

## MembranePlus™

July 2017

Dear MembranePlus™ User,

Thank you for your interest in MembranePlus. Our Simulations Plus development team continues to work hard to make MembranePlus the most advanced and reliable simulation of drug absorption and metabolism in cell based assays in the world today.

### 1. Updates in version 2.0

- New Membrane Models:
  - Modeling of Sandwich and Plated Hepatocyte Assays (biliary excretion) – NEW!
  - Modeling of Suspended Hepatocyte Assays – NEW!
- ADMET Predictor™ Module:
  - Updated models from ADMET Predictor version 8.1
  - Prediction of Km/Vmax for metabolism by cytochrome P450 enzymes (CYPs), including isoforms 1A2, 2C9, 2C19, 2D6, and 3A4 – NEW!
  - IVIVE settings for conversion to either intestinal cell monolayers or hepatocytes.
  - Allow membrane model to be specified upon structure import.
  - Classification models to predict whether imported compounds are substrates for Pgp and/or OATP1B1.
- New Simulation Outputs:
  - Fu Cell - this new output provides an estimate of Fu, Enterocytes for use in GastroPlus PBPK models. This improves the prediction of absorption & pharmacokinetics for compounds exhibiting lysosomal trapping and/or high binding in enterocytes causing extended Tmax values.
  - CLdiff - the passive diffusional clearance parameter is an output that can be used in connection with GastroPlus PBPK models to define the permeability-surface area product (PStc) in PBPK tissues.
- General Features:
  - Excel spreadsheet output for all simulations modes – NEW:
    - Single simulation
    - Parameter sensitivity analysis (PSA)
    - Batch mode
  - Cytosolic fraction unbound for intracellular protein binding – NEW!
    - Applies to all membrane models
  - New tutorials with step-by-step instructions
  - New installation option (terminal services)
  - Bug fixes



## **2. Installation of MembranePlus on your computer/network**

MembranePlus is a mechanistic modeling & simulation software program designed to run on Windows 7, 8, and 10 systems, or Mac computers through Parallels (or similar Windows virtualization).

MembranePlus can be installed from the \*.zip package retrieved from our ShareFile online portal, either as a “standalone” installation on your computer or as a “network installation” on your local area network. Refer to the installation manual for detailed instructions on the installation process.

Before MembranePlus can be run from your installation, it has to be activated. The activation process is handled via email with our licensing department. Should you have any questions, please contact one of our customer support representatives at: [licensing@simulations-plus.com](mailto:licensing@simulations-plus.com) or +1-661-723-7723.

## **3. MembranePlus tutorial**

MembranePlus includes an extensive help file with a redesigned tutorial for new users. This tutorial can be used by prospective customers during the evaluation of MembranePlus, or by new/existing customers to assist with validating a computer system (i.e., running tutorials to confirm the same results are generated on your computer versus what is reported in the tutorial).

The tutorial document contains step-by-step instructions for running MembranePlus simulations. A few standard simulations and their use in drug development are described. Data for running these simulations are also provided wherever necessary, along with the nature and source of the data. The tutorial data files are present in the Tutorials folder after installing MembranePlus on your computer.

## **4. Customer support**

As part of our Personal Consultation Program, Simulations Plus has assigned scientists to specifically serve you in your use of MembranePlus. Feel free to contact them for advice on techniques for using the program better, for suggestions, and bug reports.

We stand ready to help you. If you need assistance in getting started, or if you would like advice on techniques for using the program most effectively in your research, please feel free to contact us.

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We look forward to serving you and assisting in any way we can.

Best regards,

Walt Woltosz  
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