Common Hurdles Sponsors Face upon a Marketing Application Submission

Even before the FDA's full review of a New Drug Application (NDA) or Biologics License Application (BLA), a filing review is conducted to ensure that the submission is acceptable for a full review. A "Refuse to File" (RTF) letter from the FDA can halt years of progress in the blink of an eye.

What are the most common reasons for an RTF letter?

01

CMC deficiencies account for almost 20% of RTFs

02

After clinical efficacy and safety deficiencies (accounting for over 25% of RTFs), application organization was one of the top 5 reasons for the FDA to refuse to file a sponsor's submission

Equally as challenging as receiving an RTF letter are delays in your submission timeline. A recent analysis showed that delays in drug approval could be as much as $800,000 per day.

What are the stumbling blocks that can cause a delay in submission and approval?

01

Internal team dynamics

02

Building timelines without taking document inter-dependencies into account

03

Setting overly aggressive review schedules.

(Learn how to optimize and stagger your review schedules effectively here.)

Even well after submission, sponsors often face hurdles that can delay drug approvals:

- Quality control documentation
- Inspection readiness

Avoiding RTF letters and costly delays requires more than technical expertise. It demands foresight, alignment, and disciplined execution.

At Syner-G, we partner with sponsors to build documented, science-aligned, inspection-ready submissions from the earliest stages of development through post-submission support. From strengthening CMC packages and improving submission "reviewability," to optimizing cross-functional workflows and ensuring inspection readiness, our team helps reduce regulatory risk and accelerate time to approval.

Resources

Chahal HS, Mukherjee S, Sigelman DW, Temple R. Contents of US Food and Drug Administration Refuse-to-File Letters for New Drug Applications and E cacy Supplements and Their Public Disclosure by Applicants. JAMA Intern Med. 2021;181(4):522–529. doi:10.1001/jamainternmed.2020.8866

Kaitin K, editor. Dollar Value of One Day Delay in Drug Development is Now 20% of Blockbuster Era Levels. Tufts CSDD Impact Report. July/August 2024: 26(4).

Smith Z., DiMasi J., Getz K. New Estimates on the Cost of a Delay Day in Drug Development. Ther Inn & Reg Sci 2024.