Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG REGULATION AND RESEARCH

INITIAL APPLICATION FOR SIMILAR BIOTHERAPEUTIC PRODUCTS

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 20,000.00/3 years + PHP 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

CHECKLIST OF REQUIREMENTS

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. GMP certificate (country specific)
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. Certificate of Pharmaceutical Product (CPP) issued by the competent authority in the country of origin according to the current WHO format

If the product is not marketed in the country of origin, the following should be submitted:

c.1. CPP indicating that the product is for export only or Certificate of Export
c.2. Authenticated Certificate of Free Sale (CFS) or CPP where it is marketed

If the country of origin does not issue a CPP, the following should be submitted:

c.3. Justification that the country of origin does not issue a CPP
c.4. Authenticated CFS or CPP where it is marketed

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
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. Information on the number system of the lots or batches
15. System for the re-processing of the product in event of rejection of the lot or batch by the manufacturer's QA/QC
16. Summary Lot Protocol
    a. Summary of information on the final lot or batch
    b. Detailed information of manufacture and control
    c. Manufacturer's certification to release the lot or batch
    d. Certificate of lot or batch release issued by the National Regulatory Authority (NRA)
17. 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
  - Summary Lot Protocol
  - Lot to Lot Consistency from three (3) consecutive batches
- 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 8.1. Stability Summary and Conclusion
- P 8.2. Post-approval Stability Protocol and Stability Commitment
- P 8.3. Stability Data

P 9 Quality Comparability
- P 9.1. Reference Biotherapeutic Product
- P 9.2. Manufacturing Process
- P 9.3. Characterization
  - P 9.3.1. Physicochemical Properties
  - P 9.3.2. Biological Activity
  - P 9.3.3. Immunochemical Properties
  - P 9.3.4. Impurities
- P 9.4. Specifications
- P 9.5. Analytical Techniques
- P 9.6. Stability

Part III: Nonclinical Document

Sec. A: Table of Contents

Sec. B: Nonclinical Overview

1. General Consideration
2. Special Consideration
   - 2.1. In Vitro Studies
   - 2.2. In Vivo Studies

Part IV: Clinical Document

Sec. A: Table of Contents

Sec. B: Clinical Overview

1. Pharmacokinetic Studies
2. Pharmacodynamic Studies
3. Confirmatory Pharmacokinetic/Pharmacodynamic Studies
4. Efficacy Studies
5. Safety Studies
6. Immunogenicity
7. Extrapolation of Efficacy and Safety Data

Additional Requirements:

For products to be registered using Collaborative Registration Procedure (CRP), Expression of Interest submitted to WHO.

END