Bye Bye Novel Beta Lactams ???

Beta lactam anti infectives, whether cephalosporins, penicillins and related analogues like clavams, bactams and penems probably represent the most sustained and successful contributions to combating bacterial infections across at least three generations. They have undoubtedly saved millions of lives, young, old, and "in between". The story is a familiar one and needs little elaboration. When bacteria evolved a defense mechanism against one or other of these materials, the chemists and biologists came up with a molecular variant or combination of agents to outwit the pathogens and prolong the dominance of man over microbe. The extraordinary safety of these agents, except for their sensitizing capability in a minority of patients made them first choice therapy in many cases.

But bacteria do not stand still. Today's survivor begets tomorrow's resistant strain and, without new antibiotics, infectious diseases will once again become major "killers". Where are the future penicillins and cephalosporins?

Where indeed? To this author's knowledge there are novel cehpalosporins around, with promising antibacterial spectra against the most resistant of organisms. Why are they not being evaluated clinically?

The answer is simple. Regulatory requirements are such that beta lactams must be processed in facilities that are separate from "conventional" manufacturing areas. The admittedly laudable thinking at the outset was that cross contamination of conventional medications by beta lactams posed sensitization hazards to patients. As sensitization could be induced by extremely low levels it was deemed that the only way to ensure patient safety was to keep beta lactams apart. Separate facilities were accordingly stipulated about a quarter of a century ago. As beta lactam Patents expired, and as Generics are not noted for their willingness to manufacture sterile products, because of expense, development facilities were shut down. The upshot is that there are no facilities (to this author's knowledge) where modest quantities of beta lactams, particularly for parenteral administration can be processed in sterile mode to service investigative clinical trials. Small startup organizations (where the creativity resides these days) cannot find facilities to manufacture modest quantities of sterile material for clinical assessment. No facility! no program! CRO's will not touch beta lactams in case involvement puts their other operations at risk.

The case for separate facilities might make sense if beta lactams are likely to persist in the environment, or be difficult to remove. Yet, as every student and dispensing Pharmacist knows they are intrinsically unstable. They cannot be formulated in aqueous vehicles due to instability and are also readily degraded by temperature and humidity-related stresses. Parenterals are most likely to be sterilized and presented as lyophiles, processed as solutions. Appropriate washing removes residues and, combined with the above-mentioned instability, the availability of ultra-sensitive analytical techniques and the use of appropriate isolation technology make it eminently feasible to process beta lactams such that the likelihood of residues is extremely low to non-existent. Separation in a completely separate facility is no longer warranted.

Its time to re-think and re-define attitudes.
Otherwise, its "bye-bye beta lactams: It's been good to know-ya".