THE ASEAN COMMON TECHNICAL REQUIREMENT FOR PHARMACEUTICALS REGISTRATION QUALITY (ASEAN CTR: QUALITY)

General Information: The WHO, ICH and other established international guidelines can be referred for biologics including vaccine.

No	PARAMETERS	COMPONENTS	Comments			
			NCE	BIOLOGICS	G	
S	**DRUG SUBSTANCE**					
S1	**General Information**					
	1.1. Nomenclature	**Information from the S1**	**V**	**V**	**V**	
	1.2. Structure	– Structural formula, including relative and absolute stereochemistry, the molecular formula, and the relative molecular mass.	**V**		**V**	
		– Schematic amino acid sequence indicating glycosylation sites or other post-translational modifications and relative molecular mass as appropriate.		**V**		**-** This section is applicable for biotech products and recombinant polysaccharide/protein vaccines
		BIOLOGICS - For example, in synthetic vaccines containing polysaccharides or proteins include the schematic amino acid sequence, indicating the glycosylation sites or other modifications and relative molecular mass.		**V***		
	1.3. General Properties	– Physicochemical characteristics and other relevant properties including biological activity for biologics.	**V**	**V**	**V**	
		BIOLOGICS - For each biological starting material used to obtain or extract the active ingredient, include a summary of **viral safety** of the material **(if applicable)**		**V**		

S2	**Manufacture** **2.1. Manufacturer(s)**	– Name and address of the manufacturer (s).	**V**	**V**	**V**	
	2.2. Description of Manufacturing Process and Process Controls	– The description of the Drug substance manufacturing process and process control that represents the applicant's commitment for the manufacture of the Drug substances	**V**	**V**		
		– Information on the manufacturing process, which typically starts with a vial(s) of the cell bank, and includes cell culture, harvest(s), purification and modification reaction, filling, storage and shipping conditions. Where applicable, include the number of passages.		**V**		
	• **Flow chart of manufacturing process**	- Showing all the manufacturing steps, including intermediate processes.		**V**		
	• **Description of batch identification system**	- Identification of the lot in each stage of the process, including when mixtures are made. Also submit information on the manufacturing scale and lot size.		**V**		
		- Methods and agents used, parameters controlled, and production stage in which it is performed, when applicable.		**V**		
	• **Description of inactivation or detoxification process**	- Method, reagents, and materials used, operating parameters controlled, and specifications.		**V**		
	• **Description of purification process**	- Conditions for the use and re-use of membranes and chromatography columns and the respective validation studies.		**V**		

	• **Stabilization of active ingredient**	- Description of the steps performed to stabilize the active ingredient, for example, the addition of stabilizers or other procedures, when applicable.		**V**	
	• **Reprocessing**	- Description of the procedures established for reprocessing the active ingredient or any intermediate product; criteria and justification.		**V**	
	• **Filling procedure, in-process controls**	- Description of the procedure for packaging the active ingredient, process controls, acceptance criteria, type of container closure system, type of seal on the container used to store the active ingredient, storage and transfer conditions, when applicable.		**V**	
	2.3. Control of Materials	– Starting materials, solvents, reagents, catalysts, and any other materials used in the manufacture of the drugs subtance indicating where each material is used in the process. Tests and acceptance criteria of these materials.	**V**	**V**	
		– Control of source and starting materials of biological origin.		**V**	
		– Source, history and generation of the cell substrate.		**V**	
		– Cell banking system, characterisation and testing.		**V**	
		– Viral safety evaluation.		**V**	

	2.4. Controls of Critical Steps and Intermediates	– Critical steps : Tests and acceptance criteria, with justification including **quality specifications and** experimental data, performed at critical steps of the manufacturing process to ensure that the process is controlled.	**V**	**V**	
		– Intermediates : Specifications and analytical procedure, if any, for intermediates isolated during the process.	**V**	**V**	
		– Stability data supporting storage conditions.		**V**	
	2.5. Process Validation and/or Evaluation	Process validation and/or evaluation studies for aseptic processing and sterilization., which includes information on validation procedures, establishment of criteria for establishing the control limits on the critical steps.	**V**	**V**	
	2.6. Manufacturing Process Development	– Description and discussion of significant changes made to the manufacturing process and/or manufacturing site of the Drug substance used in producing non-clinical, clinical, scale-up, pilot and if available, production scale batches.	**V**	V	
		– The development history of the manufacturing process as described in S 2.2.		V	
S3	**Characterisation**				
	3.1. Elucidation of Structure and other characteristics	– Confirmation of structure based on e.g. synthetic route and spectral analyses.	**V**	**V**	
		– Compendial requirements or appropriate information from the manufacturer		**V**	**V**
		– Details on primary, secondary and higher-order structure and information on biological activity, purity and immunochemical properties (when relevant).		**V**	

	3.2. Impurities	– Summary of impurities monitored or tested for during and after manufacture of drug substance	**V**	**V**		
		– Compendial requirements or appropriate information from the manufacturer		**V**	**V**	
S4	**Control of Drug substance**					
	4.1. Specification	– Detailed specification, tests and acceptance criteria.	**V**	**V**		
		– Compendial specification or appropriate information from the manufacturer.		**V**	**V**	
		– Specify source, including as appropriate species of animal, type of microorganism etc.		**V**		
	4.2. Analytical Procedures	– The analytical procedures used for testing of drug substance.	**V**	**V**		
		– Compendial methods or appropriate information from the manufacturer.		**V**	**V**	
	4.3. Validation of Analytical Procedures	– Analytical validation information, including experimental data for the analytical procedures used for testing the drug substance.	**V**	**V**		
		– Non-compendial methods.		**V**	**V**	
	4.4. Batch Analyses	– Description of batches and results of the analysis to establish the specification.	**V**	**V**		
	4.5. Justification of Specification	– Justification for drug substance specification.	**V**	**V**		
S5	**Reference Standards or Materials**	– Information on the reference standards or reference materials used for testing of the Drug substance.	**V**	**V**		
		– Compendial reference standard		**V**	**V**	

S6	**Container Closure System**	– Descriptions of the container closure systems.	**V**	**V**		
		– Full description of the packaging and container closure system in which the active ingredient will be stored until used for preparing the finished product .The information should include identification of all the materials that constitute the packaging container closure system and their specifications .When applicable, discuss the types of materials selected with respect to protection of the active ingredient against humidity and light.	**V**	**V**		
S7	**Stability**	– Stability report. – Literature data.	**V**	**V**	**V**	
	7.1 Stability summary and conclusion	- Should include the study conditions, including all the storage conditions (temperature, humidity, light) in which the vaccine is evaluated, analytical method, specifications, summary of results, and conclusions.	**V**	**V**		
	7.2 Post approval stability protocol and stability commitment	- It refers to the continuation of the stability study, including the number of lots to be included in the study each year and the tests to be performed.	**V**	**V**		
	7.3 Stability Data	- Should include complete data from each batch evaluated during stability studies.	**V**	**V**		
P	**DRUG PRODUCT**					
P1	**Description and Composition**	**Description:** – Dosage form and characteristics. – Accompanying reconstitution diluent (s) if any. – Type of container and closure used for the dosage form and	**V**	**V**	**V**	

		reconstitution diluent (s), if applicable.				
		Composition: Name, quantity stated in metric weight or measures, function and quality standard reference **BIOLOGICS** **-**This should include a description of the finished product, its composition, listing each of the components, active ingredient(s), adjuvant, preservatives, stabilizers, and excipients, stating the function of each of them. For lyophilized products, also include a description of the diluents and the container closure system employed for the diluents.	**V**	**V** **V**	**V**	
P2	**Pharmaceutical Development**					
	2.1. Information on Development Studies	– Information on the studies performed to establish the dosage form, formulation, manufacturing process, and the container closure system used for final product. The studies described in this point are different from the routine quality control tests performed in accordance with the product specifications	**V**	**V**		
	2.2. Components of the Drug Product	– Active ingredient Justification of the compatibility of the active ingredient with excipients listed in P1 In case of combination products, justification of the compatibility of active ingredients with each other.	**V**	**V**		
		– Literature data.			**V**	
		– Excipients Justification of the choice of	**V**	**V**		

		excipients listed in P1, which may influence the drug product performance.				
	2.3. Finished Product	– Formulation Development A brief summary describing the development of the finished product, (taking into consideration the proposed route of administration and usage for NCE and Biologics).	**V**	**V**	**V**	
		– Overages	**V**	**V**	**V**	
		– Physicochemical and Biological Properties: Parameters relevant to the performance of the finished product e.g pH, dissolution.	**V**			
	2.4. Manufacturing Process Development	– Selection and optimisation of the manufacturing process	**V**	**V**		
		– Differences between the manufacturing process (es) used to produce pivotal clinical batches and the process described in P.3.2, if applicable	**V**	**V**		
	2.5. Container Closure System	Suitability of the container closure system used for the storage, transportation (shipping) and use of the finished product.	**V**	**V**	**V**	
	2.6. Microbiological Attributes	Microbiological attributes of the dosage form, where appropriate	**V**	**V**	**V**	
	2.7. Compatibility	– Compatibility of the finished product with reconstitution diluent(s) or dosage device.	**V**	**V**		
		– Literature data			**V**	
P	**Manufacture**					
	3.1 Manufacturer	Name, address, and responsibilities of each manufacturer involved, including contract manufacturers for production and quality control.	**V**	**V**		

	3.2. Batch Formula	Name and quantities of all ingredients.	**V**	**V**	**V**	
	3.3. Manufacturing Process and Process Control	**Description of manufacturing process and process control:** – Submit a flowchart of the process, including all the steps in the process and indicate the points, at which the material enters the process, identify the critical steps and control points in the process, intermediate products, and final product. Also include a narrative of the manufacturing process, the in process controls, and the critical points identified. – Description of batch identification system, define the lot in the stages of filling, lyophilization (if it applies) and packaging.	**V**	**V**	**V**	
	3.4. Control of Critical Steps and Intermediates	– Tests and acceptance criteria developed to identify the critical steps in the manufacturing process and how they were controlled. – Information on the quality and control of intermediates isolated during the process	**V**	**V**	**V**	
	3.5. Process Validation and/or Evaluation	– Description, documentation, and results of the validation and/or evaluation studies for critical steps or critical assays used in the manufacturing process. It is also necessary to provide information on the viral safety of the product, when applicable	**V**	**V**	**V**	
P4	**Control of Excipients**					
	4.1. Specifications	– Specifications for excipients – Compendial requirements or appropriate information from the manufacturer	**V**	**V** **V**	**V**	
	4.2. Analytical Procedures	– Analytical procedures used for testing excipients where appropriate.	**V**	**V**		

		– Compendial requirements or appropriate information from the manufacturer.		V	V	
	4.3. Excipient of Human or Animal Origin	– Information regarding sources and or adventitious agents. – Compendial requirements or appropriate information from the manufacturer	V	V	V	
	4.4. Novel Excipients	– For excipient(s) used for the first time in a finished product or by a new route of administration, full details of manufacture, characterization and controls, with cross reference to supporting safety data (non-clinical or clinical)	V	V		
P5	**Control of Finished Product**					
	5.1 Specification	– The specification(s) for the finished product.	V	V	V	
	5.2. Analytical Procedures	– Detailed description on the analytical procedures used for testing the finished product.	V	V	V	
	5.3. Validation of Analytical Procedures	– Information including experimental data, for **the validation of** analytical procedure used for testing the finished product.	V	V		
		– Non-compendial method.	V	V	V	
		– Verification of compendial method where applicable.	V	V	V	

	5.4. Batch Analyses	– Description and test results of all relevant batches **to demonstrate production consistency**.	**V**	**V**	**V**	
		BIOLOGICS				
		– Summary protocol of the production and control of three consecutive lots of active ingredient, analysis certificates in the event this information is not included in the summary protocol for the finished product, an analysis of the results of these lots in terms of production consistency, where applicable.		**V**		
	5.5. Characterisation of Impurities	– Information on the characterisation of impurities, depending on the method used to manufacture the product.	**V**	**V**		
		– Compendial requirements or appropriate information from the manufacturer.		**V**	**V**	
	5.6. Justification of Specification(s)	– Justification of the proposed finished product specification(s).	**V**	**V**		
		– Compendial requirements or appropriate information from the manufacturer		**V**	**V**	
P6	**Reference Standards or Materials**	– Information on the reference standards or reference materials used for testing of the finished product.	**V**	**V**		
		– Compendial requirements or appropriate information from the manufacturer.		**V**	**V**	
P7	**Container Closure System**	– Specification and control of primary and secondary packaging material, type of packaging and the package size, details of packaging inclusion (e.g. desiccant, etc)	**V**	**V**	**V**	

P8	**Stability** **8.1 Stability summary and conclusion**	–	Stability summary demonstrating that product is stable through its proposed shelf life.	**V**	**V**	**V**
	8.2 Post approval stability protocol and stability commitment	–	Commitment on post approval stability monitoring include the stability program or stability commitment to be carried out once the vaccine is in the market, including the number of lots to be included in the study each year and the tests to be performed. These results should be submitted periodically to update the information on the stability of the vaccine evaluated	**V**	**V**	
	8.3 Stability data	–	Should include the complete results of each lot evaluated during stability studies.	**V**	**V**	
	8.4 Description of procedures to guarantee cold chain . (where applicable)	–	Describe in detail the measures used to guarantee adequate temperature and humidity conditions for shipping the finished product from the place of production to the place of final sale, including all the storage and distribution stages and indicating the controls performed in each of the stages. This description should be signed by the professional responsible for it	**V**	**V**	
P9	**Product Interchangeability/ Equivalence evidence**	–	In Vitro Comparative dissolution study as required			**V**
		–	In Vivo Bioequivalence study as required			**V**