SCREENING CHECKLIST FOR GENERICS

CENTRE OF PRODUCT AND COSMETIC EVALUATION
NATIONAL PHARMACEUTICAL REGULATORY AGENCY (NPRA)

The objective of this document is to provide general and high level guidance to enhance the quality of submission for generics application.

Please note that this screening checklist serves as a supplementary document to Drug Registration Guidance Document (DRGD): Appendix 5: Guideline on Registration of Generics. Please refer to both documents before completing the product registration application via QUEST system. An incomplete application form or dossier is likely to be rejected.

One checklist shall be submitted for each application (per call number). A new checklist shall be submitted for the second application with a new call number.

The checklist shall be completed by checking each item against the dossier prepared for submission. The applicant is required to fill in as much detailed and accurate information as possible. Upon completion, the checklist shall be attached in the QUEST system (in PDF format) under section E14.

Any supporting documents submitted shall be scanned copies of the original documents. Original hard copies of the documents are not required. NPRA reserves the right to request for the original or or certified true copy of submitted document(s) if there is any doubt that a submitted scanned document is not an accurate reflection of the original document(s).

Screening acceptance does not preclude requests by NPRA for additional document(s) or changes to the information/ document(s) during evaluation.

NPRA reserves the right to reject/not to screen incomplete applications (refer to checklist for requirements).

SCREENING CHECKLIST FOR GENERICS APPLICATION

Note:

- Cells with ☐ indicate that the documents are mandatory.
- Cells with ⬚ indicate that the documents may be optional depending on the product.
- If applicable, any text box under the remarks column should be briefly described accordingly in the checklist.
- The application will not be processed if the documents in Annex 1 are not submitted.
- This checklist is not applicable to For Export Only (FEO)/Over the Counter (OTC) products.

REVISION HISTORY

Form Version (Publish Date)

NPRA-SUG-001 (uploaded 31-07-23)

Declaration by Applicant

☐ I_____(I/C number:_____)
on behalf of my company _____
(company no:_____) hereby confirm that the information submitted in this application is true and accurate. I acknowledged that if any of the information provided by me is false or misleading, I shall be guilty of an offence and shall be liable on conviction to penalties under Sales of Drugs Act 1952 Section 12 and Regulation 8 Clause 9 under Control of Drugs and Cosmetic Regulations 1984 respectively. I also understand that any false, misleading or any omission of information required shall render this application invalid.

Call Number :

Submission Version : ☐1/2 ☐2/2

Product Name :

Product Registration Holder :

Applicant name :

Designation :

Email :

Contact Number :

Date of Declaration :_____(1st Submission)

_____ (2nd Submission)

Part I – Administrative Documentation

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
		Submitted?	Remarks	Submitted?	Remarks
General Information (To refer DRGD for more information)	**Application Details** ▪ Product of different strengths are to be submitted as separate product applications. ▪ A separate product application is required for each dosage form. ▪ Product that are made by the same manufacturer to the same specifications, formulation and dosage form but different packaging materials or pack size (quantity/ volume) do not require separate product applications. ▪ Other generics application related to current application. Please specify: Eg. Application with a different strength/dosage form/variation under evaluation/recently approved	☐		☐	
	Reference product ▪ Innovator or latest registered generic product if innovator is not available ▪ All GPA applications – the Malaysia reference product's name and MAL number must be specified. Please specify:	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
		Submitted?	Remarks	Submitted?	Remarks
Product Validation – Product Name	**Product name** ▪ Specify the proposed product name for registration Please specify: ▪ Refer to DRGD for details ▪ The product name should include the following: Product name- Dosage Form – Strength ▪ The strength of the active ingredient (drug substance) should generally be included as part of the product name to allow differentiation between different products containing the same active ingredient. ▪ The pharmaceutical dosage form should be as specific as possible with respect to the product's actual dosage form (e.g. "Film-coated tablet" instead of "Tablet") ▪ Proposed product names comprising of the international non-proprietary name (INN) should include a differentiator (e.g. name of the product owner) to allow better product differentiation from currently registered products. ▪ The product names of generic products should generally do not result in confusion and do not pose any risks for medication errors. ▪ The proposed product names should be different from other registered products to avoid confusion to consumers/ end-users.	☐		☐	
Product Validation Dosage Form	**Dosage form** ▪ The dosage form should be as specific as possible because each form is distinctly identified, e.g. "Tablet, Film-coated, Extended Release" instead of "Tablet" or "Lyophilised powder for injection" or abbreviation FC for film-coated	☐		☐	

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	▪ If the physical form supplied is different from that which is to be administered to/used by the patient, i.e., if transformation of the product is required before it can administered/used, both forms need to be conveyed within the term. (e.g. lyophilized powder for Solution for Infusion etc.)				
Product Validation Active Ingredient; Product Validation Excipients; B2: Attachment of Batch Manufacturing Formula	**Product Formulation** ▪ The full composition of the drug product, i.e. a listing of all active ingredient and excipients (including water) that are present in the final pharmaceutical dosage form should be stated with quantity per unit dosage form ▪ The functions of the excipients should be declared correctly. Any other additional information of the excipients is to be described in the REMARKS column. ▪ The quantities of active ingredients presenting in the form of salts and chelates should be clearly stated, e.g. XX phosphate 32 mg (equivalent to XX). ▪ The full compositions of all proprietary ingredients (e.g. colourants, flavouring agents, etc.) used in the product should be stated in the Product Formula, and their uses differentiated as stated in the following sections. ▪ Any premix API will require to be declared. ▪ For multiple batch sizes, the batch formula for each batch size is to be provided. (To declare maximum batch size in B1.1 for multiple batch size proposed)	☐		☐	

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	Product Formulation (Cont.) ▪ Information on residual amounts of certain materials, such as solvent, antibiotics, thiomersal and materials of biological origin (e.g. human serum albumin), added or present in the product must be declared in the REMARKS column of that particular excipient. ▪ BMF documentation must be signed by authorised personnel ▪ Overage/excess must be declared.	☐		☐	
Product Validation - Other Information Product Validation - Other Information	**Ingredients derived from human blood or animal sources** *Only applicable for products containing ingredient(s) derived from human blood or animal sources. ▪ The information should be provided in the following format: Example: Origin; Function; Manufacturing Process; Final Product ▪ The TSE declaration should be submitted (in E17) if applicable	☐		☐	
	Premix Information (if applicable) ▪ Form of premix to be declared ▪ Manufacturer details (name and address) to be declared ▪ Valid GMP certificate/ GMP compliance evidence ▪ Composition/ formulation of the premix ▪ Manufacturing process of the premix ▪ Specifications of the premix ▪ Certificate of Analysis (CoA) of the premix (minimum two (2) batches)	☐		☐	

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	Medical Device Information ▪ If a medical device (e.g. vial adaptor, syringe and needle) is packed together with the drug product, applicants should include information of the medical device and its description, as appropriate, as a single entry with the drug product. ▪ Applicant should ensure availability of Medical Device Authority (MDA) acknowledgement receipt during screening stage or Endorsement Letter for products with medical device (if applicable). ▪ Endorsement Letter should be available before product approval.	☐		☐	
	Patent Information ▪ Applicants should ensure that there is no infringement of patent/ data protection. A declaration letter such as or carry such meaning should be submitted. ▪ Signature of the Managing Director/ Director/ President/ Chief Executive Officer/ General Manager who has overall responsibility for the PRH. ▪ For template, please refer "https://npra.gov.my/index.php/en/component/content/article/99-english/directive-general/1501-for-the-purpose-of-registration-of-generic-products-prh-shall-provide-patent-declarations-as-below-i- prh-shall-comply-with-all-legal-provisions-in-malaysia-ii-the-government-authority-is-not-liable-for-any-offence-	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
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Part 1 – Section A	**Product Particulars** ▪ Please specify source of information declared (e.g. Malaysia reference product/MAL, EmC, etc.) Please specify: - 1st choice: Malaysia Reference Product - 2nd choice: Latest Generic Product - Others: EMC ▪ Information (other than indication and recommended dosage) declared has to be standardized/ tallied as per reference product if references are made. ▪ Indication and recommended dosage should be exactly the same as per Malaysia reference product.	☐		☐	
	Route of administration ▪ All routes of administration proposed for the product must be included and specific as possible.	☐		☐	
	Pharmacotherapeutic Group (ATC Code) ▪ The WHO ATC code should be provided for each distinct therapeutic indication proposed for a product, if available. ▪ If the WHO ATC code is not available at the time of the application submission, it should be left as blank and provide declaration in section E14.	☐		☐	

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Section C- Particulars of Packing	**Packaging** ▪ The description of the container closure system (CCS) should include the capacity and type of glass used in injectable vials, ampoules or types/layers of blister. ▪ The "Pack Size" refers to the quantity of container closure systems in each commercial pack of the product and quantity/volume for each pack size (e.g. for a commercial box of 50 tablets packed as 5 blister strips of 10 tablets in each strip, the pack size is 5 x 10 Tablets (QUANTITY). ▪ For patient pack size packaging, applicant should ensure compliance with dispensing pack size requirements. ▪ Tender pack size (exceeding maximum dispensing pack) /for export only pack size can be proposed with justification ▪ Section C to only cover the packaging type (material type including closure) (Example: 10 units of 10ml amber glass vial with rubber stopper and aluminium seal in an outer carton with package insert). ▪ Measurement; colour; technical specifications etc. for container closure system is sufficient to be provided/mentioned in P7 only.	☐		☐	
Section D - Label (Mock-up) For Immediate Container, Outer Carton, Proposed Package Insert & PIL/RiMUP	**General** ▪ The product name stated on the labels should be the same as that in QUEST. ▪ Please refer DRGD for details. ▪ Labelling can be either in Bahasa Malaysia or English. Any non-English* country-specific labelling requirements on the artwork/drafts and/or if the artwork/drafts is shared with other countries should be highlighted.	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
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	*If non-English text is included in the labelling, applicants must provide an official statement to declare that the non-English text is complete, accurate and unbiased information and is consistent with the English text.				
Section D1- Label (mock-up for immediate container)	**Inner/Blister Labels** ▪ The draft/artwork of the inner/blister labels should be in the actual format, design and colour that are to be printed. All products are required to have the same label artwork for all pack sizes but may have minor differences in colour code to differentiate pack sizes ▪ For blister label, the location/placement of the tablets should be included in artwork. ▪ The full product name must be repeatedly appeared on the blister. ▪ The product name stated on the labels should be the same as that in QUEST.	☐		☐	
Section D2- Label (mock-up for immediate container)	**Outer carton labels** ▪ The draft artwork of the outer carton labels should be in the actual format, design and colour that are to be printed. All products are required to have the same label artwork for all pack sizes but may have minor differences in colour code to differentiate pack sizes. ▪ Acceptable to provide one mock-up label provided there is such statement “Applicable for all pack sizes” or any other words to that effect. ▪ Artwork for different strengths should be differentiated ▪ The product name stated on the labels should be the same as that in QUEST.	☐		☐	
Section D3- Proposed Package Insert	**Package Insert (PI)** ▪ A PI is required for all scheduled poisons: o Multiple PI/PILs per product application should be avoided unless necessary with justification o If there are different strengths or dosage forms, applicants are encouraged to submit one common PI/PIL for all strengths or dosage form	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
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	○ If separate PI/PILs are to be registered for different strengths or dosage forms, the content should be consistent across the PI/PILs, except for strength/ dosage form-specific information. ○ Font size for PIs should be readable (e.g. minimum size 7). ○ Please specify the reference of information declared (e.g. preferably Malaysia registered product) under Remarks column. Please upload the reference in E14.				
Section D4- Patient Information Leaflet (PIL) / Risalah Maklumat Ubat Pesakit (RiMUP)	**Patient Information Leaflet (PIL)/ RiMUP** ▪ Both Malay and English version should be available. It should be written in a language easily understood by consumers/ end-users. ▪ Format should be as per Garispanduan Pelaksanaan Risalah Maklumat Ubat untuk Pengguna (RiMUP). ▪ Please refer DRGD for details. ▪ Please specify the reference of information declared (e.g. preferably Malaysia registered product) under Remarks column. Please upload the reference in E14.	☐		☐	
Section D5 – Label (mock up) for diluent	**Diluent labels** ▪ The draft artwork of the outer carton labels should be in the actual format, design and colour that are to be printed. All products are required to have the same label artwork for all pack sizes but may have minor differences in colour code to differentiate pack sizes. ▪ Acceptable to provide one mock-up label provided there is such statement “Applicable for all pack sizes” or any other words to that effect. ▪ The product name stated on the labels should be the same as that in QUEST.	☐		☐	

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Section E1.1 – Product Owner; Section E1.2 – Letter of authorization from Product Owner	**Product Owner Information** Input the full name and address of the legally registered owner of the product formulation, i.e. the drug product.	☐		☐	
	Authorisation Letters ▪ All scanned copies of the authorisation letters shall be on the authorising company's (i.e. Product Owner's) letterhead, dated and signed by the designated authorised person in the company. ▪ The company names and addresses, and product name stated in the letters should be consistent with the information provided in the QUEST application form and dossier.	☐		☐	
	Letter of Authorisation from Product Owner ▪ This letter authorises the local applicant company to apply for and be the Product Registration Holder (PRH) for a specific product and be responsible for all matters pertaining to the registration of this product in Malaysia. ▪ To ensure letter of authorisation/appointment comprising Product Owner, Product Registration Holder and manufacturing site company name and address (where applicable) and the proposed product.	☐		☐	
Section E2 – Letter of Appointment/ Acceptance of Contract Manufacturer/ Repacker	**Letter of Appointment/Acceptance of Contract Manufacturer/ Repacker** ▪ A letter of appointment/acceptance of manufacturer/ repacker respectively to produce, pack and/or label the drug product intended for Malaysia market should be available.	⬚		⬚	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
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Section E3 – Certificate of Pharmaceutical Product (CPP)	**Certificate of Pharmaceutical Product (CPP)** From : ☐Country of Origin ☐Reference Agency ☐ Others: _____ ▪ CPP from the competent authority in the country of origin; OR in the event a CPP is not available from the country of manufacture, e.g. where a product is not licensed for sale in said country because its manufacturer is manufacturing under contract only for product owner from another country, the following alternatives may be considered: GMP certification/ Manufacturing License for the manufacturer from the relevant competent authority, TOGETHER with CPP from the country of the product owner; or CPP from country of release, if CPP from the country of product owner is not available. ▪ CPP shall be in the format of the WHO Certification Scheme on the Quality of Pharmaceutical Products Moving in International Commerce. ▪ CPP which is issued by EMA for products registered through the centralised procedure in EU will be accepted. ▪ CPPs that indicate that the product is not licensed in the exporting country (including the scenario where the product is licensed "solely for export only") are not acceptable. ▪ CPP should be a scanned copy of either the original document in English. ▪ If the brand name (trade name) of the product registered in the country which issued the proof of approval is different from that proposed in Malaysia, a declaration letter from the product owner should be submitted, declaring that both products marketed under the different brand names are identical in all aspects of quality, safety and efficacy except for the brand name	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
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	▪ The following are **not** acceptable to replace CPP: o WHO Prequalified Products Listing o Free Sale Certificates o Statements of Licensing Status of Pharmaceutical Product ▪ EU Decentralised/MRP procedure outcome letters/documents ▪ The CPP must be **valid at the time of submission** to NPRA.				
Section E5 – Certificate of Good Manufacturing Practice (GMP)	**Certificate of Good Manufacturing Practice (GMP)** ▪ A scanned copy of the original or certified true copy of GMP certification or an equivalent document issued by any PIC/S participating authority (as listed in PIC/S website) or others as stipulated under Directive No.4 2018 issued by the Senior Director of Pharmaceutical Services. ▪ The names and addresses of manufacturer(s)/repacker(s)/ batch releaser(s) should be consistent with the information provided in the proof of GMP compliance submitted, QUEST application form and CTD sections P and S. ▪ Diluents used for reconstituting the therapeutic product which are packaged together with the therapeutic product will be considered as part of the final therapeutic product. Manufacturer(s) of the supplied diluent(s) will follow the same requirements applicable to the therapeutic product, e.g. proof of GMP compliance. ▪ The submitted Proof of GMP compliance must be **valid at the time of submission** to NPRA.	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
		Submitted?	Remarks	Submitted?	Remarks
	Certificate of Good Manufacturing Practice (GMP) (Cont.) ▪ Examples of Acceptable Proof of GMP Compliance (other than GMP Certificate): o EU: – Screenshots of EUDRA GMP Database website – Certificate printed from EUDRA GMP website which includes the EUDRA GMP watermark o US/FDA: – EIR report **(Complete set)** – Covering letter (stating the status of the audit) – If confidentiality is an issue, the product owner/ manufacturer may provide directly to the officer in charge (screener's email) o Health Canada: – Drug Establishment Licences (DEL) **AND** – Inspection Exit Notice *If confidentiality is an issue, the product owner/ manufacturer may provide directly to the officer in charge (screener's email) ▪ Certain accreditation documents/certificates issued by other drug regulatory agencies (for example, Japan/PMDA Accreditation Certificate of Foreign Drug Manufacturer), the US/FDA Establishment Licence and the Canada/Health Canada Establishment Licence are **NOT** acceptable proof of GMP compliance.	☐		☐	
Section E6 – Manufacturer	**Manufacturer's Particular** ▪ Particulars (name and address) should be declare the same as per GMP certificate. ▪ For local finished product manufacturer, please ensure applying dosage form is covered under current manufacturing license. ▪ All manufacturers' names and addresses should be consistent throughout all of the documents submitted in the application, such as GMP certificates, CPPs, Letters of authorisation and Part II of the CTD.	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
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Section E7 – Other Manufacturer(s) involved	▪ For local finished product manufacturer, please ensure applying dosage form is covered under current manufacturing license. ▪ To declare manufacturing activities conducted by other manufacturers (if applicable) ▪ For products packed and sold together with the diluent that is used to reconstitute the product, please declare the manufacturer of the diluent in section E7 (Other manufacturer) (if applicable) ▪ If there is an update/ changes to existing address/ incomplete address, please provide declaration from product owner/ manufacturer. ▪ If there are multiple companies responsible for batch release, the applicant must declare all of the sites. ▪ The manufacturer(s) which performed the batch release must be specified (if applicable). ▪ For mock-up label artwork (section D), the manufacturer's particular of the bulk or finished good manufacturer has to be the same as declared in this section. ▪ Particulars are to be provided for manufacturing sites for all drug product, drug product intermediate and diluent used to reconstitute drug product (if packed and sold together with drug product).	☐		☐	
Section E14 – Other Supporting Documents	**Supporting Attachments** ▪ All documents relating to Part 1 of the CTD must be attached. ▪ Relevant finished product monograph to be attached along. ▪ Any other supporting documents related to the CTD to be attached.	☐		☐	

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Section E15 - Worldwide Registration Status	**Registration status in other countries** ▪ To refer template in NPRA website (8 DCA Reference countries are mandated to be declared) (if applicable). The template can be download at: https://www.npra.gov.my/index.php/en/component/content/article/436-english/announcement-main/announcement-2023/1527472-declaration-of-worldwide-registration-status-for-generic-medicines-in-quest-system.html?Itemid=1391 ▪ Declare country of origin registration status.	☐		☐	
	SmPC/PI/PIL approved by DCA reference regulatory agencies/SRA ▪ The approved SmPC/PI/PIL currently approved by each of DCA reference agencies/ SRA should be submitted, where applicable. ▪ SmPC/PI/PIL to be attached under section E14. ▪ The submitted SmPC, PI and/or PIL should state the country that the document originated from. Please specify:	☐		☐	
	SmPC/PI/PIL approved by country of origin/ country of manufacture ▪ The approved SmPC/PI/PIL currently approved by country of origin/country of manufacture should be submitted, where applicable. ▪ SmPC/PI/PIL to be attached under section E14.	☐		☐	
	SmPC/PI/PIL approved by other regulatory agency ▪ The approved SmPC/ PI/ PIL from the drug regulatory agency that issued the proof of approval, should be submitted if it is not from the country of origin.	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
		Submitted?	Remarks	Submitted?	Remarks
	▪ The submitted SmPC, PI and/or PIL should state the country that the document originated from. ▪ SmPC/PI/PIL to be attached under section E14.				

Part II – Quality

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
		Submitted?	Remarks	Submitted?	Remarks
IMPORTANT NOTES FOR PART II If the product is registered in any of DCA Reference Agencies, the submission should be the same as submitted to the chosen reference agency and any documentation submitted in subsequent variations to the quality aspects of the product (where applicable).					
1.	Quality Overall Summary	☐		☐	
2.	Table of Contents	☐		☐	
3	Body of Data	☐		☐	
Drug Substance/Active Pharmaceutical Ingredient (API) Refer to the following documents before completing product registration application (Part II Section S) via Quest System: i) DRGD Appendix 11: Regulatory Control of Active Pharmaceutical Ingredients (APIs) ii) Guidance Notes Active Pharmaceutical Ingredients (APIs) Information (Part II S) for Product Registration Application via QUEST System.					
Section P1 – Description and Composition	**Description and Composition of the Drug Product** ▪ Description of the dosage form; ▪ Composition, i.e., list of all components [including proprietary mixes (e.g. flavours, printing inks)] of the dosage form, and their amount on a per unit basis (including overages, if any) the function of the components, and a reference to their quality standards (e.g., compendial monographs or manufacturer's specifications). ▪ Description of accompanying reconstitution diluent(s); and ▪ Type of container and closure used for the dosage form and accompanying reconstitution diluent, if applicable.	☐		☐	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
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Section P2 – Pharmaceutical Development	**Pharmaceutical Development** ▪ Refer to ICH Q8 Pharmaceutical Development					
	P2.1	**Information on Development Studies**	☐		☐	
	P2.2	**Components of the Drug Product**				
	P2.2.1	**Active Ingredients** ▪ 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.	☐		☐	
	P2.2.2	**Excipients** ▪ The choice of excipients listed, their concentration and characteristics that can influence the drug product performance should be discussed and submitted. ▪ The use of antioxidant(s) and/or preservative(s), and their concentration(s) should be explained and fully justified, if applicable.	☐		☐	
	P2.3	**Finished Product**				
	P2.3.1	**Formulation Development** ▪ A brief summary describing the development of the drug product should be provided, taking into consideration the proposed route of administration and usage. The differences between clinical formulations and the formulation (i.e. composition) described in P.1 should be discussed. Results from comparative in vitro studies (e.g., dissolution) or comparative in vivo studies (e.g., bioequivalence) should be discussed when appropriate	☐		☐	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
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	P2.3.2	**Overages** ▪ The use of overages should be explained and fully justified, if applicable. ▪ The inclusion of an overage to extend the shelf-life of the drug product (stability overages where release assay is >100.0%) is generally not acceptable and discouraged.	☐		☐	
	P2.3.3	**Physiochemical and Biological Properties** ▪ Parameters relevant to the performance of the drug product, such as pH, ionic strength, dissolution, redispersion, reconstitution, particle size distribution, aggregation, polymorphism, rheological properties, biological activity or potency, and/or immunological activity, should be addressed.	☐		☐	
	P2.4	**Manufacturing Process Development** ▪ The method of manufacture of the finished product should be briefly described. ▪ Comment on any significant differences between the manufacture of batches used in pivotal clinical studies (safety, efficacy, bioavailability, bioequivalence) or primary stability studies and the manufacturing process intended for commercial production of the product. ▪ The suitability of the manufacturing equipment for the proposed products should be discussed. ▪ The method of sterilisation and its validity.	⬚		⬚	

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	P2.5	**Container Closure System**				
		▪ The container closure system (CCS) should be briefly described (reference to P7 Container Closure System)	☐		☐	
		▪ The suitability of the CCS for the storage, transportation and use of the drug product should be discussed.	☐		☐	
		▪ For liquid preparations, the suitability of Container Closure System should be demonstrated (e.g. extractable and leachable studies).	☐		☐	
		▪ If applicable, performance studies for dosing devices (e.g. pen injection device, dropper pipette, dry powder inhaler) appropriate for their intended purpose (e.g. accuracy and precision under normal conditions of use for the lowest intended dose)	⬚		⬚	
		▪ Uniformity of dose data for any associated integrated devices (e.g. pMDIs, multiuse and etc.)	⬚		⬚	
		▪ The influence of the drug product manufacturing process on the container closure system where applicable (e.g. sterilisation conditions). Compliance with appropriate guidelines should be stated.	⬚		⬚	
	P2.6	**Microbiological Attributes** ▪ Where appropriate, the microbiological attributes of the dosage form should be discussed, including the selection and effectiveness of preservative systems in products containing antimicrobial preservatives. For sterile products, the integrity of the container closure system to prevent microbial contamination should be addressed.	☐		☐	
	P2.7	**Compatibility** This is applicable for drug products which have reconstitution diluents or dosage device (e.g. infusion bags, tubings)	⬚		⬚	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
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Section P3 - Manufacturer	**Manufacturer**					
	P3.1	**Batch Formula** ▪ To refer more info under section 'B2: Attachment of Batch Manufacturing Formula'.	☐		☐	
	P3.2	**Description of Manufacturing Process and Process Controls**				
		▪ A narrative description of the manufacturing process, including packaging, that represents the sequence of steps undertaken and the scale of production should also be provided. Equipment should, at least, be identified by type (e.g., tumble blender, in-line homogeniser) ▪ Steps in the process should have the critical process parameters identified, e.g. mixing time, temperature, pH etc… ▪ Common blend, if applicable, should be described in detail and must be tally with the Batch Manufacturing Formula (B1.2).	☐		☐	
		▪ For sterile products, the description includes preparation and sterilization of components as well (i.e. containers, closure etc.)	☐		☐	
		▪ Any proposed holding time(s) should be stated for each process and accompanied by relevant supportive data; to be provided in P3.4.	⬚		⬚	
	P3.2.1	**Manufacturing Process Flowchart** ▪ A flow diagram of the manufacturing process (including packaging) should be presented giving the steps of the process and showing where materials enter the process. The critical steps and points at which process controls, intermediate tests or final product controls are conducted should be identified.	☐		☐	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
			Submitted?	Remarks	Submitted?	Remarks
	P3.3	**Controls of Critical Steps and Intermediates** ▪ Summary of the routine in-process controls should be listed (i.e., tests performed, stages at which test is done, frequency of sampling & number of sample taken each time, acceptance criteria, etc.). A tabular format is preferable.	☐		☐	
	P3.4	**Process Validation and/or Evaluation** ▪ Refer to ASEAN Guidelines on Submission of Manufacturing Process Validation Data for Drug Registration for regulatory submission requirements. (https://www.npra.gov.my/index.php/en/asean-guidance-documents.html) ▪ Refer to the latest NPRA circular/ directives related to the process validation requirements for submission ▪ NPRA reserves to right to ask for more information				
	▪ ☐ Option 1 ☐ Option 2 ☐ Option 3 ▪ Option 1: Submission of three consecutively manufactured validation batches ▪ Option 2: Submission of development pharmaceutics report and validation data from one pilot batch with validation scheme on production scale batches. ▪ In addition, the applicant is required to fulfil the following standard commitments: a) To undertake that 3 consecutive full production batches are successfully validated before the product is marketed, subject to concurrence by NPRA; b) To submit the report within a specified time frame, or to make the information from these studies available for verification post authorisation by NPRA. NOTE: This option is not recommended for biological/ biotechnological product(s), product(s) manufactured using non-standard manufacturing process and other specialised product(s). Refer to ASEAN Guidelines on		☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
		Submitted?	Remarks	Submitted?	Remarks
	Submission of Manufacturing Process Validation Data for Drug Registration for details. ▪ Option 3: For products that have been approved by a reference agency, the applicant is required to provide a declaration statement to the effect that the same pre-approval dossiers pertaining to 3 process validation that have been submitted to the reference regulatory agency are submitted to NPRA for evaluation. ▪ Under certain circumstances where validation documents may not form part of the preapproval dossiers, NPRA may request for Validation Report or Validation Scheme. ▪ In addition, the applicant is required to undertake that 3 consecutive full production batches are successfully validated before the product is marketed and to submit the report to NPRA upon request. ▪ The manufacturing site/line at which the validation is carried out should be stated and be the same as that proposed for Malaysia. ▪ The relevant validation data on sterilization and aseptic operations for sterile drug products should be submitted: o <u>For terminal sterilized products</u> a) PQ study of terminal sterilizer b) PQ study of the tunnel or sterilizer for primary packaging c) Container closure system integrity data, including a short description of method and summary of test results, demonstrating the integrity of microbiological barrier of the container-closure system.				

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
			Submitted?	Remarks	Submitted?	Remarks
	○ <u>For aseptically filled products</u> a) Media fill report b) Filtration validation data (compatibility and bacterial retentive filters integrity testing data) c) PQ study of the tunnel or sterilizer for primary packaging d) Container closure system integrity data, including a short description of method and summary of test results, demonstrating the integrity of microbiological barrier of the container-closure system). ▪ The product formula of the validation batches should be the same as that proposed for Malaysia. ▪ Information such as the batch number, date of production, batch size (must be the same/cover the proposed batch size(s) in section B2) and batch type (e.g. pilot batch, production batch, etc.) should be stated. ▪ The bracketing/matrixing approach should be stated and fully justified. ▪ If the product contains API Premix, it is mandatory to submit the Process Validation of API Premix (Refer to ASEAN Guidelines on Process Validation - Question and Answers).					
Section P4 – Control of Excipients	P4	**Control of Excipients**				
	P4.1.	**Specifications of each excipients** ▪ List of excipients, grades and standards (pharmacopoeia or 'in-house')	☐		☐	
	P4.2/ P4.3	**Analytical Procedures** ▪ Compendial requirements or equivalent information from the manufacturer.	⬚		⬚	
	P4.4	**Justification of Specifications (e.g. CoA)** ▪ This is required for in-house (IH) specifications. ▪ This is optional if the specifications are set according to BP/Ph. Eur/ USP/ JP.	⬚		⬚	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
			Submitted?	Remarks	Submitted?	Remarks
	P4.5	**Excipients of Human or Animal Origin** ▪ To declare and provide proof or origin	☐		☐	
	P4.6	**Novel Excipients** ▪ The information provided should be as per the full drug substance section (if applicable)	☐		☐	
Section P5 – Control of Finished Product	P5	**Control of Drug Product (Finished Product)**				
	P5.1	**Specifications of Drug Product** ▪ The specification document number, version number and/or effective date should be stated. ▪ To provide reference for each specification (acceptance criteria) ▪ The release and stability indicating parameters should be clearly defined or differentiated.	☐		☐	
	P5.2	**Analytical Procedures** ▪ Complete analytical procedure must be submitted which described all the test method as specified under finished product specification (P5.1). ▪ The analytical procedure(s) must be written in English or Bahasa Malaysia only. ▪ The analytical procedure(s) must be submitted in a format or standard test procedure and mainly shall contain information of name of product and name of manufacturer/ laboratory site. ▪ Statement method as “per pharmacopoeia” is not acceptable. Submission of a copy from general or specific pharmacopoeia for the analytical procedure(s) are also not acceptable.	☐		☐	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
			Submitted?	Remarks	Submitted?	Remarks
		▪ All tests and specifications listed in BP and/or USP in general monographs and specific monographs must be the minimum requirement to be submitted or otherwise must be justified. ▪ Full document (analytical procedure(s) must be uploaded under section E12. Under section P5.2, statement "Refer to Section E12" is sufficient.				
	P5.3	**Validation of Analytical Procedures** ▪ Method validation report must be submitted with validation testing procedure, complete tabulated validation result and summary result for each test parameter involved. ▪ Test parameter(s) to be submitted for full method validation (for in-house or non-compendial method): e.g. specificity, linearity, accuracy, precision (including intermediate precision or ruggedness), quantitation limit or detection limit (applicable for limit test and impurity test only). ▪ Test parameter(s) to be submitted for partial method validation (for compendial method): e.g. specificity, precision, quantitation limit or detection limit (applicable for limit test and impurity test only). ▪ Test for validation must cover for assay (including preservatives if applicable), dissolution, drug release, impurity(ies)/ related substances (including residual solvent if applicable), microbial contamination test (MCT), bacterial endotoxin test (BET) and sterility test subject to dosage form submitted, identification test is optional. ▪ For product not registered under reference country(ies), a representative chromatogram or spectrum is sufficient (e.g. chromatogram for reference solution, test solution, blank/placebo, system suitability test) which is specific to analytical method applied. ▪ Full document must be uploaded under section E13. Under section P5.3, statement "Refer to Section E13" is sufficient.	☐		☐	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
			Submitted?	Remarks	Submitted?	Remarks
		▪ The format must be uploaded as one document for each test validation. Please refer to reference published in NPRA official website Guidance for Generic Medicine – Guide on Uploading the Documents in QUEST 3+ System Section E12 & E13. ▪ The guide and checklist can be download at: https://www.npra.gov.my/index.php/en/guideline-for-prescription-medicine.html ▪ Note: The generic product registration application will be REJECTED during screening stage if the files uploaded in QUEST system under section E12/E13 (P5.2/P5.3) are not uploaded/labelled according to this guide.				
	P5.4	**Batch Analysis** ▪ Batch analysis data from a minimum of 2 batches (pilot/preferably production scale) should be submitted in tabular form. (Most recent production batches. If expired batches, please provide declaration.) ▪ The batch analysis shall be reported with actual result (numerical – where applicable) rather than reporting as "All tests meet specifications". This should include ranges of analytical results and any trends that were observed. A discussion and justification should be provided for any incomplete analysis (e.g. batches not tested according to the proposed specification) or Out of Specification. *Batch size is referring to Finished Product and not bulk batch.	☐		☐	
	P5.4.1	**Certificate of Analysis (COA)** ▪ COA of minimum 2 batches (pilot/ preferably production scale) should be submitted.	☐		☐	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
			Submitted?	Remarks	Submitted?	Remarks
		▪ For COA that is expired, declaration letter to be provided with content of "Specification of finished product and test methods for those CoA's submitted and future batches for Malaysian market remains unchanged and that changes (if any) will be informed and latest CoA will be furnished" or any similar word to the effect. ▪ CoA that is expired for more than 5 years from date of expiry on date of registration submission will be rejected. ▪ CoA provided shall represent the proposed formula, batch size, primary packaging material, and API source with declaration letter (where needed)				
	P5.5	**Characterisation of Impurities** ▪ All potential degradation products should be discussed (chemical structure, source etc). ▪ Potential degradation products may include impurities identified in drug substance and degradation products resulting from interaction of the drug substance with excipients or container-closure system. ▪ Related substances controlled in relevant pharmacopoeia dosage form monographs should be included or their absence should be justified.	☐		☐	
	P5.6	**Justification of Specifications** ▪ Summarise the justification of specifications for relevant tests and comment on the suitability, adequacy and acceptability of the tests and the proposed acceptance criteria. ▪ This is optional if the specifications are set according to BP/Ph.Eur/Ph.Int/USP/JP. A copy of the compendial monograph (as claimed) should be submitted	☐		☐	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
			Submitted?	Remarks	Submitted?	Remarks
		▪ To ensure specification (for the dosage form) established is complying to ASEAN/ICH guideline, and to justify for any exclusion.				
Section P6 – Reference Standards of Materials	P6	**Reference Standards of Materials**				
		▪ The source of the reference standard (in house or official with reference to compendial standard) used for the testing of the drug product should be stated. ▪ For in house reference standards, the specifications of the reference standard should be submitted. ▪ Evidence of characterisation for in-house / working standards (e.g. tests of NMR, MS are documented in the CoA will suffice) should be submitted.	☐		☐	
Section P7 – Container Closure System	P7	**Container Closure System**				
		▪ A description of the container closure systems should be provided, including the identity of materials of construction of each primary packaging component and its specification. The specifications should include description and identification (and critical dimensions, with drawings where appropriate). ▪ State the description, including the identity of materials of construction, and specification of secondary container closure system. ▪ Non-compendial methods (with validation) should be included where appropriate. ▪ For non-functional secondary packaging components (e.g., those that neither provide additional protection nor serve to deliver the product), only a brief description should be provided. For functional secondary packaging components, additional information should be provided.	☐		☐	

Section	Documents		Applicant Initial Submission		Applicant Screening Reply	
			Submitted?	Remarks	Submitted?	Remarks
		▪ If there are any associated components (e.g. drug delivery device) to be packaged in the market package of drug product, then their description and specification should also be captured. ▪ State if the specifications for the container closure system are acceptable which should include but not limited to description, identification, critical dimension physical and chemical properties etc. ▪ To ensure P7 information is tally with Section C.				
Section P8 – Stability Data	**Stability Data**					
	Stability Summary and Conclusion ▪ The conclusion of the stability studies, photostability study (if applicable), storage condition and proposed shelf life period should be stated in the summary. ▪ Information such as the batch size (pilot/ preferably production scale, date of manufacture, site of manufacture, container closure system, and API source used for each drug product stability batch should be stated. ▪ The stability batches should be manufactured by the same process and packaged in the same container closure system as that proposed for Malaysia. ▪ Stability batch that is expired for more than 5 years from expiry date on date of registration submission will be rejected, justification/declaration to be provided if such data not available (annual programme). ▪ Stability provided shall be reflecting the proposed formula, batch size, primary packaging material, and API source with declaration letter (where needed). ▪ The bracketing/ matrixing approach should be stated and fully justified.		☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
		Submitted?	Remarks	Submitted?	Remarks
	Post-approval Stability Protocol and Stability Commitment ▪ This should be submitted and based on the proposed storage condition. If any results fall outside of the retest / shelf-life specifications, these should be reported together with the proposed action.	☐		☐	
	Stability Data ▪ At least two batches (long term and accelerated storage conditions) should be submitted. ▪ Zone IVb long term storage condition stability data should be submitted unless fully justified with supporting data (such as Out-of-Specification data under Zone IVb storage condition and investigation reports, to demonstrate an unstable drug product stability profile). ▪ A '30^{O}C ± 2^{O}C/RH not specified' long term storage condition is permissible for products in primary containers impermeable to water vapour. ▪ A '30^{O}C ± 2^{O}C/35% RH ± 5% RH' long term storage condition is permissible for aqueous-based products packed in semi- permeable containers. Potential water loss should be evaluated in addition to physical, chemical, biological and microbiological stability. ▪ Two set of stability data (both long term and accelerated storage conditions) should be submitted for each strength, pack size and/or container closure system, unless otherwise justified. The use of reduced designs should also be fully justified. ▪ Two batches of the stability study should be provided in all orientations. If all orientations are not available, AT LEAST two batches under inverted/ on-the-side orientation (worst case) AND only one batch of upright (vertical) position should be provided. *Applicable for small volume parenteral (injections, powder for injection, suspension for injection and emulsion for injection), MDI, nasal aerosol products	☐		☐	

Section	Documents	Applicant Initial Submission		Applicant Screening Reply	
		Submitted?	Remarks	Submitted?	Remarks
Section P8 – Stability Data	**In-Use Study** ▪ For in-use stability studies, refer to ASEAN Guideline on Stability Study of Drug Product for regulatory submission requirements. ▪ Information such as the batch number, batch size, in-use storage condition(s), length of storage prior to start of in-use stability testing and completed in-use test intervals should be stated. ▪ A minimum of two batches, at least pilot scale batch, should be subjected to the test, at least one of these batches should be chosen towards the end of the shelf life. If such results are not available, one batch should be tested at the final point of the submitted stability studies. In-use information declared for the product should be backed up by in-use stability data.	☐		☐	
Section P9 - Product Interchangeability/Equivalence Evidence	**Product Interchangeability (Bioequivalence Study Reports)** ▪ Refer to DRGD/Guide on How to Upload the BE Study Report and Other Relevant Documents in Quest System under Section P9 (effective 1st March 2022)/Centre of Product and Cosmetic Evaluation Bioequivalence Study Report Submission Checklist (Effective: 18th April 2022) The guide and checklist can be download at: https://www.npra.gov.my/index.php/en/application-forms-and-checklist.html ▪ Complete checklist should be filled and attached to QUEST system. Note: The generic product registration application will be REJECTED during screening stage if the files uploaded in QUEST system under section P9 cannot be traced or not corresponding to the BE checklist.	☐		☐	

Annex 1

API

1. **Good Manufacturing Process (GMP) Compliance evidence (Only for DMF & ACTD option)**
   - Valid GMP certificate/ GMP compliance evidence of the Active Pharmaceutical Ingredient (API) manufacturing site.

2. **Certificates of Suitability (CEP) (Only for CEP option)**
   - Valid CEP of the API (as per EDQM certification database).

3. **Drug Master File (DMF) (Only for DMF option)**
   - A complete DMF* of the API (with applicant's and restricted parts) with a Letter of Access (LoA) from the DMF holder (submitted directly to NPRA).
     *with the same DMF version number (for both applicant's and restricted parts) as those stated in the LoA attached in the QUEST system

4. **Letter of Access (LoA) (Only for DMF option)**
   - Letter of Access (LoA) with: -

   (i) DMF version number (for both applicant's and restricted parts);
   (ii) name and address of the API manufacturing site;
   (iii) name of the finished product & Product Registration Holder (PRH);
   (iv) name and email address of person(s) to be contacted for additional information

5. Part II S Form
- Part II S form with the correct API name in the QUEST system.
- Part II S form with the correct submission option (ACTD/DMF/CEP) in the QUEST system.
- Part II S form with the correct API manufacturing site in the QUEST system.
- Part II S form with attachments of the original API dossier from the DMF holder/CEP holder/API manufacturer in the QUEST system.

6. Certificate of Analysis (CoA) of API
- CoA of API from the API Manufacturer for API manufactured at the same API manufacturing site as declared in Part II S of the QUEST System.
- CoA of API from the Finished Pharmaceutical Product (FPP) Manufacturer for API manufactured at the same API manufacturing site as declared in Part II S of the QUEST System.

7. Stability study data
- At least twelve (12) months of long-term data and six (6) months of accelerated data on at least three (3) primary batches of the API manufactured at the same API manufacturing site as declared in Part II S of the QUEST System.

Lab

1. **Analytical procedure:**
   - Protocol of analysis for assay testing for major active ingredients and preservatives (if applicable)
   - Protocol of analysis for dissolution testing (applicable for tablet & capsule dosage form including immediate release, delay release and extended release dosage form)
   - Protocol of analysis for drug release (applicable for transdermal drug delivery system eg. topical patches)
   - Protocol of analysis for related substances or impurity testing (including residual solvents if applicable)
   - Protocol of analysis for microbial contamination test (for all non-sterile preparation)
   - Protocol of analysis for sterility testing (for sterile dosage forms)
   - Protocol of analysis for BET testing (for injectable products)
   - Documents in PDF searchable format (OCR)

2. **Method validation (including complete analytical procedure and validation result):**
   - Method validation for assay testing for major active ingredients and preservatives (if applicable)
   - Method validation for related substances or impurity testing (including residual solvents if applicable)
   - Method validation for dissolution testing (applicable for tablet & capsule dosage form including immediate release, delay release and extended release dosage form)
   - Method validation for drug release (applicable for transdermal drug delivery system eg. topical patches)
   - Method validation for microbial contamination test (for all non-sterile preparations)
   - Method validation for sterility testing (for sterile dosage forms)
   - Method validation for BET testing (for injectable products)
   - Documents in PDF searchable format (OCR)

Product

1. **Attachment of Batch Manufacturing Formula (BMF)**
   - The proposed batch size of commercial scale should be stated in the BMF together with its calculation.

2. **Certificate of Pharmaceutical Product (CPP)**
   - Valid Certificate of Pharmaceutical Product (CPP) issued by the national certifying/issuing authority in the country or within the jurisdiction of the regional certifying authority and valid upon screening submission.

3. **Certificate of Good Manufacturing Practice (GMP)**
   - Valid GMP compliance evidence (eg. GMP certificate issued by PIC/S members or EEA).

4. **Process Validation (PV) and/or Evaluation**
   - Complete Process validation (PV) report which fulfil batch size requirements.

5. **Certificate of Analysis (CoA)**
   - Minimum two (2) batches certificate of analysis (CoA) which fulfil the batch size requirements.

6. **Stability Data**
   - Minimum two (2) batches stability studies (both long term and accelerated) which fulfil the batch size requirements using the proposed API as Part S.

7. **Product Interchangeability/ Equivalence Evidence (BE)**
   - Bieoquivalence report (BE) or biowaiver with its complete checklist form.
   - Proof of BE study centre accreditation status. For BEDE (evaluation on the need for BE study inspection), proof of submission of application is not acceptable.
   - 90% confidence interval of Cmax and AUC within 80.00% - 125.00% (for highly variable drugs in replicate design study, widening of BE limit should be in line with ASEAN guideline requirements and pre-specify in protocol.)
   - Correct number of studies (fasting and/or fed)
   - Documents in PDF searchable format (OCR) (For at least clinical study report, method validation report, bioanalytical report)