الهيئة العامة للغذاء والدواء
Saudi Food & Drug Authority

SFDA Guidance for Drafting Risk Management Plans of COVID-19 Vaccines

Version 1.0

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Saudi Food & Drug Authority

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Saudi Food and Drug Authority

Vision and Mission

Vision

To be a leading international science-based regulator to protect and promote public health

Mission

Protecting the community through regulations and effective controls to ensure the safety of food, drugs, medical devices, cosmetics, pesticides and feed

Document Control

Version	Author	Date	Comments
1.0	Executive Directorate of pharmacovigilance	05 September 2021	-

Table of Content:

1. INTRODUCTION

This guidance was mainly adopted from the European Medicines Agency document "Consideration on core requirements for RMPs of COVID19 vaccines". This guidance is a supplemental to the Saudi Food and Drug Authority (SFDA) pharmacovigilance guideline on good pharmacovigilance practices to provide further section-by-section guidance and requirements for drafting the Risk Management Plans (RMPs) of COVID-19 vaccines.

1.1. Scope

This document addresses the RMP for COVID-19 vaccines.

1.2. Objective

This document aims to provide guidance and requirements for Market Authorization holders (MAHs) for drafting the RMP of COVID-19 vaccines.

1.3. COVID-19 vaccines RMP requirements

This guidance should be read in conjunction with existing relevant SFDA guidance (including, Guideline on good pharmacovigilance practices (GVP), Guideline on GVP – Definition, GVP - Product- or Population-Specific Considerations I: Vaccines for prophylaxis against infectious diseases and National Manual for Surveillance of Adverse Events Following Immunization in Saudi Arabia) published on the SFDA website.

2. CONTENT OF THE RMP:

Part I – Overview

If the originally approved product changed to include different/additional strains, the RMP should have separate details for:

1- Originally approved product
2- The product containing different/additional strains.

Part II – Safety Specification

Module SI - Epidemiology of the indication(s) and target population(s)

This section should provide the most updated information on the epidemiology of COVID-19 in Saudi Arabia. Any existing uncertainties should be acknowledged.

Module SII - Non-clinical part of the safety specification

This section should provide the most updated information if not submitted with an initial marketing authorisation application. In addition, it should be included in the earlier versions of the RMP.

Module SIII - Clinical trial exposure

This section should provide the most updated information from clinical trial data generated post-approval date. In addition, up-to-date information from protocols of ongoing trials will be needed to provide the SFDA up-to-date information about the safety follow-up and the expected size of the safety database.

Module SIV - Populations not studied in clinical trials

SIII advice above applies

Module SV - Post-authorisation experience

This section should provide the most updated information available for post-approval of the vaccine in other regions of the world, including Saudi Arabia.

Module SVI - Additional requirements for the safety specification

This section is not expected to be relevant for COVID-19 vaccines.

Module SVII - Identified and potential risks

While information in this section may not be available during the early stage of the rolling review, it should be constructed as preliminary results from clinical trials become available, with further data added from the same trials post-approval.

Important identified risks

The important identified risks should include safety concerns observed in pre-clinical/clinical results, if inapplicable, it could be acceptable that no important identified risks are included in the RMP. This may be expected in the context of prophylactic vaccines, if the risks related to the administration procedure will have minimal impact on risk/benefit balance.

Important potential risks

Safety concerns rising from clinical and/or pre-clinical data and have potential impact on the risk/benefit balance of the vaccine should be included in the list of important potential risks; these are the safety concerns that are derived from information suggesting a causal relationship with the vaccine, but isn't solid enough to conclude a definite causality.

Important potential risks could also be derived from the experience with the vaccine construct/platforms, the growing global knowledge of the COVID-19, or based on more theoretical considerations (e.g. vaccine-associated enhanced respiratory disease, immune mediated disorders).

The list of important potential risks should not include a general comprehensive list of all theoretical risks for vaccines; rather, the list should include well-justified safety concerns for which evidence described above exists. Theoretical risks could be included in the list of adverse events of special interests (AESI) to be prioritized for followed up through routine and additional pharmacovigilance activities.

Missing information

While not all subpopulations excluded from clinical trials will essentially be viewed as missing information, the following relevant subpopulation should be considered to be added as missing information in the RMP:

- Safety in Use in pregnancy and lactation;
- Safety of the vaccine in patients with severe co-morbidities (e.g. Use in immunocompromised subjects; Use in frail subjects with unstable health conditions and co-morbidities (e.g. chronic obstructive pulmonary disease (COPD), diabetes, chronic neurological disease, cardiovascular disorders, autoimmune disorders or inflammatory disorders);
- Safety in paediatric population;
- Long-term safety;
- Interaction with other vaccines

In addition to the concerns described above, the following are further considerations for Module SVII for COVID-19 vaccines:

- Reactogenicity should be discussed in the RMP if it is shown in clinical trials that the vaccine have higher reactogenicity than control. The discussion should address the impact on the safety profile, necessary risk minimisation measures to avoid reactogenicity, reactogenicity in subgroups such as frail vaccine recipients, and the risk of flares in patients with chronic inflammatory conditions.
- If the formulation or preparation techniques may increase the chance of developing an ADR, it should be discussed in this section; e.g., sterility concerns if a diluent is required for the vaccine.
- The risk of vaccine drop out in vaccine requiring more than one dose e.g. due to reactogenicity should be evaluated as well as the risk of disease enhancement; the discussion should consider the recommendation for administration of a e.g. second dose containing replaced/additional strains instead of the original product, or a of subsequent dose containing replaced/additional strains after a full vaccination course with the original product;
- Signal from clinical trials should be adequately documented and discussed in this section;
- Risks of vaccination errors especially in situations like mass vaccination campaigns could be discussed in this section, if applicable. This include errors occurring due to the use of multi-dose vials
- The safety of using mixed vaccine schedule could be discussed in this section.

Part III - Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

The applicant should describe their plan for signal detection activities and collecting individual Case Safety Report (ICSR) reports. While drafting this part, the applicant should take into consideration the challenges caused by the pandemic that could influence this process .e.g. high volume of ADR reports to be processed.

Signal detection and management; The RMP may provide information about:

- **Data sources for signal detection:** the MAH should conduct signal detection using every data source available such as MAHs' own databases, WHO database, etc., to conduct the signal detection. The data sources should be described in the RMP. Using only single data source is not considered adequate.
- Routine signal detection methods and practices: the effect of the national COVID-19 vaccination campaign and encouraging health care professionals and the public to report any potential adverse events following the COVID-19 vaccination may lead to high volumes of ADR reports. Conduction routine signal detection should take into account when performing the analysis, the increased volume of the COViD-19 reporting, the campaign effect and the quality of the reports.
- The MAH should leverage the available national and global efforts to define lists of AESI and background rates. The signal detection activities should include, but are not limited to:
  - Observed versus expected (O/E) analyses.
  - Time-to-onset (TTO) analysis
  - Time series analyses and algorithms to detect batch issues and spurious reports
  - Cluster analyses to help identify groups of ICSRs that may point to syndromes.

ICSR reporting requirements are described in Saudi guideline on good pharmacovigilance practices.

Specific follow-up questionnaire(s): in consultation with the SFDA, the MAH can consider obtaining structured information for reports of selected safety concerns in the RMP and provide the questionnaire in the RMP annex for evaluation. The applicant should consider using lay language suitable for the reporter.

After obtaining the approval, the Marketing Authorization Holder are required to submit a **summary monthly safety report (SMSR)** for the first 6 months of marketing the COVID-19 vaccines, and report should include the following minimum requirements:

- Interval/cumulative exposure data of vaccine in Saudi Arabia and worldwide.
- Interval/cumulative number of serious and non-serious case reports, overall and by age groups and in special populations (e.g. pregnant women).
- Actions taken by regulatory agencies for safety reasons.
- Changes to reference safety information.
- List of new, ongoing, and closed signals with their evaluation.
- Causality assessment evaluation of serious adverse events, including fatal cases.
- Summary of efficacy and safety findings from clinical studies (completed or ongoing).
- Benefit-risk evaluation

III.2 - Additional pharmacovigilance activities

Safety surveillance from current clinical trials should be prioritized and integrated as part of additional pharmacovigilance activities. Protocol review of long-term follow-up should be performed early in the RMP assessment. The results of pivotal trials' final safety assessments are anticipated should be submitted for review.

In Saudi Arabia, Marketing Authorization Holders of COVID-19 vaccines are required to conduct an observational **Post Authorization Safety study (PASS)** on local population to investigate the following safety considerations, the protocol of the PASS should be included in this section:

- The estimated incidence rate of AESI, such as vaccine enhanced disease and other clinically significant events among individuals vaccinated with the COVID-19 vaccine in a cohort of patients and in sub-cohorts of interest such as women of childbearing age, immunocompromised patients, and stratified by age.
- Characterize of the utilization patterns of vaccine among recipients, dividing them in sub-cohorts of interest such as women of childbearing age, immunocompromised, and within age categories.

Part IV: Plans for post-authorisation efficacy studies

No specific/additional requirements related to RMP presentation.

Part V: Risk minimisation measures

The applicant is required to have an educational material (healthcare provider guide and vaccine recipient guide) for COVID-19 vaccines; a draft of these risk minimisation measures should be included in this section for evaluation. Templates for the healthcare provider guide and vaccine recipient guide are included in the *Annex 1* and *Annex 2* of this guideline; these templates can be used and modified by the applicant as needed. Arabic version of the Vaccine-Recipient Guide should be included.

Annex 1 - COVID-19 vaccines Healthcare Provider Guide template

<Vaccine brand name>

Healthcare Provider Guide

<Start with objectives of this document. A statement explaining that the educational material is essential to ensure the safe and effective use of the product and appropriate management of the important selected risks>

Description of COVID-19:

Coronavirus disease 2019 (COVID-19) is an infectious disease caused by the novel coronavirus, SARS-CoV-2, that appeared in late 2019. A predominantly respiratory illness that can affect other organs. People with COVID-19 have reported a wide range of symptoms, ranging from mild symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus.

What is (brand name) Vaccine?

<Summary information about the vaccine, including the MOA and the indication>

Posology, preparation, and method of administration:

- *Dosing and schedule*
- *Preparation*
- *Method of administration*

Observation time after vaccine administration:

Special warnings, precautions and contraindication:

This section should be discusses in a clear and concise manner. Including the exact transcript of the text in the SPC is not preferred.

Special population:

Advice regarding the use of the vaccine in special population (e.g. paediatric, geriatric, and pregnant or lactating women) should be discussed in this section.

Interaction:

Interaction with drugs or other vaccines should be discussed in this section.

Adverse reaction:

The most important adverse reactions that the healthcare provider should look out for are included in this part.

Storage and handling:

Information to be provided to vaccine recipients/caregivers

- As the vaccination provider, you must discuss with recipient or their caregiver the information included in the Vaccine-Recipient Guide.
- Provide a copy of Vaccine-Recipient Guide prior to the individual receiving Vaccine.
- Highlight the importance of second dose schedule.

Call for reporting
Healthcare providers are urged to report ADRs related to use of the vaccine to the following contact information:

The National Pharmacovigilance Centre (NPC) - Saudi Food and Drug Authority (SFDA)
SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa/

<Applicant's ADR reporting information should be added>

<Include a statement indicating that this document id provided in agreement with the Saudi Food and Drug Authority>
<Version number and date of drafting the document should be included>

Annex 2 - COVID-19 vaccines Vaccine-Recipient Guide template

<Vaccine brand name>

Vaccine-Recipient Guide

<Introductory text such as the following should be added: You are being offered the <Vaccine brand name> Vaccine to prevent Coronavirus Disease 2019 (COVID 19) caused by SARS-CoV-2. This guide contains information to help you understand the risks and benefits of the Vaccine.>

Read all of this guide carefully before you receive this vaccine because it contains important information for you.

- Keep this guide. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects.

What is Covid-19 disease?
COVID-19 disease is caused by a coronavirus called SARS-CoV-2. This type of coronavirus has not been seen before. You can get COVID-19 through contact with another person who has the virus. A predominantly a respiratory illness that can affect other organs**.** Wide range of symptoms have been reported, ranging from mild symptoms to severe illness. Symptoms may appear 2-14 days after exposure to the virus. Symptoms may include: fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhea

What is (brand name) vaccine?
< Brief summery about the vaccine including how it is work and the indication>

What should you know before taking the vaccine?
< Important information for the recipient should know it about the Vaccine>

What should you mention to your vaccination provider before you get the (brand name) vaccine?
< Any health condition the patient should mention it before receiving the vaccine >

Who cannot take the vaccine?
Precaution, warning, and contraindication

Special population (e.g. pediatric, geriatric, and pregnant or lactating women) can be discussed in this section.

How the vaccine is given?
Methods of administration and multi dose schedule should be discussed in this section.

What should I do immediately after taking the vaccine?
Waiting time observation should be discussed.

What are the possible side effects?

Serious adverse events such as allergic reaction should be discussed in this section and recommended actions to manage the side effects should be provided for the recipient.

Can I receive the (brand name) covid-19 vaccine with other vaccines or medications?

<Interaction with medications or other vaccines should be discussed in this section>

Please report any adverse reactions that happens to you after receiving the vaccine to:

The National Pharmacovigilance Centre (NPC) - Saudi Food and Drug Authority (SFDA)
SFDA call center: 19999
E-mail: npc.drug@sfda.gov.sa
Website: http://ade.sfda.gov.sa/

<Applicant's ADR reporting information should be added>

<Include a statement indicating that this document id provided in agreement with the Saudi Food and Drug Authority>
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