D. CERTIFICATE OF PRODUCT REGISTRATION

INITIAL CPR FOR PRESCRIPTION DRUGS, BIOLOGICALS AND VACCINE

1. CERTIFICATE OF PRODUCT REGISTRATION (CPR) OF PHARMACEUTICAL PRODUCTS (NEW CHEMICAL ENTITIES/MONITORED RELEASE)

This Certificate of Product Registration is granted to Marketing Authorization Holders of chemical or synthetic drug products classified under Monitored Release either as a New Drug/New Chemical Entity or a pharmaceutical/therapeutic innovation of a Tried and Tested/Established Drug (i.e., involving use for a new indication, a new mode of administration, a new dosage form, and/or a new fixed-dose combination of two or more active ingredients) upon compliance to the agency-prescribed Quality, Safety, Efficacy standards. It is the approval granted by FDA to market a specific product in the country.

Center/Office/Division	:	Center for Drug Regulation and Research
Classification	.	Highly Technical
Type of Transaction	.	G2B – Government-to-Businesses
Who May Avail	:	All Manufacturers, Distributors, Importers, Exporters, Wholesalers, and Traders of Pharmaceutical Products
Fees to be Paid	:	AO 50 s. 2001 FDA Advisory No. 2021-2904 New Drug/Monitored Release (for all types of products): Php 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 *If additional PV activity(ies) are necessary based on FDA Circular No. 2021-020

CHECKLIST OF REQUIREMENTS	WHERE TO SECURE
CHECKLIST OF REQUIREMENTS FOR NEW CHEMICAL ENTITIES/MONITORED-RELEASE REGISTRATION	
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. Notarized Integrated Application Form (in excel and pdf formats) (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. License of pharmaceutical industries b. GMP certificate (country specific) For imported products a. License of pharmaceutical industries/importer/wholesaler (country specific) b. Certificate of Pharmaceutical Product (CPP) issued by the competent authority in the country of origin according to the current WHO format c. Foreign GMP Clearance	Applicant Company/Manufacturer (For the whole Part I) FDA Website & Cashier

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 4.4. Batch Analyses S 4.5. Justification of Specifications S 5 Reference Standards or Materials	Applicant Company/Manufacturer (For the whole Part II: Quality)

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) 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	Applicant Company/Manufacturer (For the whole Part III: Nonclinical Document)

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-Fetal 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	Applicant Company/Manufacturer (For the whole Part IV: Clinical Document)

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 – which shall include the following: a. RMP compliant with latest EMA838713/2011 Guideline on Good Pharmacovigilance Practices (GVP) Module V – Risk Management Systems b. RMP Philippine-Specific Annex (as applicable) c. RMP Philippine-Specific Annex annotated version (with tracked changes) (as applicable) OR instead of a core or country specific annex, an RMP specifically developed for the Philippines may be submitted 2. For products to be registered using the Collaborative Registration Procedure (CRP), Expression of Interest submitted to WHO 3. Post Marketing Surveillance (PMS) Protocol [as post-approval requirement if additional activity(ies) are necessary based on FDA Circular No. 2021-020] Note: • ICH Common Technical Document format is acceptable provided that the products are approved in ICH member countries/ regions.	Applicant Company /Manufacturer

	Applicant Company /Manufacturer FDA (Applicant Company)

CLIENT STEPS	AGENCY ACTION	FEES TO BE PAID	PROCESSING TIME	PERSON RESPONSIBLE
1. Secure a schedule of appointment / submission to FDAC E-mail submission: Submits the application for pre-assessment through fdac.pacd.cdrr@fda.gov.ph	1. Sends the scheduled date of submission for pre-assessment	None		FDAC *Personnel*

	2. Pre-assesses the completeness of the application. If the application is acceptable, informs the client of the result of the pre-assessment and instructs the client to proceed with payment. If the application did not satisfactorily pass the pre-assessment, advises client to secure a new appointment schedule for pre-assessment and new Document Tracking Number (DTN).	None		CDRR *Personnel*
2. For accepted applications, pays the required fee through any of the following: • BANCNET • Landbank OnColl • Landbank Link.bizPortal Sends proof of payment to the FDAC.	3. Upon receipt of the proof of payment, endorses the application to CDRR for evaluation.	See Table Above	Day 1 1 working day	FDA Cashier/ Landbank FDAC *Personnel*
	4. Receives the application from FDAC and encodes/updates the database.	None	Day 2 1 working day	Center for Drug Regulation and Research (CDRR) – Central
	5. Queuing time of the application before decking to evaluators of Registration Section and Clinical Research Section.	None	Day 2-21 20 working days	CDRR-CRR Unit *Personnel*

	6. Decks/Assigns the application to the assigned evaluators of Registration Section and Clinical Research Section.	None	Day 22 1 working day	CDRR *Director*
	7. Evaluates the application according to requirements and prescribed standards	None	Day 23-72 50 working days	*Food-Drug Regulation Officer (FDRO) I/II (Junior Evaluator)/*

If an electronic notice of deficiencies (E- NOD) was issued by the evaluator, submits complete compliance documents to the evaluator	**a. Clinical Research Section (Safety and Efficacy evaluator)** Prepares a worksheet with Recommendations on the evaluated safety and efficacy dossier, RMP, and PMS protocol (if any), then forwards this to the Quality evaluator of the Registration Section. **b. Registration Section (Quality evaluator)** Prepares a worksheet and drafts Certificate of Product Registration (CPR) issuance when the approval of the application is recommended (Quality, and Safety & Efficacy received from the CRS) Prepares a worksheet and Letter of Disapproval (LOD) when the application does not merit an approval recommendation (Quality, and Safety & Efficacy received from the CRS) *Any minor deficiencies/ clarifications will be communicated to the clients through electronic communication	None		*FDRO I/II/III/ Medical Specialist II/III*
	8. Reviews the evaluated application bearing the recommendation of the Junior Evaluator (for Quality evaluation).	None	Day 73-112 40 working days	FDRO III

	9. Prepares the final output document (CPR/LOD), affixes initial, and forwards it to the senior evaluator (FDRO III) If with post-approval commitment/s, prepares a letter, signs, and forwards it together with the CPR For Dangerous Drugs, prepares a letter/notification to PDEA for the approval of the application	None	Day 113 1 working day	FDRO I/II
	10. Reviews the final output document, affixes initial on the worksheet, and forwards it to the Section Supervisor	None	Day 114 1 working day	FDRO III
	11. Reviews the final output document, affixes initial on the worksheet, and forwards it to the Licensing and Registration (LRD) Chief.	None	Day 115 1 working day (per batch of applications)	FDRO IV (Supervisor)
	12. Checks and recommends the decision of the evaluators and supervisor by affixing signature.	None	Day 116 1 working day (per batch of applications)	LRD Chief
	13. Signs and approves the final decision	None	Day 117 1 working day (per batch of applications)	CDRR Director
	14. Encodes/Updates the Database and endorses the final output document (CPR/LOD/Letter) to the CDRR-Records Section	None	Day 118 1 working day (per batch of applications)	CDRR-CRR Unit Personnel

	15. Scans, barcodes the final output document (CPR/LOD/Letter); and endorses the final output document to the FDAC Releasing Section	None	Day 119 1 working day (per batch of applications)	CDRR-Records Personnel
3. Receives the CPR/LOD/letter	16. Releases the CPR/LOD/letter to the client	None	Day 120 1 working day	AFS - Releasing Section Personnel
(Service is covered under Republic Act No. 3720 Section 21 as amended by Executive Order No. 175 Section 13 and Republic Act No. 7394 Article 31).		**TOTAL:**	**120 working days**	