Reviewer's report

Title: Fluoroquinolone Resistance During 2000-2005: An Observational Study

Version: 3 Date: 6 February 2008

Reviewer: Joseph M Blondeau

Reviewer's report:

I have re-reviewed the manuscript and I acknowledge that the authors have made some modifications based on previous comments from my first review. Having said that, I still have some concerns regarding this manuscript and its message. The following are some of my concerns:

1) The authors do acknowledge that some percentage of moxifloxacin is excreted in urine. What drug level does this give as this may be central to the question they are proposing. With low MIC values for moxifloxacin and E.coli (as an example) is there sufficient drug concentrations in urine to inhibit bacterial growth. Second, at the 2007 meeting of ECCMID, Blondeau et al, reported that the mutant prevention concentration of moxifloxacin against E.coli and Klebsiella spp. was from 0.5-2ug/ml; MPC90 of 1ug/ml. These values are similar to what was previously published for ciprofloxacin and levofloxacin by Hansen and Blondeau, Journal of Chemotherapy, 2006. How does such data impact on the arguments. Clearly, moxifloxacin serum drug concentrations would exceed an MPC of 1 ug/ml for the full 24 hours of the dosing interval and that was previously published as well.

2) I still have some concerns regarding the title as written and the limitation expressed by the authors that a causal relationship cannot be established.

3) In the discussion, the authors state "However, in vivo urine bactericidal concentrations may be much higher than in vitro due to biofilm and pH effects." As well, "Subtherapeutic exposure may result in selection of fluoroquinolone resistant among Gram negative bacteria dwelling in the urinary tract...." I have no idea what these statements in the arguments are trying to suggest. Where is the biofilm? All antimicrobials have issues with biofilm! Where are the organisms dwelling in the urinary tract - periurethral - ?- and what evidence suggests moxifloxacin is more likely to select for these resistant strains than other quinolones - especially if they already have pre-existing mutations.

4) Finally, I do not accept that the manuscript as presented supports the conclusions as written.