Population pharmacokinetic-pharmacodynamic model of oxfendazole in healthy adults in a multiple ascending dose and food effect study and target attainment analysis

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Running title: Oxfendazole popPKPD model and target attainment analysis

SUPPLEMENTARY MATERIALS

Table S1. Demographics and baseline characteristics of subjects participating in oxfendazole multiple ascending dose and food effect study. Continuous variables are summarized as mean ± SD (range); categorical variables are summarized as number (percentage).

Characteristics	**Group 1 (3 mg/kg)**	**Group 2 (7.5 mg/kg)**	**Group 3 (15 mg/kg)**	**Group 4A (3 mg/kg, fast → fed)**	**Group 4B (3 mg/kg, fast → fed)**	**All subjects**
N	8	8	8	6	6	36
Age (years)	29.3 ± 9.1 (21.0 – 44.0)	27.1 ± 6.1 (19.0 – 33.0)	30.1 ± 4.4 (21.0 – 35.0)	27.7 ± 5.6 (22.0 – 34.0)	32.2 ± 9.4 (23.0 – 44.0)	29.2 ± 6.9 (19.0 – 44.0)
Height (cm)	178.0 ± 10.3 (163.5 – 195.6)	173.5 ± 7.1 (165.0 – 184.0)	170.8 ± 8.6 (160.0 – 184.0)	173.9 ± 6.9 (166.0 – 184.5)	174.1 ± 13.2 (158.5 – 196.0)	174.1 ± 9.1 (158.5 – 196.0)
Weight (kg)	88.9 ± 10.7 (76.8 – 103.0)	78.4 ± 14.0 (56.8 – 97.0)	76.9 ± 16.3 (58.6 – 104.0)	82.6 ± 11.9 (69.8 – 105.0)	86.3 ± 13.2 (73.2 – 105.0)	82.4 ± 13.6 (56.8 – 105.0)
BMI (kg/m^2)	28.1 ± 2.6 (25.0 – 32.6)	26.2 ± 5.3 (18.3 – 34.8)	26.3 ± 5.3 (21.1 – 34.3)	27.3 ± 4.0 (23.9 – 34.0)	28.6 ± 4.0 (24.2 – 33.9)	27.2 ± 4.2 (18.3 – 34.8)
Sex						
Male	7 (88)	5 (63)	4 (50)	5 (83)	4 (67)	25 (69)
Female	1 (13)	3 (38)	4 (50)	1 (17)	2 (33)	11 (31)
Ethnicity						
Not Hispanic or Latino	7 (88)	8 (100)	7 (88)	4 (67)	6 (100)	32 (89)
Hispanic or Latino	1 (13)	0 (0)	1 (13)	2 (33)	0 (0)	4 (11)
Race						
Asian	1 (13)	1 (13)	1 (13)	1 (17)	0 (0)	4 (11)

Black or African American	0 (0)	1 (13)	0 (0)	0 (0)	0 (0)	1 (13)
White	7 (88)	6 (75)	6 (75)	4 (67)	6 (100)	29 (81)
Multi-racial	0 (0)	0 (0)	1 (13)	1 (17)	0 (0)	2 (6)

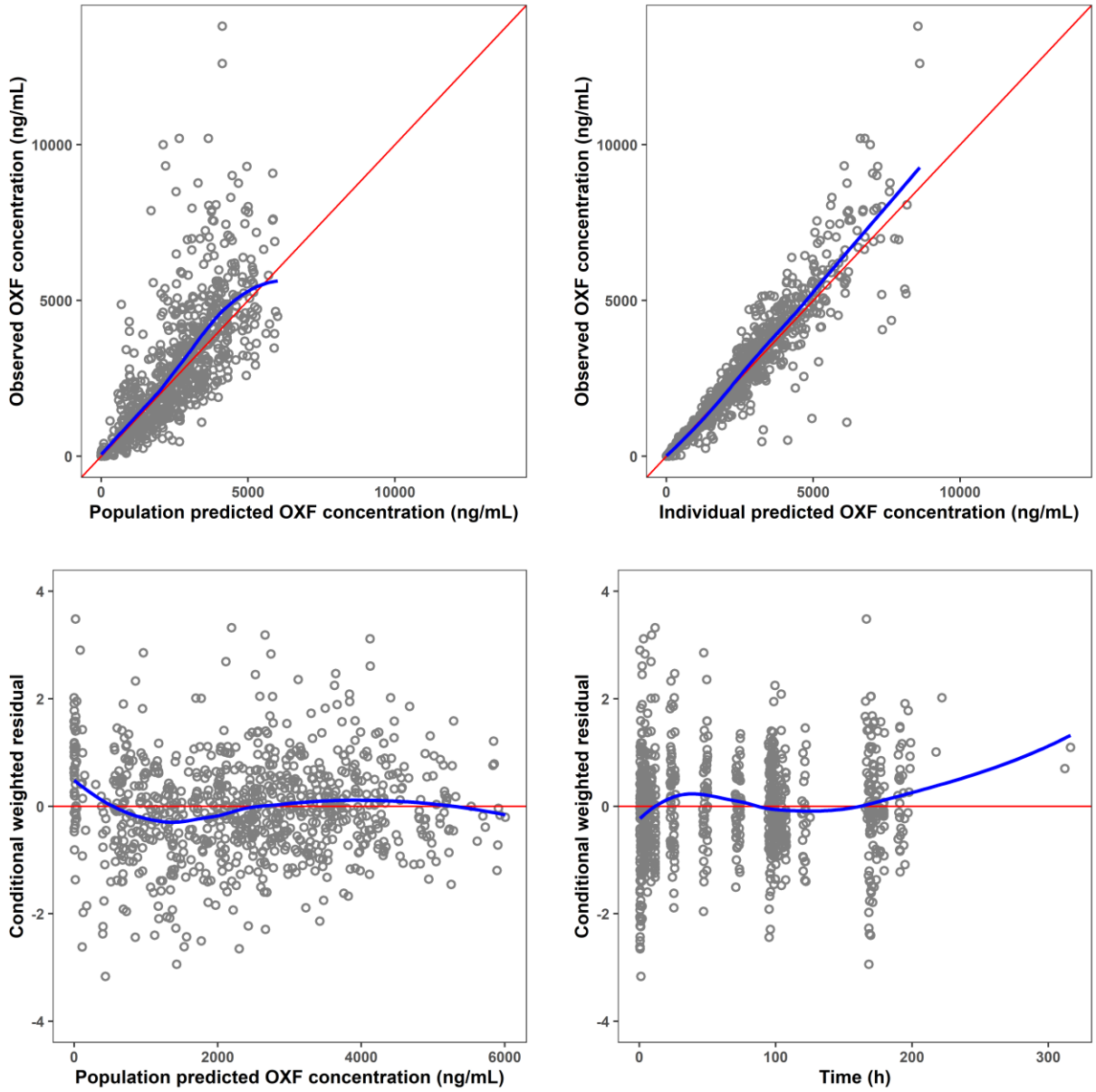

Figure S1. Goodness-of-fit plots for the oxfendazole final pharmacokinetic model. The solid blue line represents the Loess line. The solid red line represents the line of identity (upper panel) or the zero line (lower panel). No clear trend was observed in either plot indicating no systemic bias.

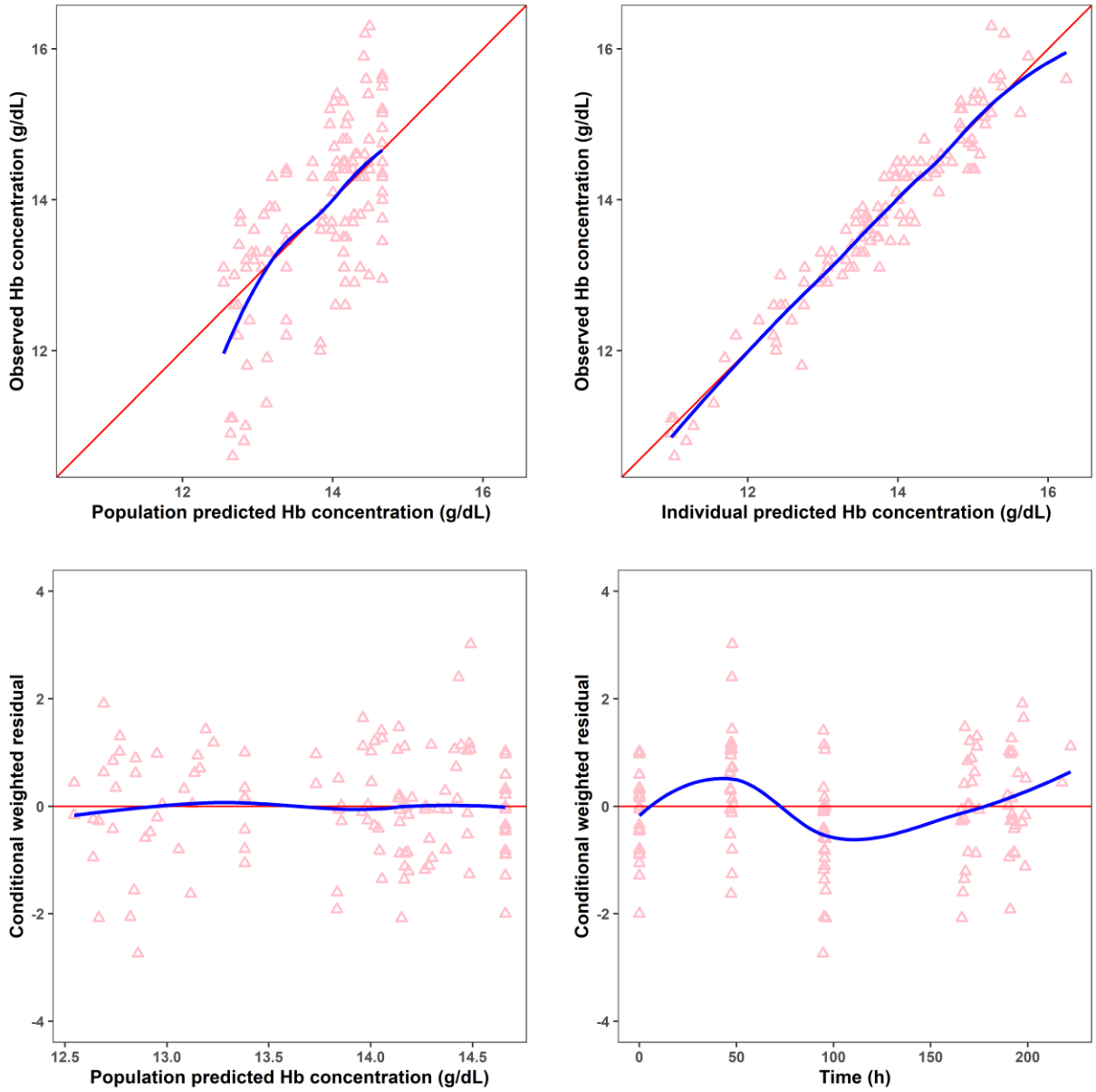

Figure S2. Goodness-of-fit plots for oxfendazole final pharmacodynamic model. The solid blue line represents the Loess line. The solid red line represents the line of identity (upper panel) or the zero line (lower panel). No clear trend was observed in either plot indicating no systemic bias.

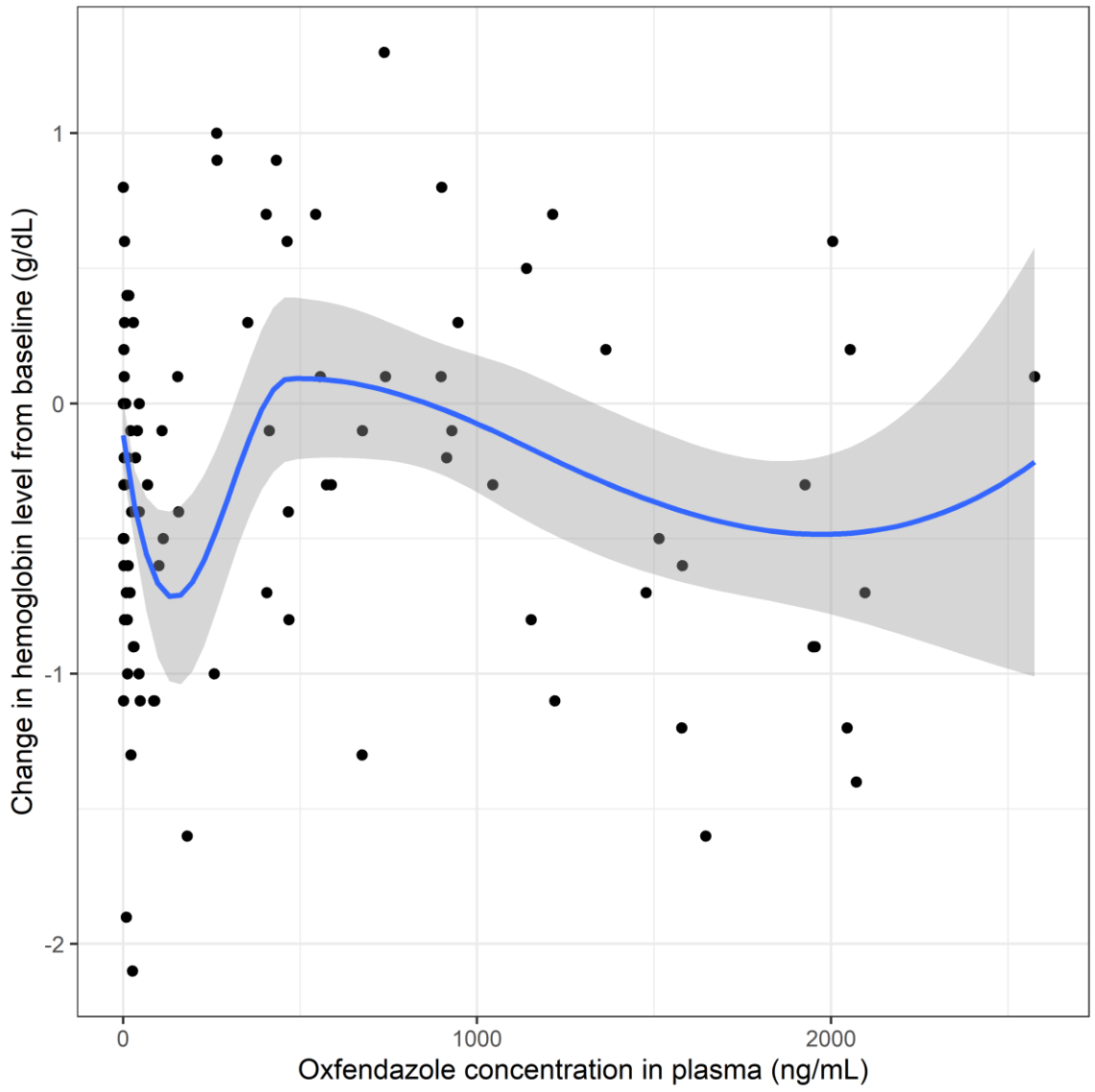

Figure S3. Plot of observed oxfendazole concentration in plasma versus observed hemoglobin concentration in plasma following the administration of multiple ascending oxfendazole doses (3, 7.5 and 15 mg/kg once daily for 5 days). Individual data are represented by black dots. The solid blue line represents the Loess line and the shaded area represents 95% confidence interval of the Loess line. The Loess line indicates neither a linear correlation or non-linear correlation as in Hill function. Thus, it is likely that the plasma oxfendazole concentration has an indirect effect on hemoglobin concentration.

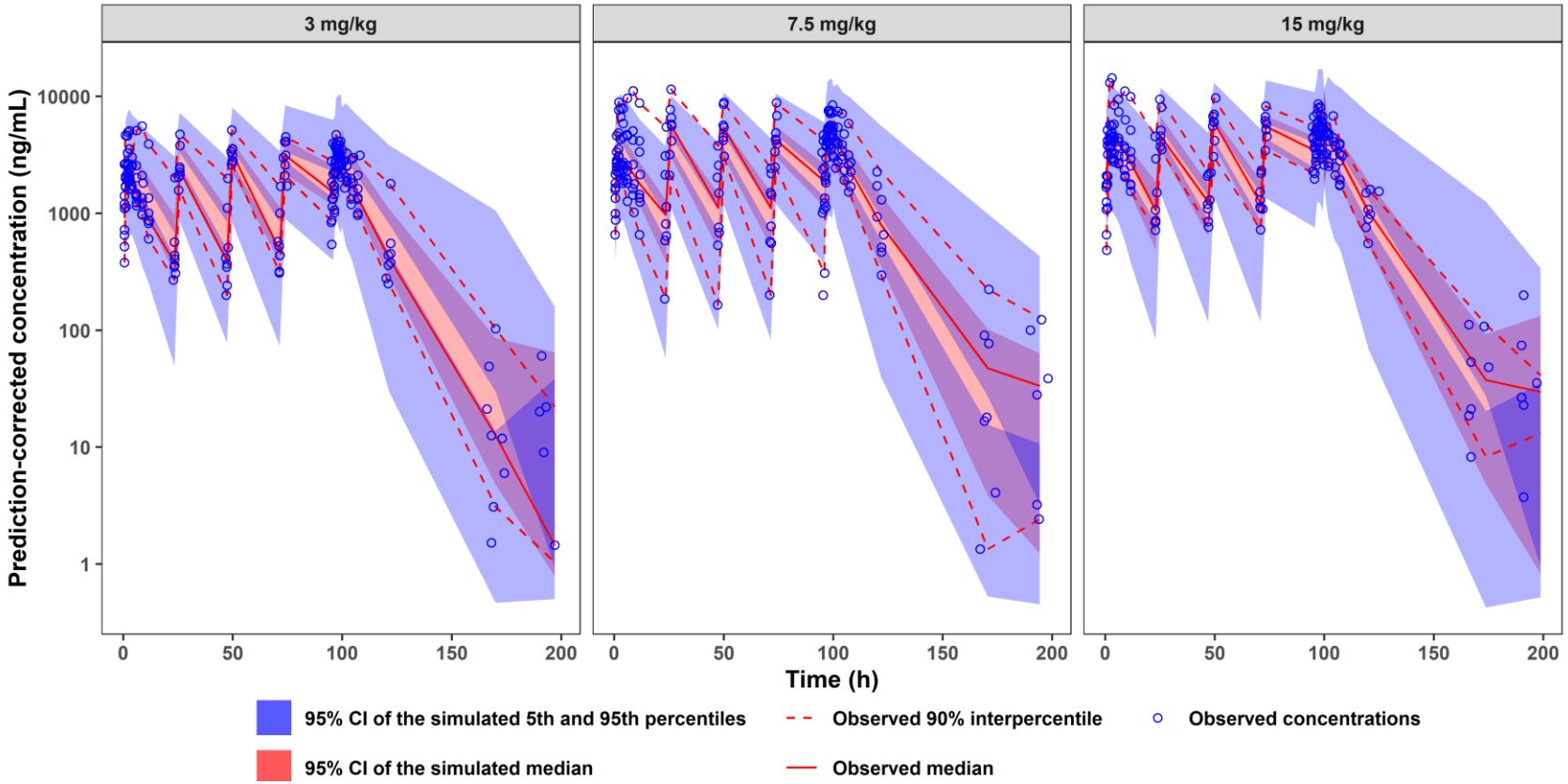

Figure S4. pcVPC plot for oxfendazole pharmacokinetic model following multiple ascending doses at 3, 7.5 and 15 mg/kg once daily for 5 days in the fasted state. pcVPC plots were constructed based on 1000 simulations at each dose level.

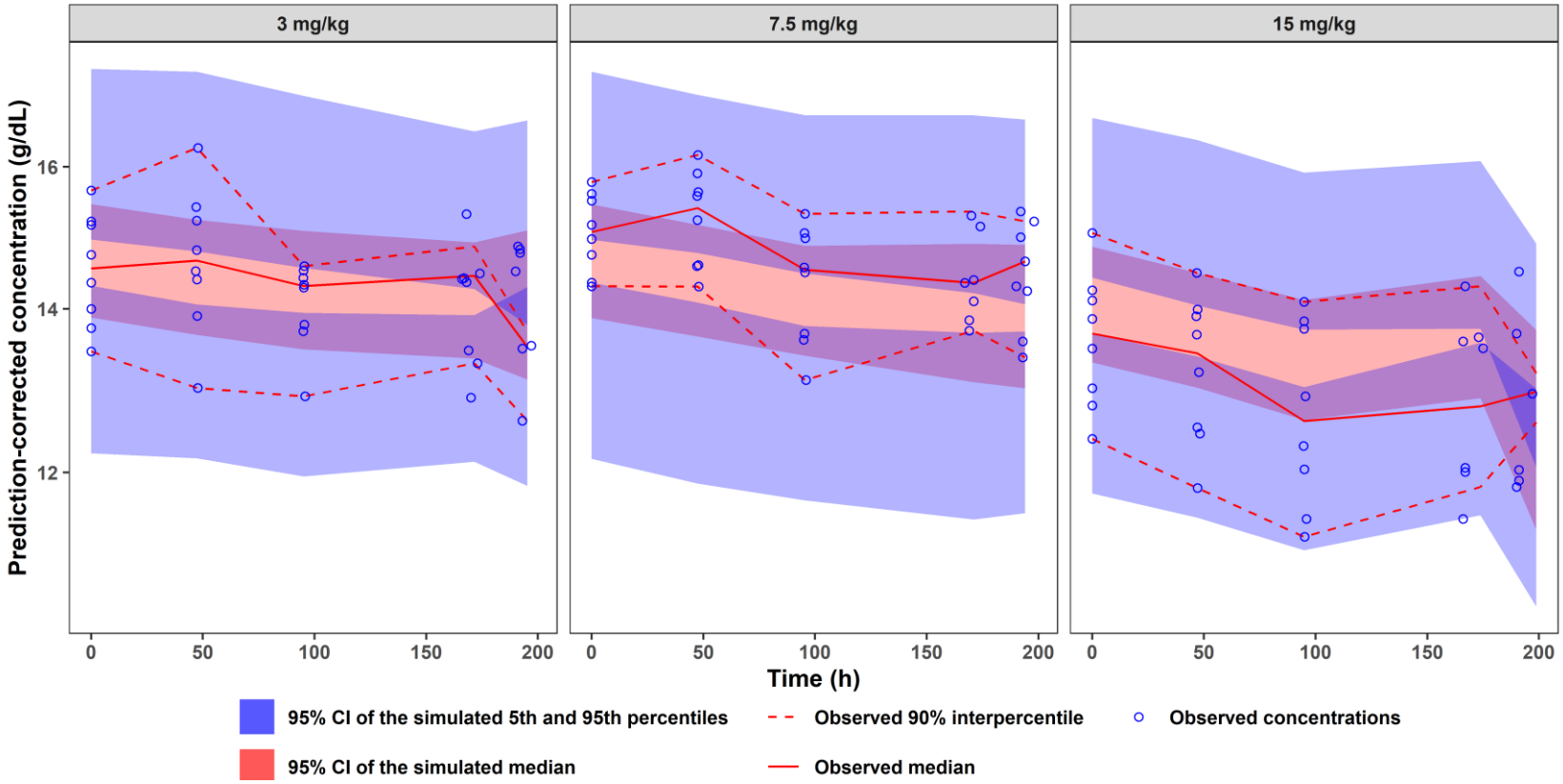

Figure S5. pcVPC plot for the change in hemoglobin concentration following multiple ascending doses of oxfendazole at 3, 7.5 and 15 mg/kg once daily for 5 days in the fasted state. pcVPC plots were constructed based on 1000 simulations at each dose level.