# **SBML Model Report**

# Model name: "Demin2013 - PKPD behaviour - 5-Lipoxygenase inhibitors"



May 6, 2016

# 1 General Overview

This is a document in SBML Level 2 Version 4 format. This model was created by the following two authors: Vijayalakshmi Chelliah<sup>1</sup> and Oleg Demin<sup>2</sup> at October fourth 2013 at 12:34 a.m. and last time modified at April 17<sup>th</sup> 2015 at 12:36 a.m. Table 1 provides an overview of the quantities of all components of this model.

Table 1: Number of components in this model, which are described in the following sections.

Element	Quantity	Element	Quantity
compartment types	0	compartments	16
species types	0	species	33
events	0	constraints	0
reactions	66	function definitions	0
global parameters	263	unit definitions	0
rules	101	initial assignments	0

#### **Model Notes**

Demin2013 - PKPD behaviour - 5-Lipoxygenaseinhibitors

This model is described in the article: Systems pharmacology models can be used to understand complex pharmacokinetic-pharmacodynamic behavior: an example using 5-lipoxygenase

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inhibitors.Demin O, Karelina T, Svetlichniy D, Metelkin E, Speshilov G, Demin O Jr, Fairman D, van der Graaf PH, Agoram BM.CPT Pharmacometrics Syst Pharmacol 2013; 2: e74Abstract:

Zileuton, a 5-lipoxygenase (5LO) inhibitor, displays complex pharmaokinetic (PK)-pharmacodynamic (PD) behavior. Available clinical data indicate a lack of dose-bronchodilatory response during initial treatment, with a dose response developing after ~1-2 weeks. We developed a quantitative systems pharmacology (QSP) model to understand the mechanism behind this phenomenon. The model described the release, maturation, and trafficking of eosinophils into the airways, leukotriene synthesis by the 5LO enzyme, leukotriene signaling and bronchodilation, and the PK of zileuton. The model provided a plausible explanation for the two-phase bronchodilatory effect of zileuton-the short-term bronchodilation was due to leukotriene inhibition and the long-term bronchodilation was due to inflammatory cell infiltration blockade. The model also indicated that the theoretical maximum bronchodilation of both 5LO inhibition and leukotriene receptor blockade is likely similar. QSP modeling provided interesting insights into the effects of leukotriene modulation.CPT: Pharmacometrics & Systems Pharmacology (2013) 2, e74; doi:10.1038/psp.2013.49; advance online publication 11 September 2013.

This model is hosted on BioModels Database and identified by: BIOMD0000000490.

To cite BioModels Database, please use: BioModels Database: An enhanced, curated and annotated resource for published quantitative kinetic models.

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#### 2 Unit Definitions

This is an overview of five unit definitions which are all predefined by SBML and not mentioned in the model.

#### 2.1 Unit substance

**Notes** Mole is the predefined SBML unit for substance.

**Definition** mol

#### 2.2 Unit volume

**Notes** Litre is the predefined SBML unit for volume.

**Definition** 1

#### 2.3 Unit area

**Notes** Square metre is the predefined SBML unit for area since SBML Level 2 Version 1.

**Definition** m<sup>2</sup>

# 2.4 Unit length

**Notes** Metre is the predefined SBML unit for length since SBML Level 2 Version 1.

**Definition** m

# 2.5 Unit time

Notes Second is the predefined SBML unit for time.

**Definition** s

# 3 Compartments

This model contains 16 compartments.

Table 2: Properties of all compartments.

Id	Name	SBO	Spatial Dimensions	Size	Unit	Constant	Outside
Default		0000290	3	1	litre		
$Vd_LTC$		0000290	3	9.47999954223633	1	$   \overline{\mathbf{Z}} $	Default
$Vd_LTD$		0000290	3	9.47999954223633	1	$   \overline{\mathbf{Z}} $	Default
$Vd_LTE$		0000290	3	9.47999954223633	1		Default
$V_B$		0000290	3	2.80999994277954	1	$\overline{\mathbf{Z}}$	Default
$V_AW$		0000290	3	0.209999993443489	1	$\overline{\mathbf{Z}}$	Default
$Vd_Hn$		0000290	3	78100	1	$\overline{\mathbf{Z}}$	Default
$Vd_{-}IL5$		0000290	3	10.1999998092651	1	$\overline{\mathbf{Z}}$	Default
$V\_BM$		0000290	3	0.824999988079071	1	$\overline{\mathbf{Z}}$	Default
$Vd\_AW\_LTC$		0000290	3	1.53999996185303	1	$   \overline{\mathbf{Z}} $	Default
$Vd\_AW\_LTD$		0000290	3	1.53999996185303	1	$   \overline{\mathbf{Z}} $	Default
$Vd_AW_LTE$		0000290	3	1.53999996185303	1	<u></u>	Default
$Vd\_AW\_Hn$		0000290	3	5640	1	$\overline{\mathbf{Z}}$	Default
$Vd_{ZF}$		0000290	3	9.44999980926514	1	$\overline{\mathbf{Z}}$	Default
$Vd_AW_ZF$		0000290	3	3.25999999046326	1	$\overline{\mathbf{Z}}$	Default
$Vd\_ML$		0000290	3	10	1	$\overline{\mathbf{Z}}$	Default

# 3.1 Compartment Default

This is a three dimensional compartment with a constant size of one litre.

# 3.2 Compartment Vd\_LTC

This is a three dimensional compartment with a constant size of 9.47999954223633 litre, which is surrounded by Default.

SBO:0000290 physical compartment

## 3.3 Compartment Vd\_LTD

This is a three dimensional compartment with a constant size of 9.47999954223633 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.4 Compartment Vd\_LTE

This is a three dimensional compartment with a constant size of 9.47999954223633 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.5 Compartment V\_B

This is a three dimensional compartment with a constant size of 2.80999994277954 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.6 Compartment V\_AW

This is a three dimensional compartment with a constant size of 0.209999993443489 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.7 Compartment Vd\_Hn

This is a three dimensional compartment with a constant size of 78100 litre, which is surrounded by Default.

SBO:0000290 physical compartment

# 3.8 Compartment Vd\_IL5

This is a three dimensional compartment with a constant size of 10.1999998092651 litre, which is surrounded by Default.

#### 3.9 Compartment V\_BM

This is a three dimensional compartment with a constant size of 0.824999988079071 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.10 Compartment Vd\_AW\_LTC

This is a three dimensional compartment with a constant size of 1.53999996185303 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.11 Compartment Vd\_AW\_LTD

This is a three dimensional compartment with a constant size of 1.53999996185303 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.12 Compartment Vd\_AW\_LTE

This is a three dimensional compartment with a constant size of 1.53999996185303 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.13 Compartment Vd\_AW\_Hn

This is a three dimensional compartment with a constant size of 5640 litre, which is surrounded by Default.

SBO:0000290 physical compartment

#### 3.14 Compartment Vd\_ZF

This is a three dimensional compartment with a constant size of 9.44999980926514 litre, which is surrounded by Default.

SBO:0000290 physical compartment

# 3.15 Compartment Vd\_AW\_ZF

This is a three dimensional compartment with a constant size of 3.25999999046326 litre, which is surrounded by Default.

# 3.16 Compartment Vd\_ML

This is a three dimensional compartment with a constant size of ten litre, which is surrounded by Default.

# 4 Species

This model contains 33 species. Section 8 provides further details and the derived rates of change of each species.

Table 3: Properties of each species.

AA_b AA_b Default HPETE_b HPETE_b Default HETE_b HETE_b Default	Derived Unit	Constant	Boundary Condi-
HPETE_b HPETE_b Default	mal 1-1		Collai-
HPETE_b HPETE_b Default	mal 1-1		tion
HPETE_b HPETE_b Default	mal 1-1		tion
HETE b HETE b Default	$\text{mol} \cdot 1^{-1}$		
	$\text{mol} \cdot 1^{-1}$		
LTA4_b LTA4_b Default	$\text{mol} \cdot 1^{-1}$		
LTC4_b LTC4_b Default	$\text{mol} \cdot 1^{-1}$		
LTC4_b_out Vd_LTC	$\text{mol} \cdot l^{-1}$	$\Box$	$\Box$
LTD4_b	$\text{mol} \cdot l^{-1}$	$\Box$	$\Box$
LTE4_b	$\text{mol} \cdot l^{-1}$		$\Box$
EO_b	$\text{mol} \cdot l^{-1}$		$\Box$
EO_i_b	$\text{mol} \cdot l^{-1}$		$\Box$
EO_a_b	$\text{mol} \cdot l^{-1}$	$\Box$	$\Box$
EO_i_aw V_AW	$\text{mol} \cdot l^{-1}$	$\Box$	$\Box$
EO_a_aw V_AW	$\text{mol} \cdot l^{-1}$	$\Box$	$\Box$
EO_aw V_AW	$\text{mol} \cdot l^{-1}$	$\Box$	$\Box$
Hn_b Vd_Hn	$\text{mol} \cdot l^{-1}$		$\Box$
IL_b Vd_IL5	$\text{mol} \cdot l^{-1}$		$\Box$
IL_bm V_BM	$\text{mol} \cdot l^{-1}$	$\Box$	$\Box$
EO_bm V_BM	$\text{mol} \cdot l^{-1}$	$\Box$	$\Box$
AA_aw Default	$\text{mol} \cdot l^{-1}$		$\Box$
HPETE_aw Default	$\text{mol} \cdot l^{-1}$		$\Box$
HETE_aw Default	$\text{mol} \cdot l^{-1}$		$\Box$
LTA4_aw Default	$\text{mol} \cdot 1^{-1}$		

Id	Name	Compartment	Derived Unit	Constant	Boundary Condi- tion
LTC4_aw	LTC4_aw	Default	$\text{mol} \cdot l^{-1}$		
LTC4_aw_out	LTC4_aw_out	$Vd_AW_LTC$	$\operatorname{mol} \cdot 1^{-1}$		
$\mathtt{LTD4}_{\mathtt{aw}}$	LTD4_aw	$Vd_AW_LTD$	$\operatorname{mol} \cdot 1^{-1}$		
$LTE4_{aw}$	LTE4_aw	$Vd_AW_LTE$	$\operatorname{mol} \cdot 1^{-1}$		$\Box$
Hn_aw	Hn_aw	$Vd\_AW\_Hn$	$\mathrm{mol}\cdot \mathrm{l}^{-1}$		
${\tt IL\_aw}$	IL_aw	$V\_AW$	$\operatorname{mol} \cdot 1^{-1}$		
${\sf ZF\_intes}$	ZF_intes	Default	$\operatorname{mol} \cdot 1^{-1}$		
${\sf ZF\_blood}$	ZF_blood	$Vd_{-}ZF$	$\operatorname{mol} \cdot 1^{-1}$		
${\sf ZF\_airways}$	ZF_airways	$Vd_AW_ZF$	$\operatorname{mol} \cdot 1^{-1}$		
$\mathtt{ML}_{\mathtt{-intes}}$	ML_intes	Default	$\operatorname{mol} \cdot 1^{-1}$		
$ML_blood$	$ML_blood$	$Vd_ML$	$\text{mol} \cdot 1^{-1}$		$\Box$

# **5 Parameters**

This model contains 263 global parameters.

Table 4: Properties of each parameter.

Id	Name	SBO	Value	Unit	Constant
Ca			1.000		
$Ca_FEV_ex$			10000.000		
${\tt Cao\_FEV}$			10000.000		
DOSE_ml			0.000		
$DOSE\_zf$			0.000		
EC50_ML_FEV			500.000		
EC50_act			0.750		
EC50_migr			0.115		
$Et_{-}LTCs$			1.000		
FL0a			1.500		
$F_ml$			0.661		
$F_zf$			0.082		
GPx			1.600		
$GSH_{\mathtt{-}}aw$			1000.000		
$GSH_b$			5000.000		
$GS_pool_aw$			10000.000		
GS_pool_b			10000.000		
HEDH5			0.500		$\Box$
${ t J\_AW\_lymfl}$			0.001		$\Box$
${\tt J\_BM\_lymfl}$			$4.9 \cdot 10^{-}$		$\Box$
KAA			10.750		
$K_Ca2$			14.367		$\Box$
$K_Ca3$			7116.527		
$K_Ca_FEV$			150000.000		
$K_GSH$			744.918		
K_LTA			1.760		
$K_LTA_GSH$			1696.600		$\Box$
$K_LTC$			0.195		
$K_PLA2_Ca$			0.100		
Kd12			0.007		
Kd50			0.430		
KdZ			20.000		
$Kd_Hn_FEV$			6300000.000		
${ t Kd_{-}IL_{-}migr}$			50.000		
$Kd_LT$			1000.000		
${\tt Kd\_LTE\_migr}$			50000.000		
Kd_LTR1_FEV			1000.000		

Id	Name	SBO	Value	Unit	Constant
Kd_LTR2_FEV			10000.000		
Kd_LT_2			10000.000		
Kd_gpx_GSSG			0.072		
Kd_gpx_HETE5			6.043		
Kd_hedh-			0.332		
_HETE5					
Kd_hedh_NADP			2.896		
Kd_hedh-			2.686		
_NADPH					
Kd_hedh-			1.667		
_oxoETE5					
Ke_ox			100.000		
Ke_red		5	$5.761955 \cdot 10^{-7}$		
$\mathtt{Ki}\_\mathtt{AA}$			551.875		
Ki_HETE			0.541		
Ki_ML_EOa			500.000		
$Km_{-}1$			2.000		
$Km\_CoA\_AA$			0.005		
Km_PLA2_APC			20.000		
Km_gpx_GSH			600.000		
Km_gpx-			5.974		$\Box$
_HPETE5					
$Kp\_Hn\_AW$			3950.000		
Kp_LTC_AW			0.220		
Kp_LTD_AW			0.220		
Kp_LTE_AW			0.220		
Kp_ZF_AW			0.204		
$Kp_ZF_IW$			0.631		
LOH_aw			0.000		
LOH_b			0.000		
$LOOH_aw$			20.000		
LOOH_b			1.000		
MAX_FEV			4.940		
$\mathtt{ML}\mathtt{\_airways}$			0.000		
$\mathtt{ML}_{-}\mathtt{ex}$			0.000		
$M\_Hn$			111.200		
$M_{-}IL5$			45000.000		
$M_LTC$			625.800		
$M\_LTD$			496.700		$\Box$
$M\_LTE$			439.600		
$M\_ML$			586.180		
$M_{-}ZF$			236.000		

Id	Name	SBO	Value	Unit	Constant
NADP_aw			2900.000		
NADP_b			2000.000		
NP_pool_aw			3000.000		
NP_pool_b			3000.000		
$N_A_pmole$			$6.02 \cdot 10^{11}$		
$OL_b_ex$			0.000		
PL			110.000		
$Q_AW_blf$			5.230		
$R1_portion-$			0.390		
_E0a					
$R1_portion-$			0.016		
_FEV					
R2_portion-			0.037		
_FEV			2.007		_
R_FEV			3.007		
R_Hn_AW			5130.000		
R_Hn_B			141.000		
R_LTC_AW			1.400		
R_LTC_B			0.538		
R_LTD_AW			1.400		
R_LTD_B			0.538		
R_LTE_AW			1.400		
R_LTE_B R_ZF_AW			0.538 2.960		
R_ZF_AW R_ZF_B			0.533		
R_in_relax-			2.073		
_FEV			2.073		
T			1440.000		
TSN_O			15.500		
V_CoA			350.000		
Vmax_PLA2			450.000		
a			1.000		
al			1.000		
ca			10.000		
diam_EO			$1.2 \cdot 10^{-4}$		
fup_Hn			0.770		
fup_LT			0.160		
fup_ML			0.004		n H
fup_ZF			0.069		n H
h_act			3.000		_ A
h_matur			1.000		– A
h_migr			3.000		
J					

Id	Name	SBO	Value	Unit	Constant
k1			10-6	6	
k1_min			$1.6 \cdot 10^{-7}$	7	
k3			34.000		
$k_{-}3$			263640.000		
k_EO_a_d			$1.5 \cdot 10^{-4}$	4	
k_EO_d			$3 \cdot 10^{-4}$		
k_EO_m			10.000		
k_EO_t_baw			0.040		
$k_E0_t_bmb$			0.020		
$k_Hn_d$			0.033		
k_Hn_p			$1.8 \cdot 10^{10}$	0	
k_IL_d			0.005		
k_IL_p			16.000		
k_IL_t_awb			0.050		
$k_{IL_t_bbm}$			0.001		
k_LTCs_back			1003.709		
k_LTCs_fow			1068016.000		
k_abs_ml			0.012		
k_abs_zf			0.018		
$k\_{acet}$			0.003		
k_dp			0.067		
k_elim_ml			0.002		
k_elim_zf			0.004		
$k_{-}fev_{-}eff$			3000000.000		
k_ggt			0.100		
k_gpx_cat			0.488		
k_hedh_1			88.338		
k_hedh_2			1724.404		
k_hedh_3			31.497		
$k_hedh_4$			8.078		Ä
k_lo			4642.680		
k_lta_syn			54420.000		
k_ltc_ltd_el			0.100		Ä
k_lte_el			0.040		
k_ox			$2.658 \cdot 10^{-2}$	4	
k_ox2			67.200		
k_red			$2.538 \cdot 10^{-4}$	4	
k_red2			$4.428 \cdot 10^{-5}$		
ka			500.000		
ki			25000.000		
kia			0.001		
n_FEV			1.000		

Id	Name	SBO	Value	Unit	Constant
naEO_LTCsyn			0.000		
npi			3.140		
oral			1.000		
$oxoETE_aw$			0.000		
$oxoETE_b$			0.000		
portion_mig	r		0.300		
$\mathtt{zf}_{\mathtt{-inh}}$			0.000		$\Box$
$\mathtt{ft}\_\mathtt{zf}$			0.000		
${\tt ft\_ml}$			0.000		
ZF_blood-			0.000		$\Box$
_conc					
ZF_airways- _conc			0.000		
ML_blood-			0.000		
_conc			0.000		
ML_airways-			0.000		
_conc			0.000		
w_EO			0.000		
V_CB			0.000		
V_aCB			0.000		
V_LTC_CB			0.000		
V_CAW			0.000		
$V_aCAW$			0.000		
V_LTC_CAW			0.000		
GSSG_b			0.000		
NADPH_b			0.000		
PLA2_D			0.000		
PLA2_Ca			0.000		
Ki_AA_AA			0.000		
K_AA_HETE			0.000		
Ki_HPETE_AA			0.000		
00H_b			0.000		
OH_b			0.000		
r1			0.000		
r2			0.000		A
REDOX_b			0.000		A
RELFL05_b			0.000		
DFLOa_b			0.000		
FL03_b			0.000		– A
FL02_b			0.000		– A
FL03t_b			0.000		– A
FLO2t_b			0.000		
					J

Id	Name	SBO	Value	Unit	Constant
FL05HP_b			0.000		
$C_b$			0.000		
$A_b$			0.000		
$B_b$			0.000		
delta_LTCs_	b		0.000		
nom_LTCs_b			0.000		
den_LTCs_b			0.000		
$C_hedh_b$			0.000		
$A_hedh_b$			0.000		
$B_hedh_b$			0.000		
$\mathtt{GSSG}_\mathtt{aw}$			0.000		
$\mathtt{NADPH}_\mathtt{aw}$			0.000		
$00H_{aw}$			0.000		
OH_aw			0.000		
REDOX_aw			0.000		
RELFL05_aw			0.000		
DFLOa_aw			0.000		
FL03_aw			0.000		
FL02_aw			0.000		
FL03t_aw			0.000		
$FLO2t_aw$			0.000		
FL05HP_aw			0.000		
$\mathtt{C}_{\mathtt{a}\mathtt{w}}$			0.000		
$\mathtt{A}_{-}\mathtt{a}\mathtt{w}$			0.000		
$\mathtt{B}_{\mathtt{a}\mathtt{w}}$			0.000		
delta_LTCs-			0.000		
_aw					
nom_LTCs_aw			0.000		
den_LTCs_aw			0.000		
$C_hedh_aw$			0.000		
$A\_hedh\_aw$			0.000		
$B_hedh_aw$			0.000		
OL_b			0.000		
$\mathtt{OL}_\mathtt{aw}$			0.000		
Rec_occup-			0.000		
_migr			0.000		
Ca_FEV			0.000		
r_out_FEV			0.000		
r_in_FEV			0.000		
FEV1			0.000		
TSN			0.000		
$\mathtt{TSN\_Hn}$			0.000		

Id	Name	SBO	Value	Unit	Constant
FEV1_percent			0.000		
time_hour			0.000		
${ t time\_day}$			0.000		
$N_EO_bm$			0.000		$\Box$
N_EO_b			0.000		$\Box$
$N_EO_i_b$			0.000		$\Box$
$N_E0_a_b$			0.000		$\Box$
$EO_b_tot$			0.000		$\Box$
$N_EO_b_{tot}$			0.000		
$N_EO_aw$			0.000		
$N_EO_i_aw$			0.000		
$N_EO_a_a$			0.000		
EO_aw_tot			0.000		
$N_EO_aw_tot$			0.000		
EO_b_tot_per-			0.000		
_SS					
$N_EO_aw_tot-$			0.000		
_perc					
$N_EO_b_{tot}$			0.000		
_perc					
N_EO			0.000		
$N_E0_a$			0.000		
$LTC4_b_pM$			0.000		
${\tt LTs\_aw\_pg}$			0.000		
$LTD4_b_free$			0.000		
$ML_uM$			0.000		
${\tt LTD4\_aw\_pers}$			0.000		
$N_EO_perc$			0.000		
Hn_aw_perc			0.000		
$N_EO_aw_perc$			0.000		
$Ca\_FEV\_LTR1$			0.000		
$Ca\_FEV\_LTR2$			0.000		
OL_ASM			0.000		

# 6 Rules

This is an overview of 101 rules.

# 6.1 Rule ft\_zf

Rule ft\_zf is an assignment rule for parameter ft\_zf:

$$ft\_zf = \left\lceil \frac{time}{T} \right\rceil + \left\lceil \frac{time - 360.0}{T} \right\rceil + \left\lceil \frac{time - 660.0}{T} \right\rceil + \left\lceil \frac{time - 960.0}{T} \right\rceil \tag{1}$$

#### **Derived unit** s

#### 6.2 Rule ft\_ml

Rule ft\_ml is an assignment rule for parameter ft\_ml:

$$ft_{-}ml = \left\lceil \frac{time}{T} \right\rceil \tag{2}$$

#### **Derived unit** s

#### 6.3 Rule ZF\_blood\_conc

Rule ZF\_blood\_conc is an assignment rule for parameter ZF\_blood\_conc:

$$ZF\_blood\_conc = fup\_ZF \cdot [ZF\_blood]$$
 (3)

#### **6.4 Rule ZF\_airways\_conc**

Rule ZF\_airways\_conc is an assignment rule for parameter ZF\_airways\_conc:

$$ZF_{airways\_conc} = [ZF_{airways}]$$
 (4)

Derived unit  $mol \cdot l^{-1}$ 

#### 6.5 Rule ML\_blood\_conc

Rule ML\_blood\_conc is an assignment rule for parameter ML\_blood\_conc:

$$ML\_blood\_conc = fup\_ML \cdot [ML\_blood]$$
 (5)

# 6.6 Rule ML\_airways\_conc

Rule ML\_airways\_conc is an assignment rule for parameter ML\_airways\_conc:

$$ML\_airways\_conc = fup\_ML \cdot [ML\_blood]$$
 (6)

#### 6.7 Rule w\_E0

Rule w\_E0 is an assignment rule for parameter w\_E0:

$$w\_EO = \frac{\text{npi} \cdot \text{diam}\_EO^{3.0}}{6.0}$$
 (7)

#### 6.8 Rule V\_CB

Rule V\_CB is an assignment rule for parameter V\_CB:

$$V_{-}CB = ([EO_{-}a_{-}b] + [EO_{-}b] + [EO_{-}i_{-}b]) \cdot N_{-}A_{-}pmole \cdot w_{-}EO \cdot vol(V_{-}B)$$
(8)

#### 6.9 Rule V\_aCB

Rule V\_aCB is an assignment rule for parameter V\_aCB:

$$V_{a}CB = [EO_{a}b] \cdot N_{A}pmole \cdot w_{E}O \cdot vol(V_{B})$$
(9)

#### 6.10 Rule V\_LTC\_CB

Rule V\_LTC\_CB is an assignment rule for parameter V\_LTC\_CB:

$$V\_LTC\_CB = (naEO\_LTCsyn \cdot ([EO\_b] + [EO\_i\_b]) + [EO\_a\_b]) \cdot N\_A\_pmole \cdot w\_EO \cdot vol (V\_B)$$

$$(10)$$

#### 6.11 Rule V\_CAW

Rule V\_CAW is an assignment rule for parameter V\_CAW:

$$V\_CAW = ([EO\_a\_aw] + [EO\_aw] + [EO\_i\_aw]) \cdot N\_A\_pmole \cdot w\_EO \cdot vol(V\_AW) \quad (11)$$

#### 6.12 Rule V\_aCAW

Rule V\_aCAW is an assignment rule for parameter V\_aCAW:

$$V_{a}CAW = [EO_{a}_{a}w] \cdot N_{A}_{p}mole \cdot w_{E}O \cdot vol(V_{A}W)$$
(12)

#### 6.13 Rule V\_LTC\_CAW

Rule V\_LTC\_CAW is an assignment rule for parameter V\_LTC\_CAW:

$$V\_LTC\_CAW = (naEO\_LTCsyn \cdot ([EO\_aw] + [EO\_i\_aw]) + [EO\_a\_aw]) \cdot N\_A\_pmole \cdot w\_EO \cdot vol(V\_AW)$$
(13)

#### 6.14 Rule GSSG\_b

Rule GSSG\_b is an assignment rule for parameter GSSG\_b:

$$GSSG_b = \frac{GS\_pool\_b - GSH\_b}{2.0}$$
 (14)

#### 6.15 Rule NADPH\_b

Rule NADPH\_b is an assignment rule for parameter NADPH\_b:

$$NADPH_b = NP_pool_b - NADP_b$$
 (15)

#### 6.16 Rule PLA2\_D

Rule PLA2\_D is an assignment rule for parameter PLA2\_D:

$$PLA2_D = 1.0 + \frac{Ca}{K_PLA2_Ca}$$
 (16)

#### 6.17 Rule PLA2\_Ca

Rule PLA2\_Ca is an assignment rule for parameter PLA2\_Ca:

$$PLA2\_Ca = \frac{\frac{Ca}{K\_PLA2\_Ca}}{PLA2\_D}$$
 (17)

#### 6.18 Rule Ki\_AA\_AA

Rule Ki\_AA\_AA is an assignment rule for parameter Ki\_AA\_AA:

$$Ki_AA_AA = Ki_AA$$
 (18)

#### 6.19 Rule K\_AA\_HETE

Rule K\_AA\_HETE is an assignment rule for parameter K\_AA\_HETE:

$$K_AA_HETE = Ki_HETE$$
 (19)

#### 6.20 Rule Ki\_HPETE\_AA

Rule Ki\_HPETE\_AA is an assignment rule for parameter Ki\_HPETE\_AA:

$$Ki\_HPETE\_AA = Ki\_AA$$
 (20)

#### **6.21 Rule OOH\_b**

Rule OOH\_b is an assignment rule for parameter OOH\_b:

$$OOH_b = [HPETE_b] + LOOH_b$$
 (21)

#### **6.22 Rule OH\_b**

Rule OH\_b is an assignment rule for parameter OH\_b:

$$OH_b = [HETE_b] + LOH_b$$
 (22)

#### **6.23** Rule r1

Rule r1 is an assignment rule for parameter r1:

$$r1 = k_{-}ox + \frac{k_{-}ox2 \cdot Ca}{K_{-}Ca2}$$
 (23)

#### **6.24 Rule** r2

Rule r2 is an assignment rule for parameter r2:

$$r2 = k red + \frac{k red2 \cdot Ca}{K Ca2}$$
 (24)

#### 6.25 Rule REDOX\_b

Rule REDOX\_b is an assignment rule for parameter REDOX\_b:

$$REDOX\_b = \frac{\frac{r2}{Ke\_red} + \frac{r1 \cdot OH\_b}{Ke\_ox} + \frac{al \cdot ki \cdot ZF\_blood\_conc}{KdZ} \cdot \left(1.0 + \frac{Ca}{K\_Ca3}\right)}{r2 + r1 \cdot OOH\_b}$$
(25)

#### 6.26 Rule RELFL05\_b

Rule RELFL05\_b is an assignment rule for parameter RELFL05\_b:

$$RELFLO5\_b = \frac{\frac{k\_lo\cdot[AA\_b]}{K\_AA} + k3\cdot[HPETE\_b]\cdot\left(1.0 + \frac{[AA\_b]}{K\_AA}\right)}{k\_lta\_syn + k\_3\cdot\left(1.0 + \frac{[AA\_b]}{K\_HPETE\_AA}\right)}$$
(26)

#### 6.27 Rule DFLOa\_b

Rule DFLOa\_b is an assignment rule for parameter DFLOa\_b:

$$DFLOa_b = \left(1.0 + \frac{Ca}{K\_Ca3}\right) \cdot \left(1.0 + \frac{REDOX\_b \cdot \left(1.0 + \frac{Ca}{K\_Ca2}\right)}{1.0 + \frac{Ca}{K\_Ca3}} + \frac{[AA\_b]}{K\_AA}\right)$$

$$\cdot \left(1.0 + \frac{[AA\_b]}{Ki\_AA\_AA}\right) + \frac{[AA\_b]}{Ki\_AA} \cdot \left(1.0 + \frac{[HETE\_b]}{K\_AA\_HETE}\right) + RELFLO5\_b$$

$$\cdot \left(1.0 + \frac{[AA\_b]}{Ki\_HPETE\_AA}\right) + \frac{[HETE\_b]}{Ki\_HETE} + \frac{al \cdot ZF\_blood\_conc}{KdZ}\right)$$
(27)

#### 6.28 Rule FL03\_b

Rule FL03\_b is an assignment rule for parameter FL03\_b:

$$FLO3_b = \frac{FLOa}{DFLOa_b}$$
 (28)

#### **6.29 Rule FL02\_b**

Rule FL02\_b is an assignment rule for parameter FL02\_b:

$$FLO2_b = FLO3_b \cdot REDOX_b \tag{29}$$

#### 6.30 Rule FLO3t\_b

Rule FLO3t\_b is an assignment rule for parameter FLO3t\_b:

$$FLO3t_b = FLO3_b \cdot \left(1.0 + \frac{Ca}{K_c Ca3}\right)$$
 (30)

#### **6.31 Rule FL02t\_b**

Rule FLO2t\_b is an assignment rule for parameter FLO2t\_b:

$$FLO2t_b = FLO2_b \cdot \left(1.0 + \frac{Ca}{K_c Ca2}\right)$$
 (31)

#### 6.32 Rule FLO5HP\_b

Rule FLO5HP\_b is an assignment rule for parameter FLO5HP\_b:

$$FLO5HP_b = FLO3t_b \cdot RELFLO5_b \tag{32}$$

#### **6.33 Rule** C\_b

Rule C\_b is an assignment rule for parameter C\_b:

$$C_{-}b = \frac{[\text{HPETE\_b}] \cdot \text{GSH\_b} \cdot \text{GSH\_b}}{\text{Km\_gpx\_HPETE5} \cdot \text{Km\_gpx\_GSH} \cdot \text{Km\_gpx\_GSH}}$$
(33)

#### **6.34 Rule A\_b**

Rule A\_b is an assignment rule for parameter A\_b:

$$\begin{split} A\_b &= \frac{GSH\_b \cdot GSH\_b}{Km\_gpx\_GSH \cdot Km\_gpx\_GSH} \cdot \left(1.0 + \frac{GSSG\_b}{Kd\_gpx\_GSSG}\right) \\ &+ \frac{[HPETE\_b]}{Km\_gpx\_HPETE5} \cdot \left(1.0 + \frac{[HETE\_b]}{Kd\_gpx\_HETE5}\right) + C\_b \end{split} \tag{34}$$

#### **6.35 Rule B\_b**

Rule B\_b is an assignment rule for parameter B\_b:

$$B\_b = \frac{k\_gpx\_cat \cdot [HPETE\_b] \cdot GSH\_b \cdot GSH\_b}{Km\_gpx\_HPETE5 \cdot Km\_gpx\_GSH \cdot Km\_gpx\_GSH}$$
(35)

#### 6.36 Rule delta\_LTCs\_b

Rule delta\_LTCs\_b is an assignment rule for parameter delta\_LTCs\_b:

$$delta\_LTCs\_b = 1.0 + \frac{[LTA4\_b]}{K\_LTA} + \frac{GSH\_b}{K\_GSH} + \frac{\frac{[LTA4\_b]\_GSH\_b}{K\_LTA}}{K\_LTA\_GSH} + \frac{[LTC4\_b]}{K\_LTC}$$
(36)

#### 6.37 Rule nom\_LTCs\_b

Rule nom\_LTCs\_b is an assignment rule for parameter nom\_LTCs\_b:

$$nom\_LTCs\_b = Et\_LTCs \cdot (K\_LTC \cdot k\_LTCs\_fow \cdot [LTA4\_b] \cdot GSH\_b - k\_LTCs\_back \\ \cdot K\_LTA\_GSH \cdot K\_GSH \cdot [LTC4\_b])$$
(37)

#### 6.38 Rule den\_LTCs\_b

Rule den\_LTCs\_b is an assignment rule for parameter den\_LTCs\_b:

$$den\_LTCs\_b = delta\_LTCs\_b \cdot K\_LTA\_GSH \cdot K\_GSH \cdot K\_LTC$$
 (38)

#### 6.39 Rule C\_hedh\_b

Rule C\_hedh\_b is an assignment rule for parameter C\_hedh\_b:

$$C\_hedh\_b = \left(1.0 + \frac{[HETE\_b]}{Kd\_hedh\_HETE5} + \frac{NADPH\_b}{Kd\_hedh\_NADPH}\right) \cdot \left(\frac{k\_hedh\_3 \cdot oxoETE\_b}{Kd\_hedh\_oxoETE5} + \frac{k\_hedh\_2 \cdot NADP\_b}{Kd\_hedh\_NADP}\right)$$
(39)

#### 6.40 Rule A\_hedh\_b

Rule A\_hedh\_b is an assignment rule for parameter A\_hedh\_b:

$$A\_hedh\_b = \left(1.0 + \frac{NADP\_b}{Kd\_hedh\_NADP} + \frac{oxoETE\_b}{Kd\_hedh\_oxoETE5}\right) \\ \cdot \left(\frac{k\_hedh\_1 \cdot [HETE\_b]}{Kd\_hedh\_HETE5} + \frac{k\_hedh\_4 \cdot NADPH\_b}{Kd\_hedh\_NADPH}\right) + C\_hedh\_b$$

$$(40)$$

#### 6.41 Rule B\_hedh\_b

Rule B\_hedh\_b is an assignment rule for parameter B\_hedh\_b:

$$B\_hedh\_b = \frac{k\_hedh\_1 \cdot k\_hedh\_2 \cdot [HETE\_b] \cdot NADP\_b}{Kd\_hedh\_HETE5 \cdot Kd\_hedh\_NADP}$$

$$- \frac{oxoETE\_b \cdot NADPH\_b \cdot k\_hedh\_3 \cdot k\_hedh\_4}{Kd\_hedh\_oxoETE5 \cdot Kd\_hedh\_NADPH}$$

$$(41)$$

#### 6.42 Rule GSSG\_aw

Rule GSSG\_aw is an assignment rule for parameter GSSG\_aw:

$$GSSG_aw = \frac{GS\_pool\_aw - GSH\_aw}{2.0}$$
 (42)

#### 6.43 Rule NADPH\_aw

Rule NADPH\_aw is an assignment rule for parameter NADPH\_aw:

$$NADPH_aw = NP_pool_aw - NADP_aw$$
 (43)

#### 6.44 Rule 00H\_aw

Rule OOH\_aw is an assignment rule for parameter OOH\_aw:

$$OOH_aw = [HPETE_aw] + LOOH_aw$$
 (44)

#### 6.45 Rule OH\_aw

Rule OH\_aw is an assignment rule for parameter OH\_aw:

$$OH_{aw} = [HETE_{aw}] + LOH_{aw}$$
 (45)

#### 6.46 Rule REDOX\_aw

Rule REDOX\_aw is an assignment rule for parameter REDOX\_aw:

$$REDOX\_aw = \frac{\frac{r2}{Ke\_red} + \frac{r1\cdot OH\_aw}{Ke\_ox} + \frac{al\cdot ki\cdot ZF\_airways\_conc}{KdZ} \cdot \left(1.0 + \frac{Ca}{K\_Ca3}\right)}{r2 + r1\cdot OOH\_aw}$$
(46)

# 6.47 Rule RELFL05\_aw

Rule RELFL05\_aw is an assignment rule for parameter RELFL05\_aw:

$$RELFLO5\_aw = \frac{\frac{k\_lo\cdot[AA\_aw]}{K\_AA} + k3\cdot[HPETE\_aw]\cdot\left(1.0 + \frac{[AA\_aw]}{K_LAA}\right)}{k\_lta\_syn + k\_3\cdot\left(1.0 + \frac{[AA\_aw]}{K_LHPETE\_AA}\right)} \tag{47}$$

#### 6.48 Rule DFLOa\_aw

Rule DFLOa\_aw is an assignment rule for parameter DFLOa\_aw:

$$\begin{aligned} \text{DFLOa\_aw} &= \left(1.0 + \frac{\text{Ca}}{\text{K\_Ca3}}\right) \cdot \left(1.0 + \frac{\text{REDOX\_aw} \cdot \left(1.0 + \frac{\text{Ca}}{\text{K\_Ca2}}\right)}{1.0 + \frac{\text{Ca}}{\text{K\_Ca3}}} + \frac{[\text{AA\_aw}]}{\text{K\_AA}} \right. \\ &\quad \cdot \left(1.0 + \frac{[\text{AA\_aw}]}{\text{Ki\_AA\_AA}}\right) + \frac{[\text{AA\_aw}]}{\text{Ki\_AA}} \cdot \left(1.0 + \frac{[\text{HETE\_aw}]}{\text{K\_AA\_HETE}}\right) + \text{RELFLO5\_aw} \\ &\quad \cdot \left(1.0 + \frac{[\text{AA\_aw}]}{\text{Ki\_HPETE\_AA}}\right) + \frac{[\text{HETE\_aw}]}{\text{Ki\_HETE}} + \frac{\text{al} \cdot \text{ZF\_airways\_conc}}{\text{KdZ}} \right) \end{aligned}$$

#### **6.49 Rule FL03\_aw**

Rule FL03\_aw is an assignment rule for parameter FL03\_aw:

$$FLO3_aw = \frac{FLOa}{DFLOa_aw}$$
 (49)

#### **6.50 Rule FL02\_aw**

Rule FLO2\_aw is an assignment rule for parameter FLO2\_aw:

$$FLO2\_aw = FLO3\_aw \cdot REDOX\_aw$$
 (50)

#### 6.51 Rule FLO3t\_aw

Rule FLO3t\_aw is an assignment rule for parameter FLO3t\_aw:

$$FLO3t_aw = FLO3_aw \cdot \left(1.0 + \frac{Ca}{K_ca3}\right)$$
 (51)

#### 6.52 Rule FLO2t\_aw

Rule FLO2t\_aw is an assignment rule for parameter FLO2t\_aw:

$$FLO2t_aw = FLO2_aw \cdot \left(1.0 + \frac{Ca}{K_Ca2}\right)$$
 (52)

#### 6.53 Rule FLO5HP\_aw

Rule FLO5HP\_aw is an assignment rule for parameter FLO5HP\_aw:

$$FLO5HP_aw = FLO3t_aw \cdot RELFLO5_aw$$
 (53)

#### 6.54 Rule C\_aw

Rule C\_aw is an assignment rule for parameter C\_aw:

$$C_{-}aw = \frac{[HPETE_{-}aw] \cdot GSH_{-}aw \cdot GSH_{-}aw}{Km_{-}gpx_{-}HPETE5 \cdot Km_{-}gpx_{-}GSH \cdot Km_{-}gpx_{-}GSH}$$
 (54)

#### 6.55 Rule A\_aw

Rule A\_aw is an assignment rule for parameter A\_aw:

$$A_{aw} = \frac{GSH_{aw} \cdot GSH_{aw}}{Km_{gpx}\_GSH \cdot Km_{gpx}\_GSH} \cdot \left(1.0 + \frac{GSSG_{aw}}{Kd_{gpx}\_GSSG}\right) + \frac{[HPETE_{aw}]}{Km_{gpx}\_HPETE5} \cdot \left(1.0 + \frac{[HETE_{aw}]}{Kd_{gpx}\_HETE5}\right) + C_{aw}$$
(55)

#### 6.56 Rule B\_aw

Rule B\_aw is an assignment rule for parameter B\_aw:

$$B_{aw} = \frac{k_{gpx\_cat} \cdot [HPETE_{aw}] \cdot GSH_{aw} \cdot GSH_{aw}}{Km_{gpx\_HPETE5} \cdot Km_{gpx\_GSH} \cdot Km_{gpx\_GSH}}$$
(56)

# 6.57 Rule delta\_LTCs\_aw

Rule delta\_LTCs\_aw is an assignment rule for parameter delta\_LTCs\_aw:

$$delta\_LTCs\_aw = 1.0 + \frac{[LTA4\_aw]}{K\_LTA} + \frac{GSH\_aw}{K\_GSH} + \frac{\frac{[LTA4\_aw]\cdot GSH\_aw}{K\_LTA}}{\frac{K\_LTA\_GSH}{K\_LTA\_GSH}} + \frac{[LTC4\_aw]}{K\_LTC}$$
(57)

#### 6.58 Rule nom\_LTCs\_aw

Rule nom\_LTCs\_aw is an assignment rule for parameter nom\_LTCs\_aw:

$$nom\_LTCs\_aw = Et\_LTCs \cdot (K\_LTC \cdot k\_LTCs\_fow \cdot [LTA4\_aw] \cdot GSH\_aw - k\_LTCs\_back \cdot K\_LTA\_GSH \cdot K\_GSH \cdot [LTC4\_aw])$$
(58)

#### 6.59 Rule den\_LTCs\_aw

Rule den\_LTCs\_aw is an assignment rule for parameter den\_LTCs\_aw:

$$den LTCs_aw = delta LTCs_aw \cdot K_LTA_GSH \cdot K_GSH \cdot K_LTC$$
 (59)

#### 6.60 Rule C\_hedh\_aw

Rule C\_hedh\_aw is an assignment rule for parameter C\_hedh\_aw:

$$C\_hedh\_aw = \left(1.0 + \frac{[HETE\_aw]}{Kd\_hedh\_HETE5} + \frac{NADPH\_aw}{Kd\_hedh\_NADPH}\right) \\ \cdot \left(\frac{k\_hedh\_3 \cdot oxoETE\_aw}{Kd\_hedh\_oxoETE5} + \frac{k\_hedh\_2 \cdot NADP\_aw}{Kd\_hedh\_NADP}\right)$$

$$(60)$$

#### 6.61 Rule A\_hedh\_aw

Rule A\_hedh\_aw is an assignment rule for parameter A\_hedh\_aw:

$$A\_hedh\_aw = \left(1.0 + \frac{NADP\_aw}{Kd\_hedh\_NADP} + \frac{oxoETE\_aw}{Kd\_hedh\_oxoETE5}\right) \\ \cdot \left(\frac{k\_hedh\_1 \cdot [HETE\_aw]}{Kd\_hedh\_HETE5} + \frac{k\_hedh\_4 \cdot NADPH\_aw}{Kd\_hedh\_NADPH}\right) + C\_hedh\_aw$$
 (61)

#### 6.62 Rule B\_hedh\_aw

Rule B\_hedh\_aw is an assignment rule for parameter B\_hedh\_aw:

$$B\_hedh\_aw = \frac{k\_hedh\_1 \cdot k\_hedh\_2 \cdot [HETE\_aw] \cdot NADP\_aw}{Kd\_hedh\_HETE5 \cdot Kd\_hedh\_NADP}$$

$$-\frac{oxoETE\_aw \cdot NADPH\_aw \cdot k\_hedh\_3 \cdot k\_hedh\_4}{Kd\_hedh\_oxoETE5 \cdot Kd\_hedh\_NADPH}$$
(62)

#### **6.63 Rule OL\_b**

Rule OL\_b is an assignment rule for parameter OL\_b:

 $OL_b$ 

$$= \frac{\text{R1\_portion\_EOa} \cdot \frac{\text{fup\_LT} \cdot [\text{LTD4\_b}]}{\text{Kd\_LT}}}{1.0 + \frac{\text{fup\_LT} \cdot [\text{LTD4\_b}]}{\text{Kd\_LT}} + \frac{\text{ML\_blood\_conc}}{\text{Ki\_ML\_EOa}}} + \frac{(1.0 - \text{R1\_portion\_EOa}) \cdot \frac{\text{fup\_LT} \cdot ([\text{LTC4\_b\_out}] + [\text{LTD4\_b}])}{\text{Kd\_LT\_2}}}{1.0 + \frac{\text{fup\_LT} \cdot ([\text{LTC4\_b\_out}] + [\text{LTD4\_b}])}{\text{Kd\_LT\_2}}}$$

$$(63)$$

#### 6.64 Rule OL\_aw

Rule OL\_aw is an assignment rule for parameter OL\_aw:

$$OL\_aw = \frac{R1\_portion\_EOa \cdot \frac{[LTD4\_aw]}{Kd\_LT}}{1.0 + \frac{[LTD4\_aw]}{Kd\_LT} + \frac{ML\_airways\_conc}{Ki\_ML\_EOa}} + \frac{(1.0 - R1\_portion\_EOa) \cdot \frac{[LTC4\_aw\_out] + [LTD4\_aw]}{Kd\_LT\_2}}{1.0 + \frac{[LTC4\_aw\_out] + [LTD4\_aw]}{Kd\_LT\_2}}$$

$$(64)$$

#### 6.65 Rule Rec\_occup\_migr

Rule Rec\_occup\_migr is an assignment rule for parameter Rec\_occup\_migr:

$$Rec\_occup\_migr = \frac{portion\_migr \cdot fup\_LT \cdot [LTE4\_b]}{Kd\_LTE\_migr + fup\_LT \cdot [LTE4\_b]} + \frac{(1.0 - portion\_migr) \cdot [IL\_b]}{Kd\_IL\_migr + [IL\_b]} \quad (65)$$

#### 6.66 Rule Ca\_FEV

Rule Ca\_FEV is an assignment rule for parameter Ca\_FEV:

$$\begin{aligned} \text{Ca\_FEV} &= \text{Cao\_FEV} + \text{k\_fev\_eff} \\ &\cdot \left( \frac{\text{R1\_portion\_FEV} \cdot \frac{[\text{LTD4\_aw}]}{\text{Kd\_LTR1\_FEV}}}{1.0 + \frac{[\text{LTD4\_aw}]}{\text{Kd\_LTR1\_FEV}}} + \frac{\text{R2\_portion\_FEV} \cdot \frac{[\text{LTD4\_aw}] + [\text{LTC4\_aw\_out}]}{\text{Kd\_LTR2\_FEV}}}{1.0 + \frac{[\text{LTD4\_aw}] + [\text{LTC4\_aw\_out}]}{\text{Kd\_LTR2\_FEV}}} \right. \\ &\quad + \frac{\left( 1.0 - \text{R1\_portion\_FEV} - \text{R2\_portion\_FEV} \right) \cdot \frac{[\text{Hn\_aw}]}{\text{Kd\_Hn\_FEV}}}{1.0 + \frac{[\text{Hn\_aw}]}{\text{Kd\_Hn\_FEV}}} \right) \end{aligned}$$

#### 6.67 Rule r\_out\_FEV

Rule r\_out\_FEV is an assignment rule for parameter r\_out\_FEV:

r\_out\_FEV

$$= R\_FEV - \frac{\left(R\_FEV - \left(R\_FEV \cdot (R\_FEV - R\_in\_relax\_FEV)^{2.0}\right)^{\frac{1.0}{3.0}}\right) \cdot Ca\_FEV^{n\_FEV}}{K\_Ca\_FEV^{n\_FEV} + Ca\_FEV^{n\_FEV}} \quad (67)$$

#### 6.68 Rule r\_in\_FEV

Rule r\_in\_FEV is an assignment rule for parameter r\_in\_FEV:

$$r_{in}FEV = r_{out}FEV - (R_{FEV} - R_{in}_{relax}FEV) \cdot \left(\frac{R_{FEV}}{r_{out}FEV}\right)^{0.5}$$
 (68)

#### 6.69 Rule FEV1

Rule FEV1 is an assignment rule for parameter FEV1:

$$FEV1 = MAX\_FEV \cdot \left(\frac{r\_in\_FEV}{R\_in\_relax\_FEV}\right)^{2.0}$$
(69)

#### 6.70 Rule TSN

Rule TSN is an assignment rule for parameter TSN:

$$TSN = \frac{TSN\_0 \cdot \left(R\_FEV - \left(R\_FEV \cdot (R\_FEV - R\_in\_relax\_FEV)^{2.0}\right)^{\frac{1.0}{3.0}}\right) \cdot Ca\_FEV\_ex^{n\_FEV}}{K\_Ca\_FEV^{n\_FEV} + Ca\_FEV\_ex^{n\_FEV}}$$
(70)

#### 6.71 Rule TSN\_Hn

Rule TSN\_Hn is an assignment rule for parameter TSN\_Hn:

$$TSN\_Hn = \frac{TSN\_0 \cdot \left(R\_FEV - \left(R\_FEV \cdot (R\_FEV - R\_in\_relax\_FEV)^{2.0}\right)^{\frac{1.0}{3.0}}\right) \cdot Ca\_FEV^{n\_FEV}}{K\_Ca\_FEV^{n\_FEV} + Ca\_FEV^{n\_FEV}}$$
(71)

#### 6.72 Rule FEV1\_percent

Rule FEV1\_percent is an assignment rule for parameter FEV1\_percent:

$$FEV1\_percent = \frac{FEV1 - 3.528}{3.528} \cdot 100.0 \tag{72}$$

#### 6.73 Rule time\_hour

Rule time\_hour is an assignment rule for parameter time\_hour:

$$time\_hour = \frac{time}{60.0}$$
 (73)

# 6.74 Rule time\_day

Rule time\_day is an assignment rule for parameter time\_day:

$$time\_day = \frac{time}{1440.0} \tag{74}$$

#### 6.75 Rule N\_EO\_bm

Rule N\_EO\_bm is an assignment rule for parameter N\_EO\_bm:

$$N_EO_bm = [EO_bm] \cdot 6.02 \cdot 10.0^{8.0}$$
 (75)

#### **6.76 Rule N\_EO\_b**

Rule N\_EO\_b is an assignment rule for parameter N\_EO\_b:

$$N_EO_b = [EO_b] \cdot 6.02 \cdot 10.0^{8.0}$$
 (76)

#### 6.77 Rule N\_EO\_i\_b

Rule N\_EO\_i\_b is an assignment rule for parameter N\_EO\_i\_b:

$$N\_EO\_i\_b = [EO\_i\_b] \cdot 6.02 \cdot 10.0^{8.0}$$
(77)

#### 6.78 Rule N\_EO\_a\_b

Rule N\_EO\_a\_b is an assignment rule for parameter N\_EO\_a\_b:

$$N\_EO\_a\_b = [EO\_a\_b] \cdot 6.02 \cdot 10.0^{8.0}$$
(78)

#### 6.79 Rule EO\_b\_tot

Rule EO\_b\_tot is an assignment rule for parameter EO\_b\_tot:

$$EO_b\_tot = [EO_b] + [EO_i\_b] + [EO\_a\_b]$$

$$(79)$$

**Derived unit**  $mol \cdot l^{-1}$ 

#### 6.80 Rule N\_EO\_b\_tot

Rule N\_EO\_b\_tot is an assignment rule for parameter N\_EO\_b\_tot:

$$N_EO_b_tot = ([EO_b] + [EO_i_b] + [EO_a_b]) \cdot 6.02 \cdot 10.0^{8.0}$$
(80)

#### 6.81 Rule N\_EO\_aw

Rule N\_EO\_aw is an assignment rule for parameter N\_EO\_aw:

$$N_EO_aw = [EO_aw] \cdot 6.02 \cdot 10.0^{8.0}$$
 (81)

#### 6.82 Rule N\_EO\_i\_aw

Rule N\_EO\_i\_aw is an assignment rule for parameter N\_EO\_i\_aw:

N.EO\_i\_aw = 
$$[EO_i_aw] \cdot 6.02 \cdot 10.0^{8.0}$$
 (82)

#### 6.83 Rule N\_EO\_a\_aw

Rule N\_EO\_a\_aw is an assignment rule for parameter N\_EO\_a\_aw:

$$N_EO_a_aw = [EO_a_aw] \cdot 6.02 \cdot 10.0^{8.0}$$
 (83)

#### 6.84 Rule E0\_aw\_tot

Rule EO\_aw\_tot is an assignment rule for parameter EO\_aw\_tot:

$$EO_{aw\_tot} = [EO_{aw}] + [EO_{i\_aw}] + [EO_{a\_aw}]$$
(84)

Derived unit  $mol \cdot l^{-1}$ 

# 6.85 Rule N\_EO\_aw\_tot

Rule N\_EO\_aw\_tot is an assignment rule for parameter N\_EO\_aw\_tot:

$$N_EO_aw_tot = ([EO_aw] + [EO_iaw] + [EO_aaw]) \cdot 6.02 \cdot 10.0^{8.0}$$
 (85)

# 6.86 Rule EO\_b\_tot\_per\_ss

Rule EO\_b\_tot\_per\_ss is an assignment rule for parameter EO\_b\_tot\_per\_ss:

$$EO_b_tot_per_ss = \frac{100.0 \cdot (EO_b_tot - 5.33E - 4)}{5.33E - 4}$$
(86)

#### 6.87 Rule N\_EO\_aw\_tot\_perc

Rule N\_EO\_aw\_tot\_perc is an assignment rule for parameter N\_EO\_aw\_tot\_perc:

$$N\_EO\_aw\_tot\_perc = \frac{N\_EO\_aw\_tot}{818735.0} \cdot 100.0$$
 (87)

## 6.88 Rule N\_EO\_b\_tot\_perc

Rule N\_EO\_b\_tot\_perc is an assignment rule for parameter N\_EO\_b\_tot\_perc:

$$N_EO_b_{tot_perc} = \frac{N_EO_b_{tot}}{4266021.0} \cdot 100.0$$
 (88)

#### **6.89 Rule N\_EO**

Rule N\_EO is an assignment rule for parameter N\_EO:

$$N\_EO = \frac{N\_EO\_b\_tot \cdot vol(V\_B) + N\_EO\_aw\_tot \cdot vol(V\_AW)}{vol(V\_B) + vol(V\_AW)}$$
(89)

#### 6.90 Rule N\_EO\_a

Rule N\_EO\_a is an assignment rule for parameter N\_EO\_a:

$$N\_EO\_a = \frac{N\_EO\_a\_b \cdot vol(V\_B) + N\_EO\_a\_aw \cdot vol(V\_AW)}{vol(V\_B) + vol(V\_AW)}$$
(90)

## **6.91 Rule** LTC4\_b\_pM

Rule LTC4\_b\_pM is an assignment rule for parameter LTC4\_b\_pM:

$$LTC4\_b\_pM = [LTC4\_b] \cdot 10000000.0 \tag{91}$$

#### **6.92 Rule LTs\_aw\_pg**

Rule LTs\_aw\_pg is an assignment rule for parameter LTs\_aw\_pg:

$$LTs\_aw\_pg = \frac{\frac{[LTC4\_aw\_out]}{fup\_LT} \cdot M\_LTC + \frac{[LTD4\_aw]}{fup\_LT} \cdot M\_LTD + \frac{[LTE4\_aw]}{fup\_LT} \cdot M\_LTE}{1000.0}$$
(92)

#### 6.93 Rule LTD4\_b\_free

Rule LTD4\_b\_free is an assignment rule for parameter LTD4\_b\_free:

$$LTD4\_b\_free = [LTD4\_b] \cdot fup\_LT \tag{93}$$

#### 6.94 Rule ML\_uM

Rule ML\_uM is an assignment rule for parameter ML\_uM:

$$ML_uM = \frac{[ML_blood]}{1000000.0}$$

$$(94)$$

## 6.95 Rule LTD4\_aw\_pers

Rule LTD4\_aw\_pers is an assignment rule for parameter LTD4\_aw\_pers:

$$LTD4\_aw\_pers = \frac{100.0 \cdot [LTD4\_aw]}{205.76}$$
 (95)

# 6.96 Rule N\_EO\_perc

Rule N\_EO\_perc is an assignment rule for parameter N\_EO\_perc:

$$N\_EO\_perc = \frac{100.0 \cdot N\_EO}{358758.0}$$
 (96)

#### 6.97 Rule Hn\_aw\_perc

Rule Hn\_aw\_perc is an assignment rule for parameter Hn\_aw\_perc:

# 6.98 Rule N\_EO\_aw\_perc

Rule N\_EO\_aw\_perc is an assignment rule for parameter N\_EO\_aw\_perc:

$$N_EO_aw_perc = \frac{100.0 \cdot N_EO_aw_tot}{818735.0}$$
 (98)

#### 6.99 Rule Ca\_FEV\_LTR1

Rule Ca\_FEV\_LTR1 is an assignment rule for parameter Ca\_FEV\_LTR1:

$$Ca\_FEV\_LTR1 = \frac{k\_fev\_eff}{\frac{R1\_portion\_FEV \cdot \frac{[LTD4\_aw]}{Kd\_LTR1\_FEV}}{1.0 + \frac{[LTD4\_aw]}{Kd\_LTR1\_FEV} + \frac{ML\_airways\_conc}{EC50\_ML\_FEV}}}{Ca\_FEV - Cao\_FEV}$$
(99)

#### 6.100 Rule Ca\_FEV\_LTR2

Rule Ca\_FEV\_LTR2 is an assignment rule for parameter Ca\_FEV\_LTR2:

Ca\_FEV\_LTR2

$$=\frac{k\_fev\_eff\cdot\left(\frac{R2\_portion\_FEV\cdot\frac{[LTD4\_aw]+[LTC4\_aw\_out]}{Kd\_LTR2\_FEV}}{1.0+\frac{[LTD4\_aw]+[LTC4\_aw\_out]}{Kd\_LTR2\_FEV}}+\frac{(1.0-R1\_portion\_FEV-R2\_portion\_FEV)\cdot\frac{[Hn\_aw]}{Kd\_Hn\_FEV}}{1.0+\frac{[Hn\_aw]}{Kd\_Hn\_FEV}}\right)}{Ca\_FEV-Cao\_FEV}$$
 (100)

# 6.101 Rule OL\_ASM

Rule OL\_ASM is an assignment rule for parameter OL\_ASM:

$$\begin{aligned} OL\_ASM &= \frac{R1\_portion\_FEV \cdot \frac{[LTD4\_aw]}{Kd\_LTR1\_FEV}}{1.0 + \frac{[LTD4\_aw]}{Kd\_LTR1\_FEV} + \frac{ML\_airways\_conc}{EC50\_ML\_FEV}} + \frac{R2\_portion\_FEV \cdot \frac{[LTD4\_aw] + [LTC4\_aw\_out]}{Kd\_LTR2\_FEV}}{1.0 + \frac{[LTD4\_aw] + [LTC4\_aw\_out]}{Kd\_LTR2\_FEV}} \\ &+ \frac{(1.0 - R1\_portion\_FEV - R2\_portion\_FEV) \cdot \frac{[Hn\_aw]}{Kd\_Hn\_FEV}}{1.0 + \frac{[Hn\_aw]}{Kd\_Hn\_FEV}} \end{aligned}$$

# 7 Reactions

This model contains 66 reactions. All reactions are listed in the following table and are subsequently described in detail. If a reaction is affected by a modifier, the identifier of this species is written above the reaction arrow.

Table 5: Overview of all reactions

N₀	Id	Name	Reaction Equation	SBO
1	v1	v1	$\emptyset \xrightarrow{AA\_b} AA\_b$	
2	v2	v2	$AA\_b \xrightarrow{AA\_b} \emptyset$	
3	v3	v3	$\emptyset \xrightarrow{AA\_b, HPETE\_b, AA\_b} HPETE\_b$	
4	v4	v4	$HPETE\_b \xrightarrow{HPETE\_b} HETE\_b$	
5	v5	v5	$HPETE\_b \longrightarrow HETE\_b$	
6	v6	v6	$\emptyset \longrightarrow LTA4_b$	
7	v7	v7	$LTA4\_b \longrightarrow LTC4\_b$	
8	v8	v8	$HETE\_b \longrightarrow \emptyset$	
9	v9	v9	$LTA4\_b \xrightarrow{LTA4\_b} \emptyset$	
10	v10in	v10in	$LTC4\_b \xrightarrow{LTC4\_b} \emptyset$	
11	v10out	v10out	$\emptyset \xrightarrow{\text{LTC4\_b}} \text{LTC4\_b\_out}$	
12	v11	v11	$LTC4\_b\_out \xrightarrow{LTC4\_b\_out} LTD4\_b$	
13	v12	v12	$LTD4\_b \xrightarrow{LTD4\_b} LTE4\_b$	
14	v13	v13	LTC4_b_out $\xrightarrow{LTC4\_b\_out} \emptyset$	
15	v14	v14	$LTD4\_b \xrightarrow{LTD4\_b} \emptyset$	
16	v15	v15	$LTE4\_b \xrightarrow{LTE4\_b} \emptyset$	
17	v16	v16	$EO\_b \xrightarrow{EO\_b} EO\_i\_b$	

N⁰	Id	Name	Reaction Equation	SBO
18	v17	v17	$EO\_i\_b \xrightarrow{EO\_i\_b} EO\_a\_b$	
19	v18	v18	$EO\_a\_b \xrightarrow{EO\_a\_b} EO\_b$	
20	v19	v19	$EO_{-}b \xrightarrow{EO_{-}b} \emptyset$	
21	v20	v20	$EO_a_b \xrightarrow{EO_a_b} \emptyset$	
22	v21	v21	$EO\_i\_b \xrightarrow{EO\_i\_b} EO\_i\_aw$	
23	v22	v22	$EO_a_b \xrightarrow{EO_a_b} EO_a_aw$	
24	v23	v23	$EO_b \xrightarrow{EO_b} EO_aw$	
25	v24	v24	∅ EO_b, EO_i_b, EO_a_b, EO_b, EO_i_b,	$\xrightarrow{EO\_a\_b} Hn\_b$
26	v25	v25	$\operatorname{Hn\_b} \overset{\operatorname{Hn\_b}}{\longrightarrow} \emptyset$	
27	v26	v26	$\emptyset \xrightarrow{\mathrm{EO}\_a\_b}, \xrightarrow{\mathrm{EO}\_a\_b} \mathrm{IL\_b}$	
28	v27	v27	$IL\_b \xrightarrow{IL\_b} \emptyset$	
29	v28	v28	$IL\_b \xrightarrow{IL\_b, IL\_bm} IL\_bm$	
30	v29	v29	$\emptyset \xrightarrow{\text{IL\_bm}, \text{IL\_bm}} \text{EO\_bm}$	
31	v30	v30	$EO\_bm \xrightarrow{EO\_bm} EO\_b$	
32	v31	v31	$\emptyset \xrightarrow{AA\_aw} AA\_aw$	
33	v32	v32	$AA_aw \xrightarrow{AA_aw} \emptyset$	
34	v33	v33	$\emptyset \xrightarrow{AA\_aw, HPETE\_aw, AA\_aw} HPETE\_$	aw
35	v34	v34	HPETE_aw HPETE_aw, HETE_aw HETE_aw	ΓE_aw
36	v35	v35	HPETE_aw → HETE_aw	
37	v36	v36	$\emptyset \longrightarrow LTA4_aw$	
38	v37	v37	$LTA4_aw \longrightarrow LTC4_aw$	
39	v38	v38	$HETE_{aw} \longrightarrow \emptyset$	

34	No	Id	Name	Reaction Equation	SBO
	40	v39	v39	$LTA4_{-aw} \xrightarrow{LTA4_{-aw}} \emptyset$	
	41	v40in	v40in	$LTC4_{-aw} \xrightarrow{LTC4_{-aw}} \emptyset$	
	42	v40out	v40out	$\emptyset \xrightarrow{\text{LTC4\_aw}, \text{LTC4\_aw}} \text{LTC4\_aw\_out}$	
	43	v41	v41	$LTC4_aw\_out \xrightarrow{LTC4_aw\_out} LTD4_aw$	
	44	v42	v42	$LTD4_aw \xrightarrow{LTD4_aw} LTE4_aw$	
	45	v43	v43	LTE4_aw $\xrightarrow{\text{LTE4\_aw}}$ LTE4_b	
E .	46	v44	v44	LTD4_aw LTD4_b LTD4_b	
Produced by SBML2l <sup>ET</sup> EX	47	v45	v45	LTC4_aw_out $\xrightarrow{LTC4\_aw\_out, LTC4\_b\_out}$ LTC4_b_ou	t
исес	48	v46	v46	EO_aw EO_i_aw	
l by	49	v47	v47	EO_i_aw EO_a_aw	
<b>8</b> ≤	50	v48	v48	$EO_a_aw \xrightarrow{EO_a_aw} EO_aw$	
N M	51	v49	v49	EO_aw $\xrightarrow{EO\_aw} \emptyset$	
<u> </u>	52	v50	v50	EO_a_aw $\xrightarrow{\text{EO}} \emptyset$	2
	53	v51	v51	Ø EO_a_aw, EO_i_aw, EO_a_w, EO_a_aw, EO_i_aw, EO	J_aw Hn_aw
	54	v52	v52	$\operatorname{Hn\_aw} \xrightarrow{\operatorname{Hn\_aw}, \operatorname{Hn\_b}} \operatorname{Hn\_b}$	
	55	v53	v53	$\emptyset \xrightarrow{\text{EO}\_a\_aw, \text{EO}\_a\_aw} \text{IL}\_aw$	
	56	v54	v54	$IL_aw \xrightarrow{IL_aw, IL_b} IL_b$	
	57	v55	v55	LTE4_aw $\xrightarrow{\text{LTE4}\_aw} \emptyset$	
	58	v56	v56	$LTD4_aw \xrightarrow{LTD4_aw} \emptyset$	
	59	v57	v57	$LTC4_aw_out \xrightarrow{LTC4_aw_out} \emptyset$	
	60	v58	v58	IL_aw $\xrightarrow{\text{IL}_a\text{aw}} \emptyset$	

N⁰	Id	Name	Reaction Equation	SBO
61	v59	v59	$Hn_aw \xrightarrow{Hn_aw} \emptyset$	
62	v60	v60	ZF_intes $\stackrel{ZF\_intes}{\longrightarrow}$ ZF_blood	
63	v61	v61	$ZF\_blood \xrightarrow{ZF\_blood, ZF\_airways} ZF\_airways$	
64	v62	v62	$ZF\_blood \xrightarrow{ZF\_blood} \emptyset$	
65	v63	v63	$ML_{intes} \xrightarrow{ML_{intes}} ML_{blood}$	
66	v64	v64	$ML\_blood \xrightarrow{ML\_blood} \emptyset$	

#### 7.1 Reaction v1

This is a fast irreversible reaction of no reactant forming one product influenced by one modifier.

Name v1

**Reaction equation** 

$$\emptyset \xrightarrow{AA\_b} AA\_b \tag{102}$$

**Modifier** 

Table 6: Properties of each modifier.

Id	Name	SBO
$AA_b$	$AA_{-}b$	

**Product** 

Table 7: Properties of each product.

Id	Name	SBO
$AA_b$	$AA_b$	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{1} = \text{vol}\left(\text{Default}\right) \cdot \left(\frac{\text{Vmax\_PLA2} \cdot \text{PLA2\_Ca} \cdot \text{PL}}{\text{Km\_PLA2\_APC} + \text{PL}} - \frac{\text{V\_CoA} \cdot [\text{AA\_b}]}{\text{Km\_CoA\_AA} + [\text{AA\_b}]}\right) \quad (103)$$

#### 7.2 Reaction v2

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v2

**Reaction equation** 

$$AA\_b \xrightarrow{AA\_b} \emptyset \tag{104}$$

Reactant

Table 8: Properties of each reactant.

Id	Name	SBO
AA_b	$AA_b$	

### **Modifier**

Table 9: Properties of each modifier.

Id	Name	SBO
AA_b	$AA_b$	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_2 = vol \left( Default \right) \cdot \frac{k\_lo \cdot [AA\_b] \cdot FLO3t\_b}{K\_AA}$$
 (105)

### 7.3 Reaction v3

This is a fast irreversible reaction of no reactant forming one product influenced by three modifiers.

### Name v3

## **Reaction equation**

$$\emptyset \xrightarrow{AA\_b, HPETE\_b, AA\_b} HPETE\_b$$
 (106)

#### **Modifiers**

Table 10: Properties of each modifier.

Id	Name	SBO
AA_b HPETE_b AA_b	AA_b HPETE_b AA_b	

## **Product**

Table 11: Properties of each product.

Id	Name	SBO
HPETE_b	HPETE_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{3} = vol\left(Default\right) \cdot \left(k\_3 \cdot FLO5HP\_b - k3 \cdot FLO3t\_b \cdot \left[HPETE\_b\right]\right) \cdot \left(1.0 + \frac{[AA\_b]}{Ki\_AA}\right) \quad (107)$$

## 7.4 Reaction v4

This is a fast irreversible reaction of one reactant forming one product influenced by two modifiers.

Name v4

### **Reaction equation**

$$HPETE\_b \xrightarrow{HPETE\_b, HETE\_b} HETE\_b$$
 (108)

#### Reactant

Table 12: Properties of each reactant.

Id	Name	SBO
HPETE_b	HPETE_b	

#### **Modifiers**

Table 13: Properties of each modifier.

Id	Name	SBO
	HPETE_b	
HETE_b	HETE_b	

### **Product**

Table 14: Properties of each product.

Id	Name	SBO
HETE_b	HETE_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_4 = \text{vol} \left( \text{Default} \right) \cdot \text{r1} \cdot \left( \left[ \text{HPETE\_b} \right] \cdot \text{FLO2\_b} - \frac{\left[ \text{HETE\_b} \right] \cdot \text{FLO3\_b}}{\text{Ke\_ox}} \right)$$
 (109)

## 7.5 Reaction v5

This is a fast irreversible reaction of one reactant forming one product.

Name v5

### **Reaction equation**

$$HPETE\_b \longrightarrow HETE\_b \tag{110}$$

#### Reactant

Table 15: Properties of each reactant.

Id	Name	SBO
HPETE_b	HPETE_b	

## **Product**

Table 16: Properties of each product.

Id	Name	SBO
HETE_b	HETE_b	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_5 = \text{vol}\left(\text{Default}\right) \cdot \frac{\text{GPx} \cdot \text{B}_{-}\text{b}}{\text{A}_{-}\text{b}}$$
 (111)

### 7.6 Reaction v6

This is a fast irreversible reaction of no reactant forming one product.

Name v6

## **Reaction equation**

$$\emptyset \longrightarrow LTA4_b$$
 (112)

### **Product**

Table 17: Properties of each product.

Id	Name	SBO
LTA4_b	LTA4_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_6 = \text{vol}\left(\text{Default}\right) \cdot \text{k\_lta\_syn} \cdot \text{FLO5HP\_b}$$
 (113)

## 7.7 Reaction v7

This is a fast irreversible reaction of one reactant forming one product.

Name v7

## **Reaction equation**

$$LTA4_b \longrightarrow LTC4_b$$
 (114)

### Reactant

Table 18: Properties of each reactant.

Id	Name	SBO
$LTA4_b$	LTA4_b	

### **Product**

Table 19: Properties of each product.

Id	Name	SBO
LTC4_b	LTC4_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_7 = \text{vol}\left(\text{Default}\right) \cdot \frac{\text{nom\_LTCs\_b}}{\text{den\_LTCs\_b}}$$
 (115)

#### 7.8 Reaction v8

This is a fast irreversible reaction of one reactant forming no product.

Name v8

## **Reaction equation**

$$HETE\_b \longrightarrow \emptyset \tag{116}$$

#### Reactant

Table 20: Properties of each reactant.

Id	Name	SBO
HETE_b	HETE_b	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_8 = \text{vol} \left( \text{Default} \right) \cdot \frac{\text{HEDH5} \cdot \text{B\_hedh\_b}}{\text{A\_hedh\_b}}$$
 (117)

### 7.9 Reaction v9

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v9

## **Reaction equation**

$$LTA4\_b \xrightarrow{LTA4\_b} \emptyset \tag{118}$$

### Reactant

Table 21: Properties of each reactant.

Id	Name	SBO
LTA4_b	LTA4_b	

### Modifier

Table 22: Properties of each modifier.

Id	Name	SBO
LTA4_b	LTA4_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_9 = \text{vol}\left(\text{Default}\right) \cdot \text{Kd}12 \cdot \left[\text{LTA4\_b}\right]$$
 (119)

## 7.10 Reaction v10in

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v10in

## **Reaction equation**

$$LTC4\_b \xrightarrow{LTC4\_b} \emptyset$$
 (120)

#### Reactant

Table 23: Properties of each reactant.

Id	Name	SBO
LTC4_b	LTC4_b	

#### **Modifier**

Table 24: Properties of each modifier.

Id	Name	SBO
LTC4_b	LTC4_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{10} = \text{vol}(\text{Default}) \cdot \text{Kd50} \cdot [\text{LTC4\_b}]$$
 (121)

#### 7.11 Reaction v10out

This is a fast irreversible reaction of no reactant forming one product influenced by two modifiers.

Name v10out

### **Reaction equation**

$$\emptyset \xrightarrow{LTC4\_b, LTC4\_b} LTC4\_b\_out$$
 (122)

#### **Modifiers**

Table 25: Properties of each modifier.

Id	Name	SBO
LTC4_b	LTC4_b	
$LTC4\_b$	LTC4_b	

#### **Product**

Table 26: Properties of each product.

Id	Name	SBO
LTC4_b_out	LTC4_b_out	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{11} = vol(Default) \cdot Kd50 \cdot [LTC4\_b] \cdot V\_LTC\_CB \cdot 10.0^{6.0}$$
 (123)

### 7.12 Reaction v11

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

#### Name v11

## **Reaction equation**

$$LTC4\_b\_out \xrightarrow{LTC4\_b\_out} LTD4\_b$$
 (124)

#### Reactant

Table 27: Properties of each reactant.

Id	Name	SBO
LTC4_b_out	LTC4_b_out	

#### **Modifier**

Table 28: Properties of each modifier.

Id	Name	SBO
LTC4_b_out	LTC4_b_out	

#### **Product**

Table 29: Properties of each product.

Id	Name	SBO
LTD4_b	LTD4_b	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{12} = \text{vol}(\text{Vd\_LTC}) \cdot \text{k\_ggt} \cdot \text{fup\_LT} \cdot [\text{LTC4\_b\_out}]$$
 (125)

### 7.13 Reaction v12

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v12

### **Reaction equation**

$$LTD4\_b \xrightarrow{LTD4\_b} LTE4\_b \tag{126}$$

#### Reactant

Table 30: Properties of each reactant.

Id	Name	SBO
LTD4_b	LTD4_b	

#### **Modifier**

Table 31: Properties of each modifier.

Id	Name	SBO
LTD4_b	LTD4_b	

#### **Product**

Table 32: Properties of each product.

Id	Name	SBO
LTE4_b	LTE4_b	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{13} = \text{vol}(\text{Vd\_LTD}) \cdot \text{k\_dp} \cdot \text{fup\_LT} \cdot [\text{LTD4\_b}]$$
 (127)

## 7.14 Reaction v13

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

## Name v13

## **Reaction equation**

$$LTC4\_b\_out \xrightarrow{LTC4\_b\_out} \emptyset$$
 (128)

Table 33: Properties of each reactant.

Id	Name	SBO
LTC4_b_out	LTC4_b_out	

### **Modifier**

Table 34: Properties of each modifier.

Id	Name	SBO
LTC4_b_out	LTC4_b_out	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{14} = \text{vol}(\text{Vd\_LTC}) \cdot \text{k\_ltc\_ltd\_el} \cdot \text{fup\_LT} \cdot [\text{LTC4\_b\_out}]$$
 (129)

### 7.15 Reaction v14

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

### Name v14

## **Reaction equation**

$$LTD4\_b \xrightarrow{LTD4\_b} \emptyset$$
 (130)

### Reactant

Table 35: Properties of each reactant.

Id	Name	SBO
LTD4_b	LTD4_b	

#### **Modifier**

Table 36: Properties of each modifier.

Id	Name	SBO
LTD4_b	LTD4_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{15} = \text{vol}(\text{Vd\_LTD}) \cdot \text{k\_ltc\_ltd\_el} \cdot \text{fup\_LT} \cdot [\text{LTD4\_b}]$$
 (131)

### 7.16 Reaction v15

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v15

#### **Reaction equation**

$$LTE4\_b \xrightarrow{LTE4\_b} \emptyset \tag{132}$$

#### Reactant

Table 37: Properties of each reactant.

Id	Name	SBO
LTE4_b	LTE4_b	

#### **Modifier**

Table 38: Properties of each modifier.

Id	Name	SBO
LTE4_b	LTE4_b	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{16} = \text{vol}(Vd\_LTE) \cdot (k\_lte\_el + k\_acet) \cdot \text{fup\_LT} \cdot [LTE4\_b]$$
 (133)

## 7.17 Reaction v16

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v16

### **Reaction equation**

$$EO_{-b} \xrightarrow{EO_{-b}} EO_{-i-b}$$
 (134)

#### Reactant

Table 39: Properties of each reactant.

Id	Name	SBO
EO_b	EO_b	·

#### **Modifier**

Table 40: Properties of each modifier.

Id	Name	SBO
EO_b	EO_b	

#### **Product**

Table 41: Properties of each product.

Id	Name	SBO
EO_i_b	EO_i_b	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{17} = \text{ca} \cdot \text{vol}(V_{-B}) \cdot \frac{\text{ka} \cdot [\text{EO}\_b] \cdot \text{OL}\_b^{\text{h\_act}}}{\text{EC50\_act}^{\text{h\_act}} + \text{OL}\_b^{\text{h\_act}}}$$
(135)

### **7.18 Reaction v17**

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

## Name v17

## **Reaction equation**

$$EO\_i\_b \xrightarrow{EO\_i\_b} EO\_a\_b$$
 (136)

## Reactant

Table 42: Properties of each reactant.

Id	Name	SBO
EO_i_b	EO_i_b	

### **Modifier**

Table 43: Properties of each modifier.

Id	Name	SBO
EO_i_b	EO_i_b	

### **Product**

Table 44: Properties of each product.

Id	Name	SBO
E0_a_b	EO_a_b	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{18} = \text{ca} \cdot \text{vol}(V_B) \cdot \text{k\_EO\_m} \cdot [\text{EO\_i\_b}]$$
(137)

## 7.19 Reaction v18

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

#### Name v18

## **Reaction equation**

$$EO_{-}a_{-}b \xrightarrow{EO_{-}a_{-}b} EO_{-}b \tag{138}$$

Table 45: Properties of each reactant.

Id	Name	SBO
EO_a_b	EO_a_b	

### **Modifier**

Table 46: Properties of each modifier.

Id	Name	SBO
EO_a_b	EO_a_b	

## **Product**

Table 47: Properties of each product.

Id	Name	SBO
EO_b	EO_b	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{19} = \operatorname{ca} \cdot \operatorname{vol}(V_B) \cdot \operatorname{kia} \cdot [EO_a_b]$$
(139)

### 7.20 Reaction v19

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

## Name v19

## **Reaction equation**

$$EO_{-b} \xrightarrow{EO_{-b}} \emptyset$$
 (140)

Table 48: Properties of each reactant.

Id	Name	SBO
EO_b	EO_b	

#### Modifier

Table 49: Properties of each modifier.

Id	Name	SBO
EO_b	EO_b	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{20} = \text{vol}(V_B) \cdot k_EO_d \cdot [EO_b]$$
 (141)

### **7.21 Reaction** v20

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

### Name v20

### **Reaction equation**

$$EO_{-a-b} \xrightarrow{EO_{-a-b}} \emptyset$$
 (142)

## Reactant

Table 50: Properties of each reactant.

Id	Name	SBO
EO_a_b	EO_a_b	

#### **Modifier**

Table 51: Properties of each modifier.

Id	Name	SBO
EO_a_b	EO_a_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{21} = \text{vol}(V_B) \cdot k_EO_a \cdot [EO_a \cdot b]$$
(143)

### **7.22 Reaction v21**

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier

Name v21

## **Reaction equation**

$$EO\_i\_b \xrightarrow{EO\_i\_b} EO\_i\_aw$$
 (144)

#### Reactant

Table 52: Properties of each reactant.

Id	Name	SBO
EO_i_b	EO_i_b	

#### **Modifier**

Table 53: Properties of each modifier.

Id	Name	SBO
EO_i_b	EO_i_b	

#### **Product**

Table 54: Properties of each product.

Id	Name	SBO
EO_i_aw	EO_i_aw	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{22} = \text{vol}(V\_B) \cdot \frac{\text{k\_EO\_t\_baw} \cdot [\text{EO\_i\_b}] \cdot \text{Rec\_occup\_migr}^{\text{h\_migr}}}{\text{EC50\_migr}^{\text{h\_migr}} + \text{Rec\_occup\_migr}^{\text{h\_migr}}}$$
(145)

### 7.23 Reaction v22

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

### Name v22

## **Reaction equation**

$$EO_{-}a_{-}b \xrightarrow{EO_{-}a_{-}b} EO_{-}a_{-}aw$$
 (146)

### Reactant

Table 55: Properties of each reactant.

Id	Name	SBO
EO_a_b	EO_a_b	

### **Modifier**

Table 56: Properties of each modifier.

Id	Name	SBO
EO_a_b	EO_a_b	

### **Product**

Table 57: Properties of each product.

Id	Name	SBO
EO_a_aw	EO_a_aw	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{23} = \text{vol}(V_B) \cdot \frac{\text{k\_EO\_t\_baw} \cdot [\text{EO\_a\_b}] \cdot \text{Rec\_occup\_migr}^{\text{h\_migr}}}{\text{EC50\_migr}^{\text{h\_migr}} + \text{Rec\_occup\_migr}^{\text{h\_migr}}}$$
(147)

# **7.24 Reaction** v23

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v23

### **Reaction equation**

$$EO_-b \xrightarrow{EO_-b} EO_-aw$$
 (148)

#### Reactant

Table 58: Properties of each reactant.

Id	Name	SBO
EO_b	EO_b	·

#### **Modifier**

Table 59: Properties of each modifier.

Id	Name	SBO
EO_b	EO_b	

#### **Product**

Table 60: Properties of each product.

Id	Name	SBO
EO_aw	EO_aw	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{24} = \text{vol}(V_B) \cdot \frac{\text{k\_EO\_t\_baw} \cdot [\text{EO\_b}] \cdot \text{Rec\_occup\_migr}^{\text{h\_migr}}}{\text{EC50\_migr}^{\text{h\_migr}} + \text{Rec\_occup\_migr}^{\text{h\_migr}}}$$
(149)

## **7.25 Reaction** v24

This is a fast irreversible reaction of no reactant forming one product influenced by six modifiers.

#### Name v24

## **Reaction equation**

$$\emptyset \xrightarrow{\text{EO\_b}, \text{ EO\_i\_b}, \text{ EO\_a\_b}, \text{ EO\_b}, \text{ EO\_i\_b}, \text{ EO\_a\_b}} \text{Hn\_b}$$
 (150)

#### **Modifiers**

Table 61: Properties of each modifier.

Id	Name	SBO
EO_b	EO_b	
$EO_i_b$	EO_i_b	
$EO_a_b$	EO_a_b	
$E0_b$	$EO_b$	
$EO_i_b$	EO_i_b	
EO_a_b	EO_a_b	

### **Product**

Table 62: Properties of each product.

Id	Name	SBO
Hn_b	Hn_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{25} = \text{vol}(V_B) \cdot k_H n_p \cdot ([EO_b] + [EO_i_b] + [EO_a_b])$$
 (151)

## **7.26 Reaction** v25

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v25

## **Reaction equation**

$$\operatorname{Hn_b} \xrightarrow{\operatorname{Hn_b}} \emptyset$$
 (152)

Table 63: Properties of each reactant.

Id	Name	SBO
Hn_b	Hn_b	

#### **Modifier**

Table 64: Properties of each modifier.

Id	Name	SBO
Hn_b	Hn_b	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{26} = \text{vol}(Vd_{-}Hn) \cdot k_{-}Hn_{-}d \cdot \text{fup}_{-}Hn \cdot [Hn_{-}b]$$
(153)

### 7.27 Reaction v26

This is a fast irreversible reaction of no reactant forming one product influenced by two modifiers.

Name v26

## **Reaction equation**

$$\emptyset \xrightarrow{\text{EO\_a\_b}, \text{EO\_a\_b}} \text{IL\_b}$$
 (154)

#### **Modifiers**

Table 65: Properties of each modifier.

Id	Name	SBO
E0_a_b	EO_a_b	
$EO_a_b$	EO_a_b	

#### **Product**

Table 66: Properties of each product.

Id	Name	SBO
$IL_b$	IL_b	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{27} = \text{vol}(V_B) \cdot k_I L_p \cdot [EO_a_b]$$
(155)

#### **7.28 Reaction** v27

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v27

## **Reaction equation**

$$IL\_b \xrightarrow{IL\_b} \emptyset \tag{156}$$

#### Reactant

Table 67: Properties of each reactant.

Id	Name	SBO
$IL_b$	$IL_{-}b$	

### **Modifier**

Table 68: Properties of each modifier.

Id	Name	SBO
IL_b	$IL_b$	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{28} = \text{vol}(\text{Vd\_IL5}) \cdot \text{k\_IL\_d} \cdot [\text{IL\_b}]$$
 (157)

#### 7.29 Reaction v28

This is a fast irreversible reaction of one reactant forming one product influenced by two modifiers.

Name v28

## **Reaction equation**

$$IL_b \xrightarrow{IL_b, IL_bm} IL_bm$$
 (158)

Table 69: Properties of each reactant.

Id	Name	SBO
IL_b	IL_b	

### **Modifiers**

Table 70: Properties of each modifier.

Id	Name	SBO
IL_b	IL_b	
${\tt IL\_bm}$	$IL_bm$	

### **Product**

Table 71: Properties of each product.

Id	Name	SBO
IL_bm	$IL_{-}bm$	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{29} = \text{k\_IL\_t\_bbm} \cdot ([\text{IL\_b}] - [\text{IL\_bm}]) - \text{J\_BM\_lymfl} \cdot [\text{IL\_bm}]$$
 (159)

### 7.30 Reaction v29

This is a fast irreversible reaction of no reactant forming one product influenced by two modifiers.

Name v29

## **Reaction equation**

$$\emptyset \xrightarrow{\text{IL\_bm}, \text{IL\_bm}} \text{EO\_bm}$$
 (160)

## **Modifiers**

Table 72: Properties of each modifier.

Id	Name	SBO
	IL_bm IL_bm	
111_0m	IL_OIII	

Table 73: Properties of each product.

Id	Name	SBO
EO_bm	EO_bm	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{30} = \text{vol}\left(V\_BM\right) \cdot \left(\frac{k1 \cdot [IL\_bm]^{h\_matur}}{Km\_1^{h\_matur} + [IL\_bm]^{h\_matur}} + k1\_min\right)$$
(161)

## 7.31 Reaction v30

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v30

## **Reaction equation**

$$EO\_bm \xrightarrow{EO\_bm} EO\_b$$
 (162)

### Reactant

Table 74: Properties of each reactant.

Id	Name	SBO
EO_bm	EO_bm	

### **Modifier**

Table 75: Properties of each modifier.

Id	Name	SBO
EO_bm	EO_bm	

Table 76: Properties of each product.

Id	Name	SBO
EO_b	EO_b	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{31} = \text{ca} \cdot \text{vol} (V\_BM) \cdot \text{k\_EO\_t\_bmb} \cdot [EO\_bm]$$
 (163)

### 7.32 Reaction v31

This is a fast irreversible reaction of no reactant forming one product influenced by one modifier.

### Name v31

## **Reaction equation**

$$\emptyset \xrightarrow{AA\_aw} AA\_aw \tag{164}$$

### **Modifier**

Table 77: Properties of each modifier.

Id	Name	SBO
AA_aw	$AA_{aw}$	

#### **Product**

Table 78: Properties of each product.

Id	Name	SBO
AA_aw	$AA_{-}aw$	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{32} = \text{vol}\left(\text{Default}\right) \cdot \left(\frac{\text{Vmax\_PLA2} \cdot \text{PLA2\_Ca} \cdot \text{PL}}{\text{Km\_PLA2\_APC} + \text{PL}} - \frac{\text{V\_CoA} \cdot [\text{AA\_aw}]}{\text{Km\_CoA\_AA} + [\text{AA\_aw}]}\right) \quad (165)$$

### 7.33 Reaction v32

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v32

#### **Reaction equation**

$$AA_{aw} \xrightarrow{AA_{aw}} \emptyset$$
 (166)

#### Reactant

Table 79: Properties of each reactant.

Id	Name	SBO
$AA_aw$	AA_aw	

#### **Modifier**

Table 80: Properties of each modifier.

Id	Name	SBO
AA_aw	AA_aw	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{33} = vol\left(Default\right) \cdot \frac{k \cdot lo \cdot [AA\_aw] \cdot FLO3t\_aw}{K\_AA}$$
(167)

#### 7.34 Reaction v33

This is a fast irreversible reaction of no reactant forming one product influenced by three modifiers.

Name v33

### **Reaction equation**

$$\emptyset \xrightarrow{AA\_aw, HPETE\_aw, AA\_aw} HPETE\_aw$$
 (168)

#### **Modifiers**

Table 81: Properties of each modifier.

Id	Name	SBO
AA_aw	AA_aw	
$ ext{HPETE\_aw}$	HPETE_aw	
$\mathtt{AA}_{-}\mathtt{aw}$	$AA_{-}aw$	

#### **Product**

Table 82: Properties of each product.

Id	Name	SBO
HPETE_aw	HPETE_aw	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{34} = \text{vol}\left(\text{Default}\right) \cdot \left(\text{k\_3} \cdot \text{FLO5HP\_aw} - \text{k3} \cdot \text{FLO3t\_aw} \cdot \left[\text{HPETE\_aw}\right]\right) \cdot \left(1.0 + \frac{[\text{AA\_aw}]}{\text{Ki\_AA}}\right)$$
(169)

#### 7.35 Reaction v34

This is a fast irreversible reaction of one reactant forming one product influenced by two modifiers.

Name v34

### **Reaction equation**

$$HPETE\_aw \xrightarrow{HPETE\_aw, HETE\_aw} HETE\_aw$$
 (170)

Table 83: Properties of each reactant.

Id	Name	SBO
HPETE_aw	HPETE_aw	

### **Modifiers**

Table 84: Properties of each modifier.

Id	Name	SBO
HPETE_aw HETE aw	HPETE_aw HETE aw	

#### **Product**

Table 85: Properties of each product.

Id	Name	SBO
HETE_aw	HETE_aw	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{35} = vol(Default) \cdot r1 \cdot \left( [HPETE\_aw] \cdot FLO2\_aw - \frac{[HETE\_aw] \cdot FLO3\_aw}{Ke\_ox} \right) \quad (171)$$

### 7.36 Reaction v35

This is a fast irreversible reaction of one reactant forming one product.

Name v35

### **Reaction equation**

$$HPETE_aw \longrightarrow HETE_aw$$
 (172)

Table 86: Properties of each reactant.

Id	Name	SBO
HPETE_aw	HPETE_aw	

Table 87: Properties of each product.

Id	Name	SBO
HETE_aw	HETE_aw	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{36} = \text{vol}\left(\text{Default}\right) \cdot \frac{\text{GPx} \cdot \text{B\_aw}}{\text{A\_aw}}$$
 (173)

### 7.37 Reaction v36

This is a fast irreversible reaction of no reactant forming one product.

Name v36

## **Reaction equation**

$$\emptyset \longrightarrow LTA4_aw$$
 (174)

#### **Product**

Table 88: Properties of each product.

Id	Name	SBO
LTA4_aw	LTA4_aw	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{37} = \text{vol}(\text{Default}) \cdot \text{k\_lta\_syn} \cdot \text{FLO5HP\_aw}$$
 (175)

### 7.38 Reaction v37

This is a fast irreversible reaction of one reactant forming one product.

Name v37

## **Reaction equation**

$$LTA4_aw \longrightarrow LTC4_aw$$
 (176)

### Reactant

Table 89: Properties of each reactant.

Id	Name	SBO
LTA4_aw	LTA4_aw	

### **Product**

Table 90: Properties of each product.

Id	Name	SBO
LTC4_aw	LTC4_aw	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{38} = \text{vol}\left(\text{Default}\right) \cdot \frac{\text{nom\_LTCs\_aw}}{\text{den\_LTCs\_aw}}$$
 (177)

## 7.39 Reaction v38

This is a fast irreversible reaction of one reactant forming no product.

Name v38

## **Reaction equation**

$$HETE_aw \longrightarrow \emptyset$$
 (178)

Table 91: Properties of each reactant.

Id	Name	SBO
HETE_aw	HETE_aw	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{39} = \text{vol}\left(\text{Default}\right) \cdot \frac{\text{HEDH5} \cdot \text{B\_hedh\_aw}}{\text{A\_hedh\_aw}}$$
 (179)

### 7.40 Reaction v39

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v39

## **Reaction equation**

$$LTA4\_aw \xrightarrow{LTA4\_aw} \emptyset$$
 (180)

#### Reactant

Table 92: Properties of each reactant.

Id	Name	SBO
LTA4_aw	LTA4_aw	

### **Modifier**

Table 93: Properties of each modifier.

Id	Name	SBO
LTA4_aw	LTA4_aw	

### **Kinetic Law**

Derived unit contains undeclared units

$$v_{40} = vol(Default) \cdot Kd12 \cdot [LTA4\_aw]$$
 (181)

### 7.41 Reaction v40in

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v40in

## **Reaction equation**

$$LTC4_aw \xrightarrow{LTC4_aw} \emptyset$$
 (182)

#### Reactant

Table 94: Properties of each reactant.

Id	Name	SBO
LTC4_aw	LTC4_aw	

#### **Modifier**

Table 95: Properties of each modifier.

Id	Name	SBO
LTC4_aw	LTC4_aw	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{41} = \text{vol}(\text{Default}) \cdot \text{Kd50} \cdot [\text{LTC4\_aw}]$$
 (183)

#### 7.42 Reaction v40out

This is a fast irreversible reaction of no reactant forming one product influenced by two modifiers.

Name v40out

### **Reaction equation**

$$\emptyset \xrightarrow{LTC4\_aw, LTC4\_aw} LTC4\_aw\_out$$
 (184)

#### **Modifiers**

Table 96: Properties of each modifier.

Id	Name	SBO
LTC4_aw	LTC4_aw	
${\tt LTC4\_aw}$	LTC4_aw	

Table 97: Properties of each product.

Id	Name	SBO
LTC4_aw_out	LTC4_aw_out	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{42} = \text{vol}\left(\text{Default}\right) \cdot \text{Kd50} \cdot \left[\text{LTC4\_aw}\right] \cdot \text{V\_LTC\_CAW} \cdot 10.0^{6.0}$$
(185)

## 7.43 Reaction v41

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

### Name v41

# **Reaction equation**

$$LTC4\_aw\_out \xrightarrow{LTC4\_aw\_out} LTD4\_aw$$
 (186)

## Reactant

Table 98: Properties of each reactant.

Id	Name	SBO
LTC4_aw_out	LTC4_aw_out	

### **Modifier**

Table 99: Properties of each modifier.

Id	Name	SBO
LTC4_aw_out	LTC4_aw_out	

Table 100: Properties of each product.

Id	Name	SBO
LTD4_aw	LTD4_aw	

## **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{43} = \text{vol}(\text{Vd\_AW\_LTC}) \cdot \text{k\_ggt} \cdot [\text{LTC4\_aw\_out}]$$
 (187)

### 7.44 Reaction v42

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v42

## **Reaction equation**

$$LTD4_aw \xrightarrow{LTD4_aw} LTE4_aw$$
 (188)

#### Reactant

Table 101: Properties of each reactant.

Id	Name	SBO
LTD4_aw	LTD4_aw	

#### **Modifier**

Table 102: Properties of each modifier.

Id	Name	SBO
LTD4_aw	LTD4_aw	

Table 103: Properties of each product.

Id	Name	SBO
LTE4_aw	LTE4_aw	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{44} = \text{vol}(\text{Vd}_{-}\text{AW}_{-}\text{LTD}) \cdot \text{k}_{-}\text{dp} \cdot [\text{LTD4}_{-}\text{aw}]$$
 (189)

### 7.45 Reaction v43

This is a fast irreversible reaction of one reactant forming one product influenced by two modifiers.

Name v43

## **Reaction equation**

$$LTE4\_aw \xrightarrow{LTE4\_aw, LTE4\_b} LTE4\_b$$
 (190)

### Reactant

Table 104: Properties of each reactant.

Id	Name	SBO
LTE4_aw	LTE4_aw	

## **Modifiers**

Table 105: Properties of each modifier.

Id	Name	SBO
LTE4_aw	LTE4_aw	
$LTE4_b$	LTE4_b	

Table 106: Properties of each product.

Id	Name	SBO
LTE4_b	LTE4_b	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{45} = Q\_AW\_blf \cdot R\_LTE\_B \cdot \left(\frac{[LTE4\_aw] \cdot R\_LTE\_AW}{Kp\_LTE\_AW} - [LTE4\_b]\right)$$
(191)

## 7.46 Reaction v44

This is a fast irreversible reaction of one reactant forming one product influenced by two modifiers.

Name v44

## **Reaction equation**

$$LTD4\_aw \xrightarrow{LTD4\_aw, LTD4\_b} LTD4\_b$$
 (192)

#### Reactant

Table 107: Properties of each reactant.

Id	Name	SBO
LTD4_aw	LTD4_aw	

### **Modifiers**

Table 108: Properties of each modifier.

Id	Name	SBO
LTD4_aw	LTD4_aw	
$LTD4_b$	LTD4_b	

Table 109: Properties of each product.

Id	Name	SBO
LTD4_b	LTD4_b	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{46} = Q\_AW\_blf \cdot R\_LTD\_B \cdot \left(\frac{[LTD4\_aw] \cdot R\_LTD\_AW}{Kp\_LTD\_AW} - [LTD4\_b]\right)$$
(193)

# **7.47 Reaction** v45

This is a fast irreversible reaction of one reactant forming one product influenced by two modi-

Name v45

# **Reaction equation**

$$LTC4\_aw\_out \xrightarrow{LTC4\_aw\_out, LTC4\_b\_out} LTC4\_b\_out$$
 (194)

#### Reactant

Table 110: Properties of each reactant.

Id	Name	SBO
LTC4_aw_out	LTC4_aw_out	

Table 111: Properties of each modifier.

Id	Name SBO	
LTC4_aw_out LTC4_b_out	LTC4_aw_out LTC4_b_out	

Table 112: Properties of each product.

Id	Name	SBO
LTC4_b_out	LTC4_b_out	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{47} = Q\_AW\_blf \cdot R\_LTC\_B \cdot \left(\frac{[LTC4\_aw\_out] \cdot R\_LTC\_AW}{Kp\_LTC\_AW} - [LTC4\_b\_out]\right) \quad (195)$$

# **7.48 Reaction** v46

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier

Name v46

# **Reaction equation**

$$EO\_aw \xrightarrow{EO\_aw} EO\_i\_aw$$
 (196)

# Reactant

Table 113: Properties of each reactant.

Id	Name	SBO
EO_aw	EO_aw	

Table 114: Properties of each modifier.

Id	Name	SBO
EO_aw	EO_aw	

Table 115: Properties of each product.

Id	Name	SBO
EO_i_aw	EO_i_aw	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{48} = ca \cdot vol(V_AW) \cdot \frac{ka \cdot [EO_aw] \cdot OL_aw^{h_act}}{EC50_act^{h_act} + OL_aw^{h_act}}$$
(197)

# 7.49 Reaction v47

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v47

# **Reaction equation**

$$EO\_i\_aw \xrightarrow{EO\_i\_aw} EO\_a\_aw$$
 (198)

#### Reactant

Table 116: Properties of each reactant.

Id	Name	SBO
EO_i_aw	EO_i_aw	

Table 117: Properties of each modifier.

Id	Name	SBO
EO_i_aw	EO_i_aw	

Table 118: Properties of each product.

Id	Name	SBO
EO_a_aw	EO_a_aw	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{49} = ca \cdot vol(V_AW) \cdot k_EO_m \cdot [EO_i_aw]$$
 (199)

# 7.50 Reaction v48

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v48

# **Reaction equation**

$$EO_aaw \xrightarrow{EO_aaw} EO_aw$$
 (200)

#### Reactant

Table 119: Properties of each reactant.

Id	Name	SBO
EO_a_aw	EO_a_aw	

Table 120: Properties of each modifier.

Id	Name	SBO
EO_a_aw	EO_a_aw	

Table 121: Properties of each product.

Id	Name	SBO
EO_aw	EO_aw	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{50} = \text{ca} \cdot \text{vol}(V_{-}AW) \cdot \text{kia} \cdot [\text{EO}_{-}a_{-}aw]$$
 (201)

# **7.51 Reaction** v49

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v49

# **Reaction equation**

$$EO_{-}aw \xrightarrow{EO_{-}aw} \emptyset$$
 (202)

# Reactant

Table 122: Properties of each reactant.

Id	Name	SBO
EO_aw	EO_aw	

Table 123: Properties of each modifier.

Id	Name	SBO
EO_aw	EO_aw	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{51} = \text{vol}(V_AW) \cdot k_EO_d \cdot [EO_aw]$$
 (203)

# 7.52 Reaction v50

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v50

### **Reaction equation**

$$EO_{-a-aw} \xrightarrow{EO_{-a-aw}} \emptyset$$
 (204)

#### Reactant

Table 124: Properties of each reactant.

Id	Name	SBO
EO_a_aw	EO_a_aw	

#### **Modifier**

Table 125: Properties of each modifier.

Id	Name	SBO
EO_a_aw	EO_a_aw	

# **Kinetic Law**

Derived unit contains undeclared units

$$v_{52} = \text{vol}(V_AW) \cdot k_EO_a_d \cdot [EO_a_aw]$$
 (205)

# 7.53 Reaction v51

This is a fast irreversible reaction of no reactant forming one product influenced by six modifiers.

Name v51

# **Reaction equation**

$$\emptyset \xrightarrow{EO\_a\_aw, EO\_i\_aw, EO\_aw, EO\_a\_aw, EO\_i\_aw, EO\_aw} Hn\_aw$$
 (206)

#### **Modifiers**

Table 126: Properties of each modifier.

Id	Name	SBO
EO_a_aw	EO_a_aw	
${\tt EO\_i\_aw}$	$EO_{-i}$ aw	
$EO_aw$	EO_aw	
$EO_a_a$	$EO_aaw$	
$EO_{i_aw}$	EO_i_aw	
${\tt EO\_aw}$	EO_aw	

# **Product**

Table 127: Properties of each product.

Id	Name	SBO
Hn_aw	$Hn_{-}aw$	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{53} = \text{vol}(V_AW) \cdot k_Hn_p \cdot ([EO_a_aw] + [EO_i_aw] + [EO_aw])$$
 (207)

# 7.54 Reaction v52

This is a fast irreversible reaction of one reactant forming one product influenced by two modifiers.

Name v52

# **Reaction equation**

$$Hn_aw \xrightarrow{Hn_aw, Hn_b} Hn_b$$
 (208)

### Reactant

Table 128: Properties of each reactant.

Id	Name	SBO
Hn_aw	Hn_aw	

# **Modifiers**

Table 129: Properties of each modifier.

Id	Name	SBO
Hn_aw	Hn_aw	
${\tt Hn\_b}$	$Hn_b$	

# **Product**

Table 130: Properties of each product.

Id	Name	SBO
Hn_b	Hn_b	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{54} = Q\_AW\_blf \cdot R\_Hn\_B \cdot \left(\frac{[Hn\_aw] \cdot R\_Hn\_AW}{Kp\_Hn\_AW} - [Hn\_b]\right)$$
(209)

# 7.55 Reaction v53

This is a fast irreversible reaction of no reactant forming one product influenced by two modifiers.

Name v53

# **Reaction equation**

$$\emptyset \xrightarrow{\text{EO\_a\_aw}, \text{EO\_a\_aw}} \text{IL\_aw}$$
 (210)

Table 131: Properties of each modifier.

Id	Name	SBO
	EO_a_aw	
EU_a_aw	EO <sub>-</sub> a_aw	

Table 132: Properties of each product.

Id	Name	SBO
IL_aw	IL_aw	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{55} = \text{vol}(V_AW) \cdot k_IL_p \cdot [EO_a_aw]$$
 (211)

# 7.56 Reaction v54

This is a fast irreversible reaction of one reactant forming one product influenced by two modifiers.

Name v54

# **Reaction equation**

$$IL_aw \xrightarrow{IL_aw, IL_b} IL_b$$
 (212)

# Reactant

Table 133: Properties of each reactant.

Id	Name	SBO
IL_aw	IL_aw	

Table 134: Properties of each modifier.

Id	Name	SBO
IL_aw	122_00	
IL_b	IL_b	

Table 135: Properties of each product.

Id	Name	SBO
IL_b	IL_b	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{56} = k_{\text{L}}\text{IL\_t\_awb} \cdot ([\text{IL\_aw}] - [\text{IL\_b}]) + J_{\text{A}}\text{W\_lymfl} \cdot [\text{IL\_aw}]$$
 (213)

# 7.57 Reaction v55

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v55

# **Reaction equation**

$$LTE4_aw \xrightarrow{LTE4_aw} \emptyset$$
 (214)

#### Reactant

Table 136: Properties of each reactant.

Id	Name	SBO
LTE4_aw	LTE4_aw	

Table 137: Properties of each modifier.

Id	Name	SBO
LTE4_aw	LTE4_aw	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{57} = \text{vol}(\text{Vd\_AW\_LTE}) \cdot (\text{k\_lte\_el} + \text{k\_acet}) \cdot [\text{LTE4\_aw}]$$
 (215)

#### 7.58 Reaction v56

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v56

# **Reaction equation**

$$LTD4\_aw \xrightarrow{LTD4\_aw} \emptyset$$
 (216)

#### Reactant

Table 138: Properties of each reactant.

Id	Name	SBO
LTD4_aw	LTD4_aw	

# **Modifier**

Table 139: Properties of each modifier.

Id	Name	SBO
LTD4_aw	LTD4_aw	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{58} = \text{vol}(Vd\_AW\_LTD) \cdot k\_ltc\_ltd\_el \cdot [LTD4\_aw]$$
 (217)

# **7.59 Reaction v57**

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v57

# **Reaction equation**

$$LTC4\_aw\_out \xrightarrow{LTC4\_aw\_out} \emptyset$$
 (218)

#### Reactant

Table 140: Properties of each reactant.

Id	Name	SBO
LTC4_aw_out	LTC4_aw_out	

#### **Modifier**

Table 141: Properties of each modifier.

Id	Name	SBO
LTC4_aw_out	LTC4_aw_out	

#### **Kinetic Law**

Derived unit contains undeclared units

$$v_{59} = \text{vol}(\text{Vd\_AW\_LTC}) \cdot \text{k\_ltc\_ltd\_el} \cdot [\text{LTC4\_aw\_out}]$$
 (219)

#### 7.60 Reaction v58

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v58

# **Reaction equation**

$$IL_{aw} \xrightarrow{IL_{aw}} \emptyset$$
 (220)

# Reactant

Table 142: Properties of each reactant.

Id	Name	SBO
IL_aw	IL_aw	

# **Modifier**

Table 143: Properties of each modifier.

Id	Name	SBO
IL_aw	IL_aw	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{60} = \text{vol}(V_AW) \cdot k_IL_d \cdot [IL_aw]$$
 (221)

# **7.61 Reaction** v59

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v59

# **Reaction equation**

$$\operatorname{Hn\_aw} \xrightarrow{\operatorname{Hn\_aw}} \emptyset$$
 (222)

# Reactant

Table 144: Properties of each reactant.

Id	Name	SBO
Hn_aw	Hn_aw	

Table 145: Properties of each modifier.

Id	Name	SBO
Hn_aw	Hn_aw	

# **Kinetic Law**

Derived unit contains undeclared units

$$v_{61} = \text{vol}(Vd\_AW\_Hn) \cdot k\_Hn\_d \cdot [Hn\_aw]$$
 (223)

# 7.62 Reaction v60

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v60

# **Reaction equation**

$$ZF\_intes \xrightarrow{ZF\_intes} ZF\_blood$$
 (224)

#### Reactant

Table 146: Properties of each reactant.

Id	Name	SBO
${\tt ZF\_intes}$	ZF_intes	

#### **Modifier**

Table 147: Properties of each modifier.

Id	Name	SBO
${\sf ZF\_intes}$	ZF_intes	

#### **Product**

Table 148: Properties of each product.

Id	Name	SBO
ZF_blood	ZF_blood	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$\begin{aligned} \nu_{62} &= vol\left(Default\right) \cdot k\_abs\_zf \\ &\cdot \left( \left[ ZF\_intes \right] + \frac{oral \cdot F\_zf \cdot \left( a \cdot ft\_zf + \left( 1.0 - a \right) \right) \cdot DOSE\_zf \cdot 1000.0}{M\_ZF} \right) \end{aligned}$$

# 7.63 Reaction v61

This is a fast irreversible reaction of one reactant forming one product influenced by two modifiers.

Name v61

# **Reaction equation**

$$ZF\_blood \xrightarrow{ZF\_blood, ZF\_airways} ZF\_airways$$
 (226)

#### Reactant

Table 149: Properties of each reactant.

Id	Name	SBO
ZF_blood	ZF_blood	

#### **Modifiers**

Table 150: Properties of each modifier.

Id	Name	SBO
ZF_blood	ZF_blood	
${\sf ZF\_airways}$	ZF_airways	

#### **Product**

Table 151: Properties of each product.

Id	Name	SBO
ZF_airways	ZF_airways	

# **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{63} = Q\_AW\_blf \cdot R\_ZF\_B \cdot \left( [ZF\_blood] - \frac{[ZF\_airways] \cdot R\_ZF\_AW}{Kp\_ZF\_AW} \right)$$
(227)

# 7.64 Reaction v62

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

Name v62

#### **Reaction equation**

$$ZF\_blood \xrightarrow{ZF\_blood} \emptyset$$
 (228)

#### Reactant

Table 152: Properties of each reactant.

Id	Name	SBO
ZF_blood	ZF_blood	

#### **Modifier**

Table 153: Properties of each modifier.

Id	Name	SBO
ZF_blood	ZF_blood	

### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{64} = \text{vol}(\text{Vd.ZF}) \cdot \text{k\_elim\_zf} \cdot [\text{ZF\_blood}]$$
 (229)

#### **7.65 Reaction** v63

This is a fast irreversible reaction of one reactant forming one product influenced by one modifier.

Name v63

#### **Reaction equation**

$$ML\_intes \xrightarrow{ML\_intes} ML\_blood$$
 (230)

# Reactant

Table 154: Properties of each reactant.

Id	Name	SBO
$\mathtt{ML}_{\mathtt{intes}}$	ML_intes	

#### **Modifier**

Table 155: Properties of each modifier.

Id	Name	SBO
$\mathtt{ML\_intes}$	ML_intes	

# **Product**

Table 156: Properties of each product.

Id	Name	SBO
$ML_blood$	ML_blood	

# **Kinetic Law**

Derived unit contains undeclared units

$$\begin{aligned} \nu_{65} &= vol\left(Default\right) \cdot k\_abs\_ml \\ &\cdot \left(\left[ML\_intes\right] + \frac{oral \cdot F\_ml \cdot \left(a \cdot ft\_ml + (1.0 - a)\right) \cdot DOSE\_ml \cdot 1.0E9}{M\_ML} \right) \end{aligned}$$

# 7.66 Reaction v64

This is a fast irreversible reaction of one reactant forming no product influenced by one modifier.

#### Name v64

# **Reaction equation**

$$ML\_blood \xrightarrow{ML\_blood} \emptyset$$
 (232)

# Reactant

Table 157: Properties of each reactant.

Id	Name	SBO
ML_blood	ML_blood	

#### **Modifier**

Table 158: Properties of each modifier.

Id	Name	SBO
ML_blood	ML_blood	

#### **Kinetic Law**

**Derived unit** contains undeclared units

$$v_{66} = \text{vol}(Vd\_ML) \cdot k\_elim\_ml \cdot [ML\_blood]$$
 (233)

# 8 Derived Rate Equations

When interpreted as an ordinary differential equation framework, this model implies the following set of equations for the rates of change of each species.

Identifiers for kinetic laws highlighted in gray cannot be verified to evaluate to units of SBML substance per time. As a result, some SBML interpreters may not be able to verify the consistency of the units on quantities in the model. Please check if

- parameters without an unit definition are involved or
- volume correction is necessary because the hasOnlySubstanceUnits flag may be set to false and spacialDimensions > 0 for certain species.

# 8.1 Species AA\_b

#### Name AA\_b

Initial concentration  $0.2890944 \text{ mol} \cdot 1^{-1}$ 

This species takes part in six reactions (as a reactant in v2 and as a product in v1 and as a modifier in v1, v2, v3, v3).

$$\frac{\mathrm{d}}{\mathrm{d}t} A A b = |v_1| - |v_2| \tag{234}$$

# 8.2 Species HPETE\_b

Name HPETE\_b

Initial concentration  $0.2965837 \text{ mol} \cdot l^{-1}$ 

This species takes part in five reactions (as a reactant in v4, v5 and as a product in v3 and as a modifier in v3, v4).

$$\frac{\mathrm{d}}{\mathrm{d}t} \mathrm{HPETE}_{b} = |v_3| - |v_4| - |v_5| \tag{235}$$

# 8.3 Species HETE\_b

Name HETE\_b

Initial concentration  $5.037703 \text{ mol} \cdot l^{-1}$ 

This species takes part in four reactions (as a reactant in v8 and as a product in v4, v5 and as a modifier in v4).

$$\frac{d}{dt}HETE_b = |v_4| + |v_5| - |v_8|$$
 (236)

# 8.4 Species LTA4\_b

Name LTA4\_b

Initial concentration  $1.081167 \text{ mol} \cdot l^{-1}$ 

This species takes part in four reactions (as a reactant in v7, v9 and as a product in v6 and as a modifier in v9).

$$\frac{d}{dt}LTA4_b = v_6 - v_7 - v_9 \tag{237}$$

# 8.5 Species LTC4\_b

Name LTC4\_b

Initial concentration  $0.8869873 \text{ mol} \cdot l^{-1}$ 

This species takes part in five reactions (as a reactant in v10in and as a product in v7 and as a modifier in v10in, v10out, v10out).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{LTC4\_b} = |v_7| - |v_{10}| \tag{238}$$

# 8.6 Species LTC4\_b\_out

Name LTC4\_b\_out

SBO:0000290 physical compartment

Initial concentration  $2168.571 \text{ mol} \cdot 1^{-1}$ 

This species takes part in seven reactions (as a reactant in v11, v13 and as a product in v10out, v45 and as a modifier in v11, v13, v45).

$$\frac{d}{dt}LTC4_b_out = |v_{11}| + |v_{47}| - |v_{12}| - |v_{14}|$$
(239)

# 8.7 Species LTD4\_b

Name LTD4\_b

Initial concentration 1308.488 mol·1<sup>-1</sup>

This species takes part in seven reactions (as a reactant in v12, v14 and as a product in v11, v44 and as a modifier in v12, v14, v44).

$$\frac{d}{dt}LTD4_b = v_{12} + v_{46} - v_{13} - v_{15}$$
 (240)

# 8.8 Species LTE4\_b

Name LTE4\_b

Initial concentration 2053.137 mol·l<sup>-1</sup>

This species takes part in five reactions (as a reactant in v15 and as a product in v12, v43 and as a modifier in v15, v43).

$$\frac{d}{dt}LTE4_b = |v_{13}| + |v_{45}| - |v_{16}|$$
(241)

#### 8.9 Species EO\_b

Name EO<sub>-b</sub>

Initial concentration  $4.68114 \cdot 10^{-7} \text{ mol} \cdot l^{-1}$ 

This species takes part in ten reactions (as a reactant in v16, v19, v23 and as a product in v18, v30 and as a modifier in v16, v19, v23, v24, v24).

$$\frac{d}{dt}EO_{-}b = |v_{19}| + |v_{31}| - |v_{17}| - |v_{20}| - |v_{24}|$$
(242)

# 8.10 Species E0\_i\_b

Name EO\_i\_b

Initial concentration  $5.479176 \cdot 10^{-8} \text{ mol} \cdot 1^{-1}$ 

This species takes part in seven reactions (as a reactant in v17, v21 and as a product in v16 and as a modifier in v17, v21, v24, v24).

$$\frac{d}{dt}EO_{i}b = v_{17} - v_{18} - v_{22}$$
 (243)

# 8.11 Species E0\_a\_b

Name EO\_a\_b

Initial concentration  $5.383185 \cdot 10^{-4} \text{ mol} \cdot 1^{-1}$ 

This species takes part in eleven reactions (as a reactant in v18, v20, v22 and as a product in v17 and as a modifier in v18, v20, v22, v24, v24, v26, v26).

$$\frac{d}{dt}EO_a_b = |v_{18}| - |v_{19}| - |v_{21}| - |v_{23}|$$
 (244)

# 8.12 Species EO\_i\_aw

Name EO\_i\_aw

Initial concentration  $1.358698 \cdot 10^{-7} \text{ mol} \cdot 1^{-1}$ 

This species takes part in six reactions (as a reactant in v47 and as a product in v21, v46 and as a modifier in v47, v51, v51).

$$\frac{d}{dt}EO_{i}aw = v_{22} + v_{48} - v_{49}$$
 (245)

# 8.13 Species EO\_a\_aw

Name EO\_a\_aw

Initial concentration  $0.001358713 \text{ mol} \cdot 1^{-1}$ 

This species takes part in ten reactions (as a reactant in v48, v50 and as a product in v22, v47 and as a modifier in v48, v50, v51, v51, v53, v53).

$$\frac{d}{dt}EO_{-}a_{-}aw = v_{23} + v_{49} - v_{50} - v_{52}$$
 (246)

# 8.14 Species E0\_aw

Name EO\_aw

Initial concentration  $1.176558 \cdot 10^{-6} \text{ mol} \cdot 1^{-1}$ 

This species takes part in eight reactions (as a reactant in v46, v49 and as a product in v23, v48 and as a modifier in v46, v49, v51, v51).

$$\frac{d}{dt}EO_{aw} = |v_{24}| + |v_{50}| - |v_{48}| - |v_{51}|$$
(247)

### 8.15 Species Hn\_b

Name Hn\_b

Initial concentration 14995.88 mol·l<sup>-1</sup>

This species takes part in five reactions (as a reactant in v25 and as a product in v24, v52 and as a modifier in v25, v52).

$$\frac{\mathrm{d}}{\mathrm{d}t} \mathrm{Hn}_{-} b = |v_{25}| + |v_{54}| - |v_{26}| \tag{248}$$

# 8.16 Species IL\_b

Name IL\_b

Initial concentration  $0.5994857 \text{ mol} \cdot 1^{-1}$ 

This species takes part in seven reactions (as a reactant in v27, v28 and as a product in v26, v54 and as a modifier in v27, v28, v54).

$$\frac{\mathrm{d}}{\mathrm{d}t} \text{IL.b} = |v_{27}| + |v_{56}| - |v_{28}| - |v_{29}| \tag{249}$$

# 8.17 Species IL\_bm

Name IL\_bm

Initial concentration  $0.4023394 \text{ mol} \cdot 1^{-1}$ 

This species takes part in four reactions (as a product in v28 and as a modifier in v28, v29, v29).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{IL}_{-}\mathrm{bm} = v_{29} \tag{250}$$

# 8.18 Species EO\_bm

Name EO\_bm

Initial concentration  $1.637391 \cdot 10^{-6} \text{ mol} \cdot l^{-1}$ 

This species takes part in three reactions (as a reactant in v30 and as a product in v29 and as a modifier in v30).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{EO\_bm} = |v_{30}| - |v_{31}| \tag{251}$$

# 8.19 Species AA\_aw

Name AA\_aw

Initial concentration  $0.1304887 \text{ mol} \cdot l^{-1}$ 

This species takes part in six reactions (as a reactant in v32 and as a product in v31 and as a modifier in v31, v32, v33, v33).

$$\frac{d}{dt}AA_aw = |v_{32}| - |v_{33}|$$
 (252)

# 8.20 Species HPETE\_aw

Name HPETE\_aw

Initial concentration  $1.780604 \text{ mol} \cdot l^{-1}$ 

This species takes part in five reactions (as a reactant in v34, v35 and as a product in v33 and as a modifier in v33, v34).

$$\frac{d}{dt}HPETE_aw = v_{34} - v_{35} - v_{36}$$
 (253)

# 8.21 Species HETE\_aw

Name HETE\_aw

Initial concentration 1.960926 mol·1<sup>-1</sup>

This species takes part in four reactions (as a reactant in v38 and as a product in v34, v35 and as a modifier in v34).

$$\frac{d}{dt}HETE_aw = v_{35} + v_{36} - v_{39}$$
 (254)

# 8.22 Species LTA4\_aw

Name LTA4\_aw

Initial concentration  $41.69257 \text{ mol} \cdot l^{-1}$ 

This species takes part in four reactions (as a reactant in v37, v39 and as a product in v36 and as a modifier in v39).

$$\frac{d}{dt}LTA4_aw = |v_{37}| - |v_{38}| - |v_{40}|$$
 (255)

# 8.23 Species LTC4\_aw

Name LTC4\_aw

Initial concentration  $6.806687 \text{ mol} \cdot l^{-1}$ 

This species takes part in five reactions (as a reactant in v40in and as a product in v37 and as a modifier in v40in, v40out, v40out).

$$\frac{d}{dt}LTC4_aw = |v_{38}| - |v_{41}| \tag{256}$$

# 8.24 Species LTC4\_aw\_out

Name LTC4\_aw\_out

Initial concentration  $359.9744 \text{ mol} \cdot l^{-1}$ 

This species takes part in seven reactions (as a reactant in v41, v45, v57 and as a product in v40out and as a modifier in v41, v45, v57).

$$\frac{d}{dt}LTC4_aw_out = |v_{42}| - |v_{43}| - |v_{47}| - |v_{59}|$$
(257)

# 8.25 Species LTD4\_aw

Name LTD4\_aw

Initial concentration  $205.7602 \text{ mol} \cdot l^{-1}$ 

This species takes part in seven reactions (as a reactant in v42, v44, v56 and as a product in v41 and as a modifier in v42, v44, v56).

$$\frac{d}{dt}LTD4_aw = |v_{43}| - |v_{44}| - |v_{46}| - |v_{58}|$$
 (258)

# 8.26 Species LTE4\_aw

Name LTE4\_aw

Initial concentration  $322.6366 \text{ mol} \cdot l^{-1}$ 

This species takes part in five reactions (as a reactant in v43, v55 and as a product in v42 and as a modifier in v43, v55).

$$\frac{d}{dt}LTE4_aw = |v_{44}| - |v_{45}| - |v_{57}|$$
 (259)

# 8.27 Species Hn\_aw

Name Hn\_aw

Initial concentration  $14162.15 \text{ mol} \cdot l^{-1}$ 

This species takes part in five reactions (as a reactant in v52, v59 and as a product in v51 and as a modifier in v52, v59).

$$\frac{d}{dt} Hn_a w = |v_{53}| - |v_{54}| - |v_{61}|$$
 (260)

# 8.28 Species IL\_aw

Name IL\_aw

Initial concentration  $0.6627439 \text{ mol} \cdot 1^{-1}$ 

This species takes part in five reactions (as a reactant in v54, v58 and as a product in v53 and as a modifier in v54, v58).

$$\frac{d}{dt}IL_aw = v_{55} - v_{56} - v_{60}$$
 (261)

# 8.29 Species ZF\_intes

Name ZF intes

Initial concentration  $0 \text{ mol} \cdot 1^{-1}$ 

This species takes part in two reactions (as a reactant in v60 and as a modifier in v60).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ZF\_intes} = -v_{62} \tag{262}$$

# 8.30 Species ZF\_blood

Name ZF\_blood

Initial concentration  $0 \text{ mol} \cdot l^{-1}$ 

This species takes part in five reactions (as a reactant in v61, v62 and as a product in v60 and as a modifier in v61, v62).

$$\frac{d}{dt}ZF\_blood = |v_{62}| - |v_{63}| - |v_{64}|$$
 (263)

# 8.31 Species ZF\_airways

Name ZF\_airways

Initial concentration  $0 \text{ mol} \cdot 1^{-1}$ 

This species takes part in two reactions (as a product in v61 and as a modifier in v61).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ZF\_airways} = v_{63} \tag{264}$$

### 8.32 Species ML\_intes

Name ML\_intes

Initial concentration  $0 \text{ mol} \cdot l^{-1}$ 

This species takes part in two reactions (as a reactant in v63 and as a modifier in v63).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ML.intes} = -v_{65} \tag{265}$$

# 8.33 Species ML\_blood

Name ML\_blood

Initial concentration  $0 \text{ mol} \cdot l^{-1}$ 

This species takes part in three reactions (as a reactant in v64 and as a product in v63 and as a modifier in v64).

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathrm{ML\_blood} = v_{65} - v_{66} \tag{266}$$

# **A Glossary of Systems Biology Ontology Terms**

**SBO:0000290 physical compartment:** Specific location of space, that can be bounded or not. A physical compartment can have 1, 2 or 3 dimensions

BML2ATEX was developed by Andreas Dräger<sup>a</sup>, Hannes Planatscher<sup>a</sup>, Dieudonné M Wouamba<sup>a</sup>, Adrian Schröder<sup>a</sup>, Michael Hucka<sup>b</sup>, Lukas Endler<sup>c</sup>, Martin Golebiewski<sup>d</sup> and Andreas Zell<sup>a</sup>. Please see http://www.ra.cs.uni-tuebingen.de/software/SBML2LaTeX for more information.

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