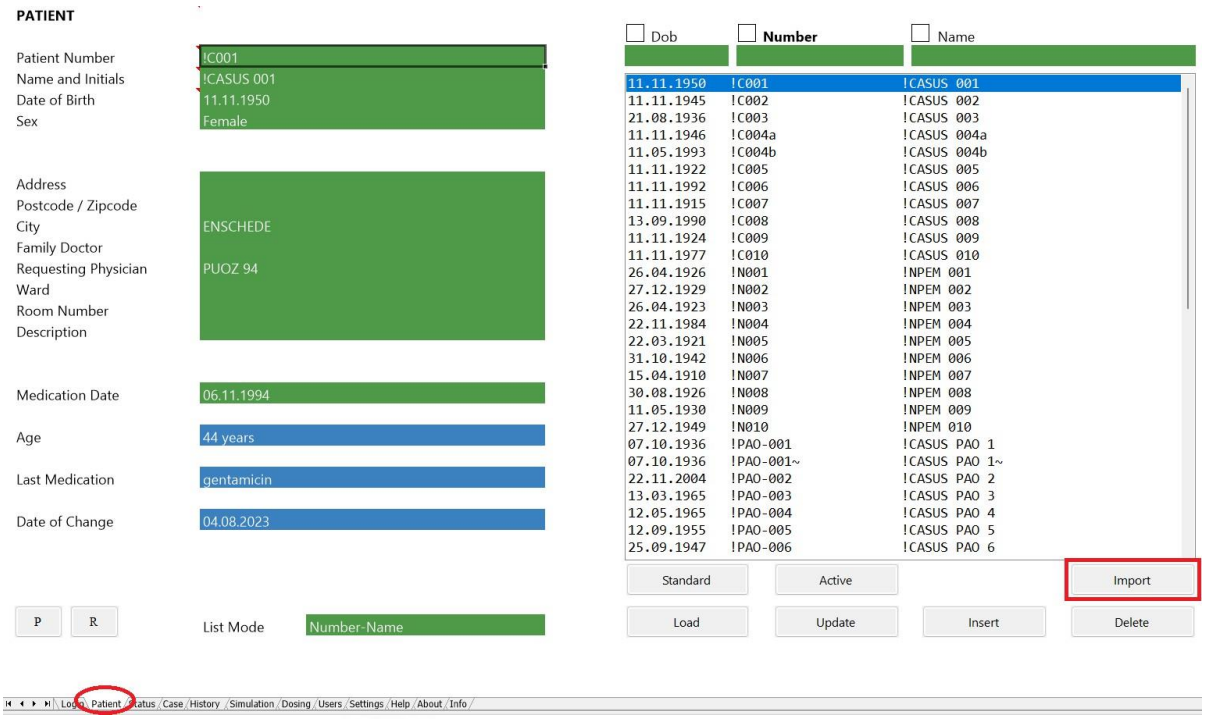
Log into your MwPharm++ application and go to the tab **Patient**. In this tab, hit the button **Import** in the right below corner as shown in the picture.



A popup window will appear. In this popup window, you can choose the downloaded file. The default folder the exported files download to is Downloads. After choosing the desired file and clicking the button **Open**, the case should be stored in your MwPharm++ database.

2.6 History

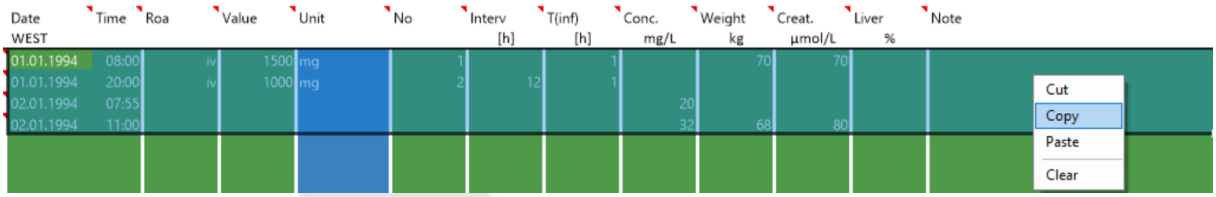
2.6.1 What parameters can I insert in History?

History section allows the user to have overview of loading and maintenance dose, that are specified by the application. User can insert specifical parameters for the actual patient such as changes in weight, drug concentration from the blood sample, creatinine, liver function and values specific for dialyses.

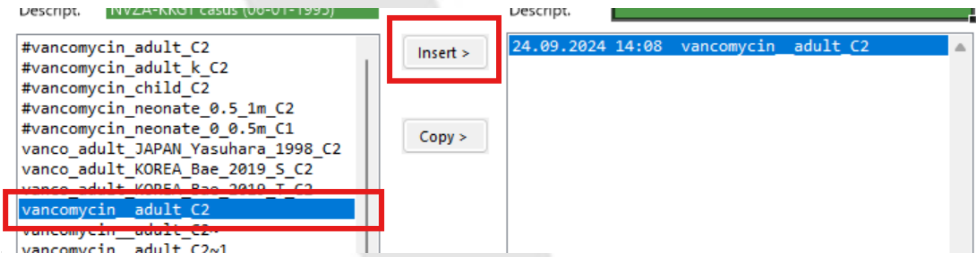
2.6.2 How to copy history between the models?

In MwPharm++ we have two ways how to copy history between the models.

Go to the **History** tab, where is your preferred history. Click the left button on the first line of the history and drag your mouse labeled everything you need. Then click the right button on the highlighted area and select Copy.



Go back to the Case tab, choose another model with which to compare the previous model and click to the Insert button.



You will be automatically brought to the **History** tab. Press **Ctrl+V** keys simultaneously or right click on the first line of the history and select **Paste**.

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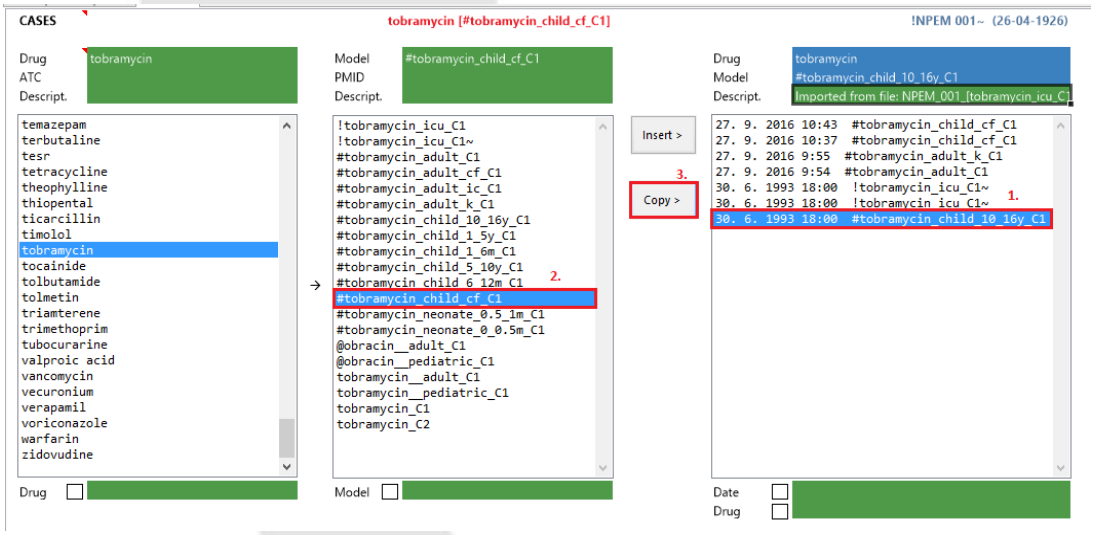
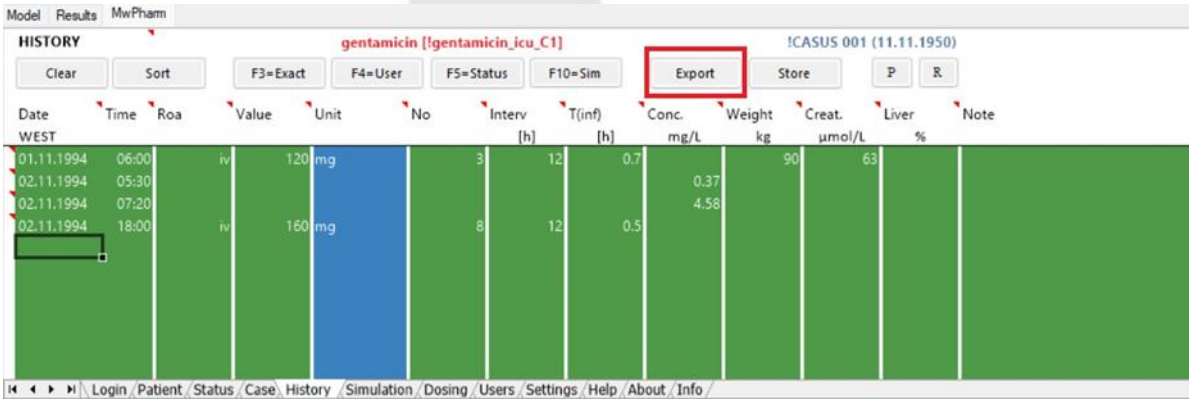
The second way would be to instantly copy model in the Case tab. In the left window, select the model which history you want to copy. In the middle window, select the model to which you want to copy history and press Copy.



2.6.3 How to export model with History

To export the model with History, go to the **History Tab** and click **Export**, as shown below.

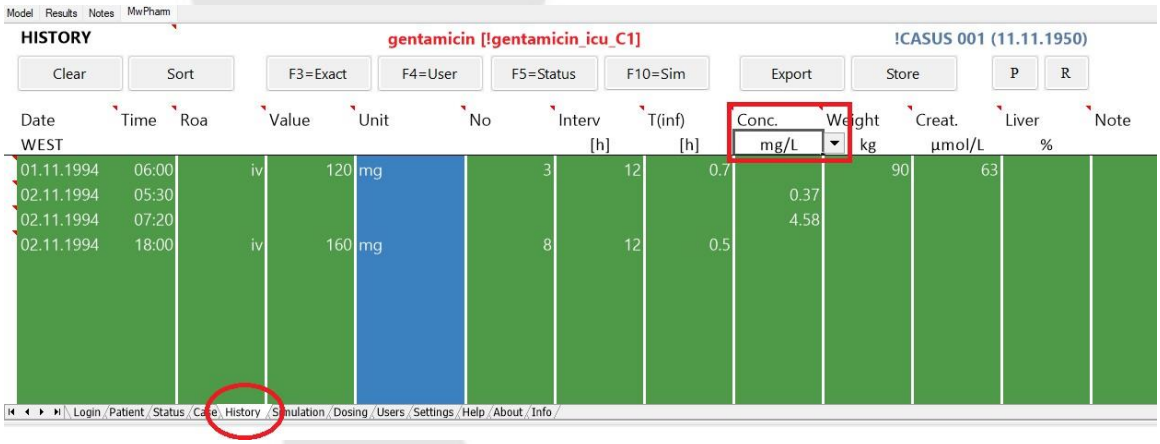


2.6.4 Why isn't PO/IV option showing in the History Tab?

This happens, when the model of a drug doesn't have the needed constants (i.e., bioavailability, absorption rate) to simulate either of the options.

2.6.5 How to change units of concentration in the History tab?

You can change units right in the **History** tab by clicking on the box with the unit and choosing the preferred one from the list. This way, the unit will be changed only in the current case.



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2.7 Dosing

2.7.1 How to generate a dose?

New dose can be generated based on concentration or AUC24 parameters. Each of these require the user to choose wanted targeted value for each parameter.

2.7.2 What does Practical mean?

MwPharm automatically calculates the Exact dose for you actual patient, which is often hard to implement in clinical setting. For this reason, we offer 4 Practical dosing regimens, that are easy for pratical clinical realization.

Profile	User	Exact	P1	P2	P3	P4	
Load	1530.9	1530.9	1500	1500	1500	1500	mg
Dose	1328.9	1328.9	1000	1250	1250	1500	mg
Tint	129.65	129.65	120	120	144	144	h
Ndos	3	3	3	4	3	4	-
Tdur	1.00	1.00	1.00	1.00	1.00	1.00	h
Max	59.73	59.73	46.20	57.46	55.01	66.04	mg/L
Min	7.93	7.93	6.97	8.63	6.15	7.38	mg/L
Tmax	1.00	1.00	1.00	1.00	1.00	1.00	h
Tmin	129.65	129.65	120.00	120.00	144.00	144.00	h
Ave	17.28	17.28	14.26	17.66	14.72	17.68	mg/L
pSS	99	99	101	100	100	100	%

Each of these dosing regimens has specified values, that can be modified by user directly. After choosing your prefered dosing regimen choose the button **Add to the history**.

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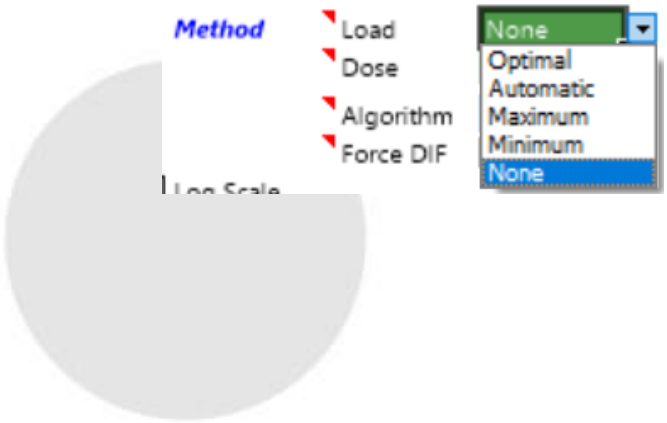
2.7.3 How to set loading dose to NONE?

In order to set loading dose to NONE, choose None for parameter Load in Dosing section. See photo below.



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2.8 Simulation

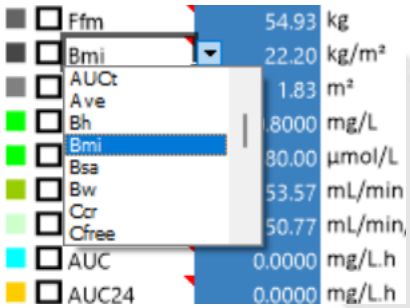
2.8.1 How to change scaling of a graph

Below the graph you can find commads for graph scaling.

2.8.2 How to add another curve?

In order to add a new curve to the graph, you can choose from the parameters automatically shown next to the graph, as in the photo below. To show any of the graphs, check the box.

If you would like to add parameter that is not listed on a default screen, choose one of the field parameters and click on Select button. Choose the desired parameter from te list. After that, tick off the white checkbox next to the name of the parameter to plot the parameter in the graph. You can also change the color of the curve by clicking on the color box next to the checkbox.



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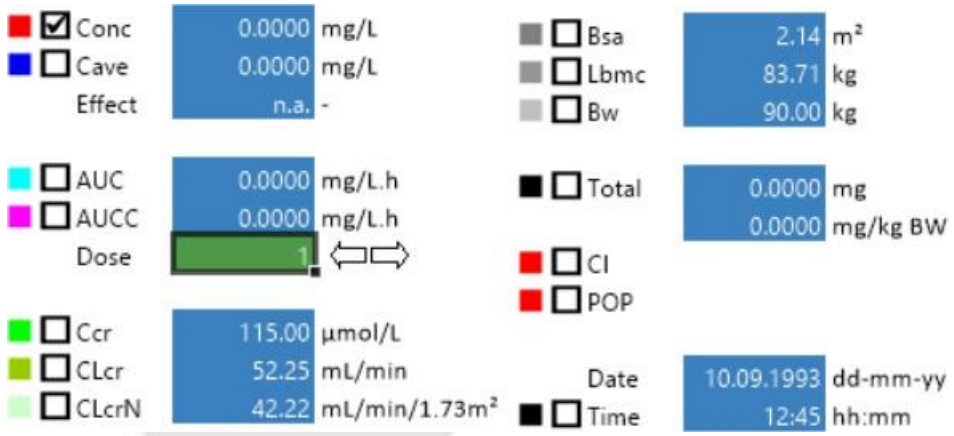
2.8.3 What are the individual checkboxes in Simulation tab good for?



Checkbox	Meaning
Conc	Shows the concentration of the drug
MIC	Minimum inhibitory concentration
AUC(C)	Area under curve (cumulative)
CI	Confidence interval
SD	Standard deviation
AUC24/MIC	Area under curve normalized to 24 h divided by MIC
Ccr	Creatinine clearance rate
Bsa, Lbmc, Bw	Body surface area, lean body mass, body weight
eGFR(n)	Estimated glomerular filtration rate (normalized)
Total	Shows the doses used
POP	Shows concentration level for population
Time	Shows vertical time lines for better reading from graph

2.8.4 What does POP check box mean?

Checkbox "POP" will show the curve based on POPulation data. When user goes back into simulation tab after fitting, the program will use the most accurate available data (fitted individual parameters). However, if the user wants to see how the curve looks based only on population data, use the check-box “POP”.

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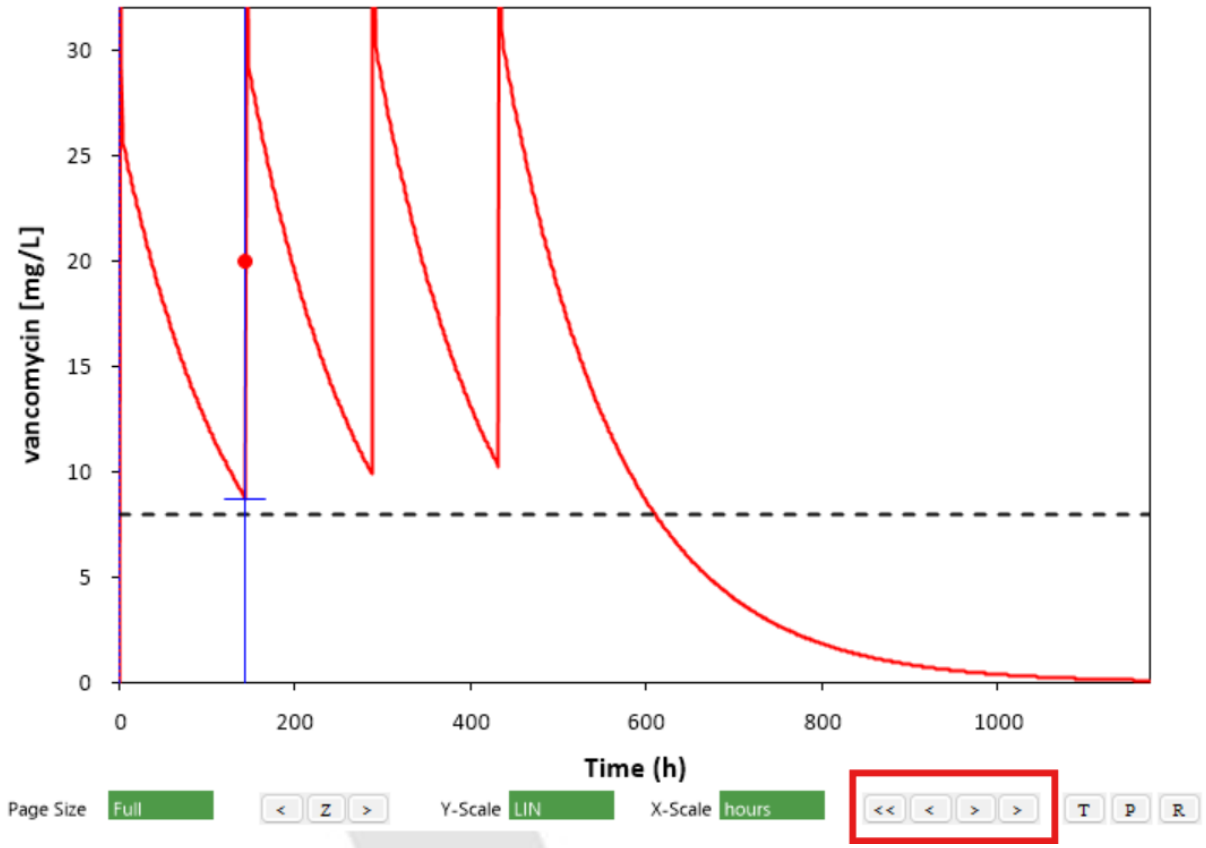
2.8.5 How to determine the concentration at time X?

Time cursor can be moved by clicking on the arrows below the graph. One arrow for minimal time step, two arrows for bigger time steps. The concentration value at a selected time will be shown on the parameter bar on the right side of the simulation tab.



2.8.6 How can I set the parameters in the Simulation tab as they used to be?

In previous versions, there used to be a default layout of the parameters visible in the Simulation tab. In order to allowing users to creating their own layout, we removed the default one. You can return to the old layout by clicking the key **Shift + the button Load** upper in the screen.

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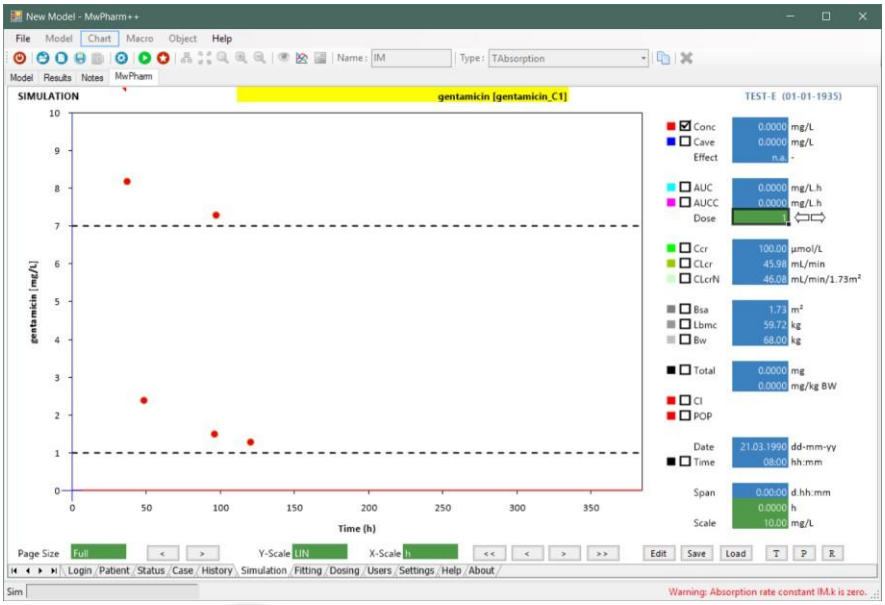
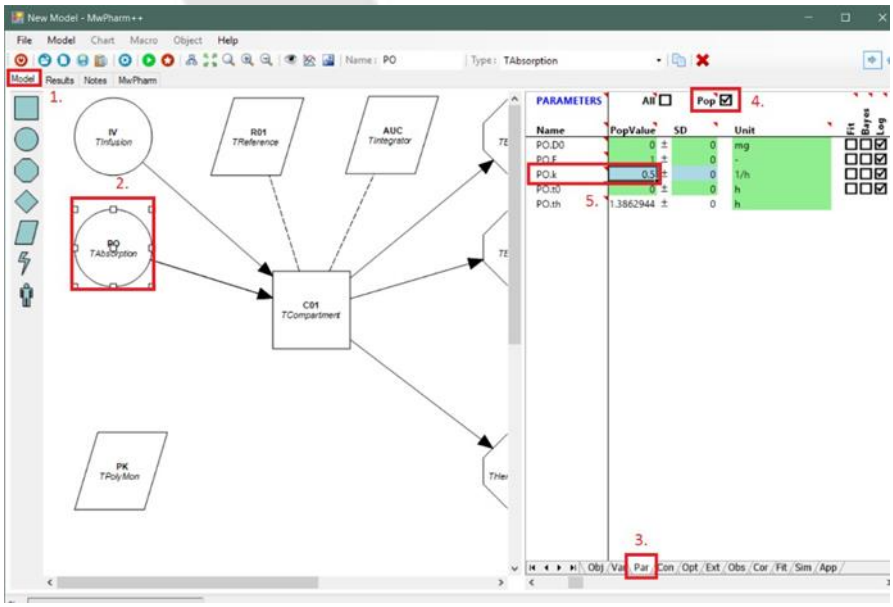
2.8.7 Why is graph staying at zero?

This can happen if you have not given you model an absorption rate constant. That means, that the constant will be zero by default. If the absorption is zero, the drug is not absorbed, and the concentration stays at zero.



This was a change made in one of the previous updates. Some drugs have default absorption rate at zero, because it deeply varies in various drug applications in per oral use. If you know the absorption rate for the drug and application, just change it in the model tab to wanted value.



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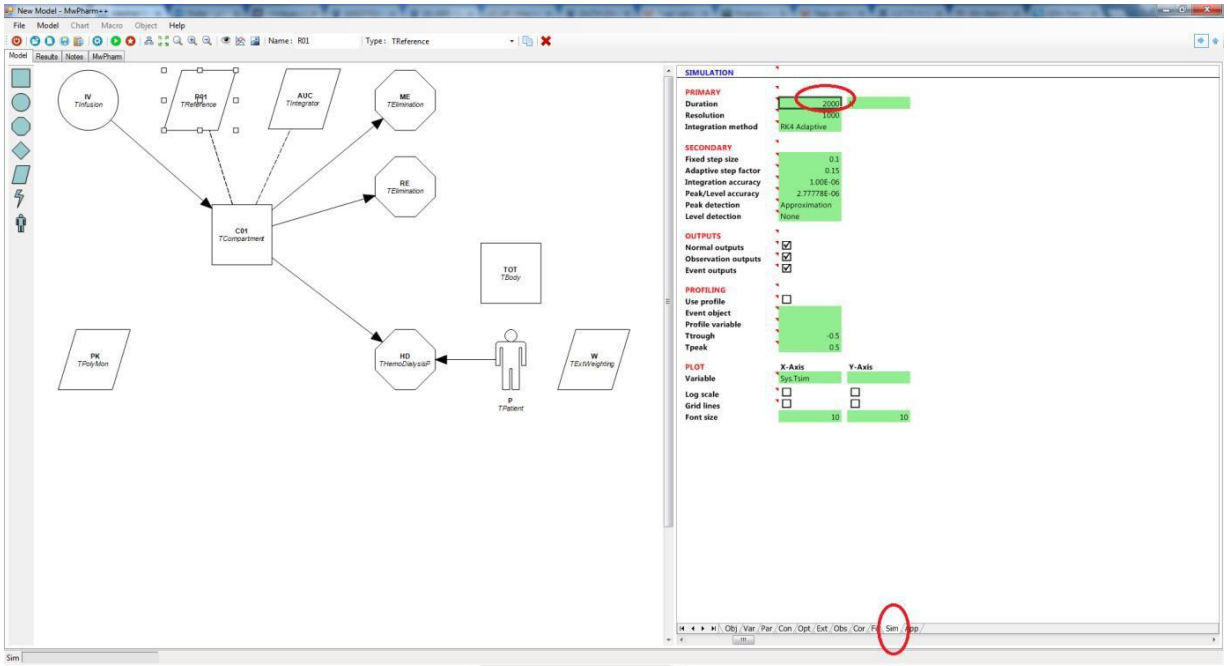
2.8.8 How to view unlimited number of days on the X axis in MwPharm++?

If you see only 25 days (for example) in simulation, even though you know the total number of days in your simulation is over 50, try the trick with adding the patient's weight to history at a time beyond the visible range. In our case at 50 days. Use the last inserted weight.

If this trick does not work, check your model settings.

The process is simple, if you have loaded a specific model where the error occurs, then flip the MwPharm tab to the Model tab in the upper left corner. Now you see a model of drug. Double-click on the TCompartment block. It opens bar on the right side, where you have to click on the Sim tab. Here, make sure that the Duration box is set to 0 h. Because if there is for example 600 h, you will only see 25 days in the simulation.

The picture below shows the location of the Duration box.



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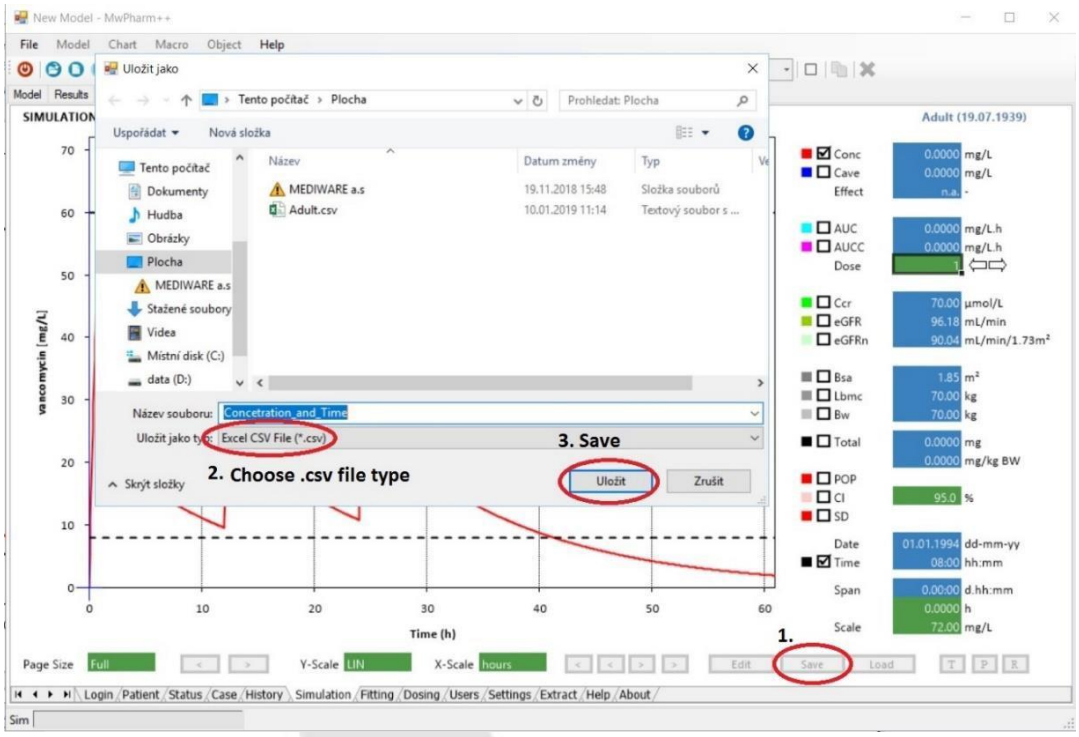
2.8.9 How to obtain complete simulation data?

When you click to **Save** button in the **Simulation** tab of MwPharm++, you can save simulation as .CSV data file. Save this file to your computer a then open in Excel. Here you will see all times and all concentrations of simulation.



2.8.10 Is it possible to show unbound concentration in Simulation tab and how?

Yes. To show the unbound concentration in Simulation tab, follow the instructions:

- Load a case and go to the history screen
- Go to **Model** tab
- Enable the observation of parameter C01.Cu variable

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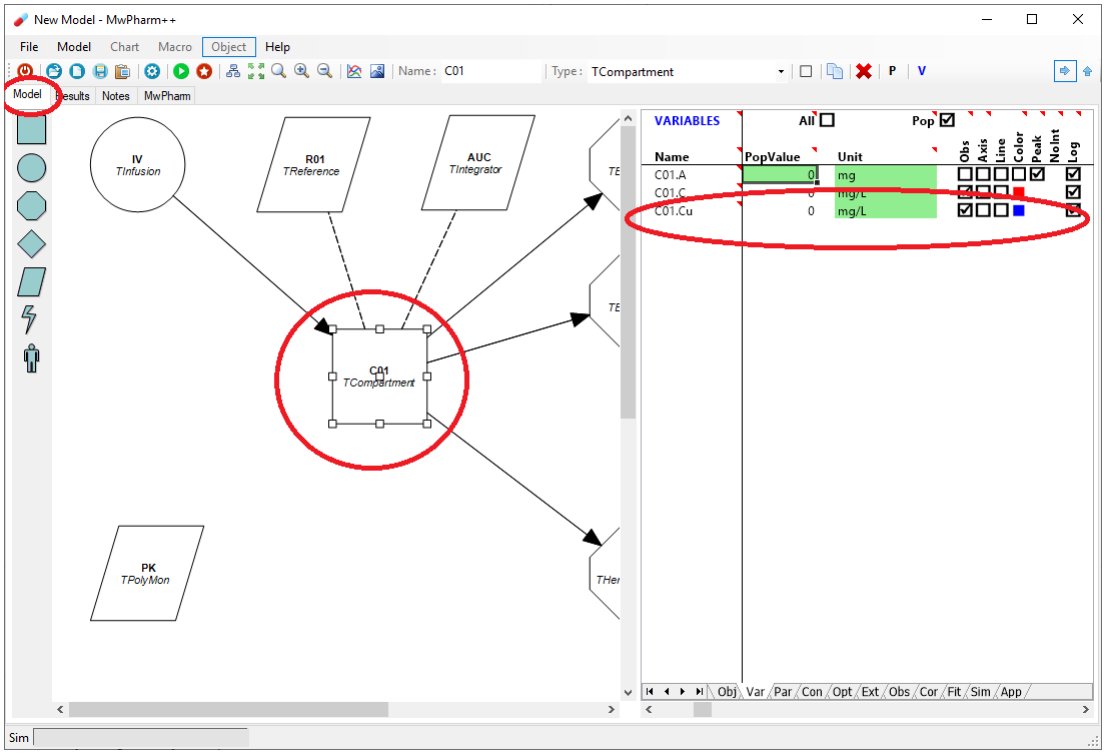
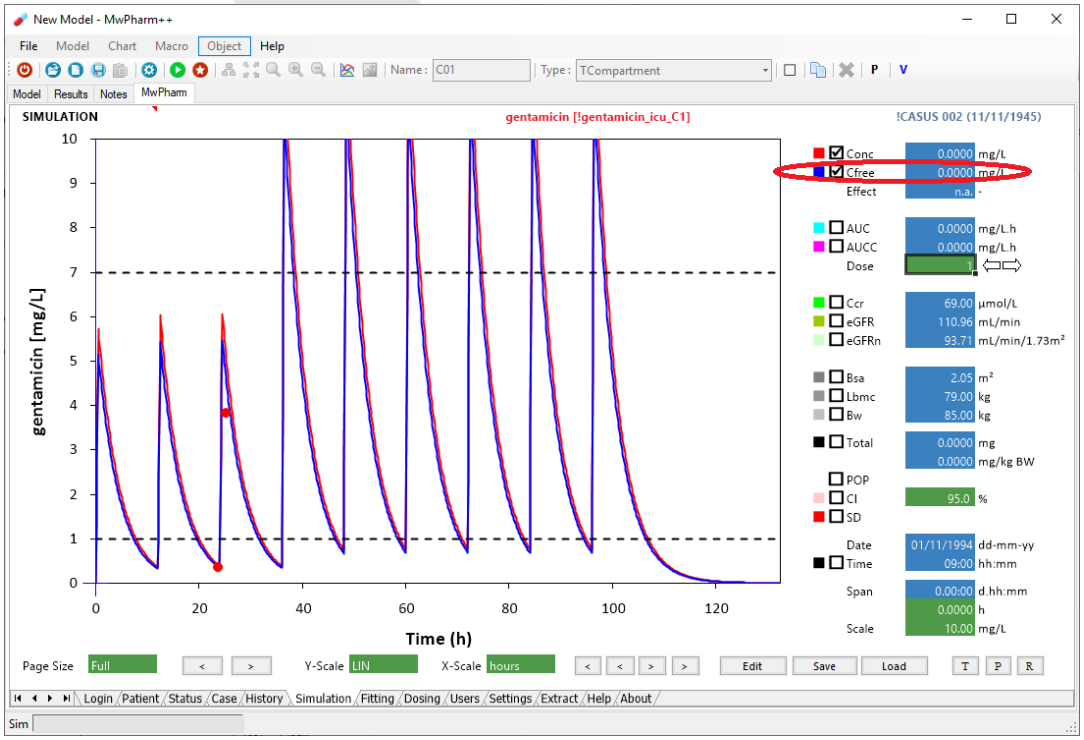


Go back to MwPharm tab to **Simulation** screen and you will see a new chart in view: concentration unbound



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2.9 Fitting

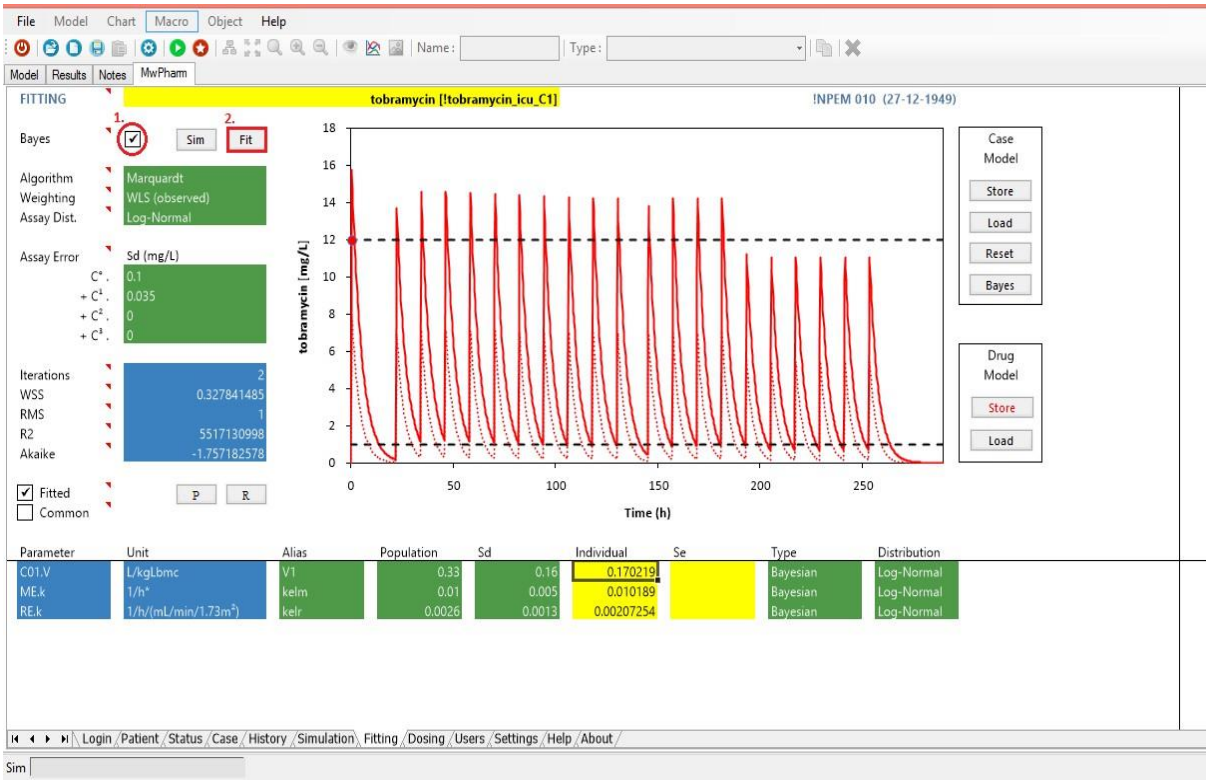
2.9.1 What is the purpose of fitting?

Fiting section enables the user to fit the simulation of the drug model based on population to its specific patient. This will lead to individual specified simulation. Fitting is done automatically with use of mathematical functions based on scientific literature. After saving the fitting, simulation curve will change. The photo shows simulation based on population with dashed line and new fitted simulation with continuous line.

2.9.2 Fitting from one point

Option A - with Bayes:

We recommend this option in 95% of cases. First, you should try tick off fitting using Bayes, if it isn't selected and press Fit. If you have a new model, you will be offered if you want to generate Bayes or not.



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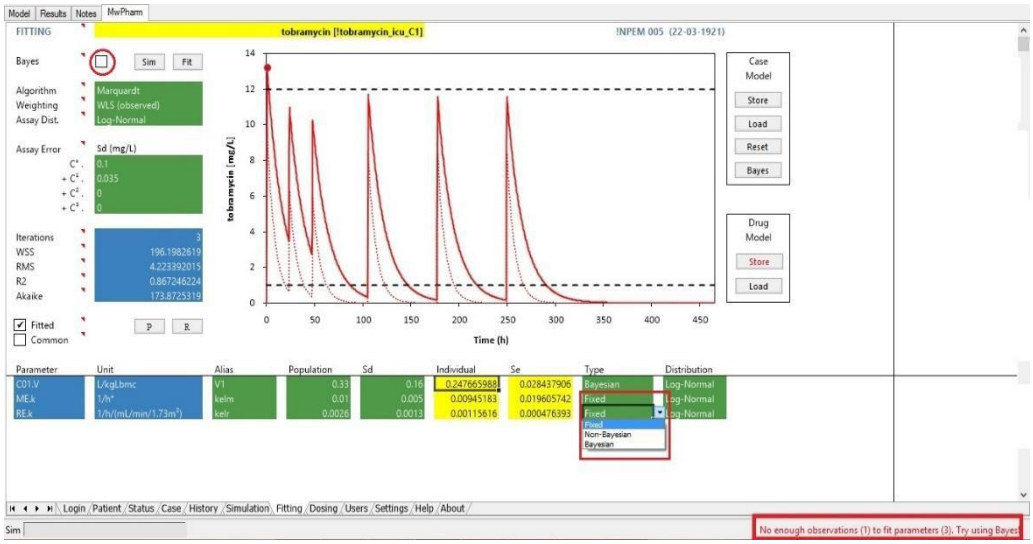
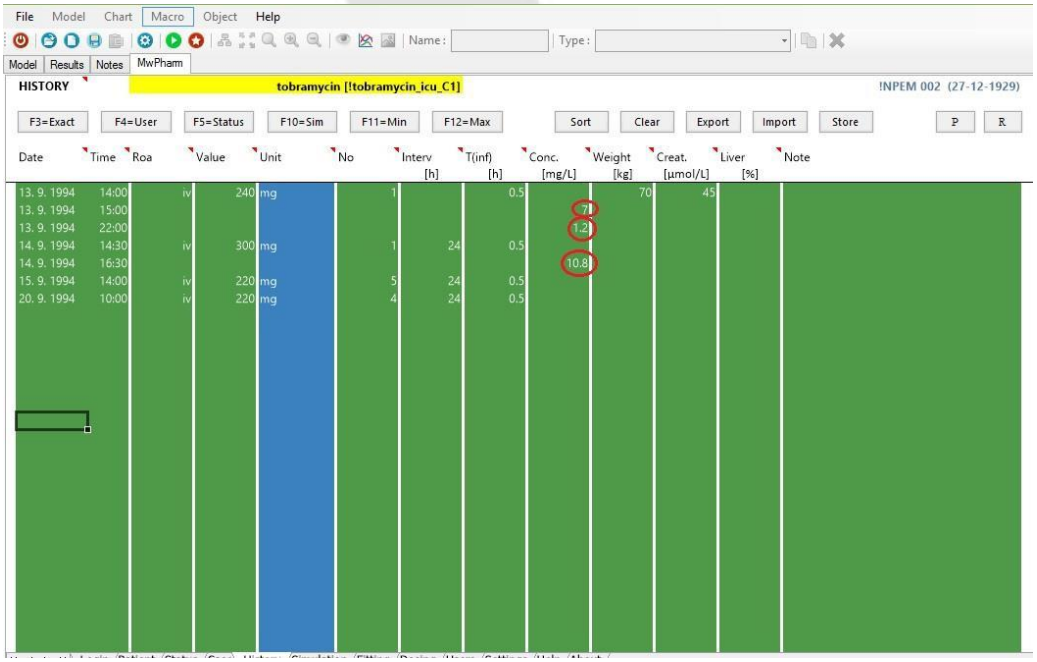
Option B - without Bayes:

If you would like to fit the model from one point without Bayes, error message will appear in the lower right corner. It is therefore necessary to reduce the number of fitting parameters. The number of fitting parameters can be reduced when you select Fixed in the column Type.



In case you want to fit all the selected parameters, you must increase the number of measurements of the concentration. You have to have at least the same number of measurements, as you have fitted parameters.



2.9.3 What is the difference between fitting with or without Bayes?

The Bayesian method combines a priori information (population data) with a posteriori information (one or more measured concentrations) for finding the statistically most likely values of the individual parameters. The number of non-Bayesian can never exceed the number of observations. That means that fitting using just one measured concentration point can be done with a model containing maximally one non-Bayesian parameter.

What is the purpose of the table called “Drug Model” on the right side in the Fitting tab?

There are two buttons in this table: Store and Load.

By clicking the button Store, you can save the parameters you set for the model so that the future models will be automatically based on these parameters.

By clicking the button Load, you can load back the population parameters we set for the model by default.

Note that this table is visible for users of the type “Administrator” or “Super user”. Users of the type “Normal user” does not have the right to change drugs and models.

2.9.4 What does it mean ‘Matrix is singular’? How to make matrix non-singular?

A typical cause for singular matrices is over-parametrization, in which an infinite set of parameter values can result in the same value of the Objective Function. For example, you cannot fit both bioavailability F and volume of distribution V.

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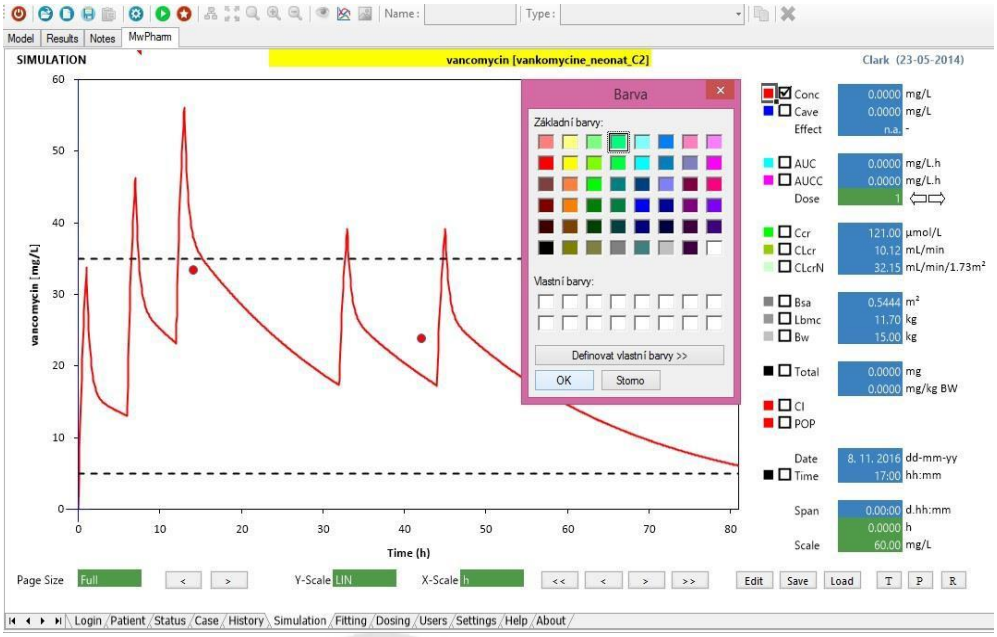
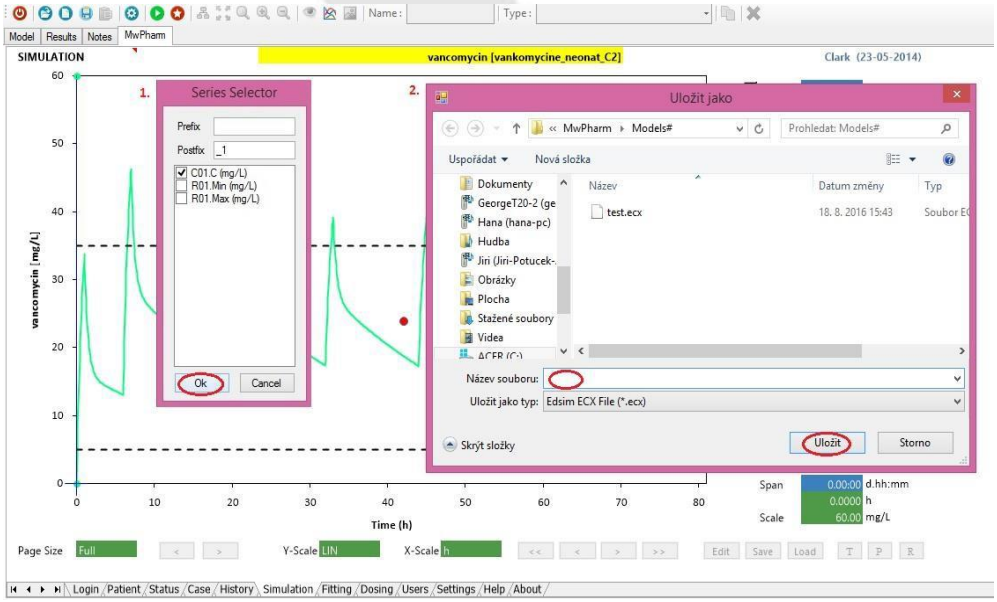
2.9.5 How to compare 2 graphs?

You can change the colour of the curve by right-clicking on the red square and choosing a new colour.



After that, click the **Save** button and a window will pop-up. Click **OK** to confirm and now popup a window where you name save the curve to a folder of your choice.



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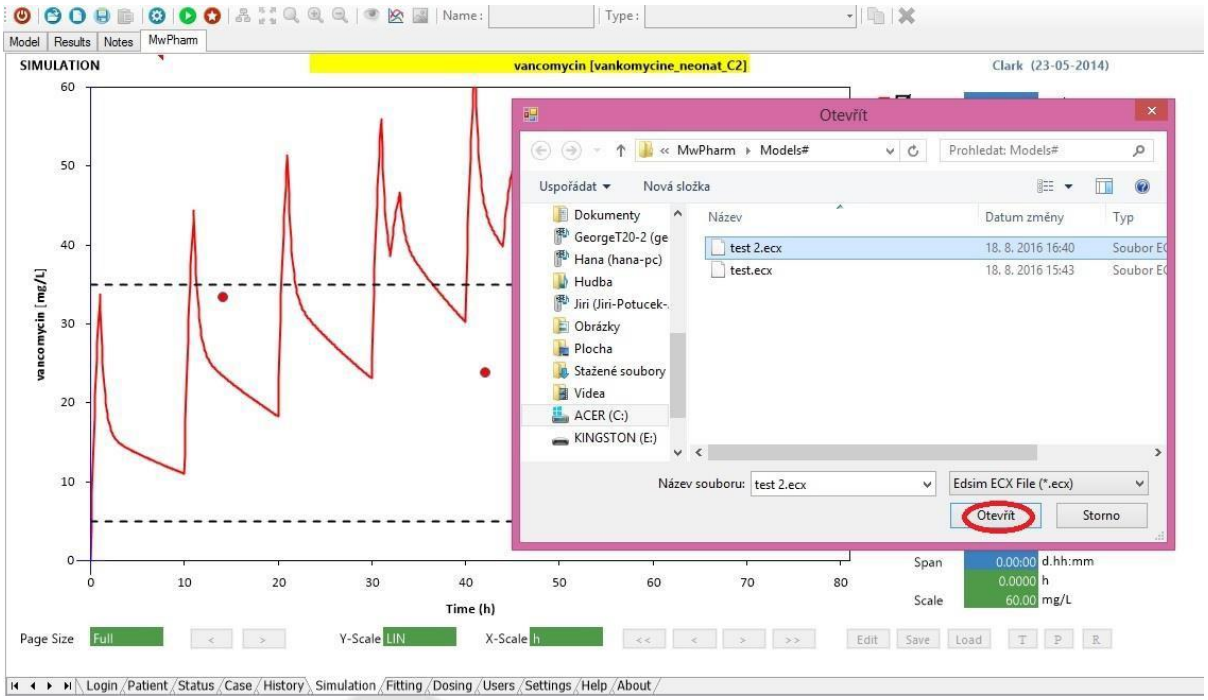
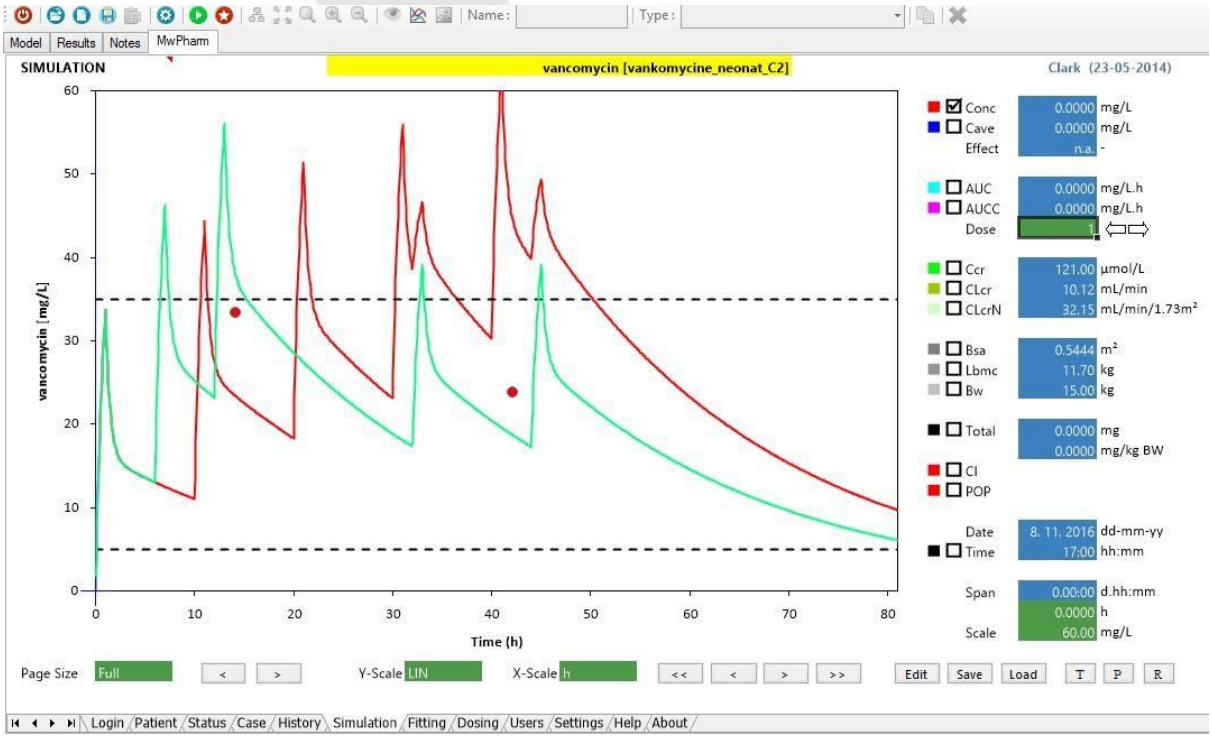
Now, you can upload a new patient or modify the parameters of the current patient. Again, you need to go to the **Simulation**, where you will see a new red dosing curve. After that, click the **Load** button, find your formerly saved curve and click **OPEN** to confirm.



Now you have successfully added another curve.



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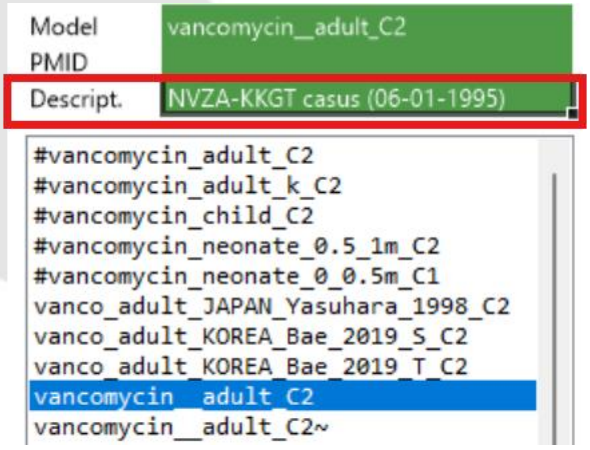
2.10 Drug models

2.10.1 How do I find the information about the sources of the models?

To find this information, you just need to go to the Case tab and select the model you want to find the information about. Above the model, there is a green row called Description, where is the information about the sources.



2.10.2 How to import a new model to your database?

In **Drug models** section choose **Import model – Select from MwPharm Library**, where you can select your model of choice. The other option is to upload file of a model.

2.10.3 How to add a new model?

At first you need to go to the **Case** tab in MwPharm++. After that go to the left column and choose the name of the drug you want to assign the model to. In case you want to assign it to a new drug, write the name of your medicament in the upper green box and click **Insert**. You might have to click the button **Insert** twice to confirm the process. The procedure is shown in the picture. To assign the new model to an existing drug simply choose the drug from the left column and proceed to the next step.

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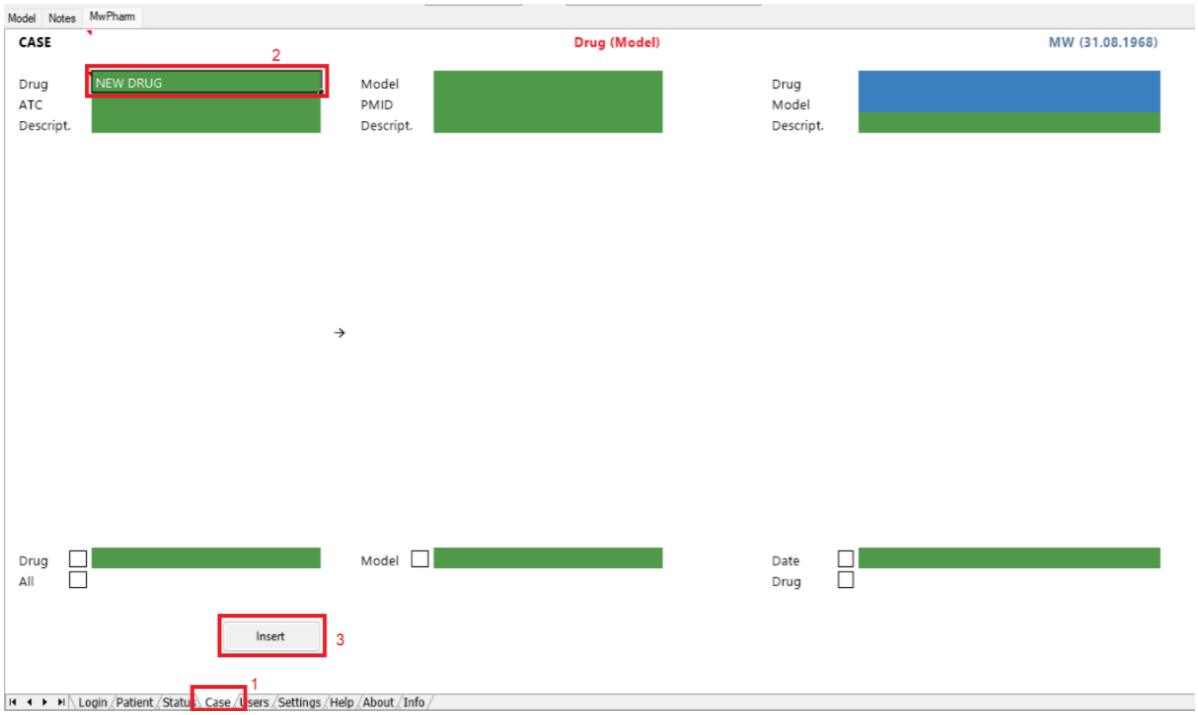
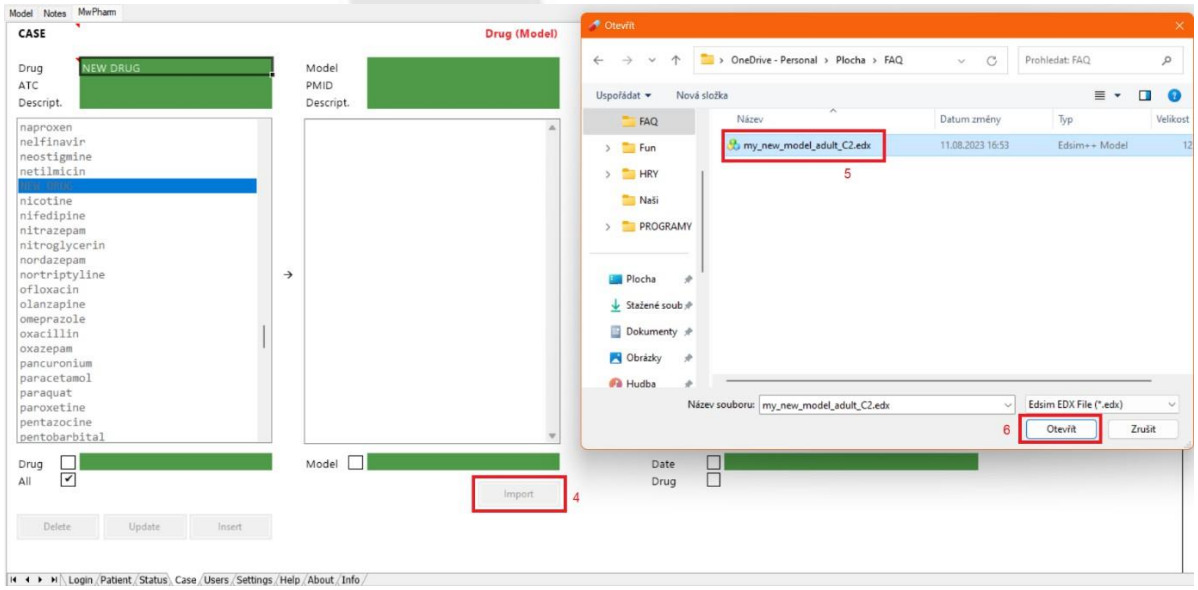


After that, click the **Import** button in the middle and a window will pop-up. There you can find the model you want to add to your database. Select it and click **Open**.



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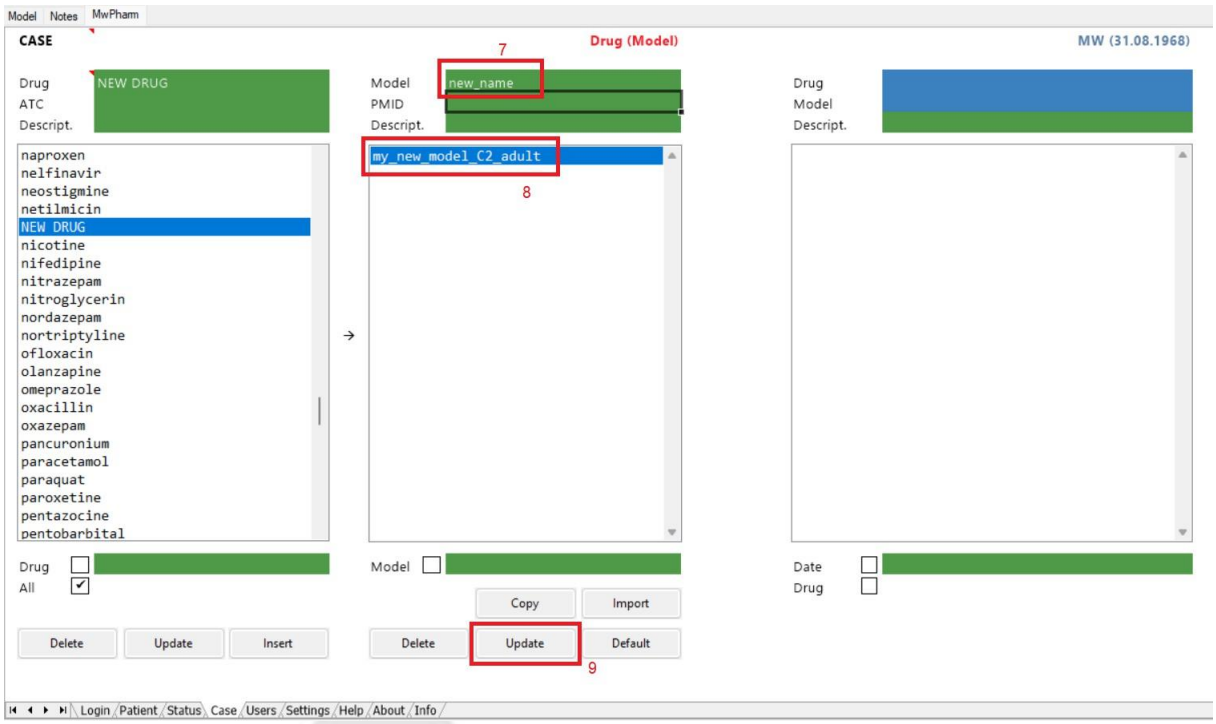
Now that you have the model inserted, you can rename it. To rename the model, you just write the new name in the upper green box and press **Enter**. After that you choose the model, you want to update, select it and click **Update**.



Now you have successfully added a new model to your database. Now you can use it like you normally would.

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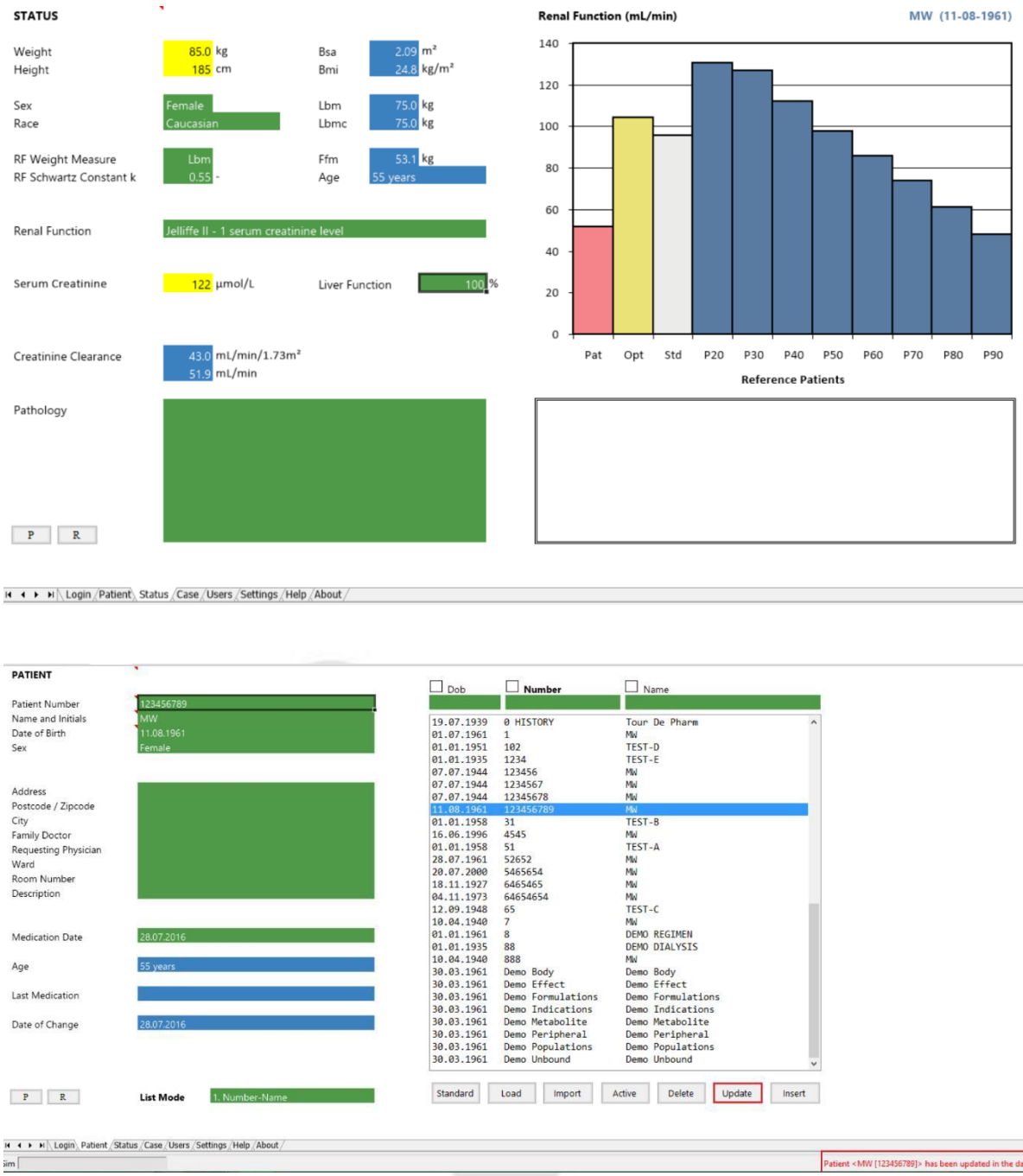

As you can see above, our software informs you, that you have successfully updated your patient.

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2.10.4 How to change model parameters?

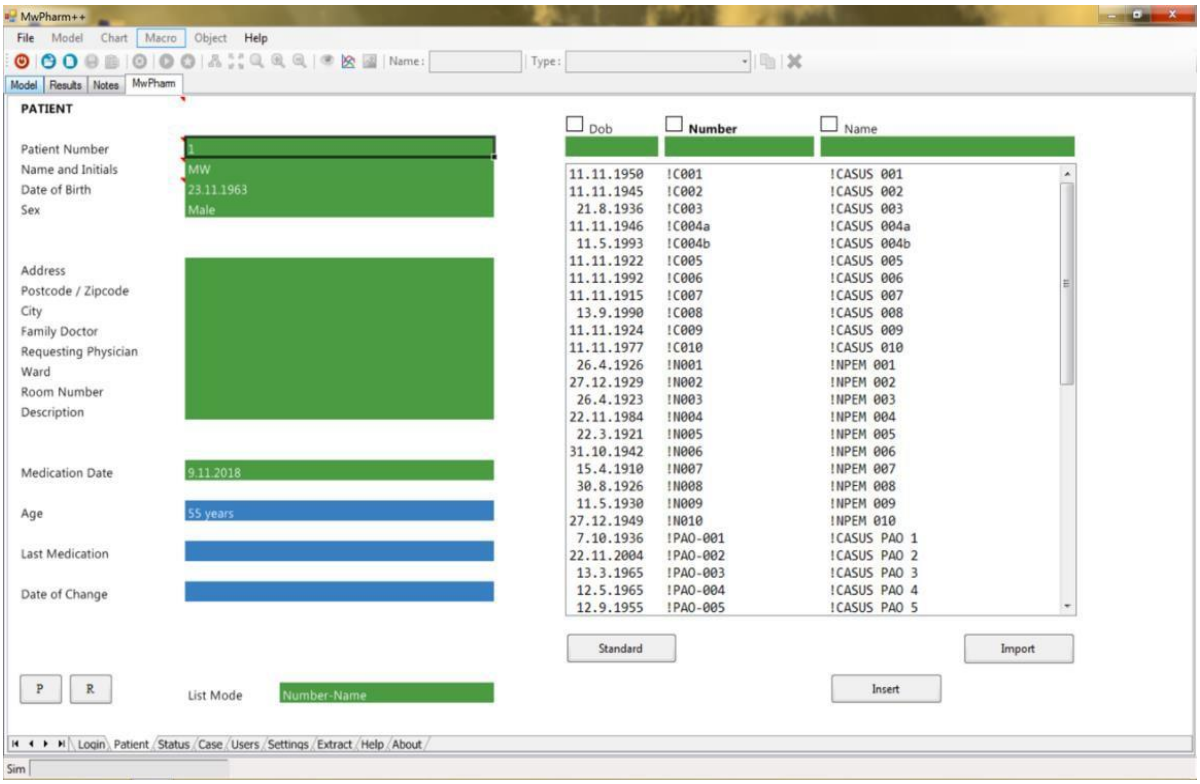
Choose the model in Drug models and press button Copy model. A copy of your model will be automatically created in the database (e.g. YourModel_C1_COPY). You can now use the **Open model details** in the roll out window to open the model editor. Go to Parameters section in order to change any parameter values.

2.10.5 Is it possible to work with drug interaction in MwPharm Online?

The software is ready for this implementation, but currently there are no drug-interactions models available in the default database. If you have data and parameters for drug interaction, you can model this in Edsim++ using special interaction building blocks.

2.10.6 How to change units of concentration in the settings of the model?

After login to the MW++ software click on "**Model**" bar (upper left corner).



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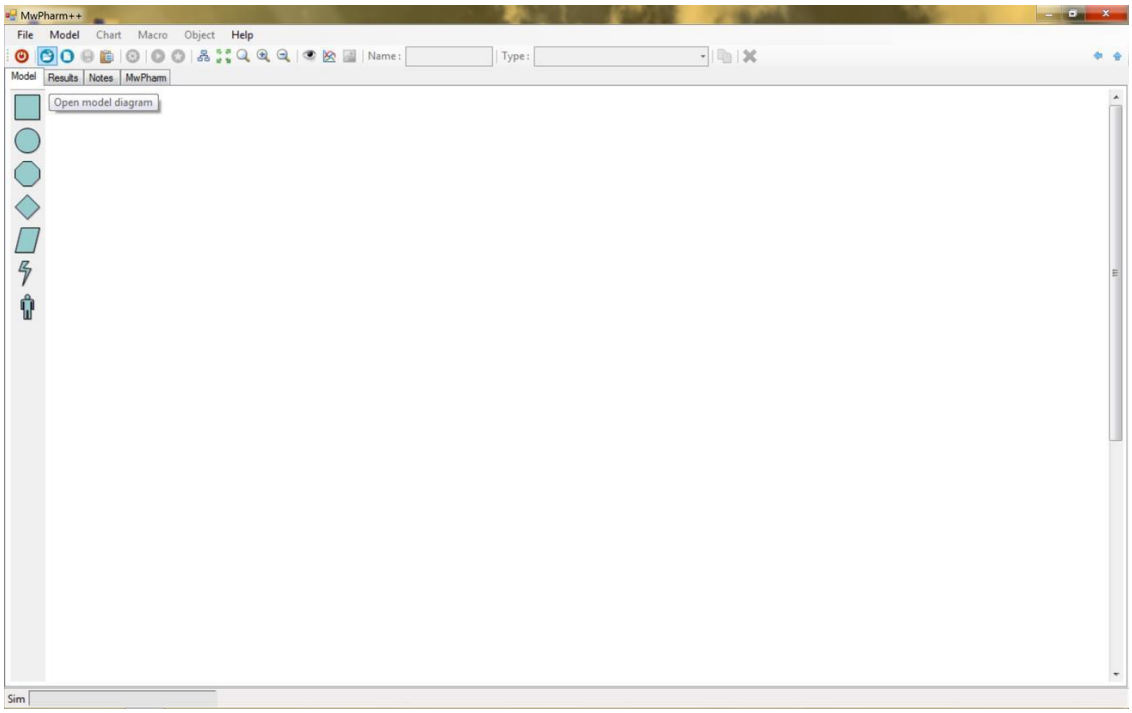
Click on „Open model diagram“.



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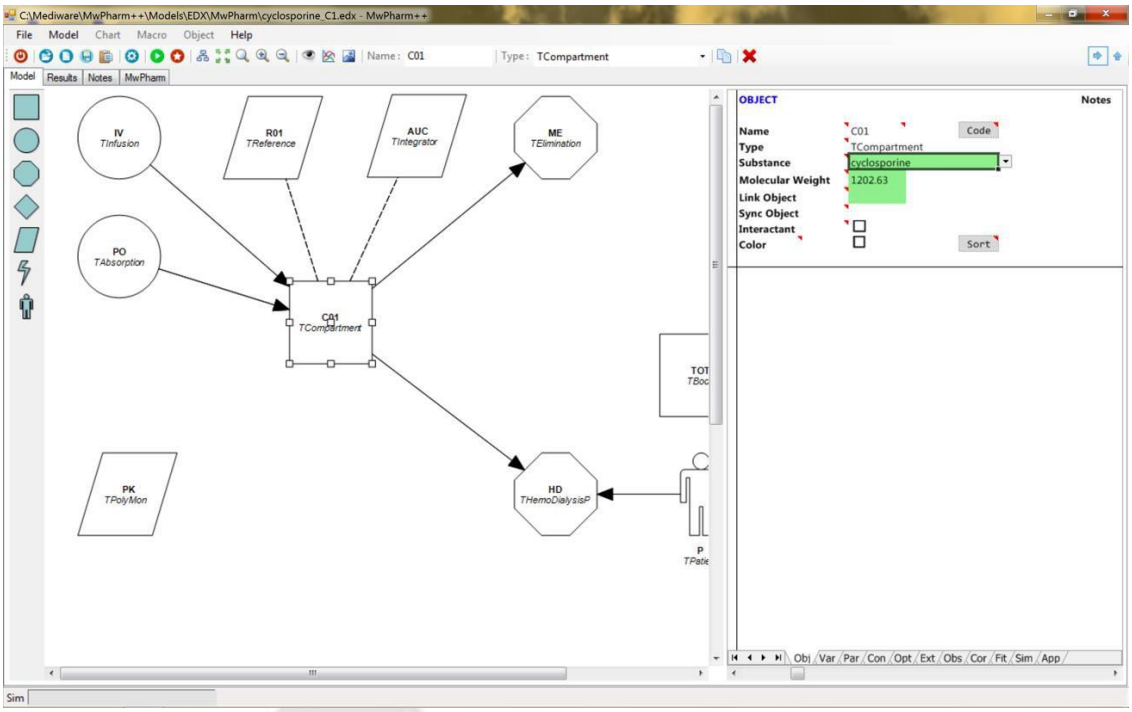
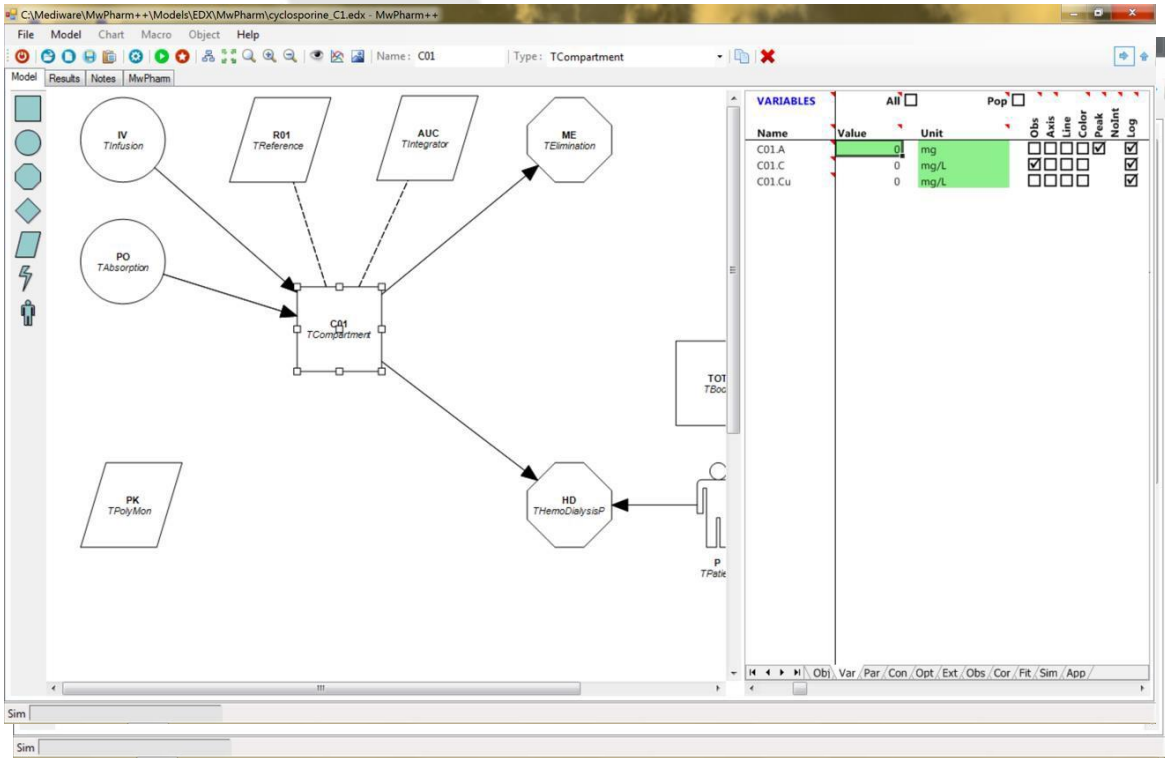
Find and open the model (folder of all models: C:\Mediware\MwPharm++\Models\EDX\MwPharm).

Double click on „C01 T Compartment “.



A window on the right side pops up => click on “**Var**” bar on the lower side of the window.



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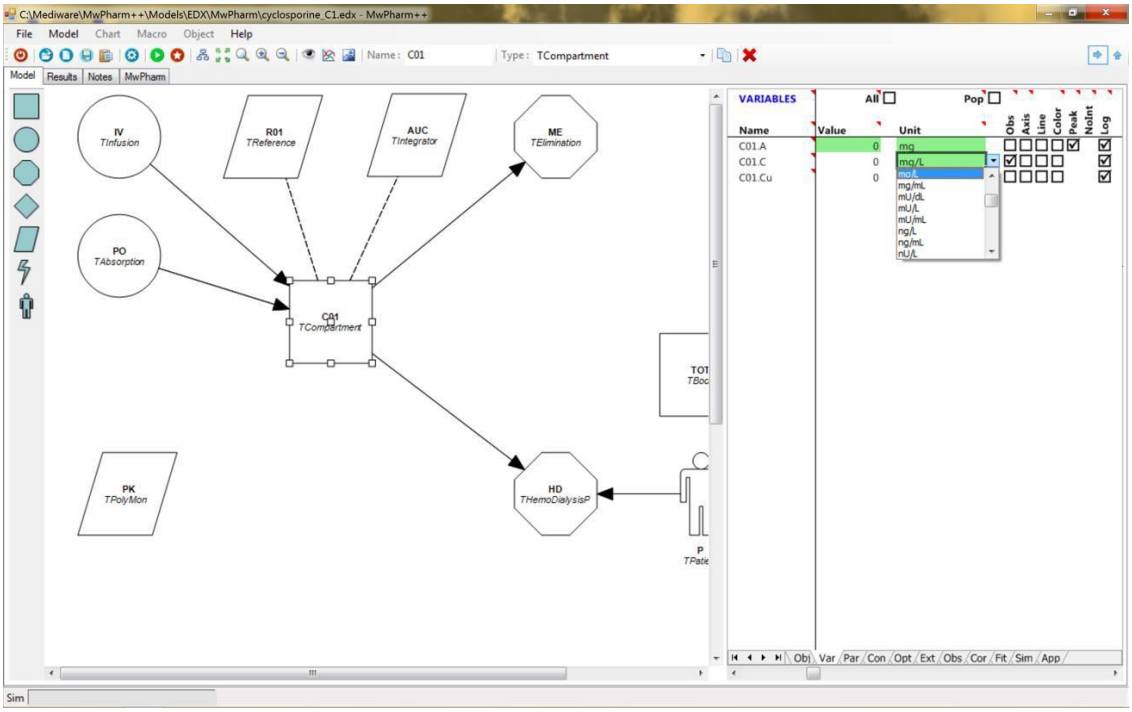
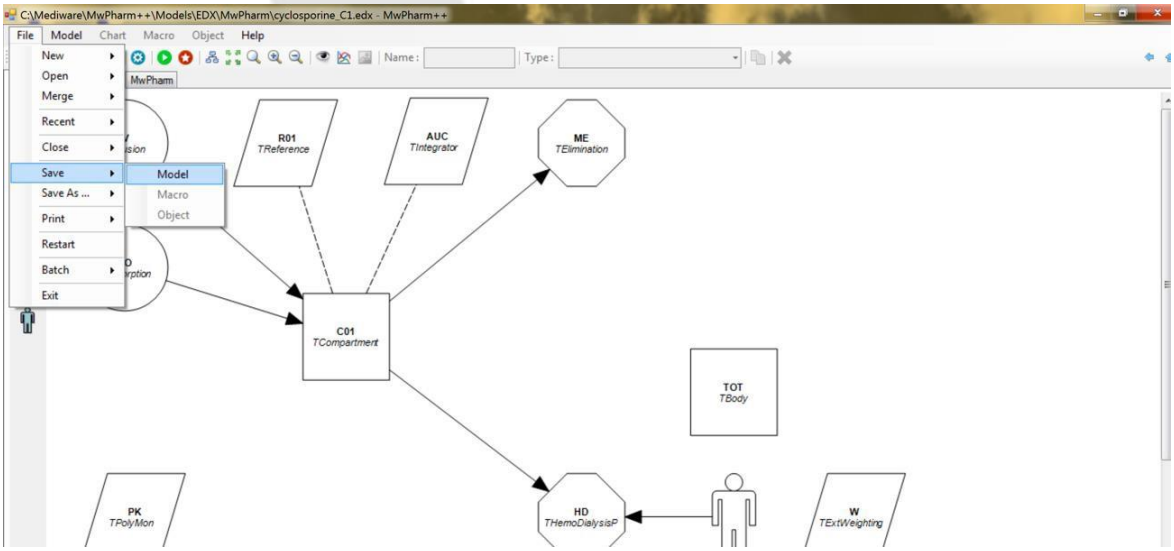
Select the unit for „C01.C“ parameter.



Finally, save your model. (either “Save as” to create new model with different units or rewrite your model by simply clicking on “Save”).



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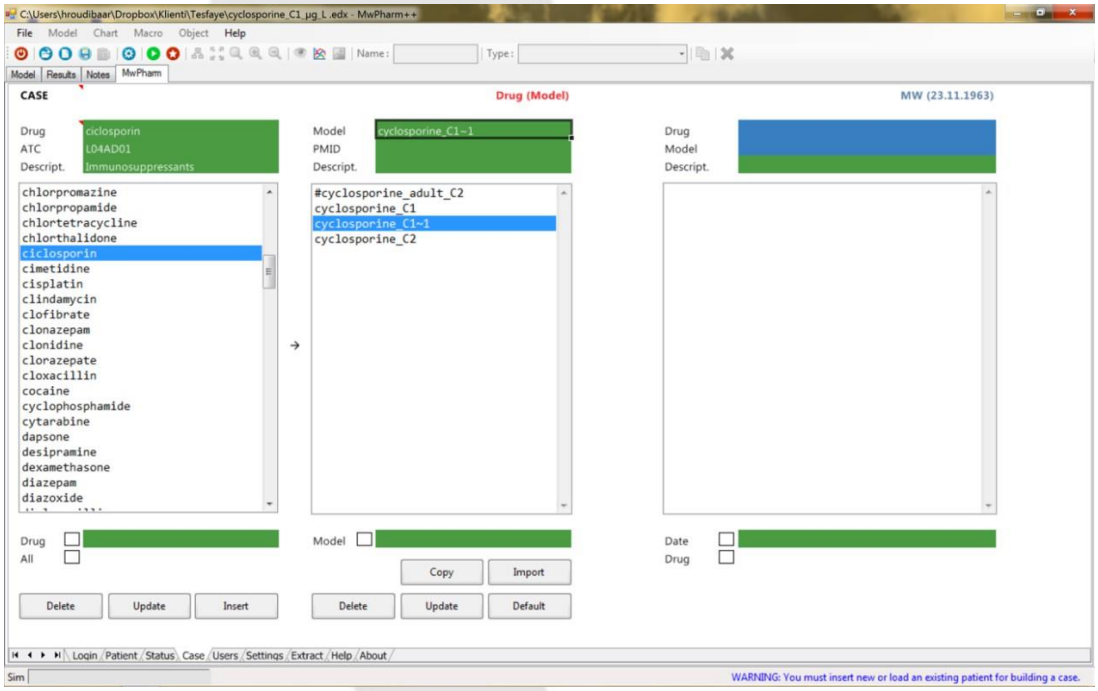
If you choose “Save as”, save the new model to your desktop or elsewhere accessible. To use the model in the MwPharm++ software import it as instructed in our **FAQ.** If you do so, don’t overwrite the original model - click on “No”. The newly added model will be named as the “original_one~1”. You can rename it as desired in the upper “Model” cell. Afterwards, click on update to change the name of the new model in the MwPharm++ database.



If you change the units to any variant including mols, be sure to check if the “Molecular weight” is input (visible after double click on “C01 TCompartment”, viz pic 4 in this chapter).

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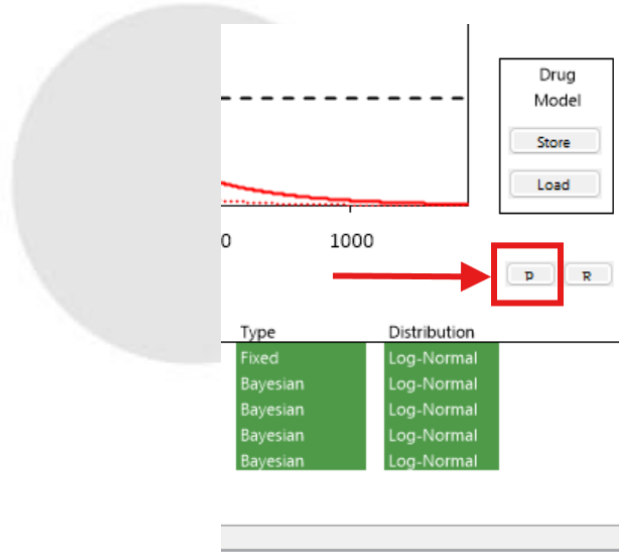
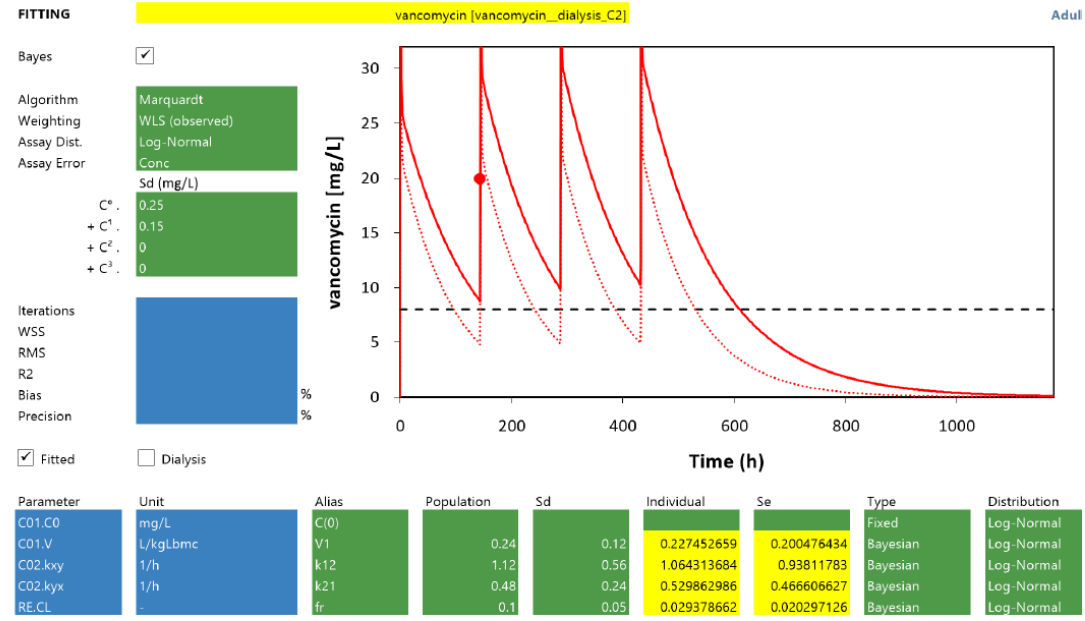
2.11 Reports

2.12 How to create a new report?

Each section in MwPharm enables user to print out a specific report. Use button **P** to get a print of the screen or button R to get a report from a specific tab.



MW PHARM ++



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2.12.1 How to change the Export Templates and Reports?

At "C:\Mediware\MwPharm++\PlugIns\MwPharm\Reports\Template", you can find the excel sheets for reports. There you have five different files, each of which contains the report templates for each tab in MwPharm++. You can change each file, as you want your final report to look like, but you need to pay attention to width of the excel final form.

The Excel sheet is using macros, which take data from MwPharm++ and put it in your final Report. To see, what macros are available, open the same folder and you can see @References.xls, which contains a list of all macros. If it is too challenging to work with macros, write an email us and we will happily prepare a template for you.

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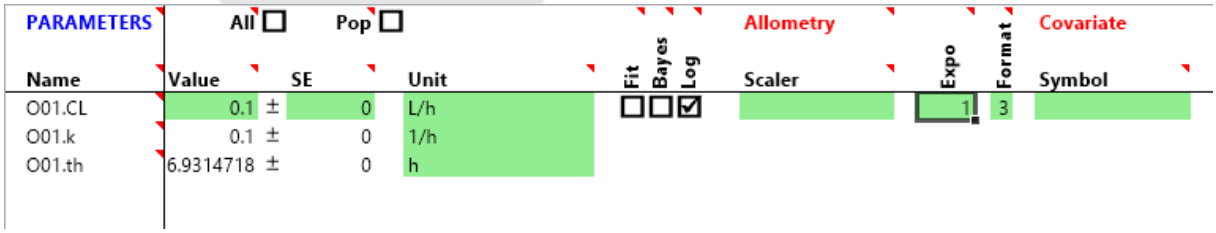
3 Edsim

3.1 What is Edsim and what is it good for?

Edsim is our software for creation of new models or for tweaking and updating old ones, that are later used in MwPharm++. Edsim is part of MwPharm++ software and can be used ed.

3.2 How to add albumin as patient variable?

There are two ways for adding covariates to model.



1) Classic MwPharm style using the Allometry field where you can specify a patient variable like Bw (requires a TPatient object). The number of patient variables is predefined and therefore limited. E.g., there is no albumin.

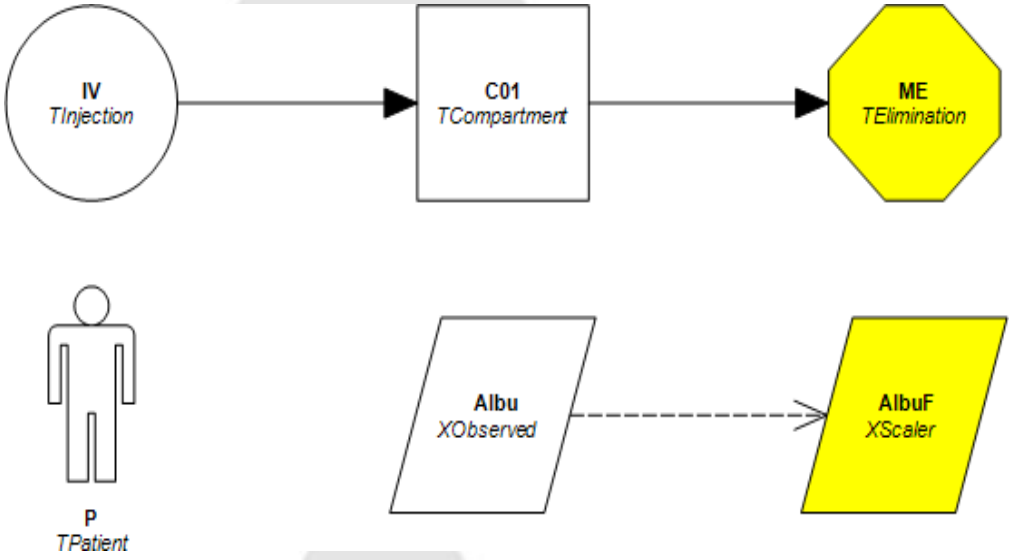
2) Advanced Edsim style using the Covariate field where you select a generic covariate (requires an XTool object). With this method we can add new covariates which are not defined in the patient object. We typically use the following to objects:

XObserved: Allows us to store a set of observed covariate values XScaler: Defines a covariate scaler formula

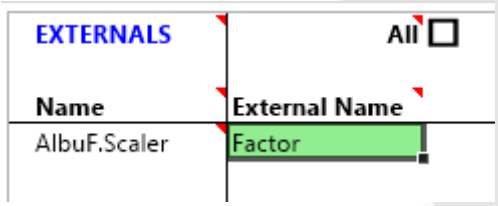
Both methods (allometry and covariates) can be combined. Furthermore, multiple covariates can be chained.

You might need to tick off the Show all types checkbox:

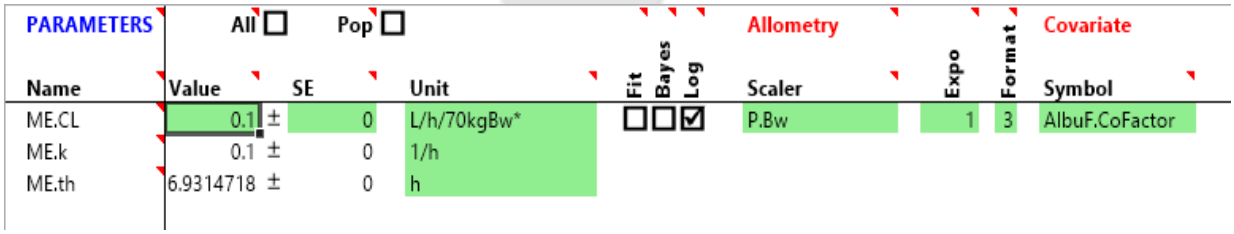
A model taking albumin into account may look like this:



It is important to set the correct external in XScaler (default Bw, must be changed to Factor).



With the clearance parameter of the ME object P.Bw is used an allometric scaler and AlbuF.CoFactor as a generic covariate.



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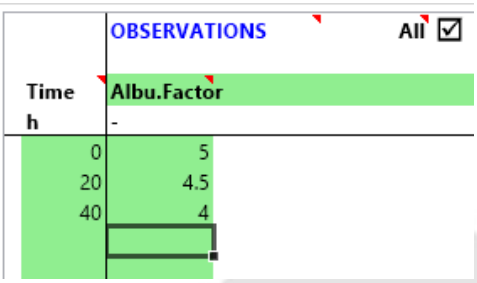
You can enter albumin observations in XObserved object:



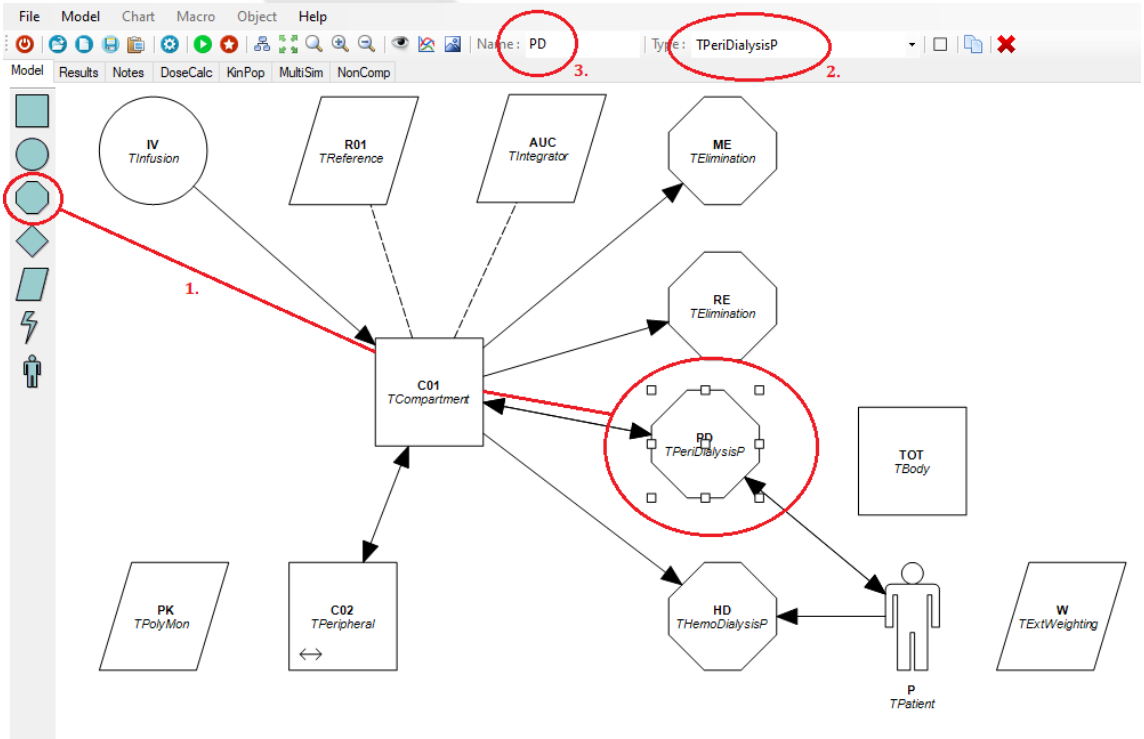
The XScaler object has two modes (Opt tab):

Absolute: CoFactor = Scaler.Value ^ Expo

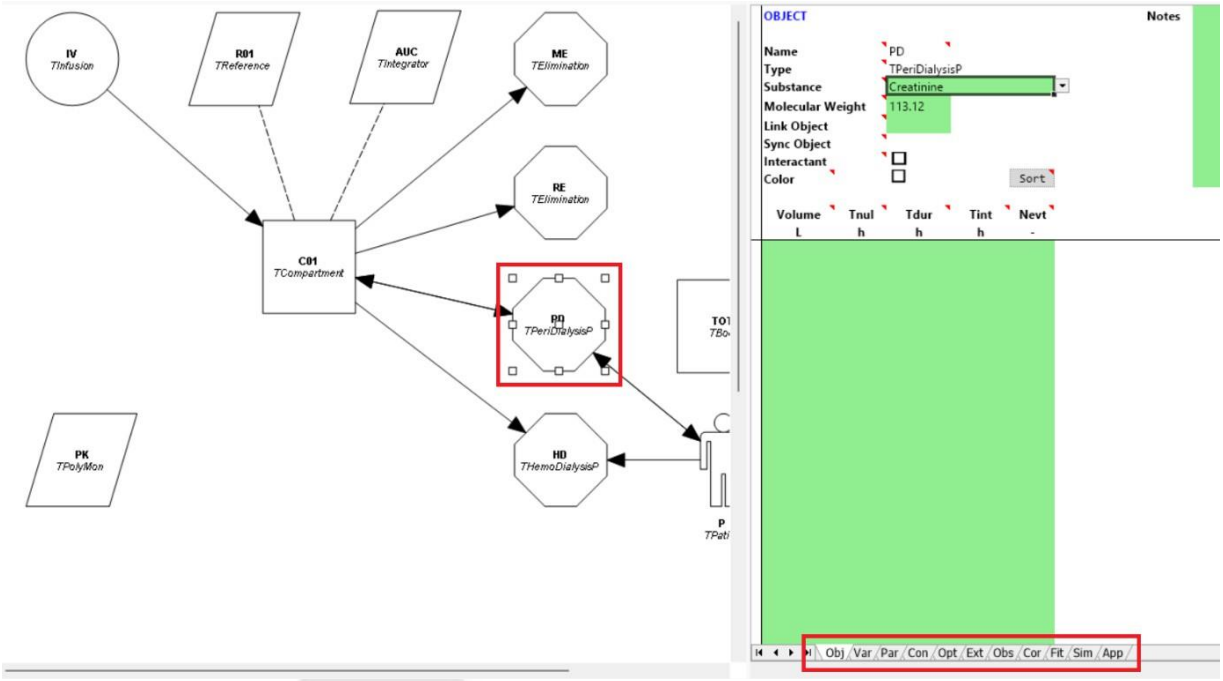
Relative: CoFactor = (Scaler.Value / Scaler.PopValue) ^ Expo

3.3 How to add Peritonela dialysis (PD) into model parameters?

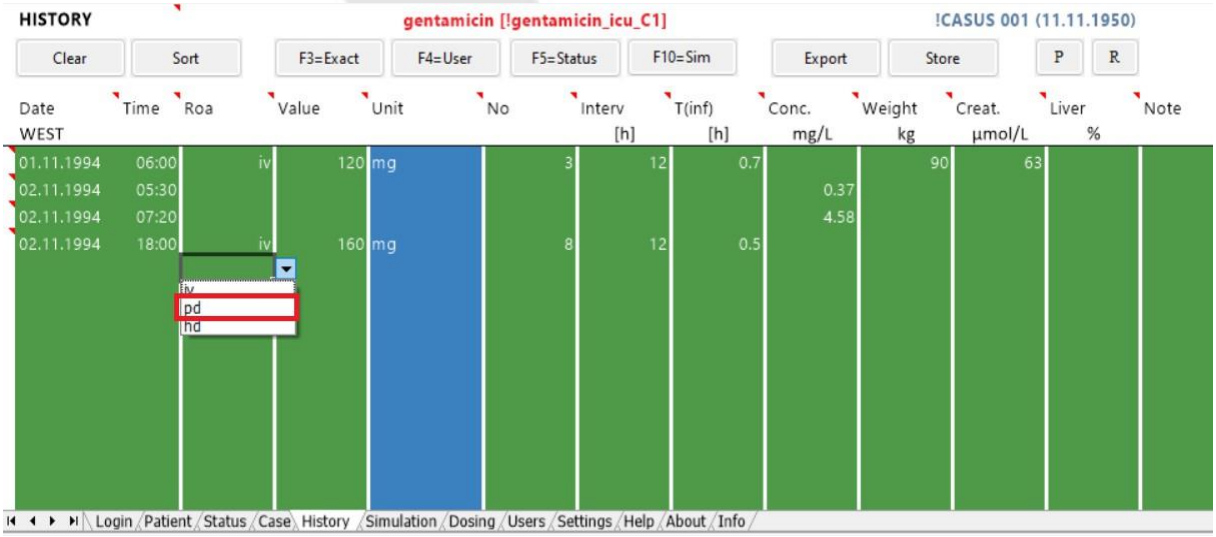
Peritoneal dialysis is not present in the default settings of the model. To add PD into your model, go to EDSIM++ (or model section in MwPharm++). Add a new **Elimination object** (drag and drop; 1) and connect it to **Patient**. Then select **TPeriDialysisP** in the TYPE section (2). Finally change the name of the object to **PD** (3).



If you double-click on the TPeriDialysisP object, a new section will open on the right side. In this section, you can change parameters of peritoneal dialysis. You can change the tab in the below part of the section.



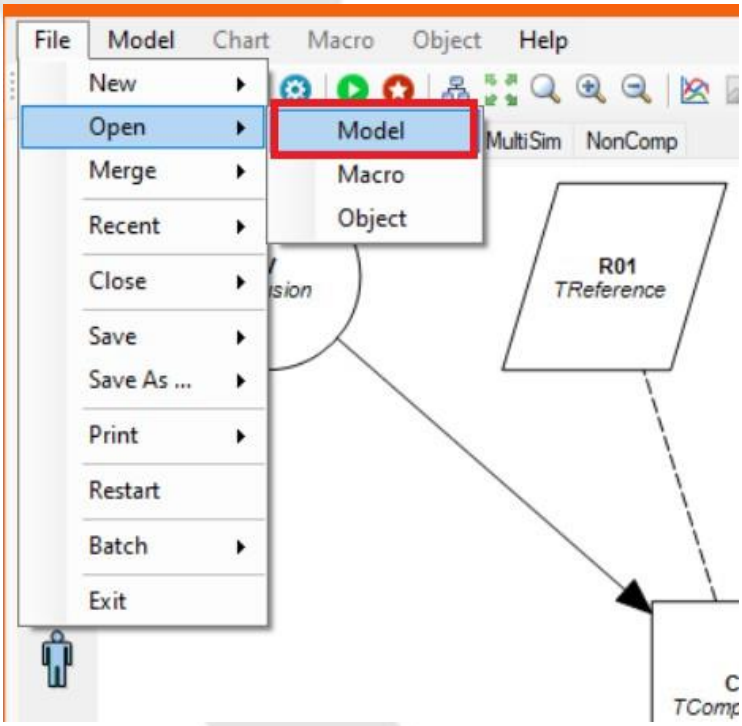
Now, go back to the History tab in MwPharm++. You can find the PD option in the routes of administration (Roa) column.



3.4 What is KinPop? How can I use it?

KinPop++ is a very easy to use PKPD population modeling tool that integrates well with MwPharm++. It is a part of Edsim++ software. With KinPop, you can fit your model parameters so that it fits to your population data. KinPop is especially useful for adjusting the basic model to the special needs of your patients in specialised units of care after you already gathered some data. Also, it is a useful tool for adjusting the model to a different population.

To use KinPop tool, start Edsim++ and select the model which parameters you want to adjust as shown in the picture. Make sure the structure of the chosen model corresponds to the population you want to use it for. In the example above, tobramycin_icu_C1 model was selected.



After selecting the model, you need to select the dataset you want to use as your new population. First, export cases you want to use from MwPharm++ (see FAQ – numbers 58 and 56). Then, go to the KinPop tab above (step 1), and choose the Project tab below (step 2). Now, click the button with two dots. A window will pop up in which you can choose a folder with a dataset you want to use. You can further omit some cases using the checkboxes on the left side (step 4). Buttons on the right side are for checking all or none of the cases (step 5). In the example, the default example dataset was used.

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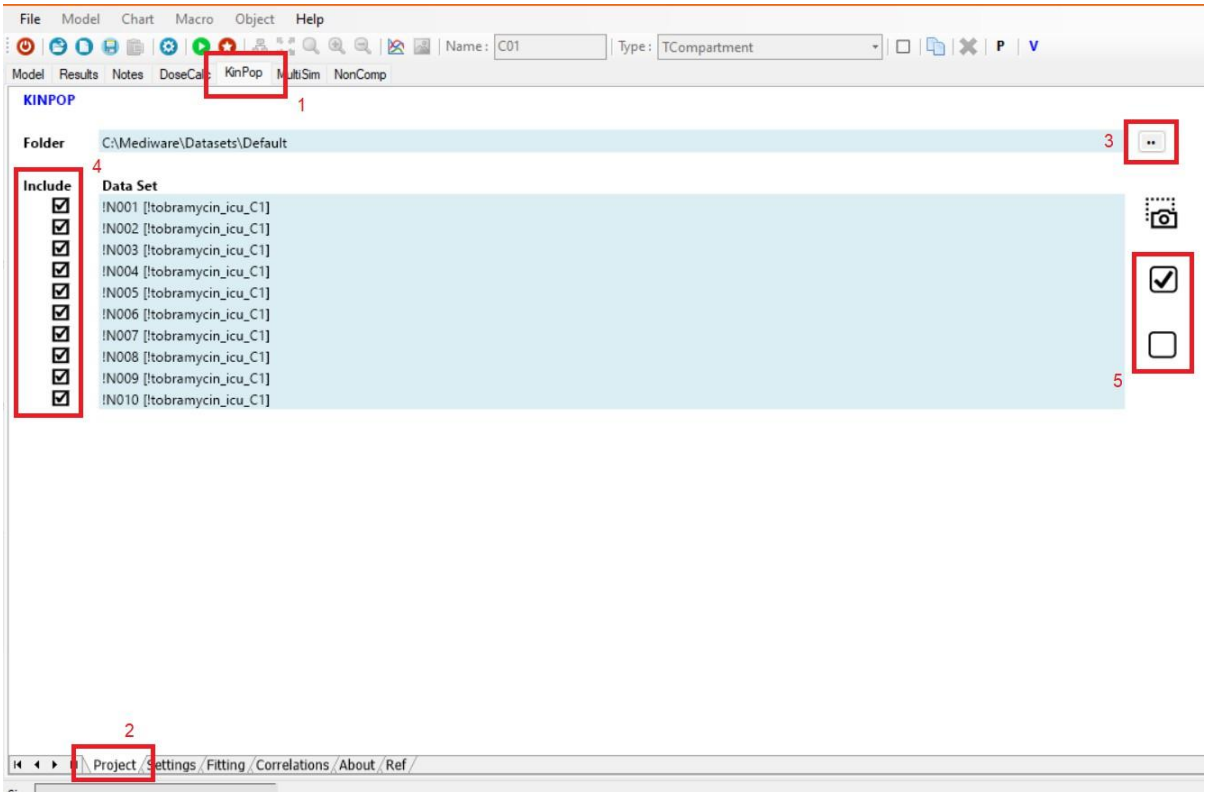
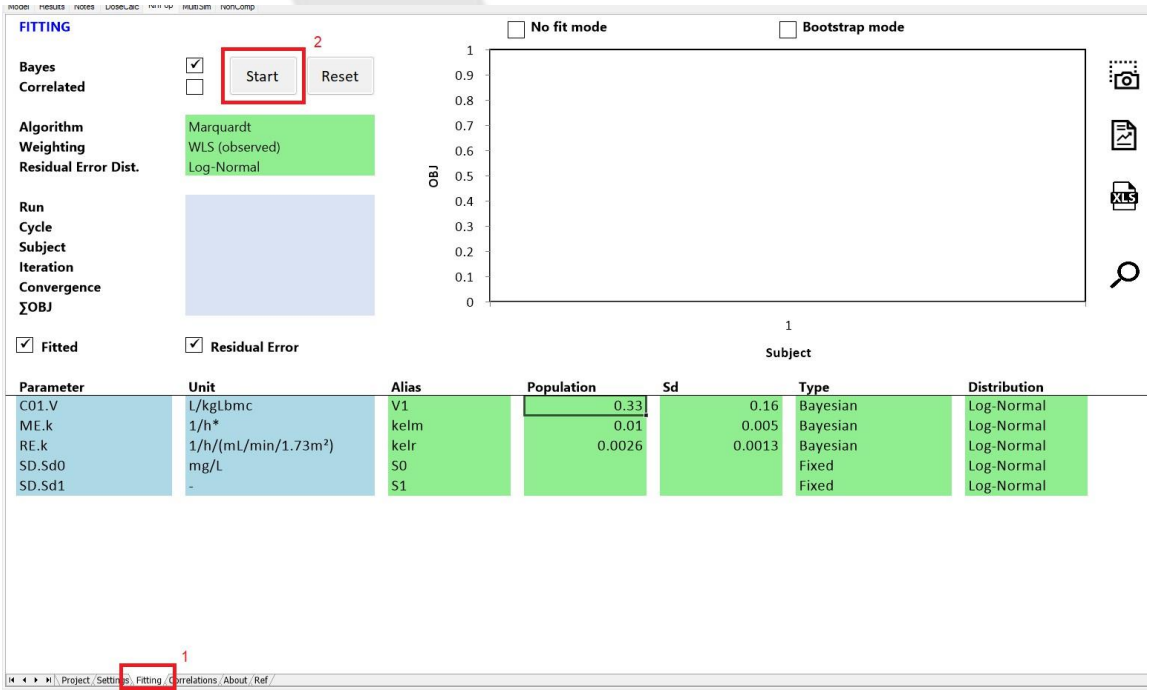


Now, that you have selected your dataset and the model, please go to the tab Fitting (step 1). Here, you can adjust the parameters you want to get fitted. You can also set correlations in the tab Correlation. Then, click the button Start (step 2).



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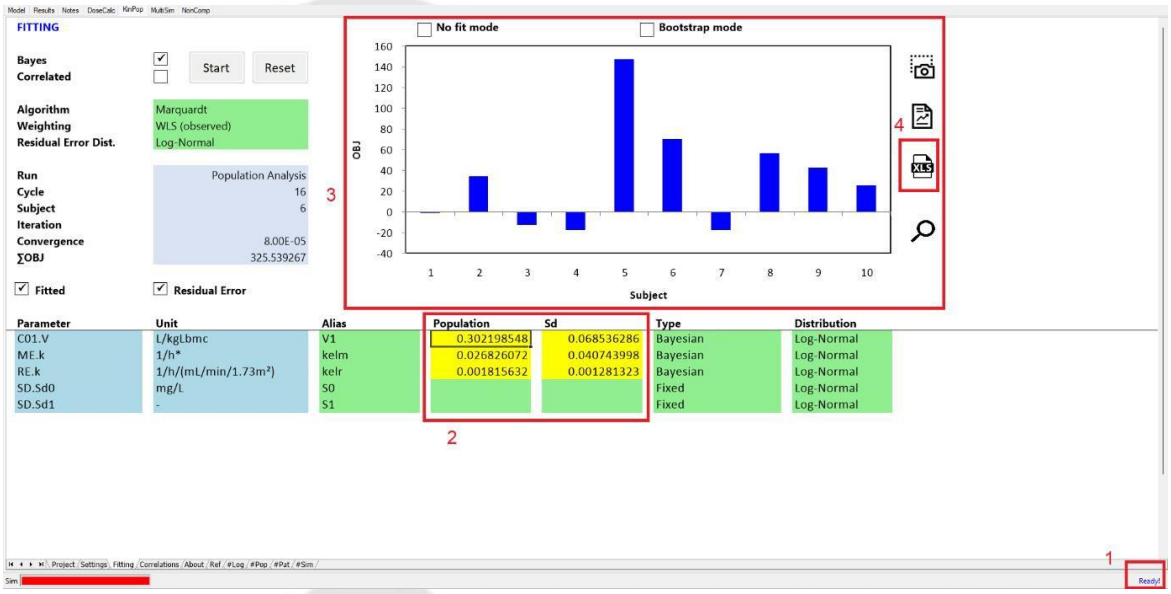
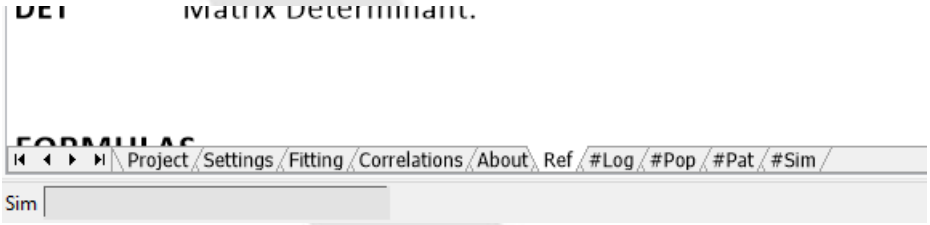
By clicking the button Start, you started the fitting. This may take a long time depending on the amount of your data, and on the parameters of your computer. Once the simulation is done, a message “Ready!” appears in the right bottom corner (step 1), new values of parameters are calculated (step 2), and a graph visually representing closeness of each chosen case to calculated values (step 3). If you click the XLS button (step 4), you can generate Excel file with results of the fitting.



At the bottom of the page there are tabs #Log, #Pop, #Pat, and #Sim.



Tab #Log, contains analysis logs. You can find here information about how the calculation of individual parameters went over individual cycles. The process of convergence of the parameter to the result value is shown in graphs.

In tab #Pop, there is a comparison of individual and population values, correlations, covariances, and statistical characteristics of the dataset. There are also graphs characterizing goodness of fit and weighted residuals.

In tab #Pat, there is information about individual patients (part Patients), their fitted parameters together with values (like median or mean value) characterizing them as a dataset (part Parameters), statistical characteristics of each patient’s values (part Statistics), and observations

made in individual cases together with values characterizing how far from calculated values are individual observed values (part Observations).

In tab #Sim, there are results of the simulation for individual cases.

In the table below, you can find the most important abbreviations used in KinPop:

Abbr.	Meaning	Abbr.	Meaning
LL	Log-Likelihood.	**MPE**	Mean Prediction Error (bias).
OBJ	Objective function.	**MDPE**	Median Prediction Error (bias).
AIC	Akaike Information Criterion.	**MAPE**	Mean Absolute Prediction Error (precision).
BIC	Bayesian Information Criterion.	**MDAPE**	Median Absolute Prediction Error (precision).
WSS	Weighted sum of squares.	**RMSE**	Root Mean Squared Error (precision).
WSSm	Weighted sum of squares (observations).	**Cest**	Predicted concentration.
WSSp	Weighted sum of squares (parameters).	**Cobs**	Observed concentration.
WSS/df	Mean weighted sum of squares.	**Cvar**	Predicted (est) or observed (obs) concentration.
SD	Standard deviation (population).	**CN**	Matrix Condition Number.
SE	Standard error (sample).	**DET**	Matrix Determinant.
PE	Prediction error (as weighted residual or relative prection error)		

The most important formulas are as follows (obs – observation-based weighting, est – estimation-based weighting):

PE *Weighted Residuals*

Normal distributed

$$PE = \frac{(C_{obs} - C_{est})}{SD_{var}}$$

Log-normal distributed

$$PE = \frac{\ln\left(\frac{C_{obs}}{C_{est}}\right)}{\left(\frac{SD_{var}}{C_{var}}\right)}$$

Relative Prediction Error

$$PE = \frac{(C_{obs} - C_{est})}{C_{obs}}$$

$$PE(\%) = PE \cdot 100\%$$

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MPE $MPE = \frac{\sum PE}{N}$ (mean PE, MDPE applies to median PE)

MAPE $MAPE = \frac{\sum |PE|}{N}$ (mean absolute PE, MDAPE applies to median absolute PE)

RMSE $RMSE = \sqrt{\frac{\sum PE^2}{N}}$ (root of mean squared PE, root mean square error)

The list of most important abbreviations and formulas used for the computing can be also found in the tab Ref.

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3.5 Others

3.5.1 How to define theta value in our software?

The THETA values are the population means. You must check the **Pop** checkbox when entering these values. The OMEGA is associated with the standard deviation.

Pop(i) = THETA(i)

Sd(i) = THETA(i) * Sqrt(OMEGA(i,i))

3.5.2 Two modes in the X Observed object (Obj tab). What is the standard mode? What is the NonMem mode?

This is just a different way of parametrizing the covariate. If you click on the **Code** button in the **Obj** tab you can see how this is done:

```
Standard    : CoFactor = Factor          (Factor >=0)
NonMem      : CoFactor = (1 + Factor)    (Factor >=-1)
```


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