RISK MANAGEMENT PLAN (RMP)
Malaysia-Specific Annex (MSA)

I. Product Overview in Malaysia

Date of Submission	
MSA Version Number	Version 2.0
Product Name	COVILO Suspension for Injection COVID-19 Vaccine (Vero Cell), Inactivated
Active Ingredient(s)	Inactivated SARS-CoV-2 (19nCoV-CDC-Tan-HB02 strain) (Vero cell)
Dosage Form	Semi-transparent suspension in slightly white colour in vials
MAL Number	
Date of First Registration Approval in Malaysia	
Product Category	Vaccine
Product Registration Holder (PRH)	Duopharma (M) Sdn Bhd Lot 2599, Jalan Seruling 59, Kawasan 3, Taman Klang Jaya 41200 Klang, Selangor Darul Ehsan, MALAYSIA
Details of Responsible Person for Pharmacovigilance (RPPV) (name, designation, email, telephone number)	**Name of primary contact:** Sabrina Binti Haron Designation: General Manager, Technical Compliance Email address: sabrina-haron@duopharmabiotech.com Phone numbers: Office: +603-3323 2759 ext: 1119 Mobile: +6012-318 9751 **Name of secondary contact:** Dr Shahnun Bin Ahmad Designation: Manager, Medical Affairs Email address: shahnun@duopharmabiotech.com Phone numbers: Office: +603-8924 2188 ext: 2298 Mobile: +6013-391 0110 **Name of secondary contact:** Saw Jia Huey Designation: Senior Executive/Pharmacist Email address: jhsaw@duopharmabiotech.com Phone numbers: Office: +603-3323 2759 ext: 1370 Mobile: +6016-384 3029
Approved Indication(s)	Prevention of Covid-19 disease

II. Changes from Previous RMP Version

- Updated section IV(a) Routine/Additional Risk Minimisation Activities by Safety Concern to align with the local package insert, revision date 09.07.2021.

- Updated section IV(c) Vaccine Reminder Card with COVILO Vaccination Card Ver 1.0 dated 12.07.2021 (Appendix 1).
- Updated section IV(e) Traceability to include additional information.

III. Summary of Changes to the MSA over time

Date of Submission	MSA Version Number	Description of Change
21 Jun 2021	V1.0	First MSA submitted.
	V2.0	▪ Updated Product name and removal of prefilled syringe ▪ Updated local risk minimisation plan to align with local package insert ▪ Additional details on Vaccine Reminder Card ▪ Additional details on Traceability

IV. Safety Specification: Summary of Safety Concerns

Important identified risks	▪ Anaphylaxis
Important potential risks	▪ Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD) ▪ Programmatic errors ▪ Reactogenicity
Missing information	▪ Use during pregnancy and breastfeeding ▪ Long-term safety data ▪ Use in paediatric population <18 years of age ▪ Interaction with other vaccines ▪ Use in immunocompromised patients, including HIV ▪ Use in patients with comorbidities (e.g., chronic obstructive pulmonary disease [COPD], diabetes, chronic neurological disease, cardiovascular disorders) ▪ Safety of subjects with acute disease, acute attack of chronic disease, severe chronic disease, allergic constitution and fever ▪ Autoimmune ▪ Inflammatory disorders ▪ Impact of the emergence of variants on vaccine efficacy/effectiveness and safety

	▪ Interchangeability or sequential use with other vaccines ▪ Subject aged 60 years and above ▪ Current or past SARS-CoV-2 infection

V. Local Pharmacovigilance Plan

Please refer to Duopharma's PVSS document.

a) Routine Pharmacovigilance Activities

All cases of spontaneous ARFI/ADR received from healthcare professional and vaccine recipients (both public and private sector) will be entered into PV safety database maintained by Duopharma. All cases will be coded using the most recent version of the MedDRA dictionary.

Each AEFI/ADR will be assessed to the greatest possible extent to determine:

- The severity of the AEFI/ADR. Severity of AEFI/ADR received from healthcare professional will be assigned by the reporter themselves. In cases where no severity was assigned by healthcare professional or AEFI/ADR was reported by vaccine recipient, severity of AEFI/ADR will be assessed according to Hartwig and Seigel severity assessment scale for adverse drug reactions[1]
- Its duration (start and end date);
- Whether drug treatment or other treatment of AE was assigned (absence of the associated drug/drug-free treatment or presence of the associated drug/drug-free treatment)
- Causality according to World Health Organization causality assessment algorithmn[2]

The frequency of AEFI/ADR will be calculated for each system organ class (SOC) and the preferred term (PT) based on the number of doses that have been supplied for the particular month (assuming that all doses will be used). Alternatively, the number of doses used for any particular month can be requested from Ministry of Health and used as denominator.

The summarized data on the AEFI/ADR severity, their relation to the vaccine and the relevant outcomes will be provided for each system organ class.

The Malaysia's Safety Summary Report will be shared across with BIBP on a monthly basis. The consolidated Safety Summary Report will thereafter be submitted to NPRA via email. This will be done on a monthly basis (on the 10th day of each month for the previous month).

PBRER will be prepared to be submitted to NPRA on a regular basis.

b) **Additional Pharmacovigilance Activities by Safety Concern**

Post Authorization Safety Study (PASS) and Post Authorization Efficacy Study (PAES)

There is currently no plan to conduct any Post Authorization Safety Study (PASS) and Post Authorization Efficacy Study (PAES) in Malaysia. Duopharma will share the result and update NPRA on various clinical studies that are currently being conducted worldwide once the results are available.

According to information from 'Program Imunisasi COVID-19 Kebangsaan' documentation and monitoring of AEFI/ADR among vaccine recipient will also be conducted by enhanced surveillance where vaccine recipient can report via MySejahtera application. Investigation for serious AEFI will be conducted by a special committee to evaluate AEFI cases and safety issue pertaining to COVID-19 vaccine. It is hoped that this information will be shared by Ministry of Health with Duopharma to ensure comprehensive capturing of all AEFI/ADR both in public and private sector.

VI. Local Risk Minimisation Plan

a. Routine/Additional Risk Minimisation Activities by Safety Concern

Safety Concerns	Local Risk Minimisation Activities	Additional Information
Important identified risks		
Anaphylaxis	***Routine:*** After vaccination, the recipients should be observed on site for at least 15 minutes. Vaccination clinics to be equipped with epinephrine and other first aid drugs in case of an occasional severe allergic reaction. (Package Insert [Contraindications] and [Precautions]) ***Additional***: Nil	Nil
Important potential risks		
Vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD)	***Routine:*** Nil ***Additional:*** Nil	Nil

Programmatic errors	***Routine:*** Training of personnel in charge of storage, distribution and use of vaccines on vaccine knowledge. (Package Insert [Precautions] and [Storage]) ***Additional:*** Nil	
Reactogenicity	***Routine:*** There is limited experience with COVILO from clinical trials. (Package Insert [Side Effects]) ***Additional:*** Nil	Nil
Missing information		
Use during pregnancy and breastfeeding	***Routine:*** Limited experience exists with use of COVILO in pregnant women. Administration of COVILO in pregnancy should be only considered when the potential benefits outweigh any potential risks for mother and foetus. It is unknown whether COVILO is excreted in human milk. (Package Insert [Use in Pregnancy & Lactation]) ***Additional:*** Nil	Nil
Current of past SARS-CoV-2 infection	***Routine:*** There is no evidence of protective efficacy of COVILO for SARS-CoV-2 infected person. (Package Insert [Precautions]) ***Additional:*** Nil	Nil
Long term safety data	***Routine:*** At present, there is no clinical data on long-term safety profile of COVILO. (Package Insert [Precautions]) ***Additional:*** Nil	Nil
Use in paediatric population <18 years of age	***Routine:*** At present, there is no clinical data on safety and efficacy of vaccination among paediatric population <18 years of age. (Package Insert [Indication]) ***Additional:*** Nil	Nil
Subjects aged 60 years and above	***Routine:*** At present, the evidence of the protective efficacy of COVILO on people aged ≥60 has not been obtained. (Package Insert [Indication] and [Precautions]) ***Additional:*** Nil	
Interaction with other vaccines	***Routine:*** At present, there is no clinical data on the interaction between COVILO with other vaccines. (Package Insert [Precautions] and [Interaction with Other Medicaments]) ***Additional:*** Nil	Nil

Use in immunocompromised patients, including HIV	***Routine:*** No data on the safety and efficacy of COVILO among population with immune impairment (such as malignant tumour, nephrotic syndrome, AIDS patients) have been obtained. The vaccination of this vaccine among such population should be subjected to individual considerations. (Package Insert [Precautions]) ***Additional:*** Nil	Nil
Use in patients with comorbidities (e.g., chronic pulmonary disease [COPD], diabetes, chronic neurological disease, cardiovascular disorders)	***Routine:*** Use with caution in patients who have diabetes, and those with a history or family history of convulsions, epilepsy, encephalopathy or mental illness. (Package Insert [Contraindications] and [Precautions]) ***Additional:*** Nil	Nil
Safety of subjects with acute disease, acute attack of chronic disease, severe chronic disease, allergic constitution and fever	***Routine:*** Use with caution in patients with acute disease, acute onset of chronic diseases and fever. Delay the vaccination after the doctor's evaluation if necessary. (Package Insert [Contraindications] and [Precautions]) ***Additional:*** Nil	Nil
Use in patients with autoimmune disorders	***Routine:*** There is limited information on the safety of COVILO in individuals with autoimmune disorders. (Package Insert [Precautions] and [Interaction with Other Medicaments]) ***Additional:*** Nil	Nil
Use in patients with inflammatory disorders	***Routine:*** There is limited information on the safety of COVILO in individuals with inflammatory disorders. (Package Insert [Precautions] and [Interaction with Other Medicaments]) ***Additional:*** Nil	Nil
Impact of the emergence of variants on vaccine efficacy/effectiveness and safety	***Routine:*** Nil ***Additional:*** Nil	Nil
Interchangeability or sequential use with other vaccines	***Routine:*** Training of personnel in charge on vaccine knowledge. (Package Insert [Precautions] and [Interaction with Other Medicaments]) ***Additional:*** Nil	Nil

b. Periodic Update of Local Package Insert

As the product will only be granted conditional registration, the product package insert will need to be updated as and when new information becomes available especially in relation to the Important Identified Risk, Important Potential Risk and Missing Information relevant to the product.

c. Vaccine Reminder Card

Vaccine reminder card will be provided for each vaccinee. The Vaccine Reminder Card Version 1.0 dated 12.07.2021 can be referred to in Appendix 1. Information on the Vaccine Reminder Card will be updated accordingly should new information becomes available.

d. Cold-chain handling and storage

Shipment of vaccines from the manufacturer to Duopharma will be done by an experienced forwarding agent. The main objective is to ensure the cold chain of the vaccines are not broken at any point in time, hence sufficient control will be put in place to manage the cold chain.

Upon the arrival of the vaccine, the regulators will perform the lot release upon inspection of the vaccines. These vaccines will be transported to the customer using a cold chain box. Each box will be accompanied by a temperature monitoring device to ensure no excursion of temperature till the customer receives the vaccines.

Duopharma has established 2°C-8°C supply chain since we have been supplying other cold chain products in Malaysia under the same condition.

In addition, each label of the vial comes with a Vaccine Vial Monitors (VVM). VVM is a time-temperature sensitive dot that provides an indication of the cumulative heat to which the vial has been exposed. It warns the end user when exposure to heat is likely to have degraded the vaccine beyond an acceptable level.

e. Traceability

Vaccine Management system (VMS) will be used to ensure traceability up to the patient level. This will eliminate the potential cause of counterfeiting of the vaccines.

Each product packaging will be furnished with a unique serial number which is generated by MIMOS. This unique serial number will serve as a point of traceability for the vaccines.

f. Training materials for healthcare professional

Product Brochure for healthcare professional will be developed based on the approved Malaysian Package Insert and Factsheet. The material will be shared for NPRA approval once available.

VII. Additional Information

Not applicable.

For Office Use Only	
NPRA Reference Number	
Date Received	
Date Assessed	
Name of Assessor	
Remarks	

References

1. Steven C. Hartwig, Siegel J., Philip J, Preventability and Severity Assessment in Reporting Adverse Drug Reactions, American Journal of Hospital Pharmacy,49:2229-32, October 1992.

2. Causality assessment of an adverse event following immunization (AEFI): user manual for the revised WHO classification, second edition, WHO, Switzerland, 2018.

1–62 p. Available from:
http://www.who.int/vaccine_safety/publications/aefi_manual.pdf?ua=1

3. Recommendation for an emergency use listing of Covid-19 Vaccine BIBP submitted by Beijing Institute of Biological Products Co. Ltd., Version 4 June 2021, WHO.

4. Package insert COVILO, COVID-19 Vaccine (Vero Cell), Inactivated, last revised June 2021. Available from:
https://extranet.who.int/pqweb/sites/default/files/documents/PI_Covid-19_Vaccine_BIBP_updated_in_June%202021_Finalized_9Jun21.pdf

5. Local package insert COVILO Suspension for Injection COVID-19 Vaccine (Vero Cell), Inactivated, last revised 09.07.2021.

Appendices

1. COVILO Vaccination Card Ver 1.0 dated 12.07.2021