SA48

Responses of Pharmaceutical Companies to Literature Review Inquiries from a Regulatory Authority: A Retrospective Analysis

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Background

In support of new marketing authorizations and variations for novel pharmaceutical products, regulatory submissions generally consist of comprehensive modules that cover all phases of clinical development, including Phase I, II, and III trials. These comprehensive submissions are essential to ensure a thorough evaluation of the product's safety and efficacy.

However, for certain submissions pertaining to products with known active substances or generics, regulatory guidelines permit applicants to submit only relevant literature references, thus exempting them from providing the complete set of documentation typically required for novel products. Although, the applicant is responsible for ensuring that the submitted literature is scientifically rigorous, directly relevant, and appropriately aligned with the specific product, including its dosage form, route of administration, and intended therapeutic indication.

Objective

This study aims to evaluate the adequacy and regulatory compliance of company responses to literature inquiries issued by the Saudi Food and Drug Authority (SFDA), focusing on the effectiveness of these responses in meeting regulatory expectations.

Methodology

A retrospective document analysis was conducted, reviewing all literature inquiries and corresponding company responses filed in the electronic Common Technical Document (eCTD) from January 2021 till November 2023. Data of product submissions were collected from the Saudi Drug Registration (SDR) and Extedo Universal Review System (EURS).

Dscriptive analysis was performed to assess the current literature review inquiries and company responses in terms of number of inquiries, type of products, submitted evidence, search strategies, and decision outcomes related to these submissions.

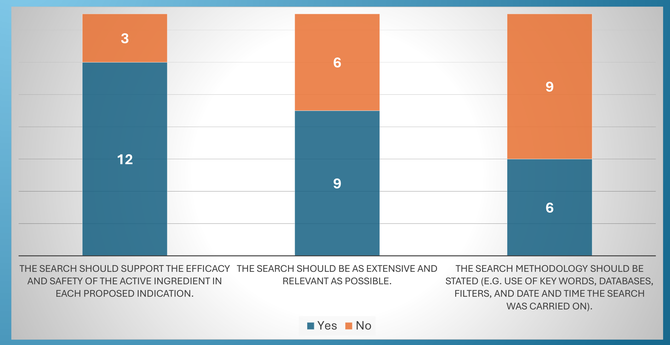
SFDA Clinical Consideration for Efficacy and Safety Assessment

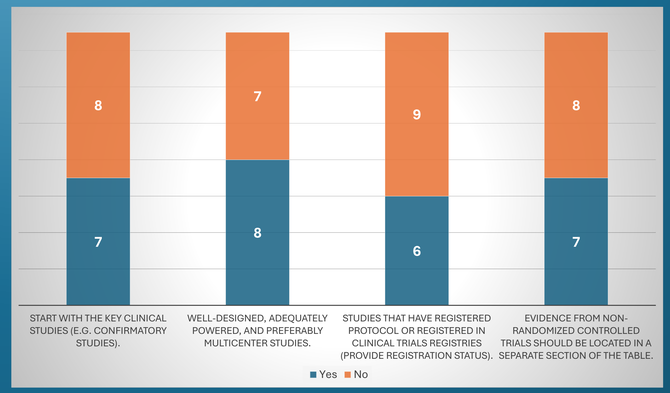
The literature review should be submitted in module 2.5 clinical overview and covers the following aspects:

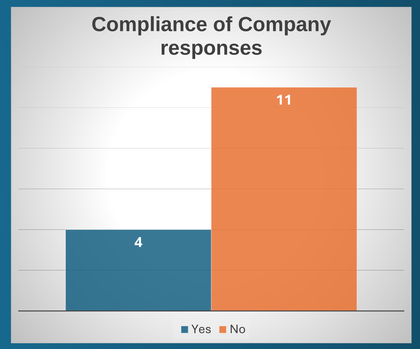
- The search should support the efficacy and safety of the active ingredient in each proposed indication.
- The search should be as extensive and relevant as possible.
- The methodology of the search used should be stated in detail (database used, keywords used, and filters applied as well as date and time the search was carried on).
- Provide a tabular listing of the identified literature with their citations and arrange the studies according to the following:
  - Start with the key clinical studies (e.g. confirmatory studies).
  - Well-designed, adequately powered, and preferably multicenter studies.
  - Studies that have registered protocol or registered in clinical trials registries (provide registration status).
  - Evidence from non-randomized controlled trials should be in a separate section of the table.

Results

Of the 28 products evaluated, 15 met the inclusion criteria. Nine products were generics compared to six new products from known active substances.







Conclusion

The study reveals a significant discrepancy between the expectations of the SFDA and the quality of company responses to literature inquiries. The findings suggest an urgent need for regulatory guidance specific to literature reviews, aiming to standardize and improve the quality of submissions.

References

1. SFDA Data Requirements for Human Drugs Submission
2. SFDA Clinical Considerations for Efficacy and Safety Assessment
3. ICH guideline M4 (R4) on common technical document (CTD) for the registration of pharmaceuticals for human use