

Antimicrobial Resistance & Europe: What Happened?



By David Shlaes — September 11, 2020

Europe used to be the voice of reason in antibiotic discovery and development, but that is no longer the case. The European Medical Agency, Europe's equivalent of the FDA, is requiring so many clinical trials for antibiotics that it is no longer feasible for companies to market the drugs in the E.U. ACSH advisor Dr. David Shlaes (pictured) explains.



I recently received a [notification](#) ^[1] from John Rex and Kevin Outterson regarding the fact that many recently approved antibiotics will not be marketed in Europe. At first glance, I assumed that these products were simply unable to obtain a price that would provide for a return on investment leading the companies to abandon the European marketplace. But, based on the information provided by Rex and Outterson, it's more complicated and more discouraging than that.

To go back in time, during the struggles at the FDA starting around 2000, Europe almost seemed like a haven of regulatory bliss for antibiotic developers. Many of you will remember how antibiotics almost always were approved in Europe one or more years after their approval in the US during the last part of the last century. We viewed Europe as slow, cumbersome, and driven by inconsistent and often academic concerns. But these perceived faults were clearly overcome when Europe became a regulatory haven as an alternative to an FDA that had lost its way.

During my consulting years, that covered the worst of the FDA antibiotic crisis, I often advised my clients to work through European regulators primarily and put the FDA aside or at least on a lower

priority in terms of trying to negotiate clinical trial designs that could lead to approval. My clients, perhaps correctly, noted that they would have a difficult time obtaining a return on their investment without the US market and as such, the FDA became a key hurdle for them to overcome. Unfortunately, years were lost in that struggle as were several of my clients.

Then, in 2012, the FDA awoke from their state of hibernation realizing that the antibiotic pipeline had all but disappeared under their regulatory restrictions – especially for antibiotics targeting pneumonia and other serious infections. They quickly established new regulatory pathways that are more efficient and rapid for new antibiotics addressing resistant infections.

And here we are in 2020. Our antibiotic pipeline remains in shambles mainly due to a lack of a sufficient marketplace. But we must remember that “sufficient” depends on costs to get there and stay there. And costs, often, still depend greatly on the regulators.

 Nabriva will not market Lefamulin in Europe partly because it is unable to find a commercial partner to drive sales. But more ominous in their recent [SEC](#) [2] filing is the statement that they may not be able to continue to survive at all given marketing restrictions associated with COVID plus outstanding obligations and debt.

Plazomicin has been withdrawn from Europe apparently because the costs of the pediatric trials required in Europe “exceed all estimates of potential sales” in the region.

Eravacycline is the victim of the financial difficulties of its parent company, Tetrphase, its limited indication and its relatively poor advantages compared to competing products.



Paratek's omadacycline was withdrawn from consideration

in Europe because the EMA [insisted](#) [3] on a second trial in community-acquired pneumonia. Omadacycline was approved in the US based on two successful trials in skin infection and a single trial in pneumonia consistent with FDA guidelines for approval in both indications. FDA [approved](#) [4] omadacycline for both indications but requested a second pneumonia study as a post-approval obligation.

In the case of both omadacycline and plazomicin, the regulators have doomed the products for the European market. Some may argue that these products do not deserve to be marketed given the availability of other agents. In fact, for omadacycline, that almost seems to be what the EMA is saying. On the other hand, the regulatory hurdles to the marketplace in Europe now become yet another nail in the coffin of new antibiotic investment in research and development. After placing

so much hope in European regulators, I find I am profoundly disappointed in their actions.

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