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Regulatory Requirements for Pharmaceutical Product Registration in Singapore

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ABSTRACT

Singapore is one of the lucrative markets for pharmaceutical companies apart from India, China and Malaysia in the Asian region. Despite its small population of around 5 million people, Singapore's affluence and notable health awareness have led to increased drug demand. Incentives such as low corporate tax rates and strong intellectual property laws encourage pharmaceutical companies to locate their operations in the city-state. The government's increased commitment to healthcare provision and an increasingly aging population that has high per-capita pharmaceutical and healthcare expenditure will continue to attract pharmaceutical and private healthcare providers to Singapore. HSA (Health Sciences Authority) is the pharmaceutical regulatory authority in Singapore that ensures the safety and efficacy of the medicinal product marketed in Singapore. HSA provides two major pathways to pharmaceutical companies, NDA (New Drug Application) and GDA (Generic Drug Application), to market their products in the Singapore pharmaceutical market. This study encompasses the organization structure of HSA, classification of the medicinal product, registration process of the medicinal product, labeling requirements, and fees structure for different types of applications.

INTRODUCTION:

The Health Sciences Authority (HSA) was formed on 1 April 2001 as a statutory board of the Singapore Ministry of Health with the integration of five specialized agencies:

1. The Centre for Drug Evaluation;
2. Institute of Science and Forensic Medicine;
3. National Pharmaceutical Administration;
4. Product Regulation Department; and
5. Singapore Blood Transfusion Service.

Its vision is to be the leading innovative authority protecting and advancing national health and safety. The scale and scope of the agency's work spans a wide spectrum of scientific and professional functions. These would typically be managed in several separate and distinct agencies elsewhere. But the agency's set-up is unique in that these functions are all housed in a single organization.

The organization serves three key functions:

- It is the national regulator for health products;
- It secures the national blood supply through its operation of the national blood bank - Bloodbank@HSA; and
- It represents the national expertise in forensic medicine, forensic science, and analytical chemistry testing capabilities.

The health products regulation group of HSA contributes to the development of biomedical sciences in Singapore by administering a robust, scientific, and responsive regulatory framework. It ensures that drugs, innovative therapeutics, medical devices, and health-related products are wisely regulated and meet appropriate safety, quality, and efficacy standards. The agency also contributes to the formulation of national drug policies.

On the pre-market front, HSA administers clinical trials for new drugs and grants approvals for these products before they are marketed in Singapore. Audits on good manufacturing and

distribution practices are also conducted. On the post-market front, HSA monitors health products in the market through regulatory surveillance activities. The agency also carries out investigations and takes enforcement action against illegal activities related to unregistered, counterfeit, and adulterated health products. HSA has an established and active pharmacovigilance monitoring program that draws on its network of healthcare professionals and overseas regulators. This allows HSA to initiate targeted and prompt alert action in response to reported adverse drug events. This allows the agency to expedite the isolation of such problems and minimize harm to public health and safety[1].

All western medicines are subject to product registration before their sale and supply in Singapore. The safety, quality, and efficacy of western medicines are scientifically assessed by HSA to meet internationally benchmarked standards before marketing approval is granted. These medicines are regulated as Prescription-Only medicines [POM], Pharmacy-Only [P] medicines, or General Sale List [GSL] medicines based on the risk profiles of medicines and the appropriate degree of medical supervision required for the management of the medical condition.

No medicine is completely free of risk. Therefore, HSA is also committed to responding promptly when safety, quality, or efficacy concerns arise. In line with regulatory systems in many developed countries, all western medicines are also subject to HSA's post-marketing surveillance program which includes regular compliance checks, product sampling, and Adverse Drug Reaction (ADR) monitoring to ensure that they continue to meet the required safety, quality and efficacy standards. Products found not to comply with HSA's requirements may be suspended from further sales or recalled from the market.

Different classes of western medicines in Singapore[2]

Medicines are substances that are used by consumers and patients for the diagnosis, treatment, or prevention of disease. The range of western medicines available in the Singapore market is classified into 3 main groups:

Table 1: Different classes of western medicines in Singapore

Classification	Description	Examples
Prescription Only Medicines (POM)	These comprise potent medicines which require medical supervision and monitoring, especially when used long-term for chronic disease conditions. They can only be prescribed by doctors and are available from clinics or may be purchased from pharmacies with a doctor's prescription.	Medicines for chronic diseases such as, • Diabetes, • high blood pressure, • high cholesterol.
Pharmacy Only Medicines (P Medicines)	These are usually medicines that are used for the management of minor ailments. They can be purchased from pharmacists without a doctor's prescription. Consultation with pharmacists is required to determine the appropriateness of treatment.	Certain medicines for conditions such as, • allergic rhinitis ("hay fever") • cough • diarrhea • nausea • hair loss • medicines to help quit • smoking
General Sales List Medicines (also known as Over-the-Counter Medicines)	These are medicines whereby sale is not restricted because they are deemed safe for self-medication without medical supervision by a doctor or a pharmacist when used appropriately and according to the instructions.	• Paracetamol for fever and headache • Antacids for heartburn and acid indigestion

Discussion:

The Health Sciences Authority (HSA) was formed on 1 April 2001 as a statutory board of the Singapore Ministry of Health with the integration of five specialized agencies:

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7. Institute of Science and Forensic Medicine;
8. National Pharmaceutical Administration;
9. Product Regulation Department; and
10. Singapore Blood Transfusion Service.

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- It is the national regulator for health products;
- It secures the national blood supply through its operation of the national blood bank - Bloodbank@HSA; and
- It represents the national expertise in forensic medicine, forensic science, and analytical chemistry testing capabilities. The health products regulation group of HSA contributes to the development of biomedical sciences in Singapore by administering a robust, scientific, and responsive regulatory framework. It ensures that drugs, innovative therapeutics, medical devices, and health-related products are wisely regulated and meet appropriate safety, quality, and efficacy standards. The agency also contributes to the formulation of national drug policies.

On the pre-market front, HSA administers clinical trials for new drugs and grants approvals for these products before they are marketed in Singapore. Audits on good manufacturing and

distribution practices are also conducted. On the post-market front, HSA monitors health products in the market through regulatory surveillance activities. The agency also carries out investigations and takes enforcement action against illegal activities related to unregistered, counterfeit, and adulterated health products. HSA has an established and active pharmacovigilance monitoring program that draws on its network of healthcare professionals and overseas regulators. This allows HSA to initiate targeted and prompt alert action in response to reported adverse drug events. This allows the agency to expedite the isolation of such problems and minimize harm to public health and safety[7].

Significance of logo of HSA[8]

A strong upward direction and movement represent a dynamic, progressive, forward-looking organization of excellence. The blue arch symbolizes our global outlook and global renown. The two white strokes suggest progression and continuous development. The integrated blue and white segments express our strong collaborative and interactive approach. The firm but fluid "tick" communicates confidence in HSA approval and regulatory authority. Choice of blue colour projects their foundation of professionalism, strength, and integrity. The refreshing golden yellow signifies our vibrant, innovative, and people-oriented culture. Viewed in its totality, the HSA logo encapsulates its vision, mission, and orientation towards the future.

2. ORGANISATION STRUCTURE[9]

Health products regulation group

The HPRG (Health Products Regulation Group) ensures that drugs, innovative therapeutics, medical devices, and health-related products in Singapore are wisely regulated to meet appropriate standards of safety, quality, and efficacy.

2.1 Blood services group

The Blood Services Group, as the national blood service, secures the nation's blood supply by ensuring a safe and adequate blood supply and providing specialist transfusion medicine services.

2.2 Applied sciences group

The applied sciences group represents the national forensic medical and scientific, analytical, and laboratory expertise to support regulatory and other compliance agencies in the administration of justice and the safeguarding of public health.

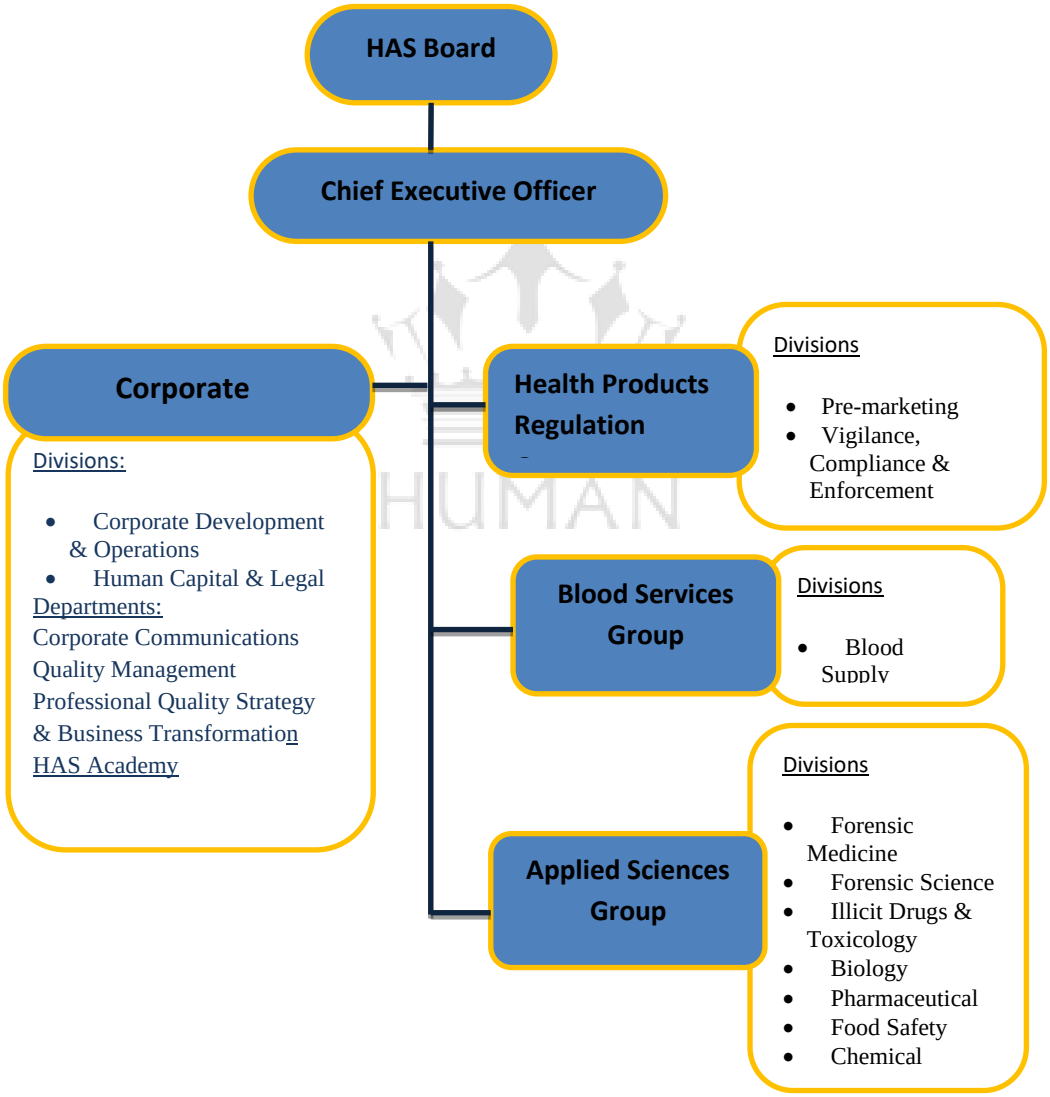

Figure 2: HSA organization structure

2.3 Corporate HQ

The corporate HQ defines the strategic direction and provides corporate support for the Authority and its three professional groups to achieve HSA's vision and mission through effective policies and guidelines, efficient processes, and strategic coordination.

a. MEDICINAL PRODUCT[10]

Under the Medicines Act, a “medicinal product” refers to any substance or article (not being an instrument, apparatus, or appliance) which is manufactured, sold, supplied, imported, or exported for use wholly or mainly in the following ways:

- use by being administered to one or more human beings for a medicinal purpose; and/or,
- use as an ingredient in the preparation of a substance or article which is to be administered to one or more human beings for a medicinal purpose.

A “medicinal purpose” means any one or more of the following purposes:

- treating or preventing disease;
- diagnosing disease or ascertaining the existence, degree, or extent of a physiological condition;
- contraception;
- inducing anesthesia; and/or,
- otherwise preventing or interfering with the normal operation of a physiological function, whether permanently or temporarily, and whether by way of terminating, reducing or postponing, or increasing or accelerating, the operation of that function or in any other way.

A product license is required before a medicinal product can be sold or supplied in Singapore unless otherwise exempted under the law. Each product license is specific to a product:

- of a particular name;
- with a particular formulation;

- in a particular dosage form (i.e. physical presentation) and strength; and
- with a particular set of approved indications and directions for use.

Any changes to the above parameters may result in the need to apply to vary the existing product license or possibly obtain a new product license altogether.

General sales list medicines

General Sales List Medicines (GSL) control is sufficient in the following situations:

a. The product is reasonably safe and can be sold or supplied without the need for supervision by a registered doctor, dentist, or pharmacist;

b. The contraindications, drug interactions, precautions, and warnings are easily recognized by the consumer; and,

c. The health hazard, the risk of misuse, the risk of misdiagnosis, or the need to take special precautions in the storage and handling of the product is small.

As healthcare products are becoming increasingly complex – e.g. combinations of a medicinal product and medical device – the regulation of such products will be based on how they are classified. Thus, if there is doubt about the product's classification, it is recommended that the applicant seek clarification via email to HSA_MedProd_Enquiry@hsa.gov.sg.

3. APPLICATION TYPES

In applying for a new product license for a medicinal product in Singapore, there are two categories of applications:

1. New Drug Application (NDA) and
2. Generic Drug Application (GDA):

3.1 New drug application

3.1.1 NDA-1:

This application is used for the first strength of a product containing a new chemical or biological entity that has never been registered before in Singapore.

3.1.2 NDA-2:

I. For the first strength of a new drug product

- containing a new combination of registered chemical or biological entities that have never been registered before in Singapore;
- containing registered chemical or biological entity(ies) in a new dosage form;
- containing registered chemical or biological entity(ies) for use by a new route of administration; or,
- containing registered chemical or biological entity(ies) for new indication(s), dosage recommendation(s) and/or patient population(s).

II. For new drug products that do not fall under the requirements for NDA-1, NDA-3, or GDA.

3.1.3 NDA-3:

This application is used for subsequent strength(s) of a new drug product that has been registered or has been submitted as an NDA-1 or NDA-2. The product name, pharmaceutical dosage form, indication, dosing regimen, and patient population shall be the same as that for the NDA-1 or NDA-2.

3.2 Generic drug application

3.2.1 GDA-1:

This application is used for the first strength of a generic chemical product.

3.2.2 GDA-2:

This application is used for subsequent strength(s) of the generic chemical product that has been registered or has been submitted as a GDA-1. The product name and pharmaceutical dosage form shall be the same as that for the GDA-1.

A generic product is essentially similar to a currently registered product in Singapore (known as the "Singapore reference product") but excludes biologics. Essentially similar4 is defined as having the same qualitative and quantitative composition in terms of active substances, having the same pharmaceutical form, and being bioequivalent. By extension, the concept of essential similarity also applies to different conventional immediate-release oral dosage forms (i.e. tablets and capsules) which contain the same active ingredient(s). A schematic diagram to illustrate the various types of applications is shown in Figure 2 below:

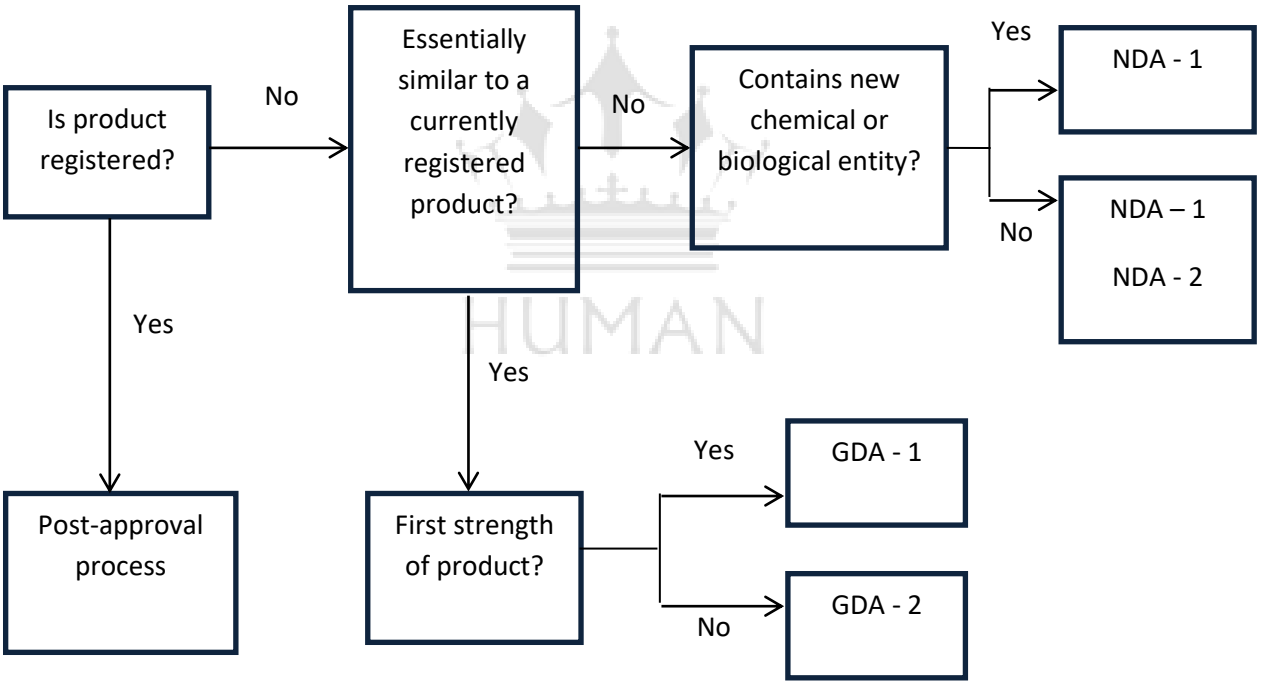

Figure 3: Schematic diagram of application routes for drug registration

REGISTRATION PROCESS

One part of a product's life cycle is the pre-marketing activities, namely registration of a product before market entry. The registration process involves a series of steps as seen in Figure 3 below:

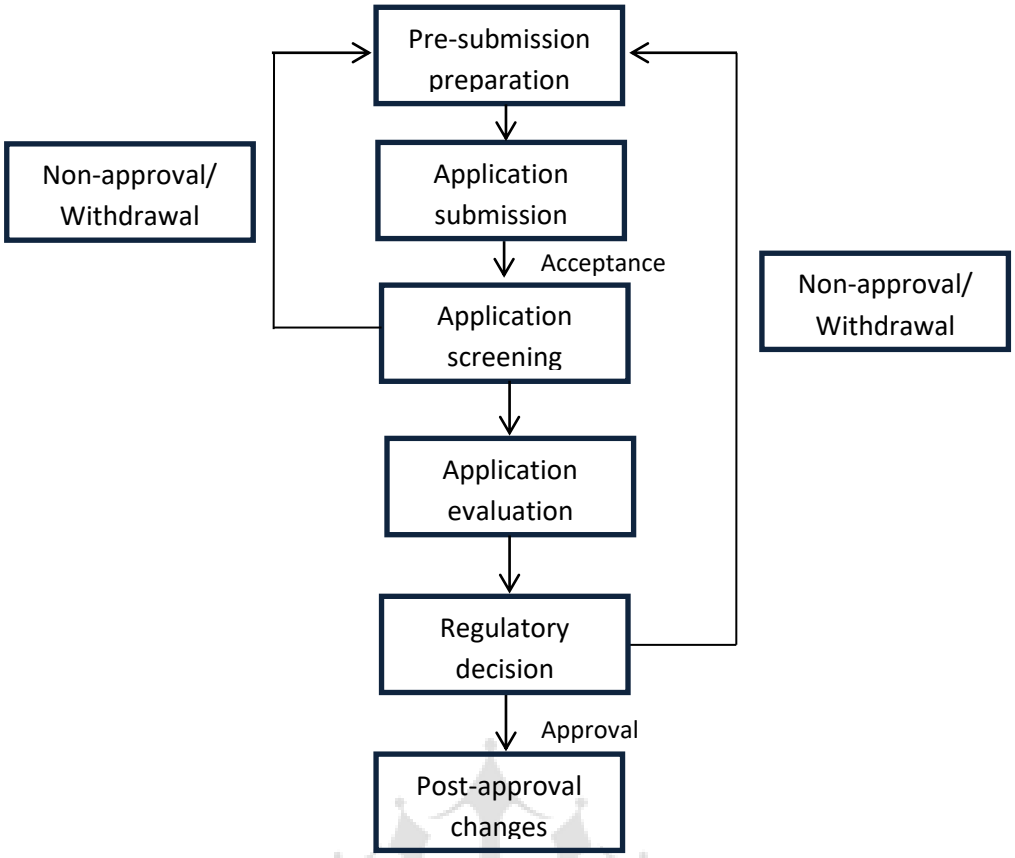

Figure 4: Steps involved in the registration process for the medicinal product

4.1 Pre-submission preparation

The first step in the registration process is one of the most important because it involves

i. Knowing which application to apply for;

ii. Knowing which evaluation route to choose; and,

iii. Arranging for a pre-submission consultation with HSA for advice, if required.

4.1.1 Evaluation routes

There are three types of evaluation dossiers for a new drug application. A schematic diagram to illustrate the various types of evaluation dossiers is given in Figure 4.

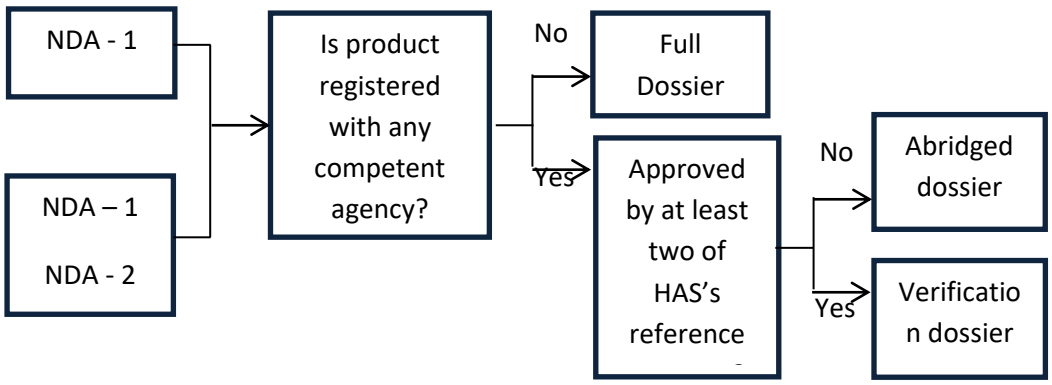

Figure 5: Schematic diagram to illustrate the various types of evaluation dossiers

1. Full dossier:

The full dossier evaluation route applies to a drug product that has not been approved by any competent drug regulatory agency at the time of submission for registration to HAS. This route applies to an innovator product containing a new chemical /biological entity, a new combination of chemical/biological entities, or innovative use of a registered product.

2. Abridged dossier:

The abridged evaluation route applies to a drug product that has been evaluated and approved by at least one competent drug regulatory agency.

3. Verification dossier:

The verification evaluation route applies to a medicinal product that has been evaluated and approved by at least two of the following HAS's reference drug regulatory agencies:

- Australia Therapeutic Goods Administration (TGA);
- Health Canada (HC);
- US Food and Drug Administration (FDA);
- The European Medicines Agency (EMA)*; or
- UK Medicines and Healthcare Products Regulatory Agency (MHRA)[#].

*For products approved via the Centralised Procedure.

#For products approved by UK MHRA through the national procedure or where the UK MHRA acted as the RMS (Reference Member State) for the Decentralised and Mutual Recognition Procedures in Europe.

However, approval by these reference regulatory agencies does not obligate HAS to approve the application. A verification dossier must be submitted within 3 years from the date of approval by the chosen primary reference agency. The primary reference agency is defined as the reference agency for which the qualifying supporting documents, as outlined in this guidance, will be submitted by the applicant.

The approved indication(s), dosing regimens(s), patient group(s), and/or direction(s) for use must be similar across the reference regulatory agencies. If there are apparent differences, the application will be re-routed to the abridged route. HAS reserves the right to accept only the most stringent indication(s), dosing regimen(s), patient group(s), and/or direction(s) of use amongst those approved by the reference regulatory agencies.

Furthermore, all aspects of the drug product's quality must be identified as currently approved by the chosen primary reference regulatory agency that has evaluated and approved the product. This includes, but is not limited to, the formulation, site(s) of manufacture, release and shelf-life specifications, primary packaging and the PI/PIL.

HAS will not accept a verification dossier if the application falls within one of the categories listed below:

- The product is a biologic;

- The product and its intended use including indication(s), dosing regimen(s) and patient group(s) have been rejected, the application withdrawn from, approved via appeal process or pending deferral by a competent drug regulatory agency for safety and/or efficacy reasons;

- The product needs a more stringent assessment as a result of differences in local disease patterns and/or medical practices (e.g. blood products, vaccines and some anti-infective).

For a product with a proposed indication that has been designated as an orphan drug by at least one reference agency, or a product that has been approved by at least one reference agency via accelerated/fast-track approval, approval under exceptional circumstances, or

equivalent approval process, the applicant should consult HAS on the eligibility of such a product through the verification route before submission.

4.1.2 Pre-submission consultation

Applicants are encouraged to contact HSA before submission of an application if questions arise or clarification is required. There are two methods to contact HSA:

i. Pre-submission inquiry via email

ii. Pre-submission meeting

Applicants are to note that all advice given by HSA will be based on the knowledge that is current at the time of the consultation. Such advice is not binding and does not have a direct bearing on the eventual outcome of the application concerned.

4.1.3 Pre-submission inquiry

The applicant may submit a pre-submission inquiry via e-mail if any clarification on medicinal product registration is needed before submission. The e-mail address is HSA_MedProd_Registration@hsa.gov.sg. The subject of the e-mail should state, “pre-submission inquiry”, for the e-mail to be sent to the relevant officer. Once the inquiry has been received, an officer will look into the matter and a response will be sent back to the applicant.

4.1.4 Pre-submission meeting

For complex issues relating to an impending submission, applicants are advised to consult with HSA in a pre-submission meeting. The request for a consultation should be made in writing, with the purpose, agenda, and proposed date & time for the meeting, via email to HSA_MedProd_Registration@hsa.gov.sg.

For a submission under the full evaluation route, the applicant is required to notify HSA via a pre-submission meeting two months prior to the intended submission date of the application dossier.

4.2 Application submission

Application submission comprises of two parts:

1. The PRISM application form and

2. The registration dossier.

4.2.1 PRISM application form

All applications must be made online via PRISM. For further information regarding submitting a PRISM application, it can be referred to chapter J for guidance notes for submitting a PRISM application[12].

4.2.2 Registration dossier

The registration dossier contains the documents to support the evaluation of the submitted application. The complete dossier should be submitted within 2 working days after the PRISM application submission to prevent delays in the processing of the application. The date of submission will be defined as the date when HSA receives the complete dataset for the application.

Registration dossiers should be in a CTD (Common Technical Document) format. The CTD provides a common format for the preparation of a well-structured submission dossier. It uses a modular framework described in ICH (International Conference Harmonization) Topic M4 or the ASEAN (Association of Southeast Asian Nations) guidelines on the CTD for Registration of Pharmaceuticals for Human use. Thus, the dossier will be in one of the two formats, either the ICH CTD or the ACTD format. According to the chosen format, the documents will be grouped into five modules (ICH CTD) or four parts (ACTD)[13,14]. The main differences between these two formats are the numbering and naming of the sections, as shown in Table 2:

Table 2: Format of the ICH CTD and ACTD

Documents	Location in	
	ICH CTD	ACTD
Administrative documents and product information	Module 1	Part I
Common technical document overview	Module 2	Incorporated in parts II, III, and IV
Quality documents	Module 3	Part II
Non-clinical documents	Module 4	Part III
Clinical documents	Module 5	Part IV

The CTD format cannot be changed once the application is submitted. Any subsequent variation applications for the product should follow the same format.

4.2.2.1 Softcopy and hardcopy requirements

In moving towards a greener environment, submission of the complete registration dossier – i.e. modules 1 to 5 of the ICH CTD or parts I to IV of the ACTD – should be in electronic format. But there is one exception: documents that require proof of authenticity (e.g. CPPs, approval letters not available online, authorization letters, GMP certificate, patent declaration, declaration letters, etc) should be submitted in electronic and hard copy format. Applicants should ensure that all soft copies – e.g. scanned documents – of the dossier are legible as illegible soft copies will cause unnecessary delays in the registration process.

Table 2 and 3 outlines the softcopy requirements for NDAs and GDAs submitted via the full, abridged, or verification evaluation route in either ICH or ACTD, respectively:

Table 3: Soft and Hard copy requirements for ICH CTD dossiers

ICH CTD	CTD Requirement [#]							
	NDA (F)		NDA (A)		NDA (V)		GDA (A + V)	
	Softcopy	Hardcopy	Softcopy	Hardcopy	Softcopy	Hardcopy	Softcopy	Hardcopy
Module 1	PRISM	1 set [*]	PRISM	1 set [*]	PRISM	1 set [*]	PRISM	1 set [*]
Module 2	PRISM/CD	N/A	PRISM/CD	N/A	PRISM/CD	N/A	PRISM/CD	N/A
Module 3			PRISM/CD		PRISM/CD		PRISM/CD	
Module 4			N/A		N/A		N/A	
Module 5			PRISM/CD		PRISM/CD		PRISM/CD	

[#] F: Full route; A: Abridged route; V: Verification route; N/A: Not applicable

[*] Only documents that require proof of authenticity are required to be submitted in hardcopy for Module 1 (e.g. CPPs, approval letters not available online, authorization letters, GMP certificate, patent declaration, declaration letters, etc.)

Table 4: Soft and Hard Copy Requirements for ACTD dossiers

ACTD	CTD Requirement [#]							
	NDA (F)		NDA (A)		NDA (V)		GDA (A + V)	
	Softcopy	Hardcopy	Softcopy	Hardcopy	Softcopy	Hardcopy	Softcopy	Hardcopy
Part I	PRISM	1 set [*]	PRISM	1 set [*]	PRISM	1 set [*]	PRISM	1 set [*]
Part II	PRISM/CD	N/A	PRISM/CD	N/A	PRISM/CD	N/A	PRISM/CD	N/A
Part III			Overview only: PRISM/CD		Overview only: PRISM/CD		N/A	
Part IV			PRISM/CD		PRISM/CD		PRISM/CD	

[#] F: Full route; A: Abridged route; V: Verification route; N/A: Not applicable.

[*] Only documents that require proof of authenticity are required to be submitted in hardcopy for Part I (e.g. CPPs, approval letters not available online, authorization letters, GMP certificate, patent declaration, declaration letters, etc.)

While module 1/ part I must be submitted in softcopy, it must also be submitted in hardcopy, notably for documents that require proof of authenticity, such as letters of authorization, GMP certificates, CPPs, patent declaration forms, and so forth. Official documents issued by other drug regulatory agencies, declaration letters, and patent declaration forms should also be submitted as the original copy. Applicants should also ensure that submitted electronic copies are identical to the hardcopy documents.

For modules 2 to 5/parts II to IV, applicants can opt to attach the documents either in full into PRISM section 7 (Supporting Attachments) or submit the soft copies (e.g. PDF format) in a CD/DVD. However, applicants are advised not to combine PRISM attachments with a CD/DVD submission – i.e. all supporting documents must be attached in PRISM or all supporting documents submitted in a CD/DVD.

To ensure that the dossier is complete, application checklists for both ICH CTD dossier is provided in Annexure 1.[14] Checklist states the required documents for each dossier type and application type. When submitting a CD/DVD, applicants are encouraged to organize the dossier via the CTD format with folders and subfolders and to include bookmarks to facilitate screening/reading of the reports.

Applicants must ensure that access to the CD/DVD is not restricted. If so, the applicant must provide the password(s) to access the CD/DVD contents. Upon acceptance of the application for evaluation, applicants will be notified if additional copies of clinical documents (in CD/DVD) will be required.

4.3 Application screening timeline

The target processing timeline for screening of the dossiers (NDA, GDA) is 25 working days before the first communication, in the form of an input request or acceptance/non-acceptance notification, is issued. The target processing timeline for screening of a dossier submitted under the CECA scheme is 14 working days[15].

The screening timeline begins from the date of the dossier submission, which should be within 2 working days after PRISM submission to prevent delays in the processing of the application. The date of submission will be defined as the date when HSA receives the complete dataset for the application (including all hard copies of original signed documents and CD/DVD- ROMs).

4.4 Evaluation timeline[16]

The target processing timeline for the evaluation of an application is the period from the date of acceptance to the issuance of a regulatory decision letter, excluding all stop clocks. The target timelines for the various evaluation routes are as follows:

The timelines stated (in working days) are subject to change.

Table 5: Evaluation timeline for different dossier type

Dossier type	NDA	GDA
Full	270	NA
Abridged	180	240
Verification	60	120
Verification - CECA	NA	90

4.5 Stop-clock

Stop clocks can occur during the screening and evaluation stages of the application. The stop-clock starts when HSA requests clarification or additional information concerning a product application. The stop-clock period ends when HSA receives a complete and satisfactory response to the query.

5. LABELING REQUIREMENTS

Labeling refers to any printed or graphic information on the immediate container, outer packaging, and any other form of printed material supplied together with the product. The product labels, PI, and/or PIL must be in English. If non-english text is included in the labeling, 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. Information provided in the labels should be consistent with the information submitted in the application dossier. Any deviation should be highlighted and brought to HSA's attention.

5.1 Outer carton and inner/blister labels

The outer carton refers to the product packaging in which the immediate packaging is placed, e.g. the carton box containing blister strips. The inner label refers to the label that is fixed onto the primary container closure system, e.g. the label affixed to a bottle, vial or ampoule. The blister label refers to the foil backing of a blister strip. In addition to the legal labeling requirements, the following information shall be present on the labeling of the product:

Table 6: Fees requirements for different types of applications and licenses

Type of Application				Fees
1.	**Application for a license – NDA & GDA**			
	a)	Screening (Payable upon submission)		
		i.	Abridged/Verification Dossier (NDA & GDA)	$550
		ii.	Full Dossier (NDA)*	$2,750
	b)	Evaluation (Payable upon acceptance)		
		i.	NDA Abridge Dossier (Chemical Drugs & Biologics)	
			• NDA-1 & NDA-2	$11,000
			• NDA-3	$5,500
		ii.	NDA Verification Dossier (Chemical Drugs & Biologics)	
			• NDA-1 & NDA-2	$16,500
			• NDA-3	$5,500
		iii.	NDA Full Dossier*	$82,500
		iv.	GDA Abridged Dossier	

Table 7: Outer carton, inner label, and blister labeling requirements

Sr. No.	Parameters	Outer carton	Inner label	Blister label
1	Product name	✓	✓	✓
2	Dosage form	✓	✓ *	NA
3	Name of active substance(s)	✓	✓	✓
4	Strength of active substance(s)	✓	✓	✓
5	Batch number	✓	✓	✓
6	Manufacturing date	✓	✓ *	NA
7	Expiry date	✓	✓	✓
8	Route of administration	✓	✓	NA
9	Storage condition	✓	✓ *	NA
10	Name & address of product owner and/or product license holder	✓	✓ *	Name/ Logo of Manufacturer/ Product owner
11	Name & address of manufacturer**	✓	✓ *	NA
12	Warnings (if applicable)	✓	✓ *	NA
13	Pack sizes (unit/volume)	✓	✓	NA
14	Special labelling (if applicable)	✓	✓ *	NA
15	Name & content of preservative(s) (if applicable)	✓	✓ *	NA

NA Applicable

* Exempted for small labels such as an ampoule or vial with a nominal volume of 10 ml or less. Other factors may be considered such as the amount of information that needs to appear on the label and the font size necessary to achieve legibility of the information.

** The name and address of either the manufacturer or the batch releaser should be present.

If the product is supplied without an outer carton, the information that is required on the outer carton should be stated on the inner label. Any handwritten information on the specimens, mock-ups, or text is not acceptable, except for statements such as “batch number and expiry dates will be printed” or similar. Email addresses and/or telephone numbers on the product’s labeling may be considered. However, website addresses are generally not allowed unless

adequately justified, for example, in the case where the information is intended for adverse drug reaction reporting.

SUMMARY AND CONCLUSION

Medicines in Singapore are classified as Prescription Only (POM), Pharmacy only (P), or General Sales List (GSL). POMs can only be supplied by a doctor or by a pharmacist according to a prescription by a doctor. P medicines can be supplied by or under the supervision of a pharmacist without a doctor's prescription, while GSL medicines can be purchased off the shelves.

Approval for the above classified medicinal products can be approved by HSA under two major applications.

1. NDA (New Drug Application)

- NDA-1
- NDA-2
- NDA-3

2. GDA (Generic Drug Application)

- GDA-1
- GDA-2

The above applications are discussed under the discussion & result section. Registration dossiers are submitted through these pathways to receive marketing authorization and registration dossiers should be in a CTD format. The CTD provides a common format for the preparation of a well-structured submission dossier. It uses a modular framework described in ICH (International Conference Harmonization) topic or the ASEAN (Association of Southeast Asian Nations) guidelines on the common technical document for registration of pharmaceuticals for human use.

Applicants should note that they are responsible for the medicinal product's quality, efficacy, and safety throughout its life cycle. What this means is that the applicant's responsibilities

start with the registration of the medicinal product and end when the product license expires or is canceled. Since the product's quality, efficacy and safety can change at any time during its life cycle, it is the applicant's responsibility to inform HSA when these changes occur as per the current guidelines.

The applicant's responsibilities include:

I. To ensure that all of the information given in the application form and supporting documents are valid and that all current data, reports and information relevant to the benefit/risk assessment of the medicinal product have been supplied at the time of the application submission;

II. To ensure that all information and material included in the application dossier on paper exactly matches the information and material included in the electronic submission dossier. No information has been added, removed, or changed;

III. To declare at the time of submission to HSA that the application submitted to HSA has not been rejected, withdrawn, approved via appeal process or pending deferral by any drug regulatory agency or HSA reference regulatory agencies, with reasons in each case if applicable;

IV. To notify HSA of any change in the information submitted in the application and of any new significant safety information during evaluation and throughout the product's life cycle in the Singapore market;

V. To notify HSA if the application submitted to HSA has been rejected, withdrawn, or deferred by any drug regulatory agency or HSA reference regulatory agencies, with reasons in each case if applicable, throughout the product's life cycle in the Singapore market;

VI. To respond to HAS's queries or requests for more data for review, within the timelines stipulated by HSA;

VII. To ensure that the product will be sold, supplied, and recommended for use following the approved PI/PIL (Package Insert/ Patient Information Leaflet) and in compliance with all license conditions, applicable legislation, and guidelines;

VIII. To ensure that all post-approval licensing conditions attached to the product license and post-approval commitments are fulfilled within the stipulated timelines;

IX. To notify HSA of any changes to the product's quality, efficacy, or safety throughout the product's life cycle in the Singapore market;

X. To notify HSA if the product's marketing authorization is withdrawn by any drug regulatory agency or the product is no longer registered in any country, with the reasons in each case, throughout the product's life cycle in the Singapore market; and,

XI. To ensure that all information provided to HSA is true and correct to the best of his/her knowledge and that he/she has not willfully suppressed any material fact. The applicant is aware that if he/she makes any false statement, representation or declaration in connection with an application submitted to HSA, he/she shall be guilty of an offense under the Medicines Act.

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