Republic of the Philippines
Department of Health
FOOD AND DRUG ADMINISTRATION

CENTER FOR DRUG REGULATION AND RESEARCH

INITIAL REGISTRATION OF REPRODUCTIVE HEALTH PRODUCTS

Who May Avail : All Manufacturers, Distributors, Importers, Exporters, Wholesalers, and Traders of Pharmaceutical Products

Fees to be Paid : **AO No. 50 s. 2001**

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 or 5-year CPR validity (Based on Bureau Circular No. 5 s. 1997).

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

New Drug/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

CHECKLIST OF REQUIREMENTS

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)

For Dangerous Drugs (as per RA 9165 and Dangerous Drugs Board):

- License to Handle Dangerous Drugs

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)

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 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
- 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 Product Interchangeability/Equivalence Evidence (if applicable)

Additional Requirements for New Chemical Entities/Monitored Release Registration:
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
4.1.4. 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. Bioavailability (BA) Study Reports
1.2. Comparative BA or Bioequivalence (BE) Study Reports
1.3. In vitro-In vivo Correlation Study Reports
1.4. 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. Risk Management Plan
2. MRE to Initial: Periodic Safety Update Report (PSUR), or proof of prior submission
3. For products to be registered using the Collaborative Registration Procedure (CRP), Expression of Interest submitted to WHO
4. FDA-Approved Local Phase IV Clinical Trial Protocol (for monitored-release applications)
5. Petitions and/or Scientific Evidence on the Mechanism of Action (to be submitted after publication of Notice of Submission of Evidence)

Note:

- For *Part II: Quality - Drug Substance (S)*, the following may be submitted:
  Option 1: Full submission (S1-S7)
  Option 2: Certificate of Suitability (CEP) –with sections/sub-sections: S1, S2.1, S4.4 and S7 (if retest period is not stated) only. Copy of the latest version of the CEP shall be provided.
  Option 3: Active Pharmaceutical Ingredient Master File (APIMF)
- ICH Common Technical Document format is acceptable provided that the products are approved in ICH member countries/ regions

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