

What were the key considerations in submissions where Clinical Pharmacology was a factor in the Complete Response Letter (non-approval)?

See NDA 217002, NDA 217338, NDA 217379, NDA 217556, NDA 218317, NDA 218828, NDA 219045, and NDA 761211.

It didn't make sense to create plots of trends in only 8 submissions.
So, instead, I list the findings.

Approvability Issues:

- *Dose: safety and/or efficacy questions remained.
- *Data not gathered in the population of interest to support dose.
- *Failed to bridge or demonstrate equivalence.
- *Exposure uncertain and there was a potential safety risk and/or nonclinical signal.

Mitigation strategies:

- *Collect additional clinical data.
- *Collect bioavailability data.
- *Characterize QT risk.
- *Perform an exposure-response analysis.
- *Reformulate.
- *Pursue contemporaneous authorization of an in vitro companion diagnostic device.
- *Pursue an accelerated approval pathway, instead.

The positive take on this is that Clinical Pharmacology has numerous tools to mitigate risk. Reading these CRLs provides insight into how Regulators view submissions so you can submit a successful application on the first go!

Note: This is my independent analysis of the Complete Response Letters released by FDA on September 4, 2025.

<https://www.fda.gov/news-events/press-announcements/fda-announces-real-time-release-complete-response-letters-posts-previously-unpublished-batch-89>