ประกาศสำนักงานคณะกรรมการอาหารและยา
เรื่อง การนำข้อตกลง ASEAN Harmonized Product on Pharmaceutical Registration
สู่การปฏิบัติเต็มรูปแบบ (ฉบับที่ ๒)
พ.ศ. ๒๕๖๔

ตามที่สำนักงานคณะกรรมการอาหารและยาได้ออกประกาศ เรื่อง การขึ้นทะเบียนตำรับยาตามข้อตกลง ASEAN Harmonization Product on Pharmaceutical Registration ลงวันที่ ๒๖ ธันวาคม พ.ศ. ๒๕๕๑ และได้กำหนดให้การยื่นคำขอขึ้นทะเบียนตำรับยาชีววัตถุ ต้องยื่นคำขอขึ้นทะเบียนตำรับยาแบบ ASEAN Harmonization ตั้งแต่วันที่ ๑ มกราคม พ.ศ. ๒๕๕๒ และคณะกรรมการที่ปรึกษาด้านคุณภาพและมาตรฐาน หรือ ASEAN Consultative Committee on Standard and Quality/Pharmaceutical Product Working Group (ACCSQ/PPWG) ได้บรรลุข้อตกลงหลักเกณฑ์ ASEAN Common Technical Requirement (ACTR) , ASEAN Common Technical Dossier (ACTD) สำหรับยาชีววัตถุในปี พ.ศ. ๒๕๖๒ ดังนั้น เพื่อให้แนวทางการควบคุม กำกับ ดูแล และการพิจารณาขึ้นทะเบียนตำรับยาชีววัตถุ ในประเทศไทยเป็นไปตามมาตรฐานสากลและมีความเหมาะสมต่อสถานการณ์ปัจจุบัน

อาศัยอำนาจตามความในข้อ ๒ แห่งประกาศกระทรวงสาธารณสุข เรื่อง กำหนดแบบคำขอและใบสำคัญการขึ้นทะเบียนตำรับยา ลงวันที่ ๑๔ พฤษภาคม พ.ศ. ๒๕๕๖ เลขาธิการคณะกรรมการอาหารและยา จึงประกาศดังต่อไปนี้

ให้ยกเลิกความใน ๑.๔.๒ ของประกาศสำนักงานคณะกรรมการอาหารและยา เรื่อง การนำข้อตกลง ASEAN Harmonized Product on Pharmaceutical Registration สู่การปฏิบัติเต็มรูปแบบ ลงวันที่ ๒ พฤศจิกายน ๒๕๕๐ และให้ใช้ความต่อไปนี้แทน

“๑.๔.๒ เอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาชีววัตถุ (Biological Products) แบบ ASEAN Harmonization จำแนกตามประเภทชีววัตถุ ตามแนบท้ายประกาศนี้”

ทั้งนี้ ตั้งแต่บัดนี้เป็นต้นไป

ประกาศ ณ วันที่ ๒๘ พฤษภาคม พ.ศ. ๒๕๖๔

(นายไพศาล ตั่นคุ้ม)
เลขาธิการคณะกรรมการอาหารและยา

เอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาชีววัตถุ (Biological Products) แบบ ASEAN HARMONIZATION

จำแนกตามประเภทยาชีววัตถุ : ข้อมูลด้าน Quality

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
	Section A. Table of Content			
	Section B. Quality Overall Summary			
S S1	DRUG SUBSTANCE General Information 1.1 Nomenclature	- Information from the S1	✓	✓
	1.2 Structure	- Structural formula, including relative and absolute stereochemistry, the molecular formula, and the relative molecular mass. - Schematic amino acid sequence indicating glycosylation sites or other post-translational modifications and relative molecular mass as appropriate. (Note: This section is applicable for biotech products and recombinant polysaccharide/protein vaccines)	✓ ✓	✓ ✓
	1.3 General Properties	- Physicochemical characteristics and other relevant properties including biological activity for 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)	✓ ✓	✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
S2	Manufacture 2.1 Manufacturer(s)	-Name and address of the manufacturer (s).	✓	✓
	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 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. Flowchart of manufacturing process, Description of batch identification system, Description of inactivation or detoxification process, Description of purification process Stabilization of active ingredient, reprocessing, Filling procedure, in process control	✓	✓
	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.	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		- Control of source and starting materials of biological origin. - Source, history and generation of the cell substrate. - Cell banking system, characterisation and testing. - Viral safety evaluation.	✓ ✓ ✓ ✓	✓ ✓ ✓ ✓
	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. - Intermediates : Specifications and analytical procedure, if any, for intermediates isolated during the process. - Stability data supporting storage conditions.	✓ ✓ ✓	✓ ✓ ✓
	2.5. Process Validation and/or Evaluation	Process validation and/or evaluation studies for aseptic processing and sterilization.	✓	✓
	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.	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		-The development history of the manufacturing process as described in S 2.2.	✓	✓
S3	Characterisation 3.1. Elucidation of Structure and other characteristics	-Confirmation of structure based on e.g. synthetic route and spectral analyses. - Compendial requirements or appropriate information from the manufacturer - Details on primary, secondary and higher-order structure and information on biological activity, purity and immunochemical properties (when relevant).	✓ ✓ ✓	✓ ✓ ✓
	3.2. Impurities	- Summary of impurities monitored or tested for during and after manufacture of drug substance - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓
S4	Control of Drug substance 4.1. Specification	- Detailed specification, tests and acceptance criteria. - Compendial specification or appropriate information from the manufacturer	✓ ✓	✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		-Specify source, including as appropriate species of animal, type of microorganism etc.	✓	✓
	4.2. Analytical Procedures	- The analytical procedures used for testing of drug substance. - Compendial methods or appropriate information from the manufacturer	✓ ✓	✓ ✓
	4.3. Validation of Analytical Procedures	- Analytical validation information, including experimental data for the analytical procedures used for testing the drug substance - Non-compendial methods	✓ ✓	✓ ✓
	4.4. Batch Analyses	- Description of batches and results of the analysis to establish the specification.	✓	✓
	4.5. Justification of Specification	- Justification for drug substance specification.	✓	✓
S5	Reference Standards or Materials	- Information on the reference standards or reference materials used for testing of the Drug substance. - Compendial reference standard	✓ ✓	✓ ✓
S6	Container Closure System	-Descriptions of the container closure systems.	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
S7	Stability	- Literature data. - Stability Summary and conclusion - Post approval stability protocol and stability commitment - Stability Data	- ✓ ✓ ✓	- ✓ ✓ ✓
P P1	DRUG PRODUCT 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 reconstitution diluent (s), if applicable. Composition Name, quantity stated in metric weight or measures, function and quality standard reference.	✓ ✓	✓ ✓
P2	Pharmaceutical Development 2.1. Information on Development Studies	Data on the development studies conducted to establish that the dosage form, formulation, manufacturing process, container closure system, microbiological attributes and usage instruction	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		are appropriate for the purpose specified in the application.		
	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. - Literature data. - Excipients Justification of the choice of 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). - Overages Justification of any overage in the formulation(s) described in P1.	✓ ✓	✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		- Physicochemical and Biological Properties Parameters relevant to the performance of the finished product e.g pH, dissolution.	✓	✓
	2.4. Manufacturing Process Development	- Selection and optimisation of the manufacturing process - Differences between the manufacturing process (es) used to produce pivotal clinical batches and the process described in P.3.2, if applicable	✓ ✓	✓ ✓
	2.5. Container Closure System	Suitability of the container closure system used for the storage, transportation (shipping) and use of the finished product.	✓	✓
	2.6. Microbiological Attributes	Microbiological attributes of the dosage form, where appropriate	✓	✓
	2.7. Compatibility	- Compatibility of the finished product with reconstitution diluent(s) or dosage devices. - Literature data	✓ -	✓ -
P3	Manufacture 3.1. Manufacturer	Name, address, and responsibilities of each manufacturer involved	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
	3.2. Batch Formula	Name and quantities of all ingredients	✓	✓
	3.3. Manufacturing Process and Process Control	Description of manufacturing process and process control	✓	✓
	3.4. Control of Critical Steps and Intermediates	Tests and acceptance criteria	✓	✓
	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. - Viral safety information	✓ ✓	✓ ✓
P4	Control of Excipients 4.1. Specifications	- Specifications for excipients - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓
	4.2. Analytical Procedures	- Analytical procedures used for testing excipients where appropriate. - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓
	4.3. Excipient of Human or Animal Origin	- Information regarding sources and or adventitious agents. - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
	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)	✓	✓
P5	Control of Finished Product			
	5.1. Specification	The specification(s) for the finished product.	✓	✓
	5.2. Analytical Procedures	Analytical procedures used for testing the finished product	✓	✓
	5.3. Validation of Analytical Procedures	- Information including experimental data, for the validation of the analytical procedure used for testing the finished product	✓	✓
		- Non-compendial method	✓	✓
		- Verification of compendial method applicability - precision & accuracy	✓	✓
	5.4. Batch Analyses	- Description and test results of all relevant batches.	✓	✓
		- Summary protocol of the production and control	✓	✓
	5.5. Characterisation of Impurities	- Justification of the proposed finished product specification(s).	✓	✓
		- Compendial requirements or appropriate information from the manufacturer	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
P6	Reference Standards or Materials	- Information on the reference standards or reference materials used for testing of the finished product. - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓
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)	✓	✓
P8	Stability	- Stability Summary and conclusion - Commitment on post approval stability monitoring - Stability report : data demonstrating that product is stable through its proposed shelf life. - Description of procedures to guarantee cold chain (where applicable)	✓ ✓ ✓ ✓	✓ ✓ ✓ ✓
P9	Product Interchangeability/ Equivalence evidence	- In Vitro Comparative dissolution study as required - In Vivo Bioequivalence study as required	- -	- -

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
A A1	ANNEX Adventitious Agents Safety Evaluation	- A discussion on measures implemented to control endogenous and adventitious agents in production should be included. - A tabulated summary of the reduction factors for viral clearance, should be provided.	✓	✓
	Section C. Body of Data			
S S1	DRUG SUBSTANCE General Information 1.2 Nomenclature	- Information from the S1	✓	✓
	1.2 Structure	- Structural formula, including relative and absolute stereochemistry, the molecular formula, and the relative molecular mass. - Schematic amino acid sequence indicating glycosylation sites or other post-translational modifications and relative molecular mass as appropriate. (Note: This section is applicable for biotech products and recombinant polysaccharide/protein vaccines)	✓ ✓	✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
	1.3 General Properties	- Physicochemical characteristics and other relevant properties including biological activity for 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)	✓ ✓	✓ ✓
S2	Manufacture 2.2 Manufacturer(s)	-Name and address of the manufacturer (s).	✓	✓
	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 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. Flowchart of manufacturing process, Description of batch identification system, Description of inactivation or detoxification process, Description of purification process Stabilization of active ingredient, reprocessing, Filling	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		procedure, in process control		
	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.	✓	✓
		- Control of source and starting materials of biological origin.	✓	✓
		- Source, history and generation of the cell substrate.	✓	✓
		- Cell banking system, characterisation and testing.	✓	✓
		- Viral safety evaluation.	✓	✓
	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.	✓	✓
		- Intermediates : Specifications and analytical procedure, if any, for intermediates isolated during the process.	✓	✓
		- Stability data supporting storage conditions.	✓	✓
	2.5. Process Validation and/or Evaluation	Process validation and/or evaluation studies for aseptic processing and sterilization.	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
	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. -The development history of the manufacturing process as described in S 2.2.	✓ ✓	✓ ✓
S3	Characterisation 3.1. Elucidation of Structure and other characteristics	-Confirmation of structure based on e.g. synthetic route and spectral analyses. - Compendial requirements or appropriate information from the manufacturer - Details on primary, secondary and higher-order structure and information on biological activity, purity and immunochemical properties (when relevant).	✓ ✓ ✓	✓ ✓ ✓
	3.2. Impurities	- Summary of impurities monitored or tested for during and after manufacture of drug substance - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
S4	Control of Drug substance			
	4.1. Specification	- Detailed specification, tests and acceptance criteria.	✓	✓
		- Compendial specification or appropriate information from the manufacturer	✓	✓
		-Specify source, including as appropriate species of animal, type of microorganism etc.	✓	✓
	4.2. Analytical Procedures	- The analytical procedures used for testing of drug substance.	✓	✓
		- Compendial methods or appropriate information from the manufacturer	✓	✓
	4.3. Validation of Analytical Procedures	- Analytical validation information, including experimental data for the analytical procedures used for testing the drug substance	✓	✓
		- Non-compendial methods	✓	✓
	4.4. Batch Analyses	- Description of batches and results of the analysis to establish the specification.	✓	✓
	4.5. Justification of Specification	- Justification for drug substance specification.	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
S5	Reference Standards or Materials	- Information on the reference standards or reference materials used for testing of the Drug substance. - Compendial reference standard	✓ ✓	✓ ✓
S6	Container Closure System	-Descriptions of the container closure systems.	✓	✓
S7	Stability	- Literature data. - Stability Summary and conclusion - Post approval stability protocol and stability commitment - Stability Data	- ✓ ✓ ✓	- ✓ ✓ ✓
P P1	DRUG PRODUCT 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 reconstitution diluent (s), if applicable. Composition	✓ ✓	✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		Name, quantity stated in metric weight or measures, function and quality standard reference.		
P2	Pharmaceutical Development 2.1. Information on Development Studies	Data on the development studies conducted to establish that the dosage form, formulation, manufacturing process, container closure system, microbiological attributes and usage instruction are appropriate for the purpose specified in the application.	✓	✓
	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. - Literature data. - Excipients Justification of the choice of 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	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		product, (taking into consideration the proposed route of administration and usage for NCE and Biologics). - Overages Justification of any overage in the formulation(s) described in P1. - Physicochemical and Biological Properties Parameters relevant to the performance of the finished product e.g pH, dissolution.	✓ ✓	✓ ✓
	2.4. Manufacturing Process Development	- Selection and optimisation of the manufacturing process - Differences between the manufacturing process (es) used to produce pivotal clinical batches and the process described in P.3.2, if applicable	✓ ✓	✓ ✓
	2.5. Container Closure System	Suitability of the container closure system used for the storage, transportation (shipping) and use of the finished product.	✓	✓
	2.6. Microbiological Attributes	Microbiological attributes of the dosage form, where appropriate	✓	✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
	2.7. Compatibility	- Compatibility of the finished product with reconstitution diluent(s) or dosage devices. - Literature data	✓ -	✓ -
P3	Manufacture 3.1. Manufacturer	Name, address, and responsibilities of each manufacturer involved	✓	✓
	3.2. Batch Formula	Name and quantities of all ingredients	✓	✓
	3.3. Manufacturing Process and Process Control	Description of manufacturing process and process control	✓	✓
	3.4. Control of Critical Steps and Intermediates	Tests and acceptance criteria	✓	✓
	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. - Viral safety information	✓ ✓	✓ ✓
P4	Control of Excipients 4.1. Specifications	- Specifications for excipients - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
	4.2. Analytical Procedures	- Analytical procedures used for testing excipients where appropriate. - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓
	4.3. Excipient of Human or Animal Origin	- Information regarding sources and or adventitious agents. - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓
	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)	✓	✓
P5	Control of Finished Product 5.1. Specification	The specification(s) for the finished product.	✓	✓
	5.2. Analytical Procedures	Analytical procedures used for testing the finished product	✓	✓
	5.3. Validation of Analytical Procedures	- Information including experimental data, for the validation of the analytical procedure used for testing the finished product - Non-compendial method - Verification of compendial method applicability - precision &	✓ ✓ ✓	✓ ✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		accuracy		
	5.4. Batch Analyses	- Description and test results of all relevant batches. - Summary protocol of the production and control	✓ ✓	✓ ✓
	5.5. Characterisation of Impurities	- Justification of the proposed finished product specification(s). - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓
P6	Reference Standards or Materials	- Information on the reference standards or reference materials used for testing of the finished product. - Compendial requirements or appropriate information from the manufacturer	✓ ✓	✓ ✓
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)	✓	✓
P8	Stability	- Stability Summary and conclusion - Commitment on post approval stability monitoring - Stability report : data demonstrating that product is stable through its proposed shelf life.	✓ ✓ ✓	✓ ✓ ✓

No.	Parameters	Components	Requirements	
			Biological Products	
			Vaccine	Other Biological Products
		- Description of procedures to guarantee cold chain (where applicable)	✓	✓
P9	Product Interchangeability/ Equivalence evidence	- In Vitro Comparative dissolution study as required - In Vivo Bioequivalence study as required	- -	- -
A A1	ANNEX Adventitious Agents Safety Evaluation	- A discussion on measures implemented to control endogenous and adventitious agents in production should be included. - A tabulated summary of the reduction factors for viral clearance, should be provided.	✓	✓

เอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาชีววัตถุ (Biological Products) แบบ ASEAN HARMONIZATION

จำแนกตามประเภทยาชีววัตถุ : ข้อมูลด้าน Non Clinical

Part III: Document	NCE	BIOLOGICS	RT	S/P	IND	Vaccine				
						NV	NC	CV/ EV	IND	S/P
Section A. Table of Content	√	√	❖	❖	❖	√	√	❖	❖	❖
Section B. Nonclinical Overview	√	√	❖	❖	❖	√	√	❖	❖	❖
1. General Aspect	√	√	❖	❖	❖	√	√	❖	❖	❖
2. Content and structural format	√	√	❖	❖	❖	√	√	❖	❖	❖
Section C. Nonclinical Summary (Written and Tabulated)										
1. **Nonclinical Written Summaries**	√	√	❖	❖	❖	√	√	❖	❖	❖
1.1 Pharmacology										
1.1.1 Primary Pharmacodynamics / Immunogenicity Study	√	√	-	-	-	√	√	-	-	-
1.1.2 Secondary Pharmacodynamics	√	√	-	-	-	-	-	-	-	-
1.1.3 Safety Pharmacology	√	√	-	-	-	❖	-	-	-	-
1.1.4 Pharmacodynamics Drug Interactions	√	√	-	-	-	❖	❖	-	-	-
1.2 Pharmacokinetics										
1.2.1 Absorption	√	❖	❖	❖	-	-	-	-	-	-
1.2.2 Distribution	√	❖	❖	❖	-	❖	❖	❖	-	❖
1.2.3 Metabolism (Inter-species comparison)	√	❖	❖	❖	-	-	-	-	-	-
1.2.4 Excretion	√	❖	❖	❖	-	-	-	-	-	-
1.2.5 Pharmacokinetics Drug Interaction (non-clinical)	√	-	-	-	-	-	-	-	-	-
1.2.6 Other Pharmacokinetics Studies	√	-	❖	-	-	-	-	-	-	-
1.3 Toxicology										
1.3.1 Single dose toxicity	√	√	-	-	-	❖	❖	❖	-	-

Part III: Document	NCE	BIOLOGICS	RT	S/P	IND	Vaccine				
						NV	NC	CV/ EV	IND	S/P
1.3.2 Repeat dose toxicity	√	√	-	-	-	√	❖	❖ *)	-	-
1.3.3 Genotoxicity	√	-	-	-	-	❖	❖	❖	-	-
1.3.4 Carcinogenicity	√	♦	-	-	-	❖	❖	❖	-	-
1.3.5 Reproductive and developmental toxicity	√	√	-	-	-	❖	❖	❖	-	-
1.3.5.1 Fertility and early embryonic development	√	√	-	-	-	❖	❖	❖	-	-
1.3.5.2 Embryo-fetal development	√	√	-	-	-	❖	❖	❖	-	-
1.3.5.3 Prenatal and postnatal development including maternal function										
1.3.6 Local tolerance	❖	❖	❖	❖	❖	❖	❖	❖	-	❖
1.3.7 Other toxicity studies, if available	❖	❖	❖	❖	❖	❖	❖	❖	-	❖
2. Nonclinical Tabulated Summaries										
Section D. Nonclinical Study Report (As requested)										
1. **Table of Content**	√	√	❖	❖	❖	√	√	❖	❖	❖
2. **Pharmacology**										
2.1 Primary Pharmacodynamics / Immunogenicity Study	√	√	-	-	-	√	√	-	❖	-
2.2 Secondary Pharmacodynamics	√	√	-	-	-	-	-	-	-	-
2.3 Safety Pharmacology	√	√	-	-	-	❖	-	-	-	-
2.4 Pharmacodynamics Drug Interactions										

Part III: Document	NCE	BIOLOGICS	RT	S/P	IND	Vaccine				
						NV	NC	CV/ EV	IND	S/P
3. **Pharmacokinetics**										
3.1 Analytical Methods and Validation Reports	√	❖	❖	❖	-	-	-	-	-	-
3.2 Absorption	√	❖	❖	❖	-	❖	❖	❖	-	❖
3.3 Distribution	√	❖	❖	❖	-	-	-	-	-	-
3.4 Metabolism (Inter-species comparison)	√	❖	❖	❖	-	-	-	-	-	-
3.5 Excretion	√	-	-	-	-	-	-	-	-	-
3.6 Pharmacokinetics Drug Interaction (non-clinical)	√	-	❖	-	-	-	-	-	-	-
3.7 Other Pharmacokinetics studies										
4. Toxicology										
4.1 Single dose toxicity	√	√	-	-	-	❖	❖	❖	-	-
4.2 Repeat dose toxicity	√	√	-	-	-	√	❖	❖ *)	-	-
4.3 Genotoxicity	√	-	-	-	-	❖	❖	❖	-	-
4.3.1 In vitro	√	-	-	-	-	❖	❖	❖	-	-
4.3.2 In vivo	√	-	-	-	-	❖	❖	❖	-	-
4.4 Carcinogenicity	√	♦	-	-	-	❖	❖	❖	-	-
4.4.1 Long term studies	√	♦	-	-	-	❖	❖	❖	-	-
4.4.2 Short or medium term studies	√	♦	-	-	-	❖	❖	❖	-	-
4.4.3 Other studies	√	♦	-	-	-	❖	❖	❖	-	-

Part III: Document	NCE	BIOLOGICS	RT	S/P	IND	Vaccine				
						NV	NC	CV/ EV	IND	S/P
4.5 Reproductive and developmental toxicity	√	√	-	-	-	❖	❖	❖	-	-
4.5.1 Fertility and early embryonic development	√	√	-	-	-	❖	❖	❖	-	-
	√	√	-	-	-	❖	❖	❖	-	-
4.5.2 Embryo-fetal development	√	√	-	-	-	❖	❖	❖	-	-
4.5.3 Prenatal and postnatal development including maternal function	√	√	-	-	-	❖	❖	❖	-	-
4.5.4 Studies in which the offspring are dosed and/or further evaluated										
4.6 Local tolerance	❖	❖	❖	❖	❖	❖	❖	❖	-	❖
4.7 Other toxicity studies, if available	❖	❖	❖	❖	❖	❖	❖	❖	-	❖
4.7.1 Antigenicity										
4.7.2 Immunotoxicity										
4.7.3 Dependence										
4.7.4 Metabolites										
4.7.5 Impurities										
4.7.6 Other										
Section E. List of Key Literature References	√	√	❖	❖	❖	❖	❖	❖	-	❖

NCE - New chemical entity
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NC - New Combination
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√ - Required

-	- Not Required
❖	- Where applicable, i.e. change of route of administration due to change in formulation, change of formulation and posology such as immediate release to sustained released) and/or for product with narrow margin of safety or variable kinetics
♦	- Generally inappropriate for Biological products, however, product-specific assessment of carcinogenic potential may be needed depending upon duration of clinical dosing, patient population and/or biological activity of the product (e.g. Growth factors, immunosuppressive agents, etc.)
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Notes:

1. As references for requirement, the following WHO Guidelines or their relevant updates are used:
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2. The term 'Biologics' used in this document does not include vaccines with the rationale that vaccines has different characteristics compared with other biological products so that in many cases the requirements are different.

เอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาชีววัตถุ (Biological Products) แบบ ASEAN HARMONIZATION

จำแนกตามประเภทยาชีววัตถุ : ข้อมูลด้าน Clinical

Part IV : Clinical Document	**NCE**	**BIOLOGICS**	**MaV**			**MiV**	**GP**	**VACCINE**				
			RT	**ST/P**	**IND**			**NV**	**NC**	**NV-EA**	**IND**	**S/P**
Section A. Table of Contents	✓	✓	✓	✓	✓	-	-	✓	✓	✓	✓	✓
Section 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								✓	✓	✓	✓	✓

Part IV : Clinical Document	NCE	BIOLOGICS	MaV			MiV	GP	VACCINE				
			RT	ST/P	IND			NV	NC	NV-EA	IND	S/P
Section C. Clinical Summary	✓	✓	✓	✓	✓	-	-					
Summary of Biopharmaceutic Studies and Associated Analytical Method 1.1 Background and Overview 1.2 Summary of Results of Individual Studies 1.3 Comparison and Analyses of Results Across Studies Appendix 1								-	-	-	-	-
Section C. Clinical Summary (Cont.) **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								* *	* *	- 	* *	-

Part IV : Clinical Document	NCE	BIOLOGICS	MaV			MiV	GP	VACCINE				
			RT	ST/P	IND			NV	NC	NV-EA	IND	S/P
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 3.4 Analysis of Clinical Information Relevant to Dosing Recommendations 3.5 Persistence of Efficacy and/or Tolerance Effects Appendix 3								✓	✓	✓	✓	✓

Part IV : Clinical Document	NCE	BIOLOGICS	MaV			MiV	GP	VACCINE				
			RT	ST/P	IND			NV	NC	NV-EA	IND	S/P
Section C. Clinical Summary (Cont.) **Summary of Clinical Safety** 4.1 Exposure to the Drug 4.2 Adverse Events 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 4.6 Post-marketing Data Appendix 4								✓	✓	✓	✓	✓
Synopses of Individual Studies								✓	✓	✓	✓	✓
Section D. Tabular Listing of All Clinical Studies	✓	✓	✓	✓	✓	-	-	✓	✓	✓	✓	✓

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