
Guidance Notes on Registration of Pharmaceutical Products: Specific requirements for New Drug Applications of Chemical Entities via Primary Evaluation Route

VERSION 1.0

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Pharmacy and Poisons Board of Hong Kong

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1. Preface

1.1 These Guidance Notes outline the requirements for new drug applications (“NDAs”) for initial registration of pharmaceutical products containing chemical entities via the primary evaluation route, in addition to the requirements in the <[Guidance Notes on Registration of Pharmaceutical Products: New Drug Applications](#)>.

1.2 This document serves as a general guide to the applicant regarding NDAs for registration of pharmaceutical products, and shall not be regarded as the complete registration requirements or authoritative statement of the relevant laws or the interpretation on any particular case. This document does not preclude requests by the Pharmacy and Poisons (Registration of Pharmaceutical Products and Substances) Committee (“the Committee”) or the Drug Office of the Department of Health for additional documents during screening or evaluation.

1.3 The Drug Office would consider whether an application for registration of pharmaceutical product is subject to the requirements specified in these Guidance Notes on a case-by-case basis.

2. Categories of NDAs

2.1 NDAs for initial registration of pharmaceutical products are categorised into three categories as shown in **Table 1**.

Table 1. Categories of NDA for initial registration of pharmaceutical products

Category	Scope of initial registration applications
NDA-1 ¹	An initial registration application of a pharmaceutical product containing a new chemical entity(ies)².
NDA-2	An initial registration application of a pharmaceutical product containing registered chemical entity(ies), which need to be supported by non-clinical and/or clinical³ data to demonstrate the efficacy and safety of the product. <ul style="list-style-type: none">● NDA-2A: new salt / ester / ether / isomer / mixture of isomers / complexes / derivatives of registered chemical entity(ies) which potentially impacts its efficacy and/or safety⁴● NDA-2B: new indication / dosage / patient population of registered entity(ies)● NDA-2C: new strength of registered entity(ies)● NDA-2D: new dose form of registered entity(ies)● NDA-2E: new route of administration of registered entity(ies)● NDA-2F: new composition or component of a registered product which potentially impacts efficacy and/or safety of the product (e.g. addition or change in adjuvant system of vaccine, change in composition that potentially affects release characteristics of modified release dose forms)● NDA-2G: new container closure system / presentation of a registered product which potentially impacts the efficacy and / or safety of the product● NDA-2H: new combination of registered entities as active ingredients● NDA-2X: other types of line extension of a registered entity(ies) which potentially impacts its efficacy and/or safety, and need to be supported by non-clinical and/or clinical data

¹ The primary evaluation route only applies to NDA-2 or NDA-3 of chemical entities during the phase 1 of the primary evaluation. Please refer to the phasic implementation of primary evaluation in <[The Hong Kong Centre for Medical Products Regulation - Towards Primary Evaluation](#)>.

² A new chemical entity refers to an active ingredient contained in a pharmaceutical product which has not previously been registered in Hong Kong under some other name or description.

³ For initial registration applications of pharmaceutical products containing registered entity(ies), of which a reference product has been registered in Hong Kong, and does not need to be supported by non-clinical or clinical (except bioequivalence study) data, please refer to the <[Guidance Notes on Registration of Pharmaceutical Products/Substances](#)>.

⁴The different salts, esters, ethers, isomers, mixtures of isomers, complexes or derivatives of an active substance (i.e. contains the same active moiety as the registered entity) shall be considered to be the same active substance, unless they differ significantly in properties with regard to safety and/or efficacy, i.e. evidence that no change in the pharmacokinetics of the active moiety, pharmacodynamics and/or in toxicity which could change the safety/efficacy profile shall be demonstrated. Should this not to be the case, the active substance shall generally be considered as an NDA-1.

Category	Scope of initial registration applications
NDA-3	<p>A subsequent initial registration application of a product registered as NDA-1 and NDA-2⁵, which does not need to be supported by non-clinical or clinical data.</p> <ul style="list-style-type: none"> ● NDA-3A: new composition of excipients which does not impact the efficacy and / or safety of the product (e.g. new colourants) ● NDA-3B: new manufacturer on label ● NDA-3C: new container closure system (e.g. primary packaging and/or functional secondary packaging components) or new presentation (e.g. pack size which is the quantities of the dose form contained in its unit package⁶) ● NDA-3D: new component which does not contain an active ingredient or impact the efficacy and / or safety of the product (e.g. reconstitution diluent) ● NDA-3E: administrative changes for which a new product registration is required (e.g. additional trade name) ● NDA-3X: other types of line extension of a registered product which does not need to be supported by non-clinical or clinical data

2.2 The Drug Office would consider whether an application for initial registration of a pharmaceutical product is subject to the requirements specified on a case-by-case basis.

3. Requirements for CTD Modules 2 to 5

3.1 The requirements for International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (“ICH”) Common Technical Document (“CTD”) Modules 2 to 5⁷ based on the NDA categories are listed in **Table 2** to **Table 5**.⁸ If an NDA involves multiple categories, all concerned modules should be provided. Relevant ICH guidelines should be applied on a case-by-case basis.

⁵ Or products which have been registered as containing new chemical entities or under screening or evaluation for registration before 31 March 2026.

⁶ Regarding non-injectable products which differ only in package sizes, please refer to <[Guidance Notes on Change of Registered Particulars of Registered Pharmaceutical Products/Substances](#)> for the addition of package sizes.

⁷ Raw data (e.g. clinical study data) may be submitted in program files, if requested.

⁸ For a subsequent application of a pharmaceutical product previously registered as containing new chemical entities before 31 March 2026, the NDA should include complete CTD modules 2 to 5.

Table 2. Requirements for CTD module 2: NDA-2⁹

Subcategory		2A	2B	2C	2D	2E	2F	2G	2H	2X
		New salt / ester / ether / isomer / mixture of isomers / complexes / derivatives	New indication / dosage / patient population	New strength	New dose form	New route of administration	New composition / component	New container closure system / presentation	New combination	others
2.1	CTD Table of Contents (Modules 2-5)	Mandatory								
2.2	CTD Introduction									
2.3	Quality Overall Summary									
	2.3.S Drug Substance (DS)	Mandatory	Not required unless there is a change from NDA-1 / NDA-2 or the product is not a line extension of an NDA.	Not required unless there is a change from NDA-1 / NDA-2 or the product is not a line extension of an NDA			Mandatory			May be required
	2.3.P Drug Product (DP)			Mandatory	Mandatory	May be required				
	2.3.A Appendices									
	2.3.R Regional Information ¹⁰	If applicable		If applicable						
2.4	Nonclinical Overview	Mandatory	May be required						Mandatory	
2.5	Clinical Overview ¹¹	Mandatory								
2.6	Nonclinical Written and Tabulated Summaries	Mandatory	May be required							
2.7	Clinical Summary	Mandatory								

⁹ For modules specified as “may be required”, the requirements will be product-specific and will be discussed during the pre-NDA meetings and the screening phase.

¹⁰ If the product is co-packaged with extra measuring cup/spoon, needle, syringe, alcohol swab, vial adapter, etc. in the secondary packaging of the product, modules 2.3.R and 3.2.R should include quality information and usability studies (if applicable).

¹¹ Module 2.5 should include the discussion of product development rationale (e.g. the clinical development programme, including ongoing and planned clinical studies and the basis for the decision to submit the application at this point in the programme), explanation of concordance or lack of concordance with current standard research approaches and regulatory guidance issued by National Medical Products Administration (NMPA) of Chinese Mainland, European Medicines Agency (EMA), and the United States’ Food and Drug Administration (FDA), regulatory guidance and advice received from regulatory authorities with discussion of how that advice was implemented). Formal advice documents (e.g. official meeting minutes, official guidance, letters from regulatory authorities) should be referenced, with copies included in the references section of Module 5.

Table 3. Requirements for CTD modules 3 to 5: NDA-2¹²

CTD module / Sub-category		2A	2B	2C	2D	2E	2F	2G	2H	2X	
		New salt / ester / ether / isomer / mixture of isomers / complexes / derivatives	New indication / dosage / patient population	New strength	New dose form	New route of administration	New composition / component	New container closure system / presentation	New combination	others	
3 Quality											
3.1	Table of Contents of Module 3	Mandatory	Not required unless there is a change from NDA-1 / NDA-2 or the product is not a line extension of an NDA	Mandatory						May be required	
3.2	Body of data										
	3.2.S Drug Substance ¹³	Mandatory	Not required unless there is a change from NDA-1 / NDA-2 or the product is not a line extension of an NDA	Not required unless there is a change from NDA-1 / NDA-2 or the product is not a line extension of an NDA			Mandatory	Mandatory	Mandatory	May be required	
	3.2.P Drug Product			Mandatory	May be required	Mandatory					
	3.2.A Appendices			If applicable							
	3.2.R Regional Information	If applicable	Not required unless there is a change from NDA-1 / NDA-2 or the product is not a line extension of an NDA	If applicable							
	3.3 Literature References	If applicable									
4 Nonclinical Study Reports											
4.1	Table of Contents of Module 4	Mandatory	May be required							May be required	
4.2	Study Reports										
4.3	Literature References	If applicable									
5 Clinical Study Reports											

¹² For modules specified as “may be required”, the requirements will be product-specific and will be discussed during pre-NDA meetings and the screening phase.

¹³ A drug master file (“DMF”) may be submitted in support of an NDA of chemical entities.

CTD module \ Sub-category		2A	2B	2C	2D	2E	2F	2G	2H	2X	
		New salt / ester / ether / isomer / mixture of isomers / complexes / derivatives	New indication / dosage / patient population	New strength	New dose form	New route of administration	New composition / component	New container closure system / presentation	New combination	others	
5.1	Table of Contents of Module 5	Mandatory								May be required	
5.2	Tabular Listing of All Clinical Studies										
5.3	Clinical Study Reports										
	5.3.1 Reports of Biopharmaceutic Studies	Mandatory	May be required	Mandatory						May be required	
	5.3.2 Reports of Studies Pertinent to Pharmacokinetics Using Human Biomaterials	May be required									
	5.3.3 Reports of Human Pharmacokinetic (PK) Studies	May be required			Mandatory	May be required		Mandatory			
	5.3.4 Reports of Human Pharmacodynamic (PD) Studies	May be required									
	5.3.5 Reports of Efficacy and Safety Studies	May be required	Mandatory	May be required	Mandatory	May be required					
	5.3.6 Reports of Post-Marketing Experience	If applicable									
	5.3.7 Case Report Forms and Individual Patient Listings	May be required	Mandatory	May be required	Mandatory	May be required					
	5.4 Literature References	If applicable									

Table 4. Requirements for CTD module 2: NDA-3

subcategory		3A	3B	3C	3D	3E	3X
		New composition of excipients	New manufacturer on label	New container closure system or presentation	New component which does not contain active ingredient	Administrative changes	Others
2.1	CTD Table of Contents (Modules 2-5)	Mandatory				Not required	Mandatory
2.2	CTD Introduction						
2.3	Quality Overall Summary						
	2.3.S Drug Substance (DS)	Not required unless there is a change from NDA-1 / NDA-2 or the product is not a line extension of an NDA				Not required	May be required
	2.3.P Drug Product (DP)	Mandatory					
	2.3.A Appendices	Mandatory					
	2.3.R Regional Information ¹⁴	If applicable					
2.4	Nonclinical Overview	Not required					
2.5	Clinical Overview						
2.6	Nonclinical Written and Tabulated Summaries						
2.7	Clinical Summary						

¹⁴ If the product is co-packaged with extra measuring cup/spoon, needle, syringe, alcohol swab, vial adapter, etc. in the secondary packaging of the product, modules 2.3.R and 3.2.R should include quality information and usability studies (if applicable).

Table 5. Requirements for CTD modules 3 to 5: NDA-3¹⁵

CTD modules \ Sub-category		3A	3B	3C	3D	3E	3X
		New composition of excipients	New manufacturer on label	New container closure system or presentation	New component which does not contain active ingredient	Administrative changes	Others
3 Quality							
3.1	Table of Contents of Module 3	Mandatory				Not required	Mandatory
3.2	Body of data						
	3.2.S Drug Substance ¹⁶	Not required unless there is a change from NDA-1 / NDA-2 or the product is not a line extension of an NDA				Not required	May be required
	3.2.P Drug Product	Mandatory					
	3.2.A Appendices	Mandatory					
	3.2.R Regional Information	If applicable					
	3.3 Literature References	If applicable					
4 Nonclinical Study Reports		Not required					
5 Clinical Study Reports							

¹⁵ Raw data (e.g. clinical study data) may be submitted in program files, if requested.

¹⁶ A drug master file (“DMF”) may be submitted in support of an NDA of chemical entities.

4. Change history

Version	Date	Description of Change
1.0	31 March 2026	New document.