**SUPPLEMENTARY MATERIALS:**

**Table Supp-I:** Serum and urine estimated population pharmacokinetic parameters, sampling importance resampling (SIR) and bootstrap confidence interval (CI) values of enalapril and enalaprilat from the **reference** f0ormulation.

**Table Supp-II:** Serum and urine estimated population pharmacokinetic parameters, sampling importance resampling (SIR) and bootstrap confidence interval (CI) values of enalapril and enalaprilat from the **ODMT** formulation

**Fig Supp-1:** Goodness of fit plots including the observed versus individual and population predicted and conditional weighted residuals (CWRES) versus population predicted (PRED) plots of enalapril and enalaprilat in serum and urine generated after the population pharmacokinetic modeling of **reference** formulation. The first and third row shows the predictive performance of the model for enalapril in serum and urine respectively. The second and fourth line shows the predictive performance of enalaprilat in serum and urine respectively.

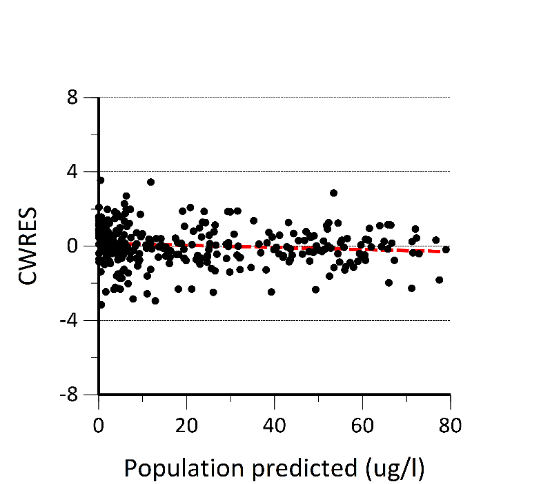
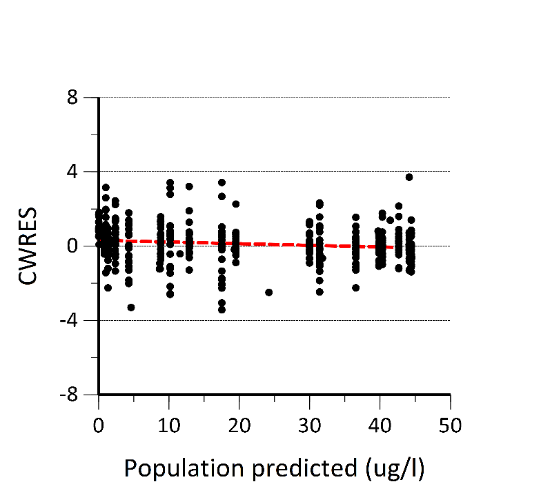
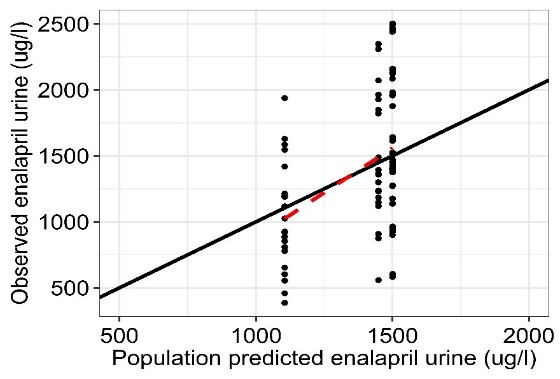
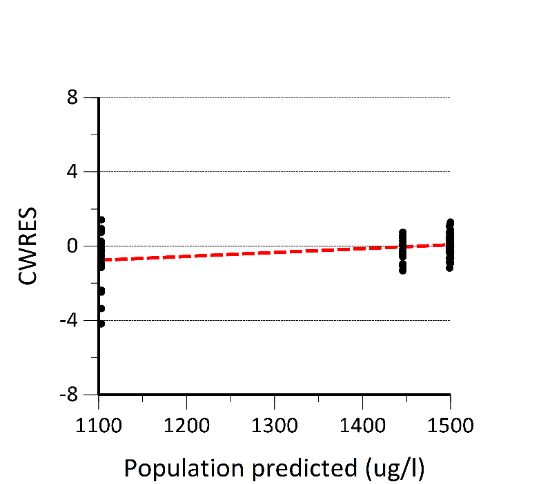
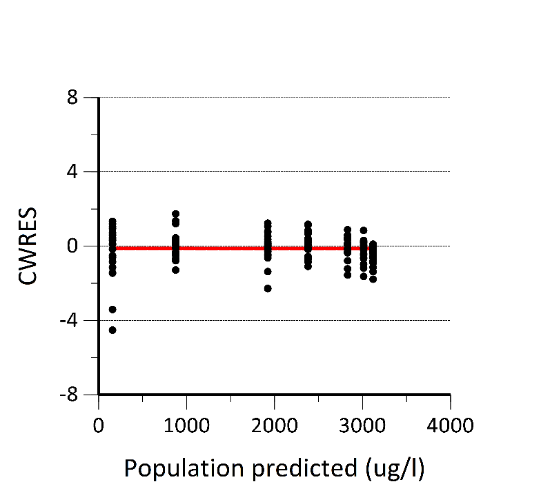
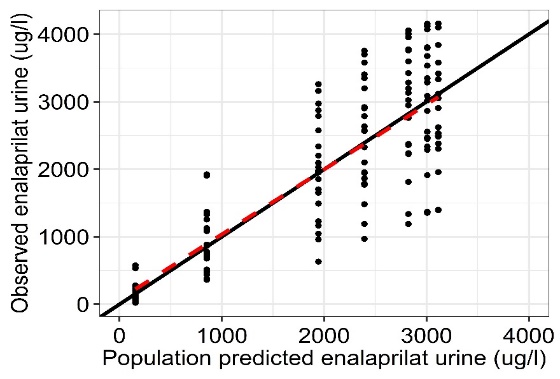
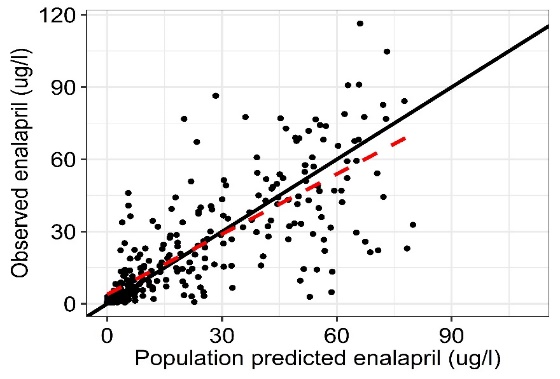
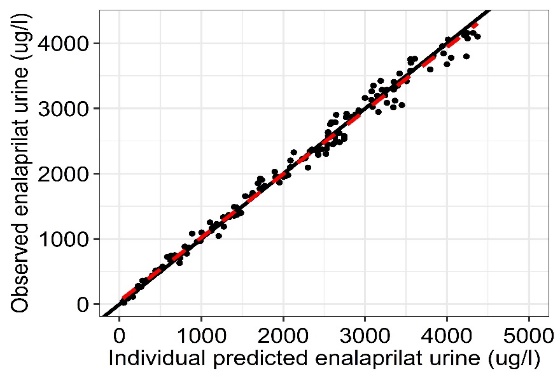
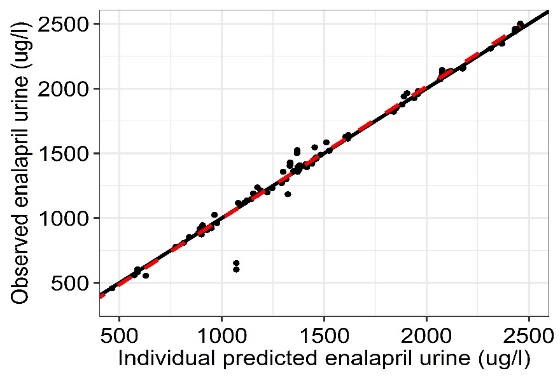
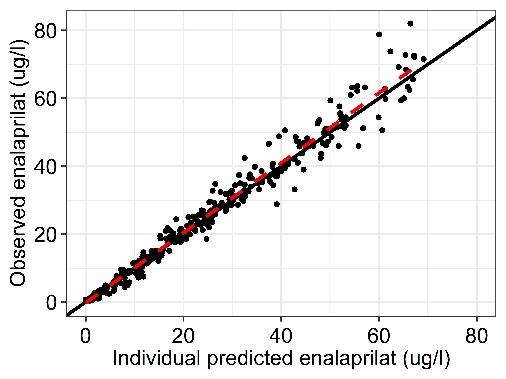
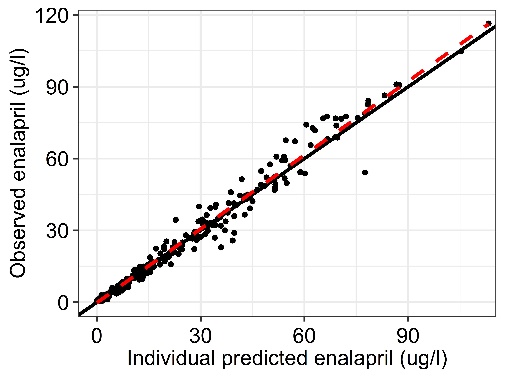
**Fig Supp-2:** Goodness of fit plots including the observed versus individual and population predicted and conditional weighted residuals (CWRES) versus population predicted (PRED) plots of enalapril and enalaprilat in serum and urine generated after the population pharmacokinetic modeling of **ODMT** formulation. The first and third row shows the predictive performance of the model for enalapril in serum and urine respectively. The second and fourth row shows the predictive performance of enalaprilat in serum and urine respectively.

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameters** | **Population Estimates (% RSE)** | **SIR 95th % CI** | **Bootstrap 95th % CI** |
| **FINAL (FULL) MODEL** | **FINAL MODEL** | **FINAL MODEL** |
| ***Basic pharmacokinetic model parameters*** | | | |
| KA (1/h) | 7.780 (37.0 %) | 5.640-11.90 | 5.541-12.10 |
| VC (L) | 51.60 (6.00 %) | 46.31-57.06 | 45.00-55.40 |
| F1 | 0.630 (5.00 %) | 0.574-0.681 | 0.562-0.667 |
| MTT1 (hr) | 0.570 (10.00 %) | 0.492-0.681 | 0.475-0.643 |
| KREN (1/h) | 0.312 (5.00 %) | 0.281-0.341 | 0.274-0.339 |
| KM (1/h) | 0.683 (7.00 %) | 0.605-0.758 | 0.635-0.746 |
| VM (L) | 44.70 (5.00 %) | 40.98-48.87 | 42.10-50.78 |
| KQ1 (1/h) | 0.060 (6.0 %) | 0.054-0.065 | 0.053-0.068 |
| KQ2 (1/h) | 0.057 (15.0 %) | 0.046-0.071 | 0.045-0.067 |
| KME (1/h) | 0.192 (6.00 %) | 0.176-0.210 | 0.175-0.210 |
| MTT2 (h) | 0.942 (13.0 %) | 0.745-1.144 | 0.741-1.025 |
| ***Interindividual variability (IIV)*** | | | |
| IIV\_KA | 1.310 (53.0 %) | 0.796-1.604 | 0.799-1.522 |
| IIV\_VC | 0.069 (34.0 %) | 0.044-0.120 | 0.049-0.090 |
| IIV\_F1 | 0.057 (31.0 %) | 0.039-0.089 | 0.041-0.750 |
| IIV\_MTT1 | 0.203 (31.0 %) | 0.132-0.338 | 0.137-0.366 |
| IIV\_KREN | 0.056 (33.0 %) | 0.036-0.097 | 0.035-0.085 |
| IIV\_KM | 0.088 (32.0 %) | 0.056-0.141 | 0.050-0.134 |
| IIV\_VM | 0.048 (35.0 %) | 0.029-0.081 | 0.036-0.102 |
| IIV\_KME | 0.053 (33.0 %) | 0.033-0.088 | 0.035-0.086 |
| IIV\_ MTT2 | 0.330 (32.0 %) | 0.225-0.420 | 0.243-0.350 |
| ***Residual unexplained variability (RUV)*** | | | |
| ***Serum Enalapril*** | | | |
| Proportional error (σ2) | 0.010 (12.0 %) | 0.007-0.011 | 0.006-0.014 |
| Additive error (ug/l) | 0.189 (21.0 %) | 0.137-0.269 | 0.125-0.245 |
| ***Serum Enalaprilat*** | | | |
| Proportional error (σ2) | 0.021 (14.0 %) | 0.016-0.026 | 0.014-0.026 |
| Additive error (ug/l) | 0.220 (22.0 %) | 0.159-0.310 | 0.147-0.316 |
| ***Urine Enalapril*** | | | |
| Proportional error (σ2) | 0.011 (14.0 %) | 0.009-0.014 | 0.007-0.016 |
| ***Urine Enalaprilat*** | | | |
| Proportional error (σ2) | 0.005 (16.0 %) | 0.004-0.006 | 0.003-0.009 |

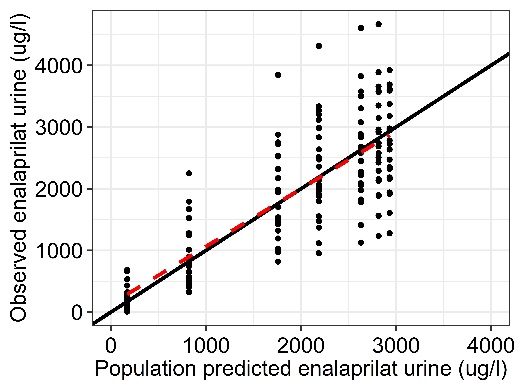
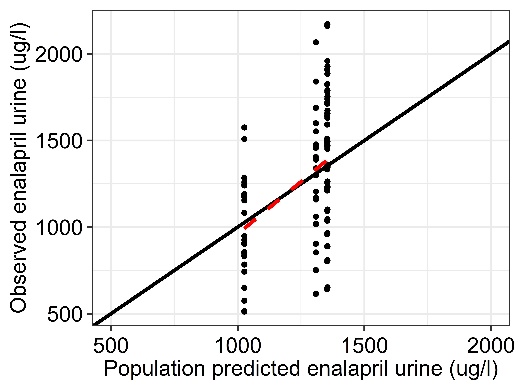
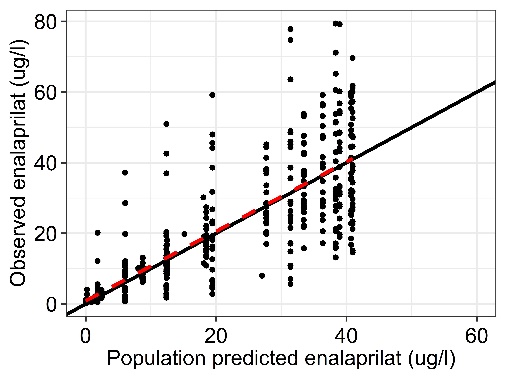
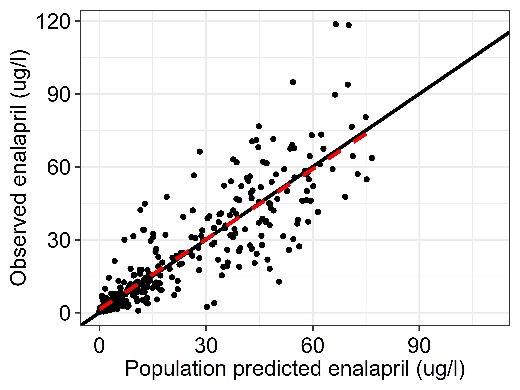
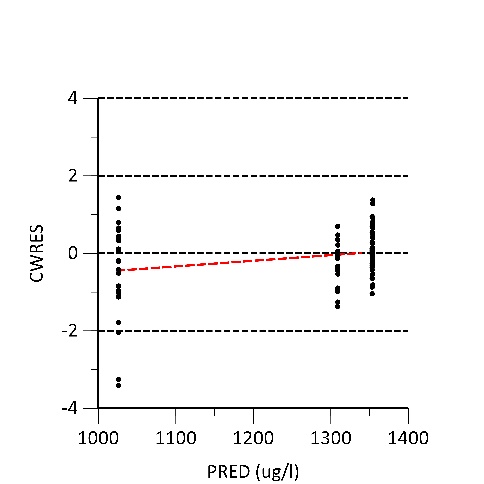
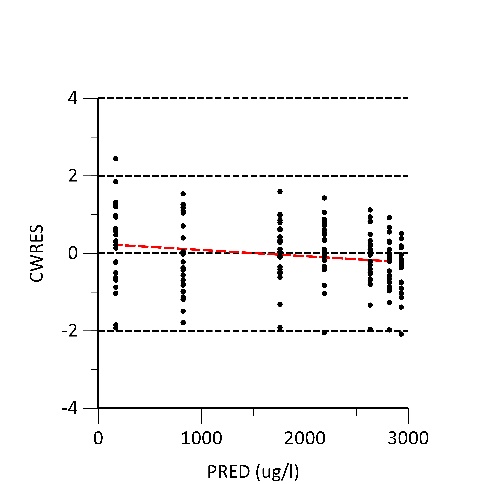
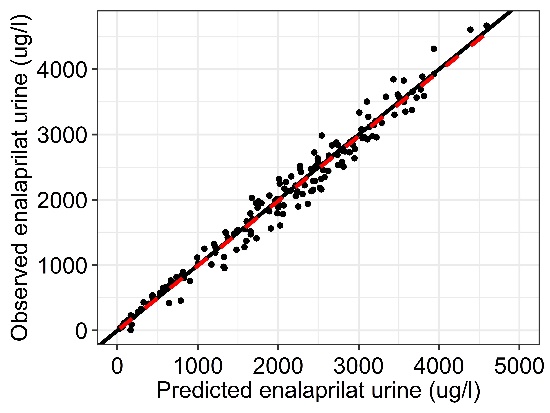
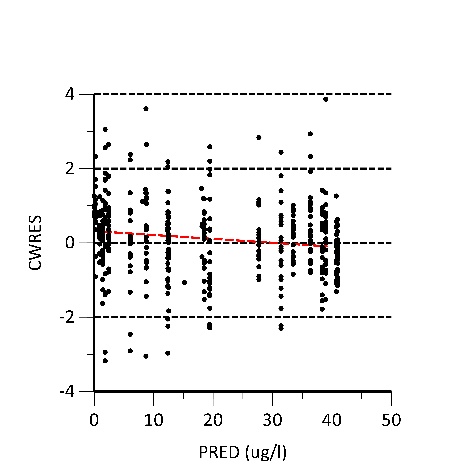
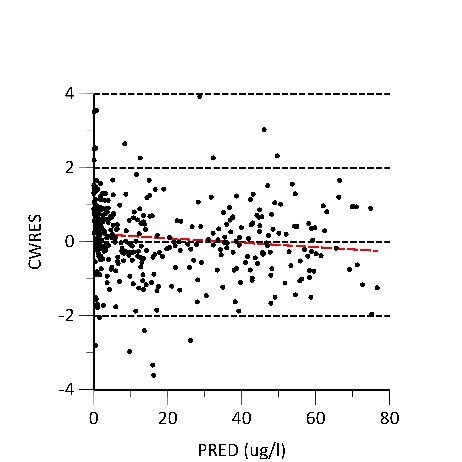
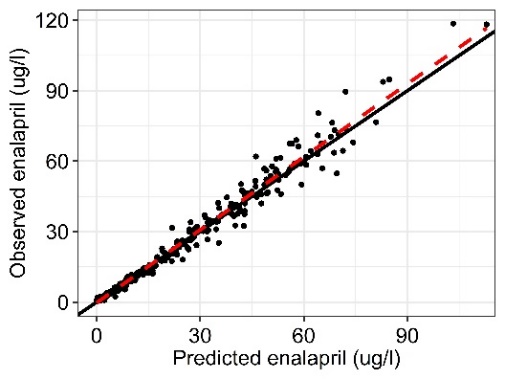
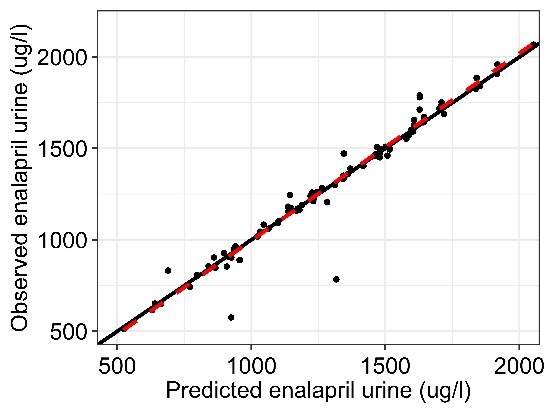
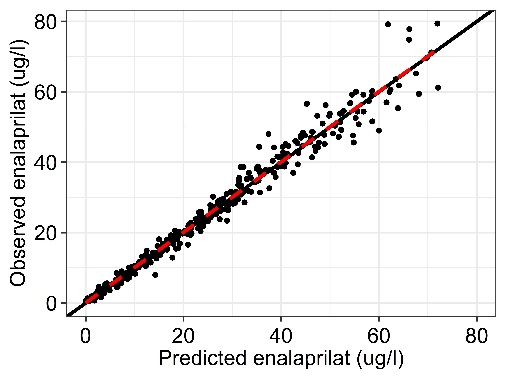
**Table Supp-I:**

**Table Supp-II:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Parameters** | **Population estimates**  **(% RES)** | **SIR 95th % CI** | **Bootstrap 95th % CI** |
| **FINAL (FULL) MODEL** | **FINAL MODEL** | **FINAL MODEL** |
| ***Basic pharmacokinetic model parameters*** | | |  |
| KA (1/h) | 7.71 (26.0 %) | 5.623-11.59 | 5.329-12.22 |
| VC (L) | 50.70 (5.00 %) | 46.87-55.05 | 47.00-55.59 |
| F1 | 0.589 (4.00 %) | 0.556-0.624 | 0.553-0.627 |
| MTT1 (hr) | 0.484 (7.00 %) | 0.438-0.551 | 0.417-0.553 |
| KREN (1/h) | 0.298 (5.00 %) | 0.274-0.323 | 0.274-0.325 |
| KM (1/h) | 0.693 (6.00 %) | 0.631-0.757 | 0.641-0.750 |
| VM (L) | 47.60 (7.00 %) | 42.52-53.20 | 42.65-52.93 |
| KQ1 (1/h) | 0.060 (5.00 %) | 0.056-0.066 | 0.054-0.066 |
| KQ2 (1/h) | 0.051 (14.0 %) | 0.040-0.064 | 0.042-0.060 |
| KME (1/h) | 0.175 (6.00 %) | 0.158-0.193 | 0.161-0.196 |
| MTT2 (h) | 0.873 (11.0 %) | 0.732-1.043 | 0.731-1.015 |
| ***Interindividual variability (IIV)*** | | |  |
| IIV\_KA | 0.779 (50.0 %) | 0.460-1.616 | 0.215-1.462 |
| IIV\_VC | 0.047 (34.0 %) | 0.031-0.082 | 0.024-0.070 |
| IIV\_F1 | 0.025 (31.0 %) | 0.017–0.042 | 0.013-0.034 |
| IIV\_MTT1 | 0.269 (30.0 %) | 0.184-0.433 | 0.137-0.366 |
| IIV\_KREN | 0.056 (31.0 %) | 0.037-0.093 | 0.033-0.076 |
| IIV\_KM | 0.067 (31.0 %) | 0.045-0.111 | 0.037-0.090 |
| IIV\_VM | 0.087 (32.0 %) | 0.059-0.146 | 0.042-0.122 |
| IIV\_KME | 0.071(31.0 %) | 0.047-0.117 | 0.039-0.090 |
| IIV\_ MTT2 | 0.094 (31.0 %) | 0.065-0.156 | 0.043-0.122 |
| ***Residual unexplained variability (RUV)*** | | |  |
| ***Serum Enalapril*** | | |  |
| Proportional error (σ2) | 0.010 (12.0 %) | 0.008-0.011 | 0.005-0.014 |
| Additive error (ug/l) | 0.186 (23.0 %) | 0.133-0.266 | 0.116-0.425 |
| ***Serum Enalaprilat*** | | |  |
| Proportional error (σ2) | 0.016 (13.0 %) | 0.013-0.019 | 0.010-0.024 |
| Additive error (ug/l) | 0.220 (17.0 %) | 0.170-0.284 | 0.117-0.316 |
| ***Urine Enalapril*** | | |  |
| Proportional error (σ2) | 0.026 (13.0 %) | 0.021-0.032 | 0.011-0.042 |
| ***Urine Enalaprilat*** | | |  |
| Proportional error (σ2) | 0.005 (15.0 %) | 0.004-0.006 | 0.001-0.009 |



**FIG Supp-1:**



**FIG Supp-2:**