GUIDANCE NOTES

ACTIVE PHARMACEUTICAL INGREDIENT (API) INFORMATION (PART II S) FOR PRODUCT REGISTRATION APPLICATION VIA QUEST SYSTEM

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

Please note that this Guidance Notes serves as a **supplementary document to *Drug Registration Guidance Document (DRGD): Appendix 11: Regulatory Control of Active Pharmaceutical Ingredients (APIs)***. Please refer to both documents before completing product registration application (Part II Section S) via QUEST system. An incomplete application form or dossier (with major deficiencies) is likely to be rejected during submission.

Table of Content

A. New Product Registration Application

1) All Part II Section S information should be submitted through QUEST system (except for Closed part of Drug Master File (DMF) for DMF option). Please refer to '**Help Button**' in QUEST system for assistance during online submission.

2) All Part II Section S information in mandatory field should be filled up according to the original dossier.

3) Original document should be uploaded to QUEST system for all API information (S1 to S10).

4) Separate Part II Section S information (in the same product registration application form) should be submitted when:
   i. A finished product contains more than one API
   ii. An API is manufactured from more than one manufacturing site
   iii. An API is manufactured using more than one synthesis route

5) Please select the **correct API manufacturer** (with the exact name & address) from QUEST database and ascertain your selection. Changes to the name or address of an API manufacturer are NOT possible once a saved form is created.

6) There are three options for Part II Section S information submission. Requirements for each submission option are available in *Drug Registration Guidance Document (DRGD): Appendix 11: Regulatory Control of Active Pharmaceutical Ingredients (APIs).* A summary of these requirements is provided in Appendix I.

7) A change of submission option is NOT allowed once screening approval is obtained.

8) Change or addition of API manufacturer is not allowed once screening approval is obtained.

9) Please also refer to Appendix II for *API Administrative Procedure.*

B. Regulatory Control of API for Product Registered Before the Implementation of Directive on Regulatory Control of API in Malaysia

1) This section is applicable for registered products containing Scheduled Poison in ALL dosage forms with the expiration of the registration period starting 1 January 2020.

2) At the point of writing, NPRA has identified anti-infective APIs as the selected category for assessment purposes. This category was selected based on current public health needs and risk-based approach which may be extended to other categories from time to time.

3) Please refer to DRGD: Appendix 11 for full information.

4) Please refer to Appendix III for *Administrative Procedure for Regulatory Control of Active Pharmaceutical Ingredient (API) In Registered Product Containing Anti Infective API*; and Appendix I for *Active Pharmaceutical Ingredient (API) Submission Checklist for Product Registration.*

C. Regulatory Control of Atypical APIs

1) This section of guidance notes is focusing on the content of regulatory control of Atypical API in Malaysia and is applicable for product registration in Malaysia.

2) Atypical APIs are excipient, food additive or cosmetic ingredient used as an active ingredient in pharmaceutical products. These substances are known to have lower risk and widely used outside of the pharmaceutical industry, that have meet recognized quality standards, as atypical APIs for the purpose of this guidance.

3) A list of Atypical APIs is available in Appendix IV. This list not meant to be exhaustive and will be reviewed by NPRA from time to time.

4) Regulatory requirement for Atypical APIs is outlined in Appendix V. Should a risk to health be identified, NPRA will take appropriate compliance and enforcement action proportional to the risk.

5) Please refer to DRGD: Appendix 11 for full information.

D. Mode of Submission for Drug Master Files (DMFs)

1) Effective 1 Jan 2021, NPRA is encouraging submission of **digital DMFs /e-DMF**.

2) A complete DMF (containing both closed part & open part information) with a Letter of Access (LoA) shall be submitted by DMF Holders to NPRA before local PRH submits a product registration application via QUEST system.

3) DMF holders may communicate the transfer matters with NPRA via email apiscreeningsub@npra.gov.my (for New Drug Products) or apiscreening@npra.gov.my for (Generic Products). Information below shall be provided as reference:
    a. Indication for submission: New Product Application/ Renewal/ Variation
    b. Name of Product
    c. Name of Product Registration Holder (PRH)
    d. Name of API
    e. Name of DMF Holder
    f. Name and Address of API Manufacturer
    g. DMF Version Number (for both Open & Closed part)

4) DMF holders may transfer the digital DMF via their preferred platform and may communicate the matters with NPRA officers via email stated above.

5) When NPRA received the digital DMF, NPRA will send acknowledgment email to confirm the receipt of digital DMF shared.

6) DMF holders that wish to continue sending DMFs via courier services may attach a cover letter with a copy of complete DMF in CD/DVD/USB together with a LoA directly to NPRA at address below:

    Head of *_____ Section
    Centre of Product and Cosmetic Evaluation
    National Pharmaceutical Regulatory Agency
    Ministry of Health Malaysia
    Lot 36, Jalan Universiti
    46200 Petaling Jaya
    Malaysia

    *indicated according to product category (e.g., New Drug Product or Generic)

E. Product Registration Application Referencing to WHO Prequalified APIs

1) World Health Organization (WHO) via the Prequalification Programme, set up in 2001, is aimed to facilitate access to medicines that meet unified standards of quality, safety and efficacy for HIV/AIDS, malaria and tuberculosis. In 2006, this was extended to cover medicines and products for reproductive health and again in 2008, to cover prequalification of zinc, for managing acute diarrhea in children. At the end of 2012, the WHO List of Prequalified Medicinal Products contained 316 medicines for priority diseases.

2) The WHO Prequalified API list contains sources of active pharmaceutical ingredients (APIs) that have been assessed by WHO and found to be acceptable, in principle, for use in finished pharmaceutical products procured by United Nations agencies.

3) Inclusion in the list of prequalified APIs does not constitute a WHO endorsement or warranty of fitness of purpose of the API for use in a particular finished pharmaceutical product (FPP), or of the safety or efficacy of the resultant FPP for treatment or health care. It remains the ultimate responsibility of the FPP manufacturer to ensure that the API, as accepted in principle, is suitable for the manufacture of the specific FPP.

4) In the spirit of harmonisation of regulatory activities and optimisation of efficient assessment, NPRA has outlined submission requirements for APIs that have been prequalified by WHO (refer to Appendix I).

5) PRH shall choose ACTD option (in QUEST system) for API source that have been prequalified by WHO. A copy of Confirmation of WHO Active Pharmaceutical Ingredient Prequalification (CPQ) shall be upload to QUEST system.

6) The submission shall be supported with a Letter of Access (LoA) from the DMF holder authorizing NPRA and PRH to incorporate as reference the content of DMF for that product registration application.

7) The LoA should include the following:
    a. Name of DMF holder
    b. Name and address of API manufacturing facility
    c. DMF version number (for Applicant's part and Restricted part) – shall be the same as prequalified API
    d. Name of the finished product (product name, dosage form and product strength
    e. Local product registration holder (PRH) responsible for product registration
    f. A declaration that the local PRH and NPRA shall be notified of any changes in the API specification or in the manufacturing process that will likely affect the product's quality or safety
    g. Name and email address of person(s) to be contacted for additional information
    h. Signature of authorizing official

8) However, submission of closed part of the DMF (by DMF Holders) to NPRA is not required unless requested during evaluation process. The PRH shall upload the required information of the open part of the DMF to QUEST system.

9) All API information submitted to QUEST system shall be the same as those assessed and accepted by WHO Prequalification Unit. Applications with any deviation from WHO prequalified API information (unless justified) will be rejected as ACTD option. Hence, a resubmission as DMF option will be required.

Appendix I

SUMMARY OF REQUIRED DOCUMENTS FOR
ACTIVE PHARMACEUTICAL INGREDIENT (API) INFORMATION IN PRODUCT REGISTRATION

NO.	SECTIONS/ FIELDS	CONTENTS	MANDATORY INFORMATION (✓)			
			ACTD	DMF	CEP	WHO PQ
1.	**Submission Option in QUEST system**	i) Drug Master File (DMF) ii) Certificate of Suitability (CEP) iii) ASEAN Common Technical Dossier (ACTD) * Refer to DRGD Appendix 11 for description	**ACTD**	**DMF**	**CEP**	**ACTD****
2.	**Certificate of Suitability**	A copy of the most current CEP including all annexes			✓	
		CEP number			✓	
		Date of issue			✓	
		Date of expiry (By default: 5 years from date of issue)			✓	
		Written Statement				
		i) Name of the finished product				
		ii) PRH responsible for the finished product				
		iii) Written assurance that no significant changes in the manufacturing methods or processing have taken place following the granting of the certificate or its last revision and			✓	
		iv) Declaration from the API Manufacturer that the PRH and the NPRA shall be notified of any future change in the API specifications or in the manufacturing process that will likely affect the product's quality or safety				
3.	**Quality Overall Summary (QOS)**	i) Overall Summary ii) Table of Contents iii) Body of Data	✓	✓	✓	✓
4.	**S1. General information**					
	S1.1 Nomenclature	International non-proprietary names/ INN: Chemical names: Synonyms: CAS No: Chemical Abstracts Service	✓	✓	✓	✓
	S1.2 Structure formula	Structural formula (relative and absolute chemistry) Molecular formula Molecular weight Molecular weight (base)	✓	✓	✓	✓
	S1.3 General Properties	Physico-chemical properties: i) Colour, physical form (powder, amorphous, crystalline, liquid, etc) ii) Solubility: - Solubility in the <u>water</u>, acid, alkali, common solvent - Solubility (mg/ml) - over the physiological pH range (pH 1.2-6.8) in several buffered media - Solubility (mg/ml) - in 250mL water at pH 1.2, 4.5 and 6.8 performed at 37ºC iii) Pka, pH, partition coefficient (log P), Melting point, hygroscopicity, isomerism, chirality and polymorphism	✓	✓	**YES**, If there are any physicochemical & relevant API properties - not controlled by the CEP, e.g. solubilities and polymorphs	✓
5	**S2. Manufacture**					
	S2.1 API Manufacturer(s)	Name and address of manufacturer that produced the API (manufacturer responsible for release of the final API). - Attach GMP certificate in S9 - Attach S2.1 Manufacturer in S10	✓	✓	✓	✓
	S2.1.1 Other API Manufacture(s) involved	Manufacturers involved in each production steps, including intermediate manufacturer, milling and quality control testing sites. * GMP Compliance evidence is required for all manufacturer involved in API manufacturing process, including intermediate manufacturing, micronization and milling sites;	✓	✓	✓	✓
	S2.1.2 Name of Synthesis Route	State the name of synthesis route. (If no specific name was assigned, please state as "Only One Route").	✓	✓	✓	✓
	S2.2 Description of Manufacturing Process and Process Controls	i) Detailed Description of the Synthesis (step & process) from starting materials until purification step. ii) Proposed starting material iii) Manufacturing scheme that indicates molecular formula; molecular weights; chemical structures of starting	✓	✓		

		materials, intermediates and the API including stereochemistry; reagents, catalysts and solvents used in each step until purification step. iv) Catalyst & solvents used (ICH class & limit). v) Control strategy of solvents. (if skip testing, etc). vi) Quantities of materials used, operating conditions and yield ranges in the description of the process. vii) Recycling of filtrates/mother liquors (maximum holding time /maximum number of times the material may be recycled/Evidence / Data on the impurity levels). viii) Final Steps (eg. Purification procedure) ix) Commercial and Maximum batch size (batch range in kg) x) Alternatives steps (no changes in the impurity profile) xi) Re-processing; identified the process/step, method, frequency/limit of reprocess, same specification of the final API, no changes in the impurity profile, control of impurity levels, etc. xii) Reworking: equivalent quality as original process, impurity profile, etc xiii) Recovery of materials or solvents: step its introduced in the process, source, ratio (or range of mixtures) of fresh and recovered solvents, specifications (including justification of specification), impurity levels xiv) Blending of batches; each batch tested & comply to final API specification				Please attach CPQ report
	S.2.2.1 Manufacturing Process Flowchart	Manufacturing Process Flow that indicates molecular formula; molecular weights; chemical structures of starting materials, intermediates and the final API, including its stereochemistry; reagents, catalysts and solvents used in each step until purification step.	✓	✓		Please attach CPQ report
	S2.3 Control of Materials	i) Starting materials; Justification on selection of starting materials, Specification, Name & address of each supplier, CoA of starting material issued by each of suppliers, CoA of starting material issued by the API manufacturer (for each of suppliers), Preparation of starting materials (Brief description), characterisation. ii) All materials (solvent, catalyst or reagent) used during manufacturing process [Specification, function and control strategy]. iii) Others. e.g. benzene contamination, Quality of water etc.	✓	✓		Please attach CPQ report
	S.2.3.1a TSE Risk Free Statement	i) Declaration; starting materials, reagents and all materials used to manufacture the API are of animal or human origin. ii) Document to demonstrate compliance on TSE/BSE requirement	✓	✓	✓	✓
	S2.4 Controls of Critical Steps and Intermediates	Controls of Critical Steps - critical steps & process control including tests and acceptance criteria (with justification including experimental data). Controls of Intermediates - List of Intermediates, specification, analytical procedure	✓	✓		Please attach CPQ report
	S2.5 Process validation and/or evaluation	Applicable to sterile API only	✓	✓	**YES**, If CEP did not specify asterile API	Please attach CPQ report
	S2.6 Manufacturing Process Development	i) Description and discussion of significant changes made to the manufacturing process and/or manufacturing site of the API used in producing non-clinical, clinical, scale-up, pilot and if available, production scale batches. ii) The development history of the manufacturing process as described in S 2.2 iii) To state the date of changes.	✓	✓		Please attach CPQ report
6	**S3. Characterisation and Impurities**					
	S3.1 Elucidation of Structure and other Characteristics	i) Pharmacopoeia API: - Comparison of spectral data between pharmacopoeia reference standard & API (If comparison is not available, assess as per non-pharmacopoeia API). ii) Non pharmacopoeia API: - Elemental analysis	✓	✓	✓	✓

		- Infrared Spectrophotometry (IR) - Ultraviolet absorption spectrum (UV) - Mass Spectrometry - Nuclear Magnetic Resonance Spectrometry (NMR) ; *^{1}H-NMR*, *^{13}C-NMR* - X-ray Diffraction - Differential Scanning Calorimetry (DSC) - Thermogravimetric analysis (TGA) - Others iii) Polymorphism - Description & characteristics of various polymorphic forms - Potential for formation of the polymorphic forms - Stability of the polymorphic forms - Evidence to prove the commercial scale process consistently produce desired polymorphic forms iv) Particle size distribution v) Isomerism				
	S3.2 Impurities	Organic Impurities, Inorganic Impurities, Residual solvents, Genotoxic Impurities - Possible carryover of impurities (during the synthesis and from the preparation of starting material and intermediates to the final API). - ll possible potential impurities that may arise from the starting materials, route of synthesis and possible degradation products should be listed with name, structure, origin, LOD and LOQ and ranges of results in at least 3 consecutive batches as well as the proposed limits taking into account the requirements of ICH guideline. - Any impurity greater than qualification threshold should be qualified and a rationale for establishing impurity limit/ acceptance criteria that includes safety considerations (eg. data from toxicology study, or batch analysis data of batches used in clinical trial with observed impurites content are equal or more than limit in the specification) should be provided. - discussion on impurities that stated in another pharmacopeia (if applicable)	✓	✓		Please attach CPQ report
7	**S4. Control of Drug Substance/ API**					
	S.4.1 Specification	Table of Specification of API from both API Manufacturer & Product Manufacturer (with **Specification version no**. & **effective date**).	✓	✓	✓	✓ (Shall be the same version as those stated on WHO CPQ)
	S4.2 Analytical Procedures	i) The analytical procedures used for testing of API should be provided in sufficient details to enable reproducible testing by another laboratory ii) Compendial methods or appropriate information from the manufacturer	✓	✓		Please attach CPQ report
	S4.3 Validation of Analytical Procedures	i) Analytical validation information, including experimental data for the analytical procedures used for testing the API ii) Typical validation characteristics to be considered: - Selectivity - Precision(repeatability, intermediate precision and reproducibility) - Accuracy - Linearity - Range - Limit of Quantitation - Limit of detection - Robustness - System suitability iii) Non-compendial methods	✓	✓		Please attach CPQ report
	S4.4 Batch Analysis	i) Batch analysis results of at least 3 batches ii) Information in table form e.g.: batch number, batch size, manufacturing date, manufacturing site and batch use (validation, stability, commercial etc.)	✓	✓	✓	✓

	S.4.4.1 Certificates of Analysis(COA)	i) From API Manufacturer (2 Batches) ii) From Product Manufacturer (2 Batches)	✓	✓	✓	✓
	S.4.5 Justification of Specification	i) Discussion on inclusion/ omission of tests and analytical procedures ii) Justification on range of acceptance criteria set for in-house tests	✓	✓	✓ (For non-monograph tests)	Please attach CPQ report
8	**S5. Reference Standards or Materials**					
	From API Manufacturer	i) Clearly stating: - Official reference standard used, with batch number - Primary reference standard used, with batch number - Working standard used, with batch number ii) For each Reference Standard should provide: - CoA of Reference Standard - IR spectra of reference standard - Overlaid IR spectra comparing the primary & working standards. - Reference standards available for impurities/related substances	✓	✓	✓	✓
	From Product Manufacturer	i) Clearly stating: - Official reference standard used, with batch number - Primary reference standard used, with batch number - Working standard used, with batch number ii) For each Reference Standard should provide: - CoA of Reference Standard - IR spectra of reference standard - Overlaid IR spectra comparing the primary & working standards. - Reference standards available for impurities/related substances	✓	✓	✓	✓
9	**S6.Container Closure System**					
	S.6 Container Closure System (CCS)	i) Description: primary packaging, secondary packaging, specifications,	✓	✓	✓	✓
		ii) IR spectra of primary packaging material, CoA, Functional secondary packaging components (If applicable), iii) Suitability: Moisture and light, compatibilty (e.g: Sorption or leeching)	✓	✓	**YES**, - If CEP did not specify a CCS or - CCS (in S.6) is different from CCS (in CEP)	**YES,** - If different with CCS stated on WHO List of Prequalified APIs
10	**S7. Stability**					
	Re-test Period or shelf life	Select (months) the proposed retest period based on stability study conclusion.	✓	✓	✓	✓
	Storage Condition	State API storage condition (including special label, if needed) based on study condition of stability data provided (eg: “Store below 25 °C, protect from light”).	✓	✓	✓	✓
	Stability Data	i) Stress Testing Study - API batch details (eg: moisture, light, acidic, basic, oxidative and thermal stress conditions).	✓	✓		
		ii) Long Term Stability Data - Minimum of 3 batches, (with recent results) - Batch information (manufacturing date, site, batch size, - Temperature/RH/Packaging iii) Accelerated Stability Data - Minimum of 3 batches, (with 6 months data) - Batch information (manufacturing date, site, batch size) - Temperature/RH/Packaging iv) Post-approval Stability Protocol and Stability Commitment	✓	✓	**YES**, If CEP did not specify a retest period with specific storage condition (CCS and specific temperature). or - CCS (in S.6 & S7) is different from CCS (in CEP)	**YES**, - If retest period & storage condition are different with WHO List of Prequalified APIs
11	**S8. Drug Master File (DMF)** General Note i) The API manufacturer may submit the DMF (both open part & closed part) as digital DMF/e-DMF with a Letter of access (LOA) to apiscreening@npra.gov.my** or apiscreeningsub@npra.gov.my**. ii) The DMF should reach NPRA at the point of screening submission. Failure to do so may result in submission rejection.					

	* Please refer to template of Cover Letter/ LOA available on NPRA website ** refer to product category Refer Part D of Guidance Note for full information					
	DMF Version No.	Current DMF version number with effective date, &		✓		✓ (Shall be the same as those stated on WHO CPQ)
	S.8.1 Letter of Access	The letter of Access authorizes NPRA to refer to the DMF, in support of the application for a finished product. Thus, the Letter of Access must state the following: - Name of DMF holder - Name and address of API manufacturing facility - DMF version number (for Applicant's part and Restricted part) - Name of the finished product (product name, dosage form and product strength - Local product registration holder (PRH) responsible for product registration - A declaration that the local PRH and NPRA shall be notified of any changes in the API specification or in the manufacturing process that will likely affect the product's quality or safety - Name and email address of person(s) to be contacted for additional information - Signature of authorizing official		✓		✓ DMF Version number shall be the same as Prequalified API
	S8.2 Name and complete address (including phone/fax no.) of DMF holder	S.8.2.1 Name of DMF Holder S.8.2.2 Address of DMF Holder S.8.2.3 Phone No. of DMF Holder S.8.2.4 Email address of Contact Person-DMF Holder		✓		✓
12	**S9. Certificate of Good Manufacturing Practice (GMP) for API Manufacturer**					
	S9. GMP Certificate	S.9. Attach a valid copy of GMP Certificate S.9.2 GMP Issuing Body S.9.3 Date of Issue of Certificate of GMP S.9.4 Date of Expiry of Certificate of GMP	✓	✓		
13	**S10. Other Supporting Document**					
	S10. Other Supporting Document	- Provide attachment for S2.1 Manufacturer in S10. - Official compendial monograph (if available) - Other supporting documents*	✓	✓	✓	✓
	Additional documents for Approved (API)	Declaration Letter from PRH (To state the changes if any) *(refer template letter)*	✓	✓	✓	
		Declaration Letter from API Manufacturer *(refer template letter)*	✓	✓		✓
		List of Additional Data - Provide all the additional data which has been requested during previous submission (approved API)	✓	✓	✓	✓
		List of Approved Variation Application - Provide list of all variation application which was approved	✓	✓	✓	✓
		Summary of other changes Table of comparison (Approved API & New submission)	✓	✓	✓	✓

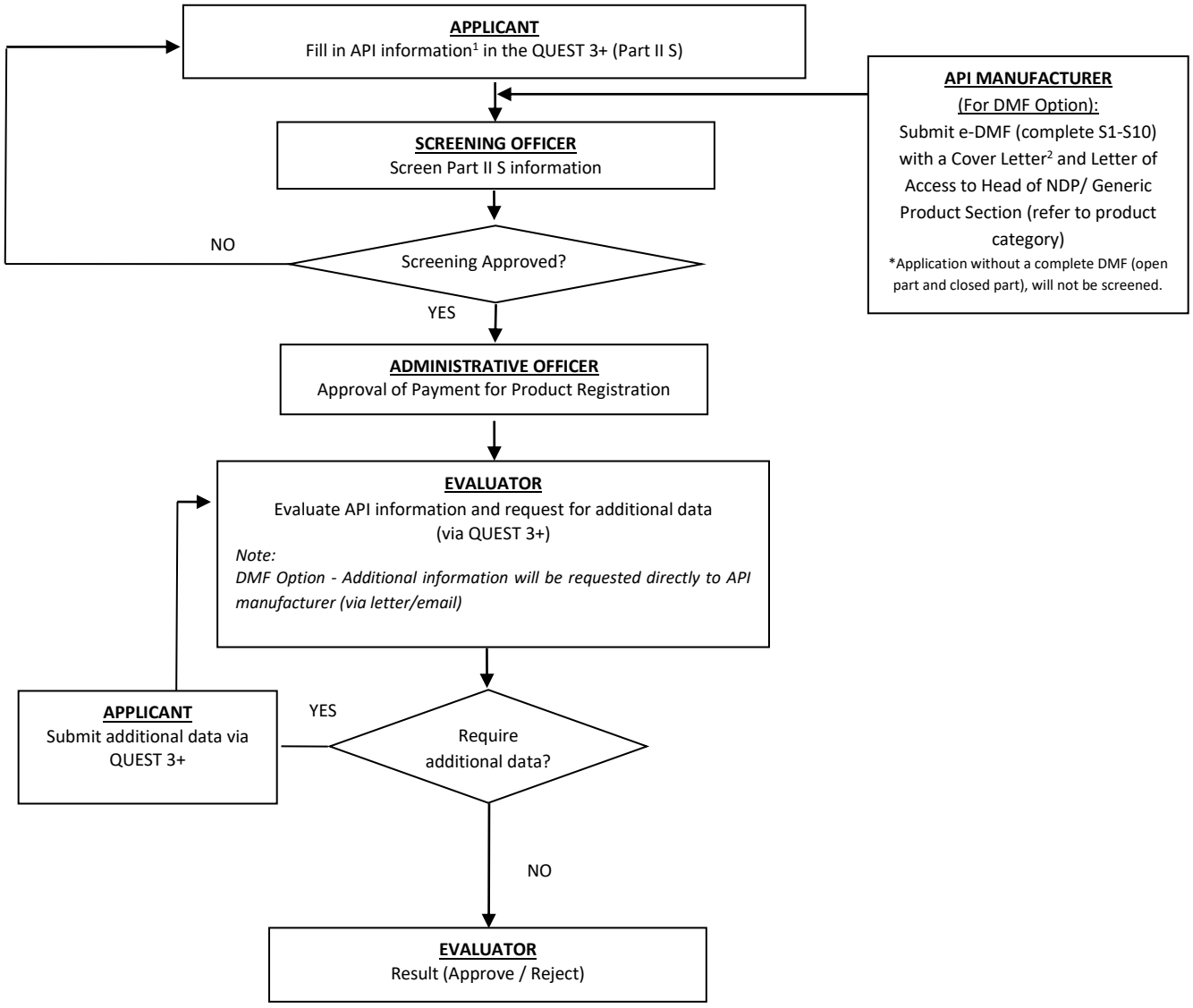
* Additional information may be requested if deemed necessary

** For new applications & variation applications (with WHO prequalified API) shall be submitted as ACTD option (e.g., for variation, please submit MaV-3)

Appendix II

API ADMINISTRATIVE PROCEDURE FOR NEW PRODUCT APPLICATION FOR NEW DRUG PRODUCT (NDP) & GENERIC PRODUCT (CONTAINING *SCHEDULED POISONS*: *ALL DOSAGE FORMS*)

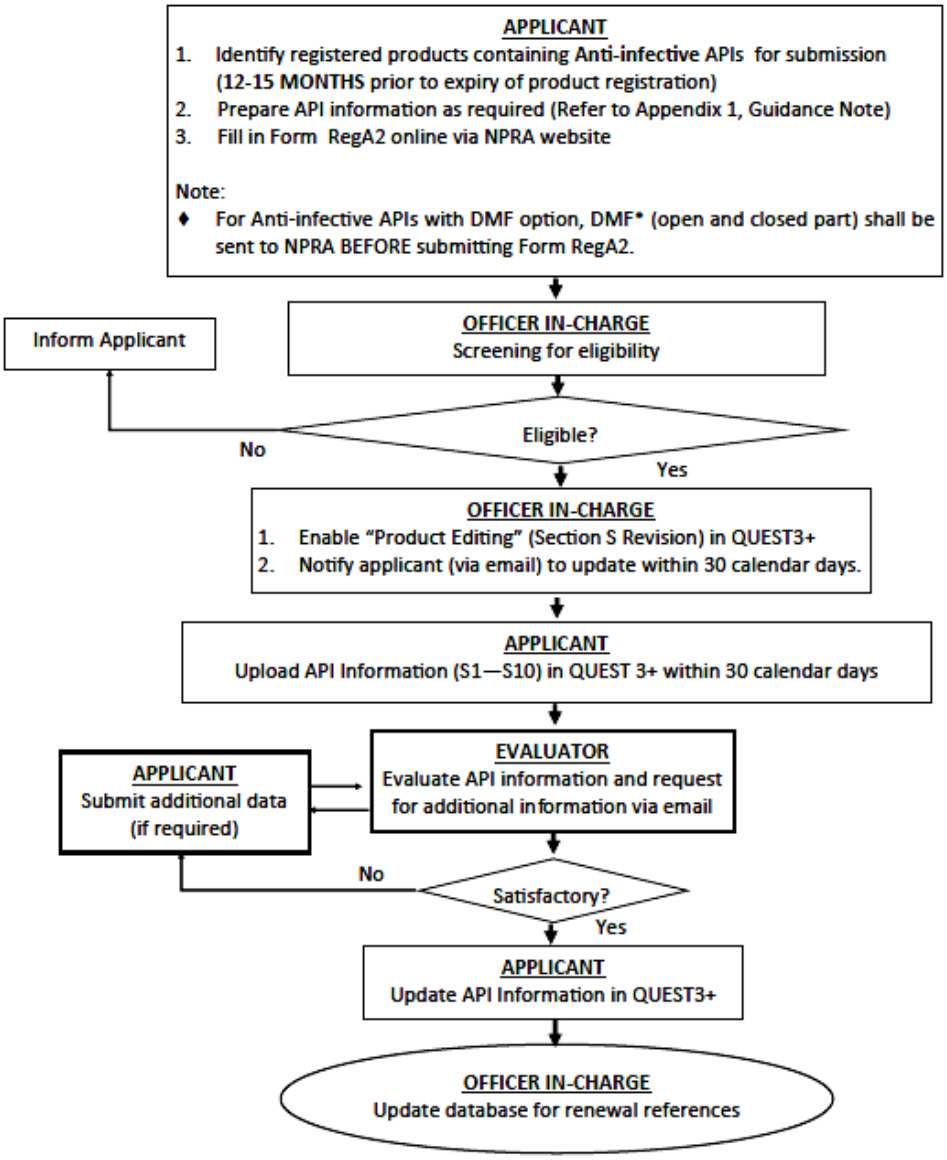
[Effective 2 Dec 2019]



Note:

1. Please Refer to Drug Registration Guidance Document (DRGD): Appendix 11: Regulatory Control of API, from website www.npra.moh.gov.my
2. Template of Cover Letter is available on NPRA website

ADMINISTRATIVE PROCEDURE FOR REGULATORY CONTROL OF ACTIVE PHARMACEUTICAL INGREDIENT (API) IN REGISTERED PRODUCT CONTAINING ANTI INFECTIVE API



Footnote:

1. *CD copy of DMF (open and closed part) with a Letter of Access and Cover Letter should be sent to: *Head of New Drug Product Section/ *Head of Generic Medicines Section (*refer to product category)
2. **For registered products not containing anti-infective APIs, part II S information shall be kept by the PRH. It is not necessary to upload to Quest 3+ system.**

Appendix IV

LIST OF ATYPICAL ACTIVE PHARMACEUTICAL INGREDIENT (API)

Examples of Atypical API:

No.	Substance Name
1	Aluminum Hydroxide
2	Ammonium Chloride
3	Ascorbic Acid
4	Calcium carbonate
5	Calcium chloride
6	Cetylpyridinium Chloride
7	Glucose / Dextrose
8	Glycerol / Glycerin
9	Glycine
10	L-Alanine
11	L-Alanyl-L-Glutamine
12	L-Arginine
13	L-Aspartic Acid
14	L-Cysteine
15	L-Glutamic Acid
16	L-Glutathione
17	L-Histidine
18	L-Isoleucine
19	L-Leucine
20	L-Lysine Acetate
21	L-Methionine
22	L-Phenylalanine
23	L-Proline
24	L-Serine
25	L-Threonine
26	L-Tyrosine
27	L-Valine
28	Magnesium Carbonate
29	Magnesium Chloride
30	Magnesium Hydroxide
31	Magnesium Oxide
32	Magnesium Sulphate
33	Malic Acid
34	Mannitol
35	Medium Chain Triglyceride
36	Olive Oil
37	Potassium Chloride
38	Potassium Dihydrogen Phosphate
39	Potassium Phosphate
40	Sodium Acetate
41	Sodium Bicarbonate
42	Sodium Chloride
43	Sodium Glycerophosphate
44	Sodium Hydroxide
45	Sodium Lactate
46	Sodium Phosphate

47	Soybean Oil
48	Zinc Acetate
49	Zinc Carbonate
50	Zinc Chloride
51	Zinc Citrate
52	Zinc Gluconate
53	Zinc Oxide
54	Zinc Sulfate

Note: This list is not meant to be exhaustive and will be reviewed from time to time.

Appendix V

SUMMARY OF REQUIRED DOCUMENTS FOR ATYPICAL ACTIVE PHARMACEUTICAL INGREDIENT (API) INFORMATION

Section S / Field		Mandatory (✓)	Remarks
S1.1	Nomenclature	✓	
S1.2	Structure formula	✓	
S1.3	General Properties	✓	
S2.1	API Manufacturer(s)	✓	
S2.1.1	Other API Manufacture(s) involved	✓ (if any)	
S2.1.2	Name of Synthesis Route	✓ (if any)	
S2.2	Description of Manufacturing Process and Process Controls	✓ (Brief description)	Brief description for: - Manufacturing process - Materials
S.2.2.1	Manufacturing Process Flowchart	✓	
S2.3	Control of Materials	Non-Mandatory	Should statement 'refer to restricted part' is given, information will be requested
S.2.3.1a	TSE Risk Free Statement	✓	
S2.4	Controls of Critical Steps and Intermediates	Non-Mandatory	
S2.5	Process validation and/or evaluation	Non-Mandatory	
S2.6	Manufacturing Process Development	Non-Mandatory	
S3.1	Elucidation of Structure and other Characteristics	Non-Mandatory	
S3.2	Impurities	Non-Mandatory	
S.4.1	API Specification from: i) API Manufacturer **and** ii) Finished Product Manufacturer	✓	
S4.2	Analytical Procedures	Non-Mandatory	
S4.3	Validation of Analytical Procedures	Non-Mandatory	
S4.4	Batch Analysis	Non-Mandatory	
S.4.4.1	Certificates of Analysis (COA) (2 batches each) from: i) API Manufacturer **and** ii) Finished Product Manufacturer	✓	
S.4.5	Justification of Specification from: i) API Manufacturer **and** ii) Finished Product Manufacturer	✓	
S5	Reference Standards or Materials from: i) API Manufacturer **and** ii) Finished Product Manufacturer	✓	If not available, please provide justification
S.6	Container Closure System (CCS)	✓	Description only
S7	Stability	Non-Mandatory	
S9	GMP Certificate	GMP Certificate Or Declaration on Quality Management System by Competent Person	Refer to template *Declaration on Quality of AAPI_V1* provided on NPRA Website
S10	Other information	✓	Additional information if deemed necessary