Silsamicin is an investigational compound being evaluated for its antimicrobial effect. The route of administration for this drug is via intravenous bolus. Approximately 99.9% of this drug is eliminated by the kidney. Tubular secretion and reabsorption do not play a role in the elimination of this drug. Silsamicin has no plasma protein binding. Assuming ideal body weight for both individuals, compute the clearance of silsamicin for the following individuals:

(1) Male, 45 years of age, 180 lbs with serum creatinine of 1.9 mg/dL

(2) Female, 60 years of age, 130 lbs with serum creatinine of 3.7 mg/dL
The blood samples of ABC13245 were obtained after an intravenous bolus administration of 100 mg ABC13245. The pharmacokinetic profile follows a bi-exponential decline. The data was fitted to a bi-exponential decay equation and the following intercepts and rate constants were obtained:

\[ C_1 = 57 \frac{mg}{L}; \quad C_2 = 8 \frac{mg}{L}; \quad \alpha = 0.9 \, h^{-1}; \quad \beta = 0.27 \, h^{-1} \]

Compute its CL, \( V_{ss} \) and MRT.

The clinical peak is defined as the concentration of the drug in the plasma 30 minutes after the end of administration. The clinical trough is the concentration 30 minutes prior to the next administration. Assume that the dosing interval is 12 hours. Compute the clinical peak and trough concentrations of ABC13245. Use the following additional equations for your computation:

\[ AUC = \frac{C_1}{\alpha} + \frac{C_2}{\beta}; \quad AUMC = \frac{C_1}{\alpha^2} + \frac{C_2}{\beta^2} \]
Drug A is administered as a racemic mixture. If the clearance of the R-isomer is 70 mL/min whereas the clearance of the S-isomer is 50 mL/min and change in urine flow has no effect on the renal clearance of either isomer, explain the difference in renal clearance of the two isomers.
Assuming that drug A exhibited a total clearance of 2.48 L/h. Its elimination is 70% hepatic metabolism and 30% renal excretion. No significant plasma protein binding was reported for Drug A. Drug A has a narrow therapeutic window. If drug C that reduces the intrinsic clearance of Drug A by 25% is added to the drug regimen of the patient receiving a constant infusion of drug A, would you change the infusion rate of drug A in this patient?
When drug C is co-administered to patients receiving drug A, the average Css of drug A decreases. No change in the pharmacologic action was observed. Explain why this is the case.