The Hollow Fiber Infection Model, Principles and Practice

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Abstract
Emerging antibiotic resistance offers a serious global health threat. 2 million people in the United States were infected with antibiotic resistant bacteria in 2014 and more than 20,000 died as a direct result of these infections, many more from complications. Antimicrobial resistance has been identified as one of the three greatest threats to human health. Antibiotic detection and growth require static susceptibility testing to screen compounds, in vitro pharmacodynamics/pharmacokinetic (PK/PD) studies to model drug dynamics and efficacy and testing in animal models to offer critical information prior to the clinical evaluation of new antibiotics. Animal models have many shortcomings though they have served as a primary development tool for many years: 1) PK/PD may not match human values 2) Cannot sample the same animal over time 3) Hard to study large statistics of bacteria to reveal resistance 4) Several infections cannot be demonstrated in a mouse or other animal. To address these shortcomings the Hollow fiber infection model (HFIM) was developed. The advantages of the HFIM are as follows: 1) Closed, bio-safe system 2) Huge number of organisms can be tested, revealing resistance 3) Quite simulates human PK/PD 4) Repetitive sampling over time, together drug and organism 5) Whole kill can be determined 6) Solitary use, disposable, reproducible 7) Double drug models can be evaluated 8) Can model both the dosing curve and elimination curve 9) Can look at bacteria in various growth phases and in combination with cells. The clinical utility of the HFIM has been established and is now recognized by the EMA. An outline of historic pk/pd models is offered and the utility of the system as it relays to antibiotics and other drugs are discussed.

Biography
John J.S. Cadwell received his degree in pharmacology from the University of Miami in 1981. He spent additional time studying at the University of Nottingham and the National Institute of Medical Research at Mill Hill, U.K. In 2000 he founded FiberCell Systems Inc., a company specializing in the research and supply of hollow fiber bioreactors. He has over 10 publications in the field and three patents relating to hollow fiber systems and is considered a world expert in the field.

Publications