## Instructions for the human model in R

1. **Installing R, R studio and packages needed to run models**

Installing R

1. In a web-browser, navigate to https://cran.r-project.org/

2. Select “Download R for Windows” under “Download and Install R”

3. Select “Install R for the first time”

4. Select “Download R 3.(version) for Windows “

5. Save and run the installer file

Installing Rstudio

1. In a web-browser navigate to https://www.rstudio.com/

2. On the homepage select Download Rstudio

3. Download the open source license version of Rstudio (first from left)

4. Select windows installer (Under Installers -> RStudio 1.(ver) – Windows Vista /7/8/10

5. Save and Run the executable file

Installing Packages:

1. Run Rstudio

2. Select Packages tab from the bottom right panel in RStudio

3. Select Install in the packages tab

4. Under packages enter deSolve and select install

This will setup the environment needed to run the models

1. **Model folder “Rsubmission\_Human”**
2. All files in the docket are provided as .txt files. Please follow the steps below to convert the files to appropriate R files in order to be able to run the PBPK model in RStudio:

**Important:** The name of the folders where you will copy the files from the docket is very important to run the PBPK model in RStudio.

* 1. Please convert “model\_human.txt” to “model.R” and placed in a folder named “model”. Simply replace the ‘\_human.txt’ part of the file name by ‘.R’.
  2. Parameter files names starting with “params”: Place the params files in 2 different folders called DLM and CPM. Replace “\_CPM.txt” and “\_DLM.txt” by “.R”.

Example: “params\_F\_2Y\_DLM.txt” will become “params\_F\_2Y.R” and will be in the folder named “DLM”.

* 1. Copy all the scenario files in a folder named “Scenarios” and replace “.txt” by “.R”.

1. This is the current version of the pyrethroid human model in R as of July 24th, 2017. Model file (model. R) is saved in the folder named ‘Model’ and parameter files for DLM and CPM simulations are saved in the folders named ‘DLM’ and ‘CPM’, respectively. R files are included in the folder named ‘Scenarios’ to simulate plasma and tissue concentration profiles of DLM and CPM at a given exposure scenario in human at specific ages.
2. Open a specific file in the folder named ‘Scenarios’ in RStudio. In all scenario files, appropriate paramFile from DLM and CPM folders corresponding to the selected exposure scenario is currently defined. To run the scenario file selected, click on Source. There are 47 files for scenario simulations of DLM and CPM. There are 4 other files named: ‘DLM\_Human\_Inh.R’, ‘DLM\_Human\_Oral.R’, ‘CPM\_Human\_Inh.R’ and ‘CPM\_Human\_Oral.R’. These files were used to generate the internal exposure to DLM and CPM at various ages in males and females after a single daily oral dose or a 1 hr inhalation exposure at steady state (results are in tables III-3,-4,-5 and -6). To run these files, you need to change the chemical, the gender and the age in #get paramFile accordingly with the scenario needed. If you want to change parameters that are in the parameter files, don’t change them in these parameter files but in the scenario files. Copy this new line: params[["NAME OF THE PARAMETER"]] <- x.

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| Scenario file in R | Note |
| CPM\_Human\_Inh | This scenario is used to generate the internal exposure to CPM at various ages in male and female after a 1 hr inhalation exposure per day at steady state. To run this file, you need to change the gender and the age accordingly with the scenario wanted. A list of the pulmonary parameters used to run this file is in the report, in appendix 9. The results are in table III3 to 6. |
| CPM\_Human\_Oral | This scenario is used to generate the internal exposure to CPM at various ages in male and female after a single daily oral dose until steady state. To run this file, you need to change the gender and the age accordingly with the scenario wanted. The results are in table III3 to 6. |
| CPM\_Scenario1\_Food\_male\_20Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for an adult of 75 kg, corresponding to an age of 20 years old. |
| CPM\_Scenario2\_Drinking\_male\_6M | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 6 months baby with a water consumption of 0.68 L/day. |
| CPM\_Scenario3\_WorkerMixerLoader\_ Inh\_male\_60 | The exposure frequency is 8 hrs/day, for 7 days/week until steady state. This scenario is for an 80-kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 1 m3/hr. |
| CPM\_Scenario4\_WorkerApplicator\_Inh\_male\_60Y | The exposure frequency is 8 hrs/day, for 7 days/week until steady state. This scenario is for an 80-kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 0.5 m3/hr. |
| CPM\_Scenario5\_WorkerPHEDcombo\_Inh\_male\_60Y | The exposure frequency is 8 hrs/day, for 7 days/week until steady state. This scenario is for an 80-kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 1.73 m3/hr. |
| CPM\_Scenario6\_ResidentialHandler\_Inh\_male\_60Y | The exposure frequency is 1 hrs/day, for 7 days/week until steady state. This scenario is for an 80-kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 0.64 m3/hr. |
| CPM\_Scenario7\_ResidentialPostAppl\_Oral\_male\_2Y | The exposure frequency is 1.5 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for a 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| CPM\_Scenario8\_ResidentialPostAppl\_Oral\_ male\_6Y | The exposure frequency is 2 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for a 19-kg child. In the EPA guideline, 19 kg is considered as the standard BW for a range of age from 3 to 6 years old. In the model, the most sensitive age was 6 years old. Therefore, the model was run for 6Y. |
| CPM\_Scenario9\_ResidentialPostAppl(indoorcarpet)\_Oral\_male\_2Y | The exposure frequency is 4 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for a 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| CPM\_Scenario10\_ResidentialPostAppl(indoorhardsurf)\_Oral\_male\_2Y | The exposure frequency is 2 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for a 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| CPM\_Scenario11\_ResidentialPostAppl(paints)\_Oral\_male\_2Y | The exposure frequency is 1.5 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for a 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| CPM\_Scenario12\_ResidentialPostAppl(pets)Oral\_male\_2Y | The exposure frequency is 1 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for a 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| CPM\_Scenario13\_ResidentialPostAppl(Indoorspacespray)\_Inh\_male\_60Y | The exposure frequency is 16 hrs/day, for 7 days/week until steady state. This scenario is for an 80-kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 0.64 m3/hr. |
| CPM\_Scenario14\_ResidentialPostAppl(Indoorspacespray)\_Inh\_male\_1Y | The exposure frequency is 18 hrs/day, for 7 days/week until steady state. This scenario is for a 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 1 year’s old. Therefore, the model was run for 1Y. The breathing rate was set to 0.33 m3/hr. |
| CPM\_Scenario15\_ResidentialPostAppl(Outdoorspacespray)\_Inh\_male\_60Y | The exposure frequency is 4 hrs/day, for 7 days/week until steady state. This scenario is for an 80-kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 0.64 m3/hr. |
| CPM\_Scenario16\_ResidentialPostAppl(Outdoorspacespray)\_Inh\_male\_1Y | The exposure frequency is 2 hrs/day, for 7 days/week until steady state. This scenario is for a 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 1 year old. Therefore, the model was run for 1Y. The breathing rate was set to 0.33 m3/hr. |
| CPM\_Scenario17\_ResidentialPostAppl(Outdoorspacespray)\_Inh\_male\_4Y5 | The exposure frequency is 2 hrs/day, for 7 days/week until steady state. This scenario is for a 19-kg child. In the EPA guideline, 19 kg is considered as the standard BW for a range of age from 3 to 6 years old. In the model, the most sensitive age was 4.5 years old. Therefore, the model was run for 4.5Y. The breathing rate was set to 0.42 m3/hr. |
| CPM\_Scenario18\_ResidentialPostAppl(Mosquitocide)\_Inh\_male\_60Y | The exposure frequency is 1.5 hrs/day, for 7 days/week until steady state. This scenario is for an 80-kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 0.64 m3/hr. |
| CPM\_Scenario19\_ResidentialPostAppl(Mosquitocide)\_Inh\_male\_1Y | The exposure frequency is 1.5 hrs/day, for 7 days/week until steady state. This scenario is for an 11-kg adult. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 1 year old. Therefore, the model was run for 1Y. The breathing rate was set to 0.33 m3/hr. |
| CPM\_ScenarioO1\_Food\_male\_6M | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 6 months baby. |
| CPM\_ScenarioO2\_Drinking\_male\_6M | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 6 months baby with a water consumption of 0.68 L/day considering 6 doses per day, every day (0.1147595 L per exposure event). |
| CPM\_ScenarioO3\_Food\_male\_1-2Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 12.6 kg child. In the EPA scenarios, 12.6 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| CPM\_ScenarioO4\_Drinking\_male\_1-2Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 12.6 kg child. In the EPA scenarios, 12.6 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 1 year old. Therefore, the model was run for 1Y with a water consumption of 0.68 L/day considering 6 doses per day, every day (0.1147595 L per exposure event). |
| CPM\_ScenarioO5\_Food\_male\_3-5Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 18.7 kg child. In the EPA scenarios, 18.7 kg is considered as the standard BW for a range of age from 3 to 5 years old. In the model, the most sensitive age was 4.5 years old. Therefore, the model was run for 4Y5. |
| CPM\_ScenarioO6\_Drinking\_male\_3-5Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 18.7 kg child. In the EPA scenarios, 18.7 kg is considered as the standard BW for a range of age from 3 to 5 years old. In the model, the most sensitive age was 3-year-old. Therefore, the model was run for 3Y with a water consumption of 0.68 L/day considering 6 doses per day, every day (0.1147595 L per exposure event). |
| CPM\_ScenarioO7\_Food\_male\_6-12Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 37.1 kg child. In the EPA scenarios, 37.1 kg is considered as the standard BW for a range of age from 6 to 12 years old. In the model, the most sensitive age was 12 years old. Therefore, the model was run for 12Y. |
| CPM\_ScenarioO8\_Drinking\_male\_6-12Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 37.1 kg adult. In the EPA scenarios, 37.1 kg is considered as the standard BW for a range of age from 6 to 12 years old. In the model, the most sensitive age was 6-year-old. Therefore, the model was run for 6Y with a water consumption of 0.68 L/day considering 6 doses per day, every day (0.1147595 L per exposure event). |
| CPM\_ScenarioO9\_Food\_male\_13-19Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 67.3 kg adult. In the EPA scenarios, 67.3 kg is considered as the standard BW for a range of age from 13 to 19 years old. In the model, the most sensitive age was 19 years old. Therefore, the model was run for 19Y. |
| CPM\_ScenarioO10\_Drinking\_male\_13-19Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 67.3 kg adult. In the EPA scenarios, 67.3 kg is considered as the standard BW for a range of age from 13 to 19 years old. In the model, the most sensitive age was 13-year-old. Therefore, the model was run for 13Y with a water consumption of 1.71062 L/day considering 4 doses per day, every day (0.427655 L per exposure event). |
| CPM\_ScenarioO11\_Food\_male\_20-49Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for an 81.5-kg adult. In the EPA scenarios, 81.5 kg is considered as the standard BW for a range of age from 20 to 49 years old. In the model, the most sensitive age was 49 years old. Therefore, the model was run for 49Y. |
| CPM\_ScenarioO12\_Drinking\_male\_20-49Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for an 81.5-kg adult. In the EPA scenarios, 81.5 kg is considered as the standard BW for a range of age from 20 to 49 years old. In the model, the most sensitive age was 20-year-old. Therefore, the model was run for 20Y with a water consumption of 1.71062 L/day considering 4 doses per day, every day (0.427655 L per exposure event). |
| CPM\_ScenarioO13\_Food\_male\_50-60Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for an 81.2-kg adult. In the EPA scenarios, 81.2 kg is considered as the standard BW for a range of age from 50 to 99 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. (NB: Our physiological parameters don't go over 60 years old) |
| CPM\_ScenarioO14\_Drinking\_male\_50-60Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for an 81.2-kg adult. In the EPA scenarios, 81.2 kg is considered as the standard BW for a range of age from 50 to 99 years old. In the model, the most sensitive age was 60-year-old. Therefore, the model was run for 60Y with a water consumption of 1.71062 L/day considering 4 doses per day, every day (0.427655 L per exposure event). (NB: Our physiological parameters don't go over 60 years old). |
| CPM\_ScenarioO15\_Food\_female\_13-49Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 72.9-kg adult. In the EPA scenarios, 72.9 kg is considered as the standard BW for a range of age from 13 to 49 years old. In the model, the most sensitive age was 49 years old. Therefore, the model was run for 49Y. |
| CPM\_ScenarioO16\_Drinking\_female\_13-49Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 72.9 kg adult. In the EPA scenarios, 72.9 kg is considered as the standard BW for a range of age from 13 to 49 years old. In the model, the most sensitive age was 13-year-old. Therefore, the model was run for 13Y with a water consumption of 1.71062 L/day considering 4 doses per day, every day (0.427655 L per exposure event). |
| DLM\_Human\_Inh | This scenario is used to generate the internal exposure to DLM at various ages in male and female after a 1 hr inhalation exposure per day at steady state. To run this file, you need to change the gender and the age accordingly with the scenario wanted. A list of the pulmonary parameters used to run this file is in the report, in appendix 9. The results are in table III3 to 6. |
| DLM\_Human\_Oral | This scenario is used to generate the internal exposure to DLM at various ages in male and female after a single daily oral dose until steady state. To run this file, you need to change the gender and the age accordingly with the scenario wanted. The results are in table III3 to 6. |
| DLM\_Scenario1\_Food\_male\_20Y | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for an adult of 75 kg, corresponding to an age of 20 years old. |
| DLM\_Scenario2\_Drinking\_male\_6M | Single oral dose per day, every day for 120 days corresponding to the steady state. This scenario is for a 6 months baby with a water consumption of 0.68 L/day. |
| DLM\_Scenario3\_Worker\_Inh\_male\_60Y | The exposure frequency is 8hrs/day, for 5 days/week until steady state. This scenario is for a 80 kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 0.64 m3/hr. |
| DLM\_Scenario4\_ResidentialHandler\_Inh\_male\_60Y | The exposure frequency is 1hrs/day, for 7 days/week until steady state. This scenario is for an 80-kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 0.64 m3/hr. |
| DLM\_Scenario5\_ResidentialAppl(Mosquitocide)\_Inh\_male\_60Y | The exposure frequency is 1.5 hrs/day, for 7 days/week until steady state. This scenario is for a 80 kg adult. In the EPA guideline, 80 kg is considered as the standard BW for a range of age from 16 to 60 years old. In the model, the most sensitive age was 60 years old. Therefore, the model was run for 60Y. The breathing rate was set to 0.64 m3/hr. |
| DLM\_Scenario6\_ResidentialAppl (Mosquitocide)\_Inh\_male\_1Y | The exposure frequency is 1.5 hrs/day, for 7 days/week until steady state. This scenario is for an 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 1 year old. Therefore, the model was run for 1Y. The breathing rate was set to 0.33 m3/hr. |
| DLM\_Scenario7\_ResidentialPostAppl (Mosquitocide)\_Oral\_male\_2Y | The exposure frequency is 4 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for an 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| DLM\_Scenario8\_IndoorCarpet\_Oral\_male\_2Y | The exposure frequency is 4 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for an 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| DLM\_Scenario9\_IndoorHardSurface\_Oral\_male\_2Y | The exposure frequency is 2 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for an 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| DLM\_Scenario10\_Turf\_Oral\_male\_2Y | The exposure frequency is 1.5 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for an 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| DLM\_Scenario11\_SurfaceDirectSpray\_Oral\_male\_2Y | The exposure frequency is 18 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for an 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |
| DLM\_Scenario12\_PetCollar\_Oral\_male\_2Y | The exposure frequency is 1 hrs/day, for 7 days/week until steady state. 4 replenishment intervals per hour are estimated (i.e., residues on the hand will be replenished every 15 minutes). This scenario is for an 11-kg child. In the EPA guideline, 11 kg is considered as the standard BW for a range of age from 1 to 2 years old. In the model, the most sensitive age was 2 years old. Therefore, the model was run for 2Y. |