ข้อกำหนดและเอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาใหม่ (New Drugs) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่ ฉบับที่ 1

[เอกสารนี้ใช้ประกอบกับ “คู่มือ/หลักเกณฑ์การขึ้นทะเบียนตำรับยาใหม่ (New Drugs) แบบ ASEAN HARMONIZATION” ฉบับที่ 1]

กลุ่มยาใหม่
กองควบคุมยา
สำนักงานคณะกรรมการอาหารและยา
กันยายน 2550

1. ข้อกำหนดและเอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาใหม่ (New Drugs) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่ : ข้อมูลด้าน Quality

สารบัญ

ข้อกำหนดในการขึ้นทะเบียนตำรับยาใหม่ (New Drugs) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่

ข้อมูลด้าน Quality

No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
S	DRUG SUBSTANCE								
S1	General Information								
	1.1 Nomenclature	- International non-proprietary name (INN) - Compendial name if relevent - Registry number of chemical abstract service (CAS) - Laboratory code(if applicable) - Chemical name (s)	√		√	√	√	√	√
	1.2 Structure	- Structural formula, including relative and absolute stereochemistry, the molecular formula, and the relative molecular mass.	√		√				
	1.3 General Properties	- Physicochemical characteristics and other relevant properties.	√		√	√	√	√	√
S2	Manufacture								
	2.1 Manufacturer (s)	Name and address of the manufacturer (s).	√		√				

NCE = New Chemical Entity , NI = New Indication , NCO = New Combination , ND = New Delivery System , NR= New Route of administration,

NDOS= New Dosage Form of Approved New Drug , NS= New Strength of Approved New Drug

[a] If the product contains previously registered NCE but not submitted by the same applicant the requirement of NCE must be followed.

[b] NI must be submitted the copy of Approved Document.

No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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.	√						
	2.3 Control of Materials	- Starting materials, solvents, reagents, catalysts, and any other materials used in the manufacture of the drugs substance indicating where each material is used in the process. Tests and acceptance criteria of these materials.	√						
	2.4 Controls of Critical Steps and Intermediates	- Critical steps : Tests and acceptance criteria, with justification including experimental data, performed at critical step of the manufacturing process to ensure that the process is controlled.	√						
		- Intermediates : Specifications and analytical procedure, if any, for intermediates isolated during the process.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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, scale-up, pilot and if available, production scale batches. - The development history of the manufacturing process as described in S2.2.	√						
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	√		√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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			√				
	4.2 Analytical Procedures	- The analytical procedures used for testing of drug substance.	√						
		Compendial methods or appropriate information from the manufacturer			√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
S7	Stability	- Stability report.	√						
		- Literature data.			√	√	√	√	√
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 reconstitution diluent (s), if applicable.	√		√	√	√	√	√
		Composition Name, quantity stated in metric weight or measures, function and quality standard reference.	√		√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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).	√		√	√	√	√	√
		- Overages Justification of any overage in the formulation (s) described in P1.	√		√	√	√	√	√
		- Physicochemical 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	√		√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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 Batch Formula	- Name and quantities of all ingredients	√		√	√	√	√	√
	3.2 Manufacturing Process and Process Control	- Description of manufacturing process and process control	√		√	√	√	√	√
	3.3 Control of Critical Steps and Intermediates	- Tests and acceptance criteria	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
P3	3.4 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.	√						
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			√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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 analytical procedure used for testing the finished product	√						
		Non-compendial method	√		√	√	√	√	√
		- Verification of compendial method applicability- precision & accuracy			√	√	√	√	

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			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
P5	5.4 Batch Analyses	- Description and test results of all relevant batches.	√		√	√	√	√	√
	5.5 Characterisation of Impurities	- Information on the characterisation of impurities	√						
		Compendial requirements or appropriate information from the manufacturer			√	√	√	√	√
	5.6 Justification of Specification(s)	- 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			√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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 report : data demonstrating that product is stable through its proposed shelf life. Commitment on post approval stability monitoring	√		√	√	√	√	√
P9	Product Interchangeability					√	√	√	√
	Equivalence evidence	- In Vitro Comparative dissolution study as required				√	√	√	√
		- In Vivo Bioequivalence study as required							

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ข้อมูลด้าน Quality

No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	Section A. Table of content		√	√	√	√	√	√	√
	Section B. Quality Overall Summary								
S	DRUG SUBSTANCE								
S1	General Information								
	1.1 Nomenclature	- International non-proprietary name (INN) - Compendial name if relevent - Registry number of chemical abstract service (CAS) - Laboratory code(if applicable) - Chemical name (s)	√		√	√	√	√	√
	1.2 Structure	- Structural formula, including relative and absolute stereochemistry, the molecular formula, and the relative molecular mass.	√		√				
	1.3 General Properties	- Physicochemical characteristics and other relevant properties.	√		√	√	√	√	√
S2	Manufacture								
	2.1 Manufacturer (s)	Name and address of the manufacturer (s).	√		√				

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			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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.	√						
	2.3 Control of Materials	- Starting materials, solvents, reagents, catalysts, and any other materials used in the manufacture of the drugs substance indicating where each material is used in the process. Tests and acceptance criteria of these materials.	√						
	2.4 Controls of Critical Steps and Intermediates	- Critical steps : Tests and acceptance criteria, with justification including experimental data, performed at critical step of the manufacturing process to ensure that the process is controlled.	√						
		- Intermediates : Specifications and analytical procedure, if any, for intermediates isolated during the process.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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, scale-up, pilot and if available, production scale batches. - The development history of the manufacturing process as described in S2.2.	√						
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			√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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			√				
	4.2 Analytical Procedures	- The analytical procedures used for testing of drug substance.	√						
		Compendial methods or appropriate information from the manufacturer			√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
S7	Stability	- Stability report. - Literature 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.	√ √		√ √	√ √	√ √	√ √	√ √

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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).	√		√	√	√	√	√
		- Overages Justification of any overage in the formulation (s) described in P1.	√		√	√	√	√	√
		- Physicochemical 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	√		√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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 Batch Formula	- Name and quantities of all ingredients	√		√	√	√	√	√
	3.2 Manufacturing Process and Process Control	- Description of manufacturing process and process control	√		√	√	√	√	√
	3.3 Control of Critical Steps and Intermediates	- Tests and acceptance criteria	√						

NCE = New Chemical Entity , NI = New Indication , NCO = New Combination , ND = New Delivery System , NR= New Route of administration,

NDOS= New Dosage Form of Approved New Drug , NS= New Strength of Approved New Drug

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[b] NI must be submitted the copy of Approved Document.

No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
P3	3.4 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.	√						
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			√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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 analytical procedure used for testing the finished product	√						
		Non-compendial method	√		√	√	√	√	√
		- Verification of compendial method applicability- precision & accuracy			√	√	√	√	√

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[b] NI must be submitted the copy of Approved Document.

No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
P5	5.4 Batch Analyses	- Description and test results of all relevant batches.	√		√	√	√	√	√
	5.5 Characterisation of Impurities	- Information on the characterisation of impurities	√						
		Compendial requirements or appropriate information from the manufacturer			√	√	√	√	√
	5.6 Justification of Specification(s)	- 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			√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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 report : data demonstrating that product is stable through its proposed shelf life. Commitment on post approval stability monitoring	√		√	√	√	√	√
P9	Product Interchangeability								
	Equivalence evidence	- In Vitro Comparative dissolution study as required				√	√	√	√
		- In Vivo Bioequivalence study as required				√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	Section C. Body of Data								
S	DRUG SUBSTANCE								
S1	General Information								
	1.1 Nomenclature	- International non-proprietary name (INN) - Compendial name if relevent - Registry number of chemical abstract service (CAS) - Laboratory code(if applicable) - Chemical name (s)	√		√	√	√	√	√
	1.2 Structure	- Structural formula, including relative and absolute stereochemistry, the molecular formula, and the relative molecular mass.	√		√				
	1.3 General Properties	- Physicochemical characteristics and other relevant properties.	√		√	√	√	√	√
S2	Manufacture								
	2.1 Manufacturer (s)	Name and address of the manufacturer (s).	√		√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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.	√						
	2.3 Control of Materials	- Starting materials, solvents, reagents, catalysts, and any other materials used in the manufacture of the drugs substance indicating where each material is used in the process. Tests and acceptance criteria of these materials.	√						
	2.4 Controls of Critical Steps and Intermediates	- Critical steps : Tests and acceptance criteria, with justification including experimental data, performed at critical step of the manufacturing process to ensure that the process is controlled.	√						
		- Intermediates : Specifications and analytical procedure, if any, for intermediates isolated during the process.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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, scale-up, pilot and if available, production scale batches. - The development history of the manufacturing process as described in S2.2.	√						
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			√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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			√				
	4.2 Analytical Procedures	- The analytical procedures used for testing of drug substance.	√						
		Compendial methods or appropriate information from the manufacturer			√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
S7	Stability	- Stability report.	√						
		- Literature data.			√	√	√	√	√
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 reconstitution diluent (s), if applicable.	√		√	√	√	√	√
		Composition Name, quantity stated in metric weight or measures, function and quality standard reference.	√		√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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.	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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).	√		√	√	√	√	√
		- Overages Justification of any overage in the formulation (s) described in P1.	√		√	√	√	√	√
		- Physicochemical 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	√		√				

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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 Batch Formula	- Name and quantities of all ingredients	√		√	√	√	√	√
	3.2 Manufacturing Process and Process Control	- Description of manufacturing process and process control	√		√	√	√	√	√
	3.3 Control of Critical Steps and Intermediates	- Tests and acceptance criteria	√						

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
P3	3.4 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.	√						
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			√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	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 analytical procedure used for testing the finished product	√						
		Non-compendial method	√		√	√	√	√	√
		- Verification of compendial method applicability- precision & accuracy			√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
P5	5.4 Batch Analyses	- Description and test results of all relevant batches.	√		√	√	√	√	√
	5.5 Characterisation of Impurities	- Information on the characterisation of impurities	√						
		Compendial requirements or appropriate information from the manufacturer			√	√	√	√	√
	5.6 Justification of Specification(s)	- 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			√	√	√	√	√

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[ab]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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 report : data demonstrating that product is stable through its proposed shelf life. Commitment on post approval stability monitoring	√		√	√	√	√	√
P9	Product Interchangeability								
	Equivalence evidence	- In Vitro Comparative dissolution study as required				√	√	√	√
		- In Vivo Bioequivalence study as required				√	√	√	√
	Section D. Key Literature references		√	√	√	√	√	√	√

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2. ข้อกำหนดและเอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาใหม่ (New Drugs) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่ : ข้อมูลด้าน Nonclinic

ข้อกำหนดในการขึ้นทะเบียนตำรับยาใหม่ (NEW DRUGS) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่

ข้อมูลด้าน Nonclinic

ICH NO.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
M3	1.Pharmacology	-Studies designed to examine effects other than the primary therapeutic effect of a drug substance.							
	1.1.Primary Pharmacodynamics	-Studies are done to identify the mode of action and/or effects of a substance in relation to its desired therapeutic target	√						
	1.2.Secondary Pharmacodynamics	-Studies are done to identify the mode of action and/or effects of a substance not related to its therapeutic target	√						
S7A S6	1.3. Safety Pharmacology	-Studies focus on identifying adverse effects on physiological functions	√		❖				

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[a]If the product contains previously registered NCE but not submitted by the same applicant the requirement of NCE must be followed.

❖ When applicable, especially for major variation (i.e. change of route of administration due to change of formulation, change of formulation and posology such as immediate release to sustained released, and/or for products with narrow margin of safety or variable kinetics.

ICH NO.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	1.3. Safety Pharmacology (continued)	-Core battery includes the assessment of effects on the vital functions, such as cardiovascular, central nervous and respiratory systems, and these should be evaluated prior to human exposure. -These evaluations may be conducted as addition to toxicity studies or as separate studies					❖		
	1.4.Pharamacodyna-mics Drug Interactions	-If they have been performed, pharmacodynamic drug interaction studies should be briefly summarized in this section.	√						

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ICH NO.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
S3B S3A	2. Pharmacokinetics	-PK data form the basis for prediction of therapeutic doses and suitable dosage regimen							
	2.1. Absorption	-Extent and rate of absorption, in-vivo and in situ studies -Kinetic parameters, bioequivalence and/ or bioavailability (serum/ plasma/ blood PK studies)	√		❖	❖	❖		❖
	2.2. Distribution	-Tissue distribution studies -Protein binding and distribution in blood cells -Placental transfer studies	√		❖	❖	❖		❖
	2.3. Metabolism (inter -species comparison)	-Chemical structure and quantities of metabolites in biological samples -Possible metabolic pathways -Pre-systemic metabolism (GI/ Hepatic First-Pass Effects)	√		❖	❖	❖		❖

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ICH NO.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
		-In vitro metabolism including P450 studies -Enzyme induction and inhibition							
	2.4. Excretion	-Route and extent of excretion -Excretion in milk	√		❖	❖	❖		❖
	2.5. Pharmacokinetic Drug Interaction (Non-clinical)	-If they have been performed, non-clinical Pharmacokinetic drug interaction studies (in-vitro and/or in-vivo) should be briefly summarized in this section.	√		❖	❖	❖		❖
	2.6. Other Pharmacokinetic studies	-If studies have been performed in non-clinical models of disease (e.g. Renally impaired animals), should be summarized in this section.	√		❖	❖	❖		❖

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ICH NO.	PARAMETERS	COMPONENTS	REQUIREMENTS						
			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	3.Toxicology	-The scope of the toxicologic evaluation should be described in relation to the proposed clinical use.							
S4	3.1. Single Dose Toxicity	-The single dose data should be briefly summarized, in order by species, by route. -It should be evaluated in two mammalian species prior to the first human exposure. -A dose escalation study is considered an acceptable alternative to the single dose design.	√		❖				
S4A	3.2. Repeat Dose Toxicity	-Studies should be summarized in order by species, by route, and by duration, giving brief details of the methodology and highlighting important findings (e.g. nature and severity of target organ toxicity, dose (exposure)/ response relationships, no observe adverse	√		❖				

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	3.2. Repeat Dose Toxicity (continued)	effect levels(NOEL)) -It's performed on rodents and non-rodents with a study duration of 6 months and 9 months respectively -Studies are related to the duration, therapeutic indication and scale of the proposed clinical trial of the pharmaceutical.	√						
S2A S2B	3.3. Genotoxicity	-Brief summaries of in vitro and in vivo tests designed to detect compounds which induce genetic damage directly or indirectly by various mechanism: ●In vitro tests include tests for the detection of bacterial mutagens ●In vivo tests include tests for the detection of clastogens (either by chromosomal aberrations or micronuclei	√						

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		polychromatic erythrocytes)							
S1A S1B S1C S1C (R)	3.4. Carcinogenicity	-Studies are conducted to identify a tumorigenic potential in animals and to assess the relevant risk in humans. -The strategy for testing the carcinogenic potential of a pharmaceutical is developed only after acquisition of information: results of genetic toxicology, intended patient population,clinical dosage regimen, pharmacodynamics in animals and in humans, repeated dose toxicology studies. No single approach can be expected to predict the carcinogenic potential. -Other factors may also be considered : such as the intended patient population, prior assessment of carcinogenic potential, extent of systemic exposure etc.	√						

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	3.4. Carcinogenicity (continued)	-A brief rationale should explain why the studies were chosen and the basis for high dose selection. -Individual studies should be summarized and comprises: ● one long-term rodent studies, ● and either, short / medium term studies (in-vivo rodent test systems) or a long term studies in a second rodent species ●Other studies	√						
S5A S5B (M)	3.5. Reproductive and Developmental Toxicity	-Studies are designed to evaluate the effect of the drug on the general reproductive performance of animals starting at implantation and continuing through the weaning period in dose significantly greater than those intended for man or in doses that give greater significantly higher blood	√						

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	3.5. Reproductive and Developmental Toxicity (continued)	and/or other tissue concentration than those achieved in man. -Studies should be conducted in mammalian species, same species and strain as in other toxicological studies, i.e. rats. For embryotoxicity studies, a second mammalian species is required, rabbit being the preferred choice as a non-rodent. -Dosages : choice of high dose should be based on data from all availble studies - Route and frequency of administration : similar to the intended route for human usage and usual frequency is once daily or more or less frequent depending on the kinetic profile	√						

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			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
S5A S5B (M)	3.5.1. Fertility and Early Embryonic Development	-Control group : use of vehicle as control group vs test group -Studies are conducted to test for toxic effects/ disturbances resulting from treatment from before mating (males/ females) through mating and implantation -Effects of a potentially toxic substance could be determined by assessment of: maturation of gametes, mating behavior, fertility, preimplantation stages of the embryo, implantation.	√						
	3.5.2. Embryo-fetal Development	-Studies conducted to detect adverse effects on the pregnant female and development of the embryo and fetus consequent to exposure of the female from implantation to closure of the hard palate.	√						

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			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
	3.5.2. Embryo-fetal Development	-The potential adverse effects to be assessed include: enhanced toxicity relative to that in non-pregnant females, embryofetal death, altered growth and structural changes. - Studies should include: ● characterization of the type and incidence of malformations in comparison with the negative and positive controls through detailed skeletal and visceral organ examination ● calculation of the pregnancy rate, implantation efficiency and fetal viability ● evaluation of the effect of treatment or chemical on maternal weight, mortality, behavior, and fetal weight including male / female ratio	√						

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			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
S5A	3.5.3. Pre-natal and Post-natal Development including Maternal Function	-The study determines the adverse effects of drugs or chemical on the pregnant/ lactating female and on development of the conceptus and the offspring following exposure of the female from implantation through weaning. Since manifestations of effect induced during this period may be delayed, observations should be continued through sexual maturity. -The potential adverse effects to be assessed shall include: enhanced toxicity relative to that in non-pregnant females, pre- and postnatal death of offspring, altered growth and development, functional deficits in offspring, including behavior, maturation (puberty) and reproduction (F1).	√						

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			NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
S5A	3.5.3. Pre-natal and Post-natal Development including Maternal Function (continued)	-studies should provide data on: a. labor – as to the presence of dystocia, duration of labor, onset of labor b. gestation – as to duration and weight gain of dams during pregnancy c. litter – as to number of pups (litter size) weight of pups, bursing behavior of pups, physiologic and anatomic parameters (food and water consumption, length, etc.) and effect of cross over nursing of pups -concurrent negative control of animal must be run together with the treated groups(at least 3 dose levels)	√						

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	4.Local Tolerance	-Studies are summarized in order by species, by route and by duration on the following; ●Eye irritation test ●Dermal toxicity testing	√	❖	❖	❖	❖		❖
	5.Other Toxicity studies	-Rationale for conducting the studies should be provided -Other studies may include : antigenicity, immunotoxicity, machanistic studies, dependence, studies on metabolites, impurities and other studies	❖	❖	❖	❖	❖		❖
	6.List of Key Literature Reference	List of key reference must be submitted.	√	❖	❖	❖	❖		❖

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เอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาใหม่ (NEW DRUGS) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่ ข้อมูลด้าน Nonclinic

PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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	√						
1.1.2 Secondary Pharmacodynamics	√						
1.1.3 Safety Pharmacology	√		❖		❖		
1.1.4 Pharmacodynamics Drug Interactions	√						

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PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
1.2 Pharmacokinetics							
1.2.1 Absorption	√		❖	❖	❖		❖
1.2.2 Distribution	√		❖	❖	❖		❖
1.2.3 Metabolism	√		❖	❖	❖		❖
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	√		❖				
1.3.2 Repeat dose toxicity	√		❖				
1.3.3 Genotoxicity	√						
1.3.4 Carcinogenicity	√						
1.3.5 Reproductive and developmental toxicity	√						

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PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
1.3.5.1 Fertility and early embryonic development	√						
1.3.5.2 Embryo-fetal development	√						
1.3.5.3 Prenatal and postnatal development	√						
1.3.6 Local tolerance	√	❖	❖	❖	❖		❖
1.3.7 Other toxicity studies, if available	❖	❖	❖	❖	❖		❖
2. Nonclinical Tabulated Summaries	√	❖	❖	❖	❖		❖
<u>Section D.</u> **Nonclinical Study Report (As requested)**							
1. Table of Content	√	❖	❖	❖	❖		❖
2. Pharmacology							
2.1 Primary Pharmacodynamics	√						
2.2 Secondary Pharmacodynamics	√						
2.3 Safety Pharmacology	√	❖			❖		
2.4 Pharmacodynamics Drug Interactions	√						

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PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
3. Pharmacokinetics							
3.1 Analytical Methods and Validation Report	√						
3.2 Absorption	√		❖	❖	❖		❖
3.3 Distribution	√		❖	❖	❖		❖
3.4 Metabolism	√		❖	❖	❖		❖
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	√						

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4.4 Carcinogenicity	√						
4.4.1 Long term studies	√						
4.4.2 Short or medium term studies	√						
4.4.3 Other studies	√						
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	√						
4.5.4 Studies in which the offspring are dosed and/or further evaluated	√						
4.6 Local tolerance	√	❖	❖	❖	❖		❖

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PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
4.7 Other toxicity studies, if available	❖	❖	❖	❖	❖		❖
4.7.1 Antigenicity							
4.7.1 Immunotoxicity							
4.7.3 Dependence							
4.7.4 Metabolites							
4.7.5 Impurities							
4.7.6 Other							
Section E. List of Key Literature Reference	√	❖	❖	❖	❖		❖

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3. ข้อกำหนดและเอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาใหม่ (New Drugs) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่ : ข้อมูลด้าน Clinic

ข้อกำหนดในการขึ้นทะเบียนตำรับยาใหม่ (New Drugs) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่

ข้อมูลด้าน Clinic

No.	PARAMETERS	COMPONENTS	REQUIREMENTS*						
			NCE	NI [a]	NCO [a]	ND [a]	NR [a]	NDOS [a]	NS [a]
1	Bioavailability (BA) and Bioequivalence (BE) Studies	BA studies evaluate the rate and extent of absorption of the active substance from the medicinal product. Comparative BA or BE studies may use PK, PD, clinical, or in vitro dissolution endpoints, and may be either single dose or multiple dose.							
	a) BA Studies	1) Studies comparing the rate and extent of absorption of a drug substance from a non-intravenous dosage form compared to intravenous injection (Absolute BA study) or compared to that of non-intravenous clear solution dosage form (Relative BA study)	√		√	√	√		√
		2) Dosage form proportionality studies	√			√	√		√
		3) Food –effect studies	√		√	√	√		√

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❖ If non-linear Pharmacokinetics

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	b) Comparative BA or BE studies	Studies compare the rate and extent of absorption of the drug substance from similar drug products (e.g., tablet to tablet, tablet to capsule etc.) Comparative BA or BE studies may include comparison between :	√		√	√	√		√
		1) The drug product used in clinical studies supporting effectiveness and the to-be-marketed drug product if applicable.	√		√	√	√		√
		2) The drug product used in clinical studies supporting effectiveness and the drug product used in stability batches if applicable.	√		√	√	√		√
		3) Same drug products from different manufacturers if applicable.	(see Quality Part)		√	√	√		√

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			NCE	NI [a]	NCO [a]	ND [a]	NR [a]	NDOS [a]	NS [a]
2	Studies Pertinent to Pharmacokinetics Using Human Biomaterials	To study metabolic pathways relative to drug absorption and elimination and to assess drug-drug interactions with these pathways							
	a) Plasma Protein Binding Studies	Ex vivo protein binding study	√		√	√	√		❖
	b) Hepatic Metabolism and Drug Interaction Studies	Hepatic metabolism and metabolic drug interaction studies with hepatic tissue	√		√	√	√		❖
	c) Studies Using Other Human Biomaterial	Studies with other biomaterials	√		√	√	√		❖
3	Human Pharmacokinetic (PK) Studies)								
	a) Healthy Subject PK and Initial Tolerability Studies	Studies of PK and initial tolerability in healthy subjects	√		√	√	√	√	❖
	b) Patient PK and initial Tolerability Studies	Studies of PK and initial tolerability in patients	√		√	√	√	√	❖

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No.	PARAMETERS	COMPONENTS	REQUIREMENTS*						
			NCE	NI [a]	NCO [a]	ND [a]	NR [a]	NDOS [a]	NS [a]
	c) Intrinsic Factor PK Studies	PK studies to assess intrinsic factors such as age, gender, racial, weight, height, disease, genetic polymorphism, and organ dysfunction	√		√	√	√		❖
	d) Extrinsic Factor PK Studies	PK studies to assess extrinsic factors such as drug-drug interactions, diet, smoking, and alcohol use.	√		√	√	√		❖
	e) Population PK Studies	Population PK studies base on sparse samples obtained in clinical trials including efficacy and safety trials	√		√	√	√		❖
4	Human Pharmacodynamics (PD) Studies								
	a) Healthy Subject PD and PK/PD studies	PD and/or PK/PD studies	√		√	√	√		❖
	b) Patient PD and PK/PD studies	PD and/or PK/PD studies in patients	√	√	√	√	√	√	❖
5	Efficacy and Safety								
	a) Controlled Clinical Studies Pertinent to the Claimed Indication	The controlled clinical studies should be sequenced by type of control:	√	√	√	√	√	√	√

NCE = New Chemical Entity, NI = New Indication , NCO = New Combination, ND = New Delivery System, NR= New Route of administration, NDOS= New Dosage Form of Approved NCE, NS= New Strength of Approved NCE

[a] If the product contains previously registered NCE but not submitted by the same applicant the requirement of NCE must be followed.

❖ If non-linear pharmacokinetics

No.	PARAMETERS	COMPONENTS	REQUIREMENTS*						
			NCE	NI [a]	NCO [a]	ND [a]	NR [a]	NDOS [a]	NS [a]
		- Placebo control (could include other control groups, such as an active comparator or other doses) - No-treatment control - Dose-response (without placebo) - Active control (without placebo) - External (Historical) control, regardless of the control treatment							
	b) Uncontrolled Clinical Studies	Uncontrolled clinical studies (e.g., open label safety studies)	√	√		√	√		√
6	Post Marketing Data (If available)		√	√	√	√	√	√	√
7	References		√	√	√	√	√	√	√

* = All studies should be complied to ICH guideline on Efficacy Topics (currently E1-E12)

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❖ If non-linear pharmacokinetics

เอกสารที่ต้องยื่นในการขึ้นทะเบียนตำรับยาใหม่ (New Drugs) แบบ ASEAN HARMONIZATION จำแนกตามประเภทยาใหม่

ข้อมูลด้าน Clinic

PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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	√	√	√	√	√	√	√
Section C. Clinical Summary 1. 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	√	√	√	√	√	√	√

NCE = New Chemical Entity, NI = New Indication, NCO = New Combination, ND = New Delivery System, NR = New Route of Administration

NDOS = New Dosage Form of Approved New Drug, NS = New Strength of Approved New Drug

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❖ Where applicable, i.e. change of route of administration due to change in formulation

PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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							
3.4 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							
4.2 Adverse Events							
4.3 Clinical Laboratory Evaluations							

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PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
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							
5. Synopses of Individual Studies							
Section D. Tabular Listing of All Clinical Studies	√	√	√	√	√	√	√
Section E. Clinical Study Reports (if applicable)	√		√	√	√		❖
1. Reports of Biopharmaceutic Studies	√		√	√	√		√
1.1 BA Study Report							
1.2 Comparative BA or 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 Report of Studies Using Other Human Biomaterials							

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PARAMETERS	REQUIREMENTS						
	NCE	NI[a]	NCO[a]	ND[a]	NR[a]	NDOS[a]	NS[a]
3. Report 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. Report of Post-Marketing Experience							
7. Case Report Forms and Individual Patient Listing	√	√	√	√	√	√	√
Section F. List of Key Literature References	√	√	√	√	√	√	√

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