Corrigendum

Corrigendum to “Semiphenological versus Empirical Modelling of the Population Pharmacokinetics of Free and Total Cefazolin during Pregnancy”

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Our paper “Semiphenological versus Empirical Modelling of the Population Pharmacokinetics of Free and Total Cefazolin during Pregnancy” contains three textual errors we wish to correct. Furthermore we wish to make a textual clarification. The corrections are as follows.

Table 2: the equations in footnotes a and b have been erroneously switched. The correct footnotes should be as follows: ^aEmpirical model: $CL = \theta_{CL0} + \theta_{CLPre} * (1 + (GA/40))$. ^bSemiphenological model: $CL = \theta_{CL0} + \theta_{CLPre} * (CrCL_{ij}(t)/CrCL_0)$. Figure 1: the units of time in the x -axis label are incorrectly labeled as hours. The correct units are minutes; hence the correct x -axis label is “Time (min).” Figure 4: the caption of Figure 4 starts incorrectly with “Simulations of typical free and total cefazolin concentration-time . . .,” while the figure’s y -axis labels state “Free cefazolin (mg/L).” The figure actually only depicts free cefazolin. Hence, the caption of Figure 4 should be corrected to “Simulations of typical free cefazolin concentration-time . . .” Clarification: we would like to make a clarification to the implementation of our model which included free and total cefazolin concentrations. The parameters CL_0 , V_C , V_P , and Q were fit based on the free cefazolin concentration.

The individual total cefazolin concentrations were then predicted based on the individually predicted free cefazolin concentration together with the estimation of the fraction unbound (f_u) (7). Other PK analyses of cefazolin have reported the total cefazolin concentrations. Hence, in order to convert our CL based on unbound cefazolin (CL_{free}) to CL based on total concentration (CL_{total}), multiplication with f_u is necessary: $CL_{total} = CL_{free} * f_u$.

These corrections do not influence the results, discussion, or conclusion of this work.

TABLE 2: Parameter estimates of the base and final population PK models (empirical and semiphysiological) for cefazolin.

Description	Parameter	Unit	Estimates (RSE %)		
			Base model	Empirical model CL~GA ^a	Semiphysiological model CL~CrCL ^b
Structural model					
Clearance	θ_{CL0}	L/min	0.49 (7)	0.119 (58)	0.142 (44)
Central volume	V_C	L	32.5 (16)	33.1 (17)	14.1 (25)
Peripheral volume	V_P	L	12.8 (25)	12.8 (27)	17.1 (7)
Intercompartmental clearance	Q	L/min	0.335 (21)	0.326 (25)	0.436 (10)
Free fraction	F_U	—	0.289 (5)	0.286 (5)	0.291 (9)
Gestation effect on clearance	θ_{CLPreg}	—	—	0.217 (16)	0.212 (38)
Between-subject variability					
Clearance	ω_{CL}	CV%	22.1 (25)	19.9 (24)	10.4 (70)
Central volume	ω_{V1}	CV%	49.1 (22)	47.6 (21)	101.5 (21)
Peripheral volume	ω_{V2}	CV%	32.7 (41)	34.2 (41)	68 (26)
Free fraction	ω_{F_U}	CV%	18.9 (36)	17.5 (37)	19.1 (38)
Residual unexplained variability variances					
Proportional, free concentration	σ_{FP}		0.0162 (8)	0.0158 (11)	0.0153 (8)
Additive, free concentration	σ_{FA}		0.176 (34)	0.229 (42)	0.217 (36)
Proportional, total concentration	σ_{TP}		0.0348 (8)	0.0328 (10)	0.0328 (9)
Additive, total concentration	σ_{TA}		0.662 (48)	0.842 (46)	0.681 (25)

RSE: relative standard error; GA: gestational age (weeks).
^aEmpirical model: $CL = \theta_{CL0} + \theta_{CLPreg} * (1 + (GA/40))$.
^bSemiphysiological model: $CL = \theta_{CL0} + \theta_{CLPreg} * (CrCL_{ij}(t)/CrCL_0)$.

FIGURE 1: Simulated (areas) and observed (solid circles, lines) free and total cefazolin concentrations versus time as predicted by the empirical model (a) and semiphysiological model (b) for trimesters 2 and 3 of pregnancy. Simulations are represented as the parametric 95% confidence intervals of the simulated 50th (red), 5th, and 95th (blue) percentiles. For the observed values, the 50th (continuous line), 5th, and 95th (dashed lines) percentiles are depicted in red.

FIGURE 4: Simulations of typical free cefazolin concentration-time profiles using the empirical and the semiphysiological approach at different periods of pregnancy (gestational weeks) based on a dose regimen of 2 g cefazolin every 6 or 8 hours administered over 30 minutes. The expected 90% minimum inhibitory concentration is depicted as horizontal black line. GW: gestational weeks.