22. CERTIFICATE FOR MAJOR VARIATION - STRAIN CLEARANCE (MAV-SC) AND MINOR VARIATION – STRAIN CLEARANCE (MIV-SC) OF HUMAN INFLUENZA VACCINES

This Certificate of Product Registration is granted to Marketing Authorization Holders once the proposed change in the strains has been approved (MaV-SC)/to continue the manufacture, distribution and sale of Seasonal Influenza Vaccines based on compliance with quality, safety and efficacy standards (MiV-SC).

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 Human
Fees to be Paid	:	**Major Variation – Strain Clearance (MaV-SC)** Php 20,000 + LRF **Minor Variation – Strain Clearance (MiV-SC)** Php 500 + LRF

CHECKLIST OF REQUIREMENTS	WHERE TO SECURE
CHECKLIST OF REQUIREMENTS FOR MAJOR VARIATION – STRAIN CLEARANCE (MaV-SC) OF HUMAN INFLUENZA VACCINES (Only relevant and adequate sections of the ACTD/CTD should be submitted. All sections not felt to be necessary should however be justified adequately in the Summary/Overview)	
Part I: Administrative Data and Product Information Sec. A Introduction Sec. B Table of Contents Sec. C Guidance on the Administrative Data and Product Information	Applicant Company
1. Integrated Application Form (with proof of payment)	Applicant Company
2. Certifications	Applicant Company

For contract manufacturing:	
a. License of pharmaceutical industries and contract manufacturer	Applicant Company/Manufacturer
b. Contract manufacturing agreement	Applicant Company/Manufacturer
c. GMP certificate of contract manufacturer	Applicant Company/Manufacturer
For manufacturing "under-license"	
a. License of pharmaceutical industries	Applicant Company/Manufacturer
b. GMP certificate of the manufacturer	Applicant Company/Manufacturer
c. Copy of "under-license" agreement	Applicant Company/Manufacturer
For locally manufactured products:	
a. License of pharmaceutical industries	Applicant Company/Manufacturer
b. GMP certificate (country specific)	Applicant Company/Manufacturer
For imported products	
a. Foreign GMP Clearance	Applicant Company/Manufacturer
b. License of pharmaceutical industries/importer/wholesaler (country specific)	Applicant Company/Manufacturer
c. Certificate of Pharmaceutical Product (CPP) issued by the competent authority in the country of origin according to the current WHO format	Applicant Company/Manufacturer
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; and	Applicant Company/Manufacturer
c.2 Authenticated Certificate of Free Sale (CFS) or CPP where it is marketed;	Applicant Company/Manufacturer
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; and	Applicant Company/Manufacturer
c.4 Authenticated CFS or CPP where it is marketed	Applicant Company/Manufacturer
3. Labeling (new strains)	
4. 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 (addendum to “previous” QOS) Sec. C Body of Data Drug Substance (S) S 2 Manufacture S 2.1. Manufacturer(s) S 2.2. Description of Manufacturing Process and Process Controls S 2.3. Control of Materials - seed lots: history: - passage level - characterization of Haemagglutinin and Neuraminidase - analytical protocols (including test results on seed lots)* S 2.4. Control of Critical Steps and Intermediates S 2.5. Process Validation and/or Evaluation - monovalent bulks: - manufacturing process strain specific changes - validation of critical manufacturing steps (e.g. inactivation, splitting efficiency) (new strains) 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 - validation study reports and summaries of test method [e.g. validation of Single Radial Diffusion (SRD) test for the new strain(s)] S 4.4. Batch Analyses - results of monovalent bulks: results (including test for neuraminidase): Each working seed lot from previously approved master seed lot where the procedure of working seed lot preparation is different from the approved procedure S 4.5. Justification of Specifications S 7 Stability (Stability tests on the active substances: results from monovalent bulks where they are used for more than one year)	Applicant Company/Manufacturer (For the whole Part II: Quality Document)

Drug Product (P) P 1 Description and Composition P 2 Pharmaceutical Development P 2.2. Components of the Drug Product P 2.2.1. Active Ingredients (new strains) P 3 Manufacture P 3.1. Batch Formula 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 8 Product Stability	
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. D Tabular Listing of All Clinical Studies Sec. E Clinical Study Reports (if applicable)	Applicant Company/Manufacturer (For the whole Part IV: Clinical Document) Applicant Company/ Manufacturer Applicant Company/Manufacturer Applicant Company/Manufacturer
Additional Requirements: 1. Representative Samples (w/COA) may be submitted at a later date, e.g. when the application has already been decked as indicated in the Document Tracking System. 2. Risk Management Plan 3. Periodic Safety Update Report (PSUR)/Periodic Benefit-Risk Evaluation Report (PBRER) 4. List of Countries where the product is already licensed and the date of approval 5. Information on the number system of the lots or batches 6. Summary Lot Protocol 7. Lot to Lot Consistency from three (3) consecutive batches 8. Copy of valid CPR	Applicant Company/Manufacturer Applicant Company/Manufacturer Applicant Company/Manufacturer Applicant Company/Manufacturer Applicant Company

Notarized Letter of Request for Major Variation – Strain Clearance (refer to Appendix 2) indicating the affected product, as well as declaration that there is/are no other change/s except from the update on the annual strain. This shall be signed by the Head of Regulatory Office.	Applicant Company
9. Adverse event following immunization report (summary of annual reports)	Applicant Company
CHECKLIST OF REQUIREMENTS FOR MINOR VARIATION – STRAIN CLEARANCE (MiV-SC) OF HUMAN INFLUENZA VACCINES	
1. Notarized Integrated Application Form (in excel and pdf format) (with proof of payment)	Applicant Company
2. Certifications	Applicant Company
For contract manufacturing:	
a. License of pharmaceutical industries and contract manufacturer	Applicant Company/ Manufacturer
b. Contract manufacturing agreement	Applicant Company/Manufacturer
c. GMP certificate of contract manufacturer	Applicant Company/Manufacturer
For manufacturing "under-license"	
a. License of pharmaceutical industries	Applicant Company/ Manufacturer
b. GMP certificate of the manufacturer	Applicant Company/Manufacturer
c. Copy of "under-license" agreement	Applicant Company/Manufacturer
For locally manufactured products:	
a. License of pharmaceutical industries	Applicant Company/ Manufacturer
b. GMP certificate (country specific)	Applicant Company/Manufacturer
For imported products	
a. Foreign GMP Clearance	Applicant Company/ Manufacturer
b. License of pharmaceutical industries/importer/wholesaler (country specific)	Applicant Company/Manufacturer

3.Labeling (new strains) 4.Product Information	
c. Package Insert	Applicant Company/Manufacturer
d. Summary of Product Characteristics (Product Data Sheet)	Applicant Company/Manufacturer
5. Representative Samples (w/COA)	Applicant Company/Manufacturer
6. Risk Management Plan	Applicant Company/Manufacturer
7. Periodic Safety Update Report (PSUR)/Periodic Benefit-Risk Evaluation Report **(PBRER)**	Applicant Company/Manufacturer
8. List of Countries where the product is already licensed and the date of approval	Applicant Company/Manufacturer
9. Information on the number system of the lots or batches	Applicant Company/Manufacturer
10. Summary Lot Protocol	Applicant Company/Manufacturer
11. Copy of valid CPR	Applicant Company/Manufacturer
12. Notarized Letter of Request for Minor Variation – Strain Clearance (refer to Appendix 3) indicating the affected product, as well as declaration that there is/are no other change/s. This shall be signed by the Head of Regulatory Office.	Applicant Company/Manufacturer
13. Adverse event following immunization report (summary of annual reports)	Applicant Company/Manufacturer

*Where the seed virus is tested for extraneous agents using Polymerase Chain Reaction (PCR), these data should be included in this application

CLIENT STEPS	AGENCY ACTION	FEES TO BE PAID	PROCESSING TIME	PERSON RESPONSIBLE
1. Secure a schedule of appointment / submission to FDAC	1. Sends the scheduled date of submission for pre-assessment	None		FDAC *Personnel*

2. E-mail submission: Submits the application for pre-assessment through fdac.pacd.cdrr@fda.gov.ph	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*
3. For accepted applications, pays the required fee through any of the following: • FDA Cashier • 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 Receiving and Releasing (CRR) Unit

	5. Queuing time of the application before decking to evaluators	None	Day 3-7 5 working days	CDRR-CRR Unit
	6. Decks/Assigns the application to the assigned evaluator	None	Day 8 1 working day	LRD *Chief*
	7. Evaluates the application according to requirements and prescribed standards	None	Day 9-30 22 working days	*Food-Drug Regulation Officer (FDRO) I/II (Junior Evaluator)/ FDRO III (Senior Evaluator)*
If an electronic notice of deficiencies (E-NOD) was issued by the evaluator, submits complete compliance documents to the evaluator	Prepares a worksheet and drafts certification when the approval of the application is recommended Prepares a worksheet and Letter of Disapproval (LOD) when the application does not merit an approval recommendation For applications with proposed brand names, requests clearance from the Brand Name Clearance evaluator. If the proposed brand name is disapproved, this shall be cited in the electronic deficiencies (E-NOD) or Letter of Disapproval (LOD) to be issued *Any minor deficiencies/ clarifications will be communicated to the clients through electronic communication	None	Day 31 1 working day	*FDRO I/II/III*

	8. Reviews the evaluated application bearing the recommendation of the	None	Day 32-47 16 working days	*FDRO III*
	9. Prepares the final output document (Certification/LOD), affixes initial, and forwards it to the senior evaluator	None	Day 48 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 49 1 working day	*FDRO III*
	11. Reviews the final output document, affixes initial on the worksheet, and forwards it to the Licensing and	None	Day 50-52 3 working days	*FDRO IV (Supervisor)*
	12. Checks and recommends the decision of the evaluators and supervisor by affixing initial/signature	None	Day 53-55 3 working days (per batch of applications)	*LRD Chief*
	13. Signs and approves the final decision	None	Day 56 1 working day (per batch of applications)	*CDRR Director*
	14. Encodes/Updates the Database and endorses the final output document (Certification/LOD/Letter) to the CDRR-Records Section	None	Day 57 1 working day (per batch of applications)	*CDRR-CRR Unit Personnel*
	15. Scans and emails the scanned copy of the final output document (Certification/LOD/ Letter) to the client; and endorses the final output document to the AFS- Releasing Section	None	Day 58-59 2 working days (per batch of applications)	*CDRR-Records Personnel*
4. Receives the Certification /LOD/letter	16. Releases the Certification /LOD to the client	None	Day 60 1 working day	*AFS-Releasing Section*

TOTAL:	**60 working days^**
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, wherein 60 working days was proposed instead of 180 working days.	

Additional processing time shall be applied if consequential changes that are related to the strain change are filed together with the MaV-SC.