

**Department of Pharmacology
Rouen University Hospital**

Dr Thomas DUFLOT

Associate Professor - Hospital Practitioner

thomas.duflot@chu-rouen.fr

Prof. Dr. James Leggett
*Editor of the Antimicrobial Agents and
Chemotherapy journal*

November 14th, 2024

Dear Prof. Dr. James Leggett,

I am writing you to resubmit the revised manuscript titled "State of the art of unbound ceftriaxone as a pharmacodynamic tool: Are we ready for its implementation in clinical practice?" for consideration for publication in the Antimicrobial Agents and Chemotherapy journal. The initial version was originally attributed under the reference AAC00014-24 and required extensive revisions.

Firstly, I would like to express my gratitude for considering the initial manuscript for the review process in AAC, and extend my thanks to the reviewers for their valuable comments. Attached, you will find a point-by-point response to the issues raised in the review, provided in a "Response to Reviewers" file, along with a PDF indicating the changes made from the original submission, highlighted or underlined, in a "Marked Up Manuscript" file, in addition to the revised manuscript.

I also created a repository on github: <https://github.com/ThomasDufлот/Ceftriaxone-AAC/> that will be made freely available to reproduce all analyses if the revised manuscript is accepted for publication.

In summary, we have made every effort to address all the reviewers' comments comprehensively. Notably, we conducted additional experiments, including external validation of the nine studied models using 62 samples with total and free ceftriaxone trough levels and albumin measurements, following approval from the local ethics committee (Approval Number: E2024-19).

Thank you for dedicating your time and attention to our submission. We eagerly anticipate your feedback and sincerely hope that you will find our work a fitting addition to your esteemed journal.

Sincerely,

Dr. Thomas DUFLOT

