## Problems in establishing PK/PD: binding to proteins, plastics, etc.

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It is now well established that PK/PD relationships of antibiotics determined in animal infection models can translate very well to the clinical situation. Thus, results from such preclinical studies provide a good understanding of the plasma concentration vs. time profile (exposure) needed in patients to achieve the desired pharmacological response (bacteriological/clinical cure). Key in this process is the ability to reliably estimate the PK/PD indices for unbound drug in plasma: *f*Cmax/MIC; *f*AUC/MIC; and, *f*T>MIC. Clearly, this requires the reliable estimation of the following for the antibiotic: pharmacokinetics; fraction of the drug unbound in plasma; and, MIC. This is relatively straightforward for many antibiotics. However, for antibiotics with certain physicochemical properties (e.g. 'sticky' molecules prone to bind to MIC wells and other labware) and/or for which the unbound fraction in plasma is very small, the process of establishing PK/PD relationships is more complex and challenging. This lecture will discuss issues relating to these aspects, including the use of polysorbate 80 to decrease antibiotic binding in MIC microtitre wells.