Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG REGULATION AND RESEARCH

MONITORED RELEASE AND INITIAL REGISTRATION OF VACCINES AND BIOLOGICALS

Who May Avail : All Manufacturers, Distributors, Importers, Exporters, Wholesalers, and Traders of Vaccines, Biologicals, Stem Cell, and Blood and Blood Products

Fees to be Paid : **Monitored Release:**
Php 33,333.33/5 years + 500.00 (Brand Name Clearance, if applicable) + Php 5,000.00 (clinical review) + Php 2,500.00* [Post-Marketing Surveillance (i.e., Local Phase IV Clinical Trial) Protocol Review] + 1% LRF

Initial
Branded: PHP 3,000.00/year + PHP 500.00 (Brand Name Clearance) + 1% LRF
Unbranded: PHP 2,000.00/year + 1% LRF
The applicant may apply for 2/5-year CPR validity.

2-year validity:
Branded: PHP 6,000.00 + PHP 500.00 (for Brand Name Clearance) = PHP 6,500.00 + 1% LRF
Unbranded: PHP 4,000.00 + 1% LRF

5-year validity:
Branded: PHP 15,000.00 + PHP 500.00 (for Brand Name Clearance) = PHP 15,500.00 + 1% LRF
Unbranded: PHP 10,000.00 + 1% LRF

Variation-turned-Initial:
PHP 15,000.00 + 1% LRF

**If additional PV activity(ies) are necessary based on FDA Circular No. 2021-020*

CHECKLIST OF REQUIREMENTS

- **AO No. 47-a s. 2001: Rules and Regulations on the Registration, including Approval and Conduct of Clinical Trials, and Lot or Batch Release Certification of Vaccines and Biological Products**
- **ASEAN Common Technical Dossier**

Part I: Administrative Data and Product Information
Sec. A: Introduction
Sec. B: Overall ASEAN Common Technical Dossier Table of Contents
Sec. C: Guidance on the Administrative Data and Product Information

1. Duly accomplished and notarized Integrated Application Form (with proof of payment)
2. Letter of Authorization (where applicable)
3. Certifications

For contract manufacturing:
a. License of pharmaceutical industries and contract manufacturer

b. Contract manufacturing agreement
c. GMP certificate of contract manufacturer

For manufacturing "under-license":
a. License of pharmaceutical industries
b. GMP certificate of the manufacturer
c. Copy of "under-license" agreement

For locally manufactured products:
a. Valid License to Operate (LTO) (Manufacturer/Packer/Repacker/Trader/Distributor/ Wholesaler)
b. Valid GMP certificate
c. Valid agreement between the manufacturer, trader, distributor (where applicable)

For imported products:
a. Valid License to Operate (LTO) (Packer/Repacker/ Trader/Importer/Distributor/ Wholesaler)
b. Valid Foreign GMP Clearance
c. Valid Certificate of Pharmaceutical Product (CPP) issued by the competent authority in the country of origin according to the current WHO format
d. Valid agreement between the manufacturer, trader, importer, distributor (where applicable)

4. Site Master File
5. Labeling
6. Representative Sample with corresponding Certificate of Analysis (upon request of the evaluator)
7. Product Information
   a. Package Insert
   b. Summary of Product Characteristics (Product Data Sheet)
8. Risk Management Plan (RMP)
9. Periodic Safety Update Report (PSUR)/Periodic Benefit Risk Evaluation Report
10. List of Countries where the product is already licensed and the date of approval (for vaccines)
11. Names of the medical director of the importer/distributor and local manufacturer who will monitor event/s reactions and prepare appropriate report to be submitted to FDA
12. Person/s responsible for production and control of the product (Name/s Position, Department, and sample of signature)
13. Description of the cold-chain procedures employed from the origin to the port of entry and in the Philippines (how and where)
14. Summary Lot Protocol (for vaccines, toxoids and immunoglobulins)
15. Lot to Lot Consistency from three (3) consecutive batches

Part II: Quality
Sec. A: Table of Contents
Sec. B: Quality Overall Summary
Sec. C: Body of Data

Drug Substance (S)
S 1 General Information

S 1.1. Nomenclature
S 1.2. Structural Formula
S 1.3. General Properties

S 2 Manufacture
S 2.1. Manufacturer(s)
S 2.2. Description of Manufacturing Process and Process Controls
S 2.3. Control of Materials
S 2.4. Control of Critical Steps and Intermediates
S 2.5. Process Validation and/or Evaluation
S 2.6. Manufacturing Process Development

S 3 Characterization
S 3.1. Elucidation of Structure and Characteristics
S 3.2. Impurities

S 4 Control of Drug Substance
S 4.1. Specifications
S 4.2. Analytical Procedures
S 4.3. Validation of Analytical Procedures
S 4.4. Batch Analyses
S 4.5. Justification of Specifications

S 5 Reference Standards or Materials
S 6 Container Closure System
S 7 Stability

Drug Product (P)

P 1 Description and Composition
P 2 Pharmaceutical Development
P 2.1. Information on Development Studies
P 2.2. Components of the Drug Product
P 2.2.1. Active Ingredients
P 2.2.2. Excipients
P 2.3. Finished Product
P 2.3.1. Formulation Development
P 2.3.2. Overages
P 2.3.3. Physicochemical and Biological Properties
P 2.4. Manufacturing Process Development
P 2.5. Container Closure System
P 2.6. Microbiological Attributes
P 2.7. Compatibility

P 3 Manufacture
P 3.1. Batch Formula
P 3.2. Manufacturing Process and Process Control
- Information on the number system of the lots or batches
- System for the re-processing of the product in the event of rejection of the lot or batch by the manufacturer's QA/QC

P 3.3. Controls of Critical Steps and Intermediates
P 3.4. Process Validation and/or Evaluation

P 4 Control of Excipients
P 4.1. Specifications
P 4.2. Analytical Procedures
P 4.3. Excipients of Human and Animal Origin

P 4.4. Novel Excipients
P 5 Control of Finished Product
P 5.1. Specifications
P 5.2. Analytical Procedures
P 5.3. Validation of Analytical Procedures
P 5.4. Batch Analyses
P 5.5. Characterization of Impurities
P 5.6. Justification of Specifications
P 6 Reference Standards or Materials
P 7 Container Closure System
P 8 Product Stability
P 9 Head to Head Comparability – for Biosimilars

Part III: Nonclinical Document
Sec. A: Table of Contents
Sec. B: Nonclinical Overview
1. General Aspect
2. Content and Structural Format
Sec. C: Nonclinical Written and Tabulated Summaries
1. Nonclinical Written Summaries
    1.1. Introduction
    1.2. General Presentation Issues
2. Content of Nonclinical Written and Tabulated Summaries
    2.1. Pharmacology
        2.1.1. Written Summary
            2.1.1.1. Primary Pharmacodynamics
            2.1.1.2. Secondary Pharmacodynamics
            2.1.1.3. Safety Pharmacology
            2.1.1.4. Pharmacodynamic Drug Interactions
        2.1.2. Tabulated Summary
    2.2. Pharmacokinetics
        2.2.1. Written Summary
            2.2.1.1. Absorption
            2.2.1.2. Distribution
            2.2.1.3. Metabolism
            2.2.1.4. Excretion
            2.2.1.5. Pharmacokinetic Drug Interaction (Nonclinical)
        2.2.2. Tabulated Summary
    2.3. Toxicology
        2.3.1. Written Summary
            2.3.1.1. Single-Dose Toxicity
            2.3.1.2. Repeat-Dose Toxicity
            2.3.1.3. Genotoxicity
            2.3.1.4. Carcinogenicity
            2.3.1.5. Reproductive and Developmental Toxicity
                2.3.1.5.1. Fertility and Early Embryonic Development
                2.3.1.5.2. Embryo-Foetal Development
                2.3.1.5.3. Prenatal and Postnatal Development
            2.3.1.6. Local Tolerance
            2.3.1.7. Other Toxicity Studies (if available)

2.3.2. Tabulated Summary
3. Nonclinical Tabulated Summaries

Sec. D: Nonclinical Study Reports

1. Table of Contents
2. Pharmacology
    2.1. Written Study Reports
        2.1.1. Primary Pharmacodynamics
        2.1.2. Secondary Pharmacodynamics
        2.1.3. Safety Pharmacology
        2.1.4. Pharmacodynamic Drug Interactions
3. Pharmacokinetics
    3.1. Written Study Reports
        3.1.1. Analytical Methods and Validation Reports
        3.1.2. Absorption
        3.1.3. Distribution
        3.1.4. Metabolism
        3.1.5. Excretion
        3.1.6. Pharmacokinetic Drug Interaction (Nonclinical)
        3.1.7. Other Pharmacokinetic Studies
4. Toxicology
    4.1. Written Study Reports
        4.1.1. Single-Dose Toxicity
        4.1.2. Repeat-Dose Toxicity
        4.1.3. Genotoxicity
            4.1.3.1. In vitro Reports
            4.1.3.2. In vivo Reports
        4.1.4. Carcinogenicity
            4.1.4.1. Long Term Studies
            4.1.4.2. Short- or Medium-Term Studies
            4.1.4.3. Other Studies
        4.1.5. Reproductive and Developmental Toxicity
            4.1.5.1. Fertility and Early Embryonic Development
            4.1.5.2. Embryo-Foetal Development
            4.1.5.3. Prenatal and Postnatal Development
            4.1.5.4. Studies in which the Offspring are Dosed and/or further Evaluated
        4.1.6. Local Tolerance
        4.1.7. Other Toxicity Studies (if available)
            4.1.7.1. Antigenicity
            4.1.7.2. Immunotoxicity
            4.1.7.3. Dependence
            4.1.7.4. Metabolites
            4.1.7.5. Impurities
            4.1.7.6. Other

Sec. E: List of Key Literature References

Part IV: Clinical Document

Sec. A: Table of Contents

Sec. B: Clinical Overview

1. Product Development Rationale

2. Overview of Biopharmaceutics
3. Overview of Clinical Pharmacology
4. Overview of Efficacy
5. Overview of Safety
6. Benefits and Risks Conclusions

Sec. C: Clinical Summary

1. Summary of Biopharmaceutic Studies and Associated Analytical Methods
    - 1.1. Background and Overview
    - 1.2. Summary of Results of Individual Studies
    - 1.3. Comparison and Analyses of Results across Studies

    Appendix 1
2. Summary of Clinical Pharmacology Studies
    - 2.1. Background and Overview
    - 2.2. Summary of Results of Individual Studies
    - 2.3. Comparison and Analyses of Results across Studies
    - 2.4. Special Studies

    Appendix 2
3. Summary of Clinical Efficacy
    - 3.1. Background and Overview of Clinical Efficacy
    - 3.2. Summary of Results of Individual Studies
    - 3.3. Comparison and Analyses of Results across Studies
        - 3.3.1. Study Populations
        - 3.3.2. Comparison of Efficacy Results of all Studies
        - 3.3.3. Comparison of Results in Sub-populations
    - 3.4. Analysis of Clinical Information Relevant to Dosing Recommendations
    - 3.5. Persistence of Efficacy and/or Tolerance Effects

    Appendix 3
4. Summary of Clinical Safety
    - 4.1. Exposure to the Drug
        - 4.1.1. Overall Safety Evaluation Plan and Narratives of Safety Studies
        - 4.1.2. Overall extent of Exposure
        - 4.1.3. Demographic and Other Characteristics of Study Population
    - 4.2. Adverse Events
        - 4.2.1. Analysis of Adverse Events
            - 4.2.1.1. Common Adverse Events
            - 4.2.1.2. Deaths
            - 4.2.1.3. Other Serious Adverse Events
            - 4.2.1.4. Other Significant Adverse Events
            - 4.2.1.5. Analysis of Adverse Events by Organ System or Syndrome
        - 4.2.2. Narratives
    - 4.3. Clinical Laboratory Evaluations
    - 4.4. Vital Signs, Physical Findings, and Other Observations Related to Safety
    - 4.5. Safety in Special Groups and Situations
        - 4.5.1. Patient Groups
        - 4.5.2. Drug Interactions
        - 4.5.3. Use in Pregnancy and Lactation
        - 4.5.4. Overdose
        - 4.5.5. Drug Abuse
        - 4.5.6. Withdrawal and Rebound
        - 4.5.7. Effects on Ability to Drive or Operate Machinery or Impairment of

Mental Ability

4.6. Post-Marketing Data

Appendix 4

5. Synopses of Individual Studies

Sec. D: Tabular Listing of All Clinical Studies

Sec. E: Clinical Study Reports (if applicable)

1. Reports of Biopharmaceutic Studies
    - 1.1. In vitro-In vivo Correlation Study Reports
    - 1.2. Reports of Bioanalytical and Analytical Methods for Human Studies
2. Reports of Studies Pertinent to Pharmacokinetics Using Human Biomaterials
    - 2.1. Plasma Protein Binding Study Reports
    - 2.2. Reports of Hepatic Metabolism and Drug Interaction Studies
    - 2.3. Reports of Studies Using Other Human Biomaterials
3. Reports of Human Pharmacokinetic (PK) Studies
    - 3.1. Healthy Subject PK and Initial Tolerability Study Reports
    - 3.2. Patient PK and Initial Tolerability Study Reports
    - 3.3. Population PK Study Reports
4. Reports of Human Pharmacodynamic (PD) Studies
    - 4.1. Healthy Subject PD and PK/PD Study Reports
    - 4.2. Patient PD and PK/PD Study Reports
5. Reports of Efficacy and Safety Studies
    - 5.1. Study Reports of Controlled Clinical Studies Pertinent to the Claimed Indication
    - 5.2. Study Reports of Uncontrolled Clinical Studies
    - 5.3. Reports of Analyses of Data from more than One Study, Including any Formal Integrated Analyses, Meta-Analyses, and Bridging Analyses
    - 5.4. Other Clinical Study Reports
6. Reports of Post-Marketing Experience
7. Case Report Forms and Individual Patient Listing

Sec. F: List of Key Literature References

Additional Requirements:

1. For products to be registered using the Collaborative Registration Procedure (CRP), Expression of Interest submitted to WHO
2. For MRE/MR to Initial applications, proof of approval/clearance/extension of Post-Marketing Surveillance (PMS) Report and Post Approval Commitments as specified in the provided RMP.
3. For MR, Post Marketing Surveillance (PMS) Protocol [if additional activity(ies) are necessary based on FDA Circular No. 2021-020]

END