Saudi: SFDA issues new pharmaceutical variations guidelines

Christina Sochacki - Senior Associate - Corporate / Mergers and Acquisitions
c.sochacki@tamimi.com - Jeddah

Effective 7 October 2020, the Saudi Food and Drug Authority ("**SFDA**") issued a new Guidelines for Variation Requirements, Version 6.1 ("**Guidelines**"). The Guidelines classify variations and provide the basic data required for each type of variation. Namely, the new guidelines change certain variations to a new "Type" and several variations were added with various "Types" associated thereto. The Guidelines apply to changes made to drug products that have already received a marketing authorisation from the SFDA.

The Guidelines were adopted from the European Medicines Agency (EMA) Guidelines on the details of the various categories of variations, Regulation (EC) No. 1234/2008. Below, we discuss the different types of variations and the associated requirements to assist applicants in the preparation and submission of drug applications for variations to a marketing authorisation.

Below, we examine the main categories of variations, or post-marketing changes, and provide several examples and the requirements for implementing such variations.

Types of Variations

The variation or post-marketing changes can be classified into two categories: 1) minor variations; and 2) major variations.

Minor variations that are of "Type IA" do not require prior approval before implementation. Within Type IA, those variations that are of "Type IA_{IN}" should be submitted immediately, within 14 days following implementation, to the SFDA. Other Type IA variations can be complied and submitted to the SFDA in a single variation application no later than 31 January of each year. In general, editorial changes and typos are treated as Type IA changes.

Minor variations that are of "Type IB" must be submitted to the SFDA by the marketing authorisation holder ("**MAH**") before implementation, but do not require formal approval; however, the MAH should wait to implement the change to ensure that the application is deemed acceptable before implementing the change.

Major variations of "Type II", which may have a significant impact on the quality, safety, and efficacy of a medicinal product, do require prior approval before implementation.

Classification of variation or post-market changes

Several examples of minor variations include:

- changes in the MAH name and address or transfer of the product to a new MAH (a different legal entity);
- removing an agent name from the artwork;

- changes in the name of the active substance;
- deletion of a manufacturing site(s) (including for: an active substance; intermediate; or finished product; packaging site; manufacturer responsible for batch release; site where batch control takes place; or supplier of a starting material, reagent, or excipient, when mentioned in the dossier); and
- change or addition of imprints, bossing, or other markings, including replacement or addition of inks used for product marking.

Several example of major variations include:

- change in the manufacturer of a starting material/reagent/intermediate used in the manufacturing process of the active substance or change in the manufacturer of the active substance, where no Certificate of Suitability is available and:
  - it is an introduction of a manufacturer of the active substance supported by a drug master file ("**DMF**") or not supported by a DMF and requires significant update to the relevant active substance section of the dossier;
  - the proposed manufacturer uses a substantially different route of synthesis or manufacturing conditions, which may have a potential to change important quality characteristics of the active substance, such as qualitative and/or quantitative impurity profile requiring qualification, or physico-chemical properties impacting on bioavailability; and
  - changes to quality control testing arrangements for a biological active substance: replacement or addition of a site where batch control/testing including a biological/immunological/immunochemical method takes place;
- change in test procedure for active substance or starting material/reagent/intermediate used in the manufacturing process of the active substance where it is a change (including replacement or addition) to a biological/immunological/immunochemical test method or a method using a biological reagent for a biological active substance; and
- change in the specification parameters and/or limits of an active substance, starting material/intermediate/reagent used in the manufacturing process of the active substance where the change is outside the approved specifications limits range for the active substance.

Changes that make a new pharmaceutical application necessary, rather than a variation, include, but are not limited to:

1. changes to the active pharmaceutical ingredient ("**API**"), such as:
   - changes of the API to a different API;
   - inclusion of an additional API in a multi-component product; and
   - change in the dose of one or more APIs;
2. changes to the pharmaceutical form/dosage form, such as:
   - change from an immediate-release product to a slow or delayed-release dosage form or vice versa;
   - a change from multi-dose to single-dose or vice-versa; and
   - change from a liquid to a powder for reconstitution, or vice-versa;
3. change in the strength;
4. change or addition of route of administration;
5. addition or replacement of measuring or administration device being an integrated part of the primary packaging that results in a change to the strength, pharmaceutical form, or route of administration of the product; and
6. other changes specific to veterinary medicinal products to be administered to food-producing animals, including a change or addition of target species.

Changes to the API supplier

Focusing in on additions and changes to the API supplier that has already been submitted, the following will be required to be submitted to the SFDA:

1. a declaration letter indicating that the DMF of the new API supplier has been evaluated by SFDA during the last five years and no changes have been made since that time;
2. a letter of commitment to immediately initiate accelerated and long term (covering the shelf life) stability studies on at least on production batch of the finished product according to the GCC guidelines using API from the new supplier and submit stability data immediately to the authority only in case of any out of specification results or potentially outside specifications at the end of the approved shelf life, along with the proposed action; and
3. where appropriate, comparative dissolution profile data for the finished product on at least one pilot batch containing the active substance from both the current and proposed sites. For herbal products, comparative disintegration data may be acceptable.

Slightly different requirements must be met in the event a Certificate of Suitability ("**CEP**") is available or where a CEP is not available.

The SFDA is responsible for putting in place regulations and effective controls to ensure the safety of food, drugs, medical devices, cosmetics, pesticides and feed in the Kingdom of Saudi Arabia. Please join our healthcare email list to receive more healthcare and life sciences legal and regulatory updates impacting the industry across the Middle East.

Al Tamimi & Company's Healthcare Sector regularly advises on laws and regulations impacting the healthcare sector. For further information please contact healthcare@tamimi.com.