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Lifestyle Diseases Possessing Threat to People of Malaysia and Drug Product Registration

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ABSTRACT

The increasing incidence of Lifestyle Diseases has much concern on the maintenance of well-being of many people. Present day around 60% of the people are prone to be suffering by these diseases and the ASEAN region is having higher incidence of occurrence of these diseases, with maximum growth reported in the grey population which nearly accounts for the 60% of the population in the region. The effect of changes of lifestyle had direct impact on the wellness of the people in this region. The ASEAN region is marked by continuous growth in the pharmaceutical segment with maximum growth recorded in the generic sectors which are rapidly progressing with profits. The ASEAN Region is considered as a destination of value for the money, emergent region with the promising profits for Pharmaceutical industry. The value for the generics is ever demanding and increasing with many manufacturers setting up their industries or forming collaborations with firms present in the local market. Nowadays there is considerable shift in the use of medicines from innovative medicines to Generic medicines, as these are easily affordable and available. Since the lifestyle diseases are of prime concern the regulations need to be understood and followed. The present study focuses on the incidence of these diseases in the region and the regulations that are followed by each country in order to get the Generic products registered, and also highlights the special regulations that are applicable for the generic drugs that are used in the treatment of the lifestyle diseases.

INTRODUCTION:

This study mainly centres on the registration requirements of Generic drugs used in treatment of Lifestyle diseases. Present day whole world is trying to tackle the issue of NCD (Non communicable diseases) which are the group of diseases which arise out of changes in the lifestyle[1]. Presently there is notable shift of the diseases from being infectious to a life style disease. In the South-East Asia Region there is a great concern about the growing incidence of Non-communicable diseases, or **NCDs**. Among these, cardiovascular diseases account for the largest share of **NCD** deaths. Today, non-communicable diseases, mainly cardiovascular diseases, cancers, chronic respiratory diseases and diabetes represent a leading threat to human health and development. These four diseases are the world's biggest killers, causing an estimated 35 million deaths each year - 60% of all deaths globally - with 80% in low- and middle-income countries[2]. In 1998 alone NCD contributed to 60% of deaths alone in this region. By 2020 these diseases are going to be known as diseases of concern.

The core lifestyle diseases possessing threat to people of Southeast Asia are the following diseases:

1. Cardiovascular Diseases
2. Diabetes Mellitus.
3. Cancer

The aforementioned diseases are caused mainly due to changes in the lifestyle and nearly effecting 73% of population in this region. The life style diseases like oncology, cardiovascular, diabetes give a wide choice for the companies to work for the investigation of the new drugs and enmasse production of Generic Drugs, thereby resulting in the procuring of medicines by the patients who can afford a premium price[3]. The most common and serious NCD's cardiovascular disease, cancer, and diabetes mellitus are linked by common preventable risk factors related to life style. A third of these deaths are expected to be among middle aged adults under the age of 60 years[4]. The cancer in the South East Asia is more prevalent and is expected to be a matter of high concern in the years to come. There has been a considerable rise in the occurrence of the cancer in this region. The life style drugs contribute much betterment for the people suffering from the various life style disorders[5,6] .

Selection of Market:

The process of getting approval and the timelines associated with the approval play a crucial role in the process of establishing a product of a pharmaceutical company in a particular market region and segment. The selection of the particular region for the launch of a product will have a substantial impact on the sales and profit of the market as the product manufacturers are always faced with the time constraints and the timeline matters. Timelines in turn are a matter of concern to the company as more the time it takes for the approval of a drug more delayed it gets for the launch of the product and in turn leads to loss of the capital to the manufacturer. The availability of the medicines and the accessibility of them make the growth of the pharmaceutical manufacturing companies as well as establish a product in the mind of the consumers.

Malaysian pharmaceutical market is projected to grow at a healthy rate. The market is small and relies heavily on the imported medicines. The medicines imported by the multinational companies command a lion's share of the market at over 70% in value terms. Free trade agreements with the Malaysian regulatory authority shall render the import of the products more easily.

In the 10 years from 1996 to 2006, there was an 88% increase in the incidence of diabetes in Malaysia and a 43% increase in high blood pressure cases. 70% of the drugs that treat these and other non-communicable as well as infectious diseases in the country are imported. The multinational pharmaceutical companies responsible for developing these treatments take on average 13 to 15 years to produce one drug, at a cost of about US$1.3 billion.

Malaysia is heavily dependent on the import of the retail medicaments representing over three quarters of the total imports. The increase in the incidence of the life style diseases will certainly find a significant place for the manufacturers as well as the importers. The amount of money spent on the health care is increasing by 13% every year, which is an indicative of the increasingly healthy lifestyle. The multinational companies reign for the branded and the ethical drugs.

The key contributors for the growth of the pharmaceutical industry are:

- Value for money destination with world class health and medical facilities.

- **Market for the generic products:** in keeping with pace with the global trends, the patent expiry of blockbuster drugs, coupled with the government support and rising health care costs, is likely to spur the demand for the generic products.

- **Specialist driven market:** the greater incidence of the top five diseases related diseases and the booming biotechnology industry will facilitate the rise of the market for the specialist therapies.

- **Demand for the generics:** The demand for the generics is on the rise and the government continues to be the major purchaser of the generic products in order to reduce of the health care financing. The increase in the public hospital has generated the demand for the generics as well.

Trade Opportunities:

The Pharmaceutical sector relies heavily on the imported products, which are fulfilling 70% of demand of the local market, as the Malaysians place a higher trust in the imported brands. The major market holding drugs in the Malaysia are the ***Life style drugs*** such as ***cholesterol lowering drugs***, and ***anti-diabetic drugs***, supplements to treat ***Erectile Dysfunction***, ***cardiovascular drugs*** and ***oncology products.***

Malaysian government initiatives are as follows:

1. Financing schemes for R&D.
2. The industrial master plan 3 (IMP-3).
3. The PICS.
4. Intellectual property protection.

Opportunities in the Malaysia pharmaceutical industry:

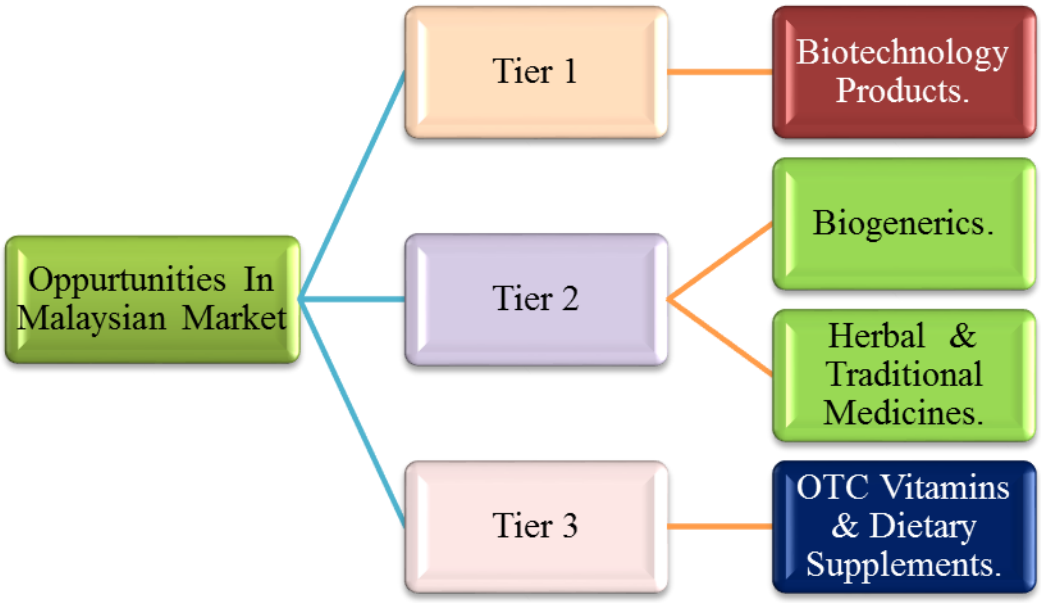

Figure 1: Opportunities in Malaysian Pharmaceutical Industry

Drug product registration in Malaysia

The different procedures applicable to the drug product registration are given in the guidance document released by the Malaysian government for the facilitating the drug manufacturers and their agents to follow the guidelines and to give them an idea about the drug registration procedure.

The daily operations of the drug registration and cosmetic notification, together with the monitoring and surveillance activities have been delegated to National Pharmaceutical Control Bureau (NPCB). Regulation 7(1)(a) of the Control of Drugs and Cosmetics (Amendment) Regulations 2006 requires all products to be registered with the DCA prior to being manufactured, sold, supplied, imported or possessed or administered, unless the product is exempted under the specific provisions of the Regulations.

Any drug in a pharmaceutical dosage form intended to be used, or capable or, purported or claimed to be capable of being used on humans or any animals. Whether internally or externally, for a medicinal purpose is required to be registered with the DCA.

Procedure for the registration of the New Application:-

There are three types of applications for the registration of the drugs, which are as follows:-

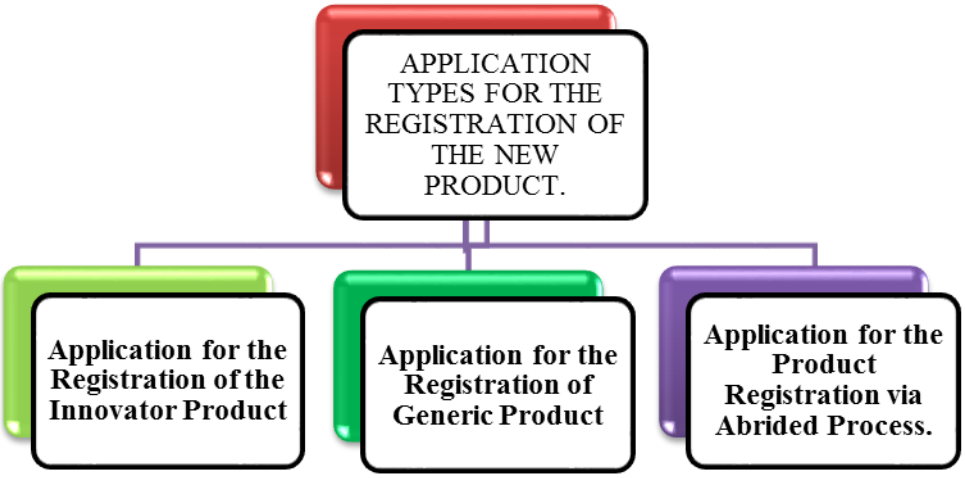

Figure 2: Categorization of applications

1. Application for the innovator product can be filed in the following conditions;

➢ Containing New Chemical Entity,

➢ Containing a new combination of the new combination of existing chemical/biological activity,

➢ Containing present chemical entity for use by a different route of administration

2. Application for the generic product,

3. Application for the product registration via abridged procedure.

Registration of the drugs by the overseas company:

➢ All the products must be registered with the drug control authority before it can be marketed.

➢ For a foreign company wishing to bring the company into Malaysia it should appoint a local agent to carry out the works of the company.

➢ The appointed agent is responsible for all the matters pertaining to the registration of the products.

➢ There are specific forms to complete during the process of registration and under the labeling requirements for products registered with the Drug Control Authority, the name and address of the actual manufacturer must be declared on the label.

Procedure of the registration of products in Malaysia:

Currently, only on-line submission is accepted for product's registration. This could be done by through NPCB's website www.bpfk.gov.my. An applicant must buy a membership for Quest before the applicant can proceed with registration. There are several packages available to choose to become a member of Quest. Any assistance/advice shall be forwarded to Digicert Customer Service Department: 03-89928888. Once the applicant has received the user and password from BPFK (via email), he/she will be able to enter the registration site and proceed with online submission. This online registration system is also applicable for NCE and biotech products, traditional registration, re-registration of products and licensing.

Every application for registration shall be accompanied with a processing fee. The amount of fees is as stipulated in The Control of Drugs and Cosmetics (Amendment) Regulations 2002.The DCA will charge any applicant such costs it may incur for the purpose of carrying out any evaluation investigation relating to the registration of any product. Any payment made is **not** refundable once an application has been submitted and payment confirmed. Applications without the correct fees will not be processed.

- Letter of authorization and certificates required;
- Letter of authorization must be valid and should be current at the time of submission.

All the applications for the registration must be accompanied with the following:

1. Letter of authorization from the product owner. (not applicable if the applicant is the product owner);

2. Where a product is contract manufactured, letters of authorization of contract manufacture and acceptance to and from the manufacturer and also each subcontractor, if applicable.

3. The letter of authorization should be on the original letter head of the company, dated and signed by the managing director, president CEO or an equivalent person who has the rights to do so.

4. Acceptance letter from the manufacturer.

5. The letter of authorization and the letter of acceptance should contain both the name of the product, actual plant address of the manufacturer involved in the manufacture of the product.

Imported products requirements:

1. Must accompany with the certificate of Pharmaceutical product (CPP) from the competent authority in the country of origin. (or)

2. Certificate of free sales (CFS) and good manufacturing practice (GMP) from the relevant competent authorities.

3. If more than one manufacturer is involved in the manufacture of the product then the GMP certification should be available for all the manufacturers[30].

Processing of the application

1. Initiation of review

Applications for the review follow a queue system. There is separate queue system for the different categories of the products.

- NCE
- Biotech
- Generics – follow full procedure.
- Abridged procedure (OTC Products)
- Traditional products.

Priority review- granted for the products where it is intended for the treatment of a serious life threatening condition or diseases.

Data requirements:

The data required to support application is divided into following:

- **(Part I)** -- Administrative data

- **(Part II)** -- Data to support product quality
- **(Part III)** -- Data to support product safety and
- **(Part IV)** -- Data to support product efficacy

Data to be submitted would be based on the type of the application as follows:

- Data for the innovator product : **Parts I to IV**
- Generic products : **Parts I, II**
- Abridged procedure : **Part I only**

The explanatory section must be read by the applicant carefully before the filling the application. In some conditions, the Regulatory Authorities would require additional information and it becomes the duty of the applicant to supplement the additional information within the stipulated interval of time.

Part I – Administrative Data and Product Information

Details include:

1. Product name,
2. Dosage form,
3. Formulation (actives. Excipients),

Section A: Product particulars

1. Product Description

- **Visual and physical characteristics** of the product, including where applicable :-

1. Shape,
2. Size,
3. Superficial markings for identification purposes,
4. Colour,
5. Odour,

6. Taste,

7. Consistency,

8. Type of tablet coating,

9. Type of capsule, etc.

10. For the description of the liquids a statement indicating whether it is a solution, emulsion, suspension must be accompanied.

2. Pharmacodynamics & Pharmacokinetics (for full evaluation only)

Comprehensive summary of the pharmacological profile should be provided which includes the following things:

➢ Main and supplementary pharmacological effects (mechanism of action, actions other than the therapeutic effects);

➢ Relevant pharmacokinetics (absorption, plasma-protein binding, distribution, biotransformation, metabolism, excretion, etc.);

➢ Bioavailability and bioequivalence studies in man.

3. Indication/Usage:

The clinical use/uses of the product should be described in the following manner;

- Curative,
- Palliative,
- Adjunctive,
- Diagnostic

4. Dose/dose instruction.

5. Recommended dose & Route of Administration:

The severity, side effects, adverse reactions, toxic effects etc including reactions such as allergy, hypersensitivity, drug dependence, addiction, carcinogenicity, tolerance, liver/Kidney toxicity etc. shall be stated in order.

6. Pregnancy and lactation;

The following data shall be mentioned in the pregnancy and lactation section.

- Conclusions from the animal reproduction/fertility study and the human experience.
- The risk in humans at different times of pregnancy, as assessed.
- Information on the possibility of using the medical product in fertile and pregnant women.

Use in lactation:

- When the active substance(s) or its metabolites are excreted in the milk recommendation as to whether to stop or continue breast feeding, and the likelihood and degree of adverse reaction in the infant should be given.

7. Signs and symptoms

The symptoms of overdose/ poisoning shall be mentioned in appropriate places also including the information suggesting the treatment methods available for the treatment of the overdose and the poisoning.

8. Storage conditions

The recommended storage conditions, temperature, humidity should be mentioned in the appropriate places accompanied by the stability data to support the storage conditions.

9. Shelf life

Shelf life should be supported by the stability data.

Information should also include shelf life before first opening, after reconstitution and/or after opening where applicable. Stability data to support such shelf life should be available.

Suitable evidence is required demonstrate that during the period of the product life that toxic decomposition products are not produced in significant amounts during this period, and that potency, sterility, efficacy of preservative, etc. are maintained.

Section B- Product Formula

This section consists of the following information;

Batch manufacturing formula:

The batch size and the actual manufacturing formula should be given. Data from the validation step shall be captured in terms of substance name, type (active or excipient ingredient), function and quantity per unit dose.

Manufacturing process:

The brief description of the manufacturing process should be entered. Essential parts of each manufacturing process should be covered. A brief description of final assembly of the product into the containers also should be mentioned. If the product is repacked/assembled by another manufacturer, details of repacking/assembly and quality control must be supplied.

In- process Quality control, Finished Process Quality Control (for abridged evaluation only):

Includes the summary of the tests done at various stages, frequency of the sampling, number of the samples taken at each time, specifications for quality assurance of the product should be supplied.

Stability data (for abridged evaluation only):

Reports of the stability data providing the details of the batches placed under the studies, containers/packaging type, conditions of storage during study (temperature, humidity, etc) duration of study and frequency (interval) of the tests/observations, and the tests performed (including degradation products being monitored) and acceptance limits.

Section C: Particulars of Packing

The details of the packing should include the following information:

- The selected pack size of the container and fill details by weight, or volume or quantity.
- Selected container type, barcoding, recommended distributors price, retail price.

Table 1: *Section D* Label mock-up for immediate container, outer carton and proposed package insert

SLNO	PARAMETERS	Unit Carton	Inner labels	Blister/ strips
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.	Expiration date	✓	✓	✓
8.	Route of administration	✓	✓	**NA**
9.	Storage condition	✓	✓*	**NA**
10.	Country's registration number	✓	✓*	**NA**
11.	Name & Address of Marketing Authorization (Product Licence) Holder	✓	✓*	Name/Logo of Manufacturer/ Product Owner
12.	Name and address of the manufacturer	✓	✓*	**NA**
13.	Warnings	✓	✓*	**NA**
14.	Pack sizes	✓	✓	**NA**
15.	Name and content of the preservative where present.	✓	✓	**NA**
16.	Name & content of alcohol where present.	✓	✓	**NA**
17.	Declare source of ingredients derived from animal origin, including gelatin (active, excipient,	✓	✓	**NA**

	and/or capsule shell).			
18.	Recommended daily allowance (RDA) for vitamins/multivitamins/ mineral preparations used as dietary supplements.	✓	✓	**NA**
19.	Words like keep out of the reach of the children both in Malaysian and English.	✓	✓*	**NA**
20.	Other country specific labelling requirements	✓	✓*	**NA**
21.	The words like controlled medicine(for scheduled poison only)	✓	✓*	**NA**
22.	Security label	✓	✓	**NA**
NA- Not applicable, * exempted for small labels, ** for multivitamins, minerals preparations, it is suggested to label as multi vitamins and minerals.				

If the product is without label, the inner label should bear all the information required.

Information not to be mentioned on the label;

1. Official website of the company.

2. Website for any purpose of product promotion from the MAH/ product owner /manufacturer is not allowed to be printed on the product label.

Labelling for the products containing following classes of the drugs;

Labelling for the oncological products:

Ex; Methotrexate 1000 mg

FOR THE ONCOLOGIST'S USE ONLY
(BAGI **PAKAR ONKOLOGI MENGGUNAKAN SAHAJA)**

The label should contain a box warning stating that the products is for the treatment by the oncologists only.

FOR THE SPECIALIST'S USE ONLY

(UNTUK KEGUNAAN HANYA PAKAR)

Labelling for the cardiovascular products:

Ex; Amiadarone

Labelling for the Anti-Diabetic products

Ex; Metformin.

FOR THE SPECIALIST'S USE ONLY

(UNTUK KEGUNAAN HANYA PAKAR)

Package insert information;

1. Brand or product name.
2. Name and strength of active substance.
3. Product description.
4. Pharamcodynamics/ pharmacokinetics.
5. Indication
6. Recommended dosage.
7. Mode of administration

8. Contraindications

9. Warnings and precautions

10. Interactions with other medicaments

11. Statement on usage during pregnancy and lactation

12. Adverse effects/ undesirable effects

13. Overdose treatment

14. Incompatibilities (for injections only)

15. Storage conditions (not required if mentioned on the outer label)

16. Dosage forms and packing available.

17. Name and address of the manufacturing/ marketing authorization holder

18. Date of revision of package insert.

Package inserts are required for the products classified as controlled poisons, also submitted for OTC products. If the product is sold in retail without the PIL the information should be mentioned on the outer label and it should be conspicuous enough to be readable by a person without any difficulty[31].

Supplementary information;

1. Summary of product characteristics if any, PIL approved by the county of origin should be submitted with the application.

2. Documentary evidence of nature and extent of the patents and the details of the holder of the patent.

For the quality guidelines, non-clinical guidelines, clinical documentation Malaysia Regulatory authorities follow **ASEAN** guidelines.

Generic Drug Registration

Step 1: Applicant submits application with data completely filled in it, and submitted within 30 days. The submitted application is screened by unit head to verify the completeness of

application. If the application is not complete the applicant has to submit the completed application within 30 days.

Step 2: Once the application is screened to be complete for the data submitted the application is accepted and approved for the payment fee. Once after the approval the applicant has 14 days to make the payment, if not the application is rejected and once again the applicant has to file the application as new application.

If the applicant does not submit the application within the due response time the details are deleted from the database and application has to be resubmitted freshly again.

Bioequivalence (BE) Study Requirements for Generic Product:

In general, for a second source application of a generic product (immediate release, oral solid dosage form), BE study report from the actual manufacturing site must be submitted during the submission of application for registration. The base of this requirement is due to the difference in manufacturing site from the first source that may change the characteristic and specifications of a second source product.

Bio-waiver:

Bio-waiver is considered in following cases:

If comparative dissolution profile (CDP) report against the registered first source product is submitted as surrogate to BE study conducted for the second source product and meeting the following cases:

- BE study conducted using the registered first source product, after it has been found satisfactory by NPCB.

- The second source product is the same as registered first source product used in the bioequivalence study in terms of:

i) Product formulation;

ii) Equipment used in the manufacturing process;

iii) Source and supplier of raw material;

iv) Quality control and specifications of raw material;

v) Manufacturing process of product and standard operating procedures;

vi) Environmental conditions during the manufacturing process of product;

vii) Quality control and specifications of finished product.

Comparative Dissolution Profile must be conducted in accordance to ASEAN Guidelines for the Conduct of Bioavailability and Bioequivalence Studies including the calculation of similarity factor (f2) to prove the similarity of these two products.

Process validation has been conducted on 3 pilot or commercial batches of the second source product and found satisfactory by the NPCB[32].

Application review process

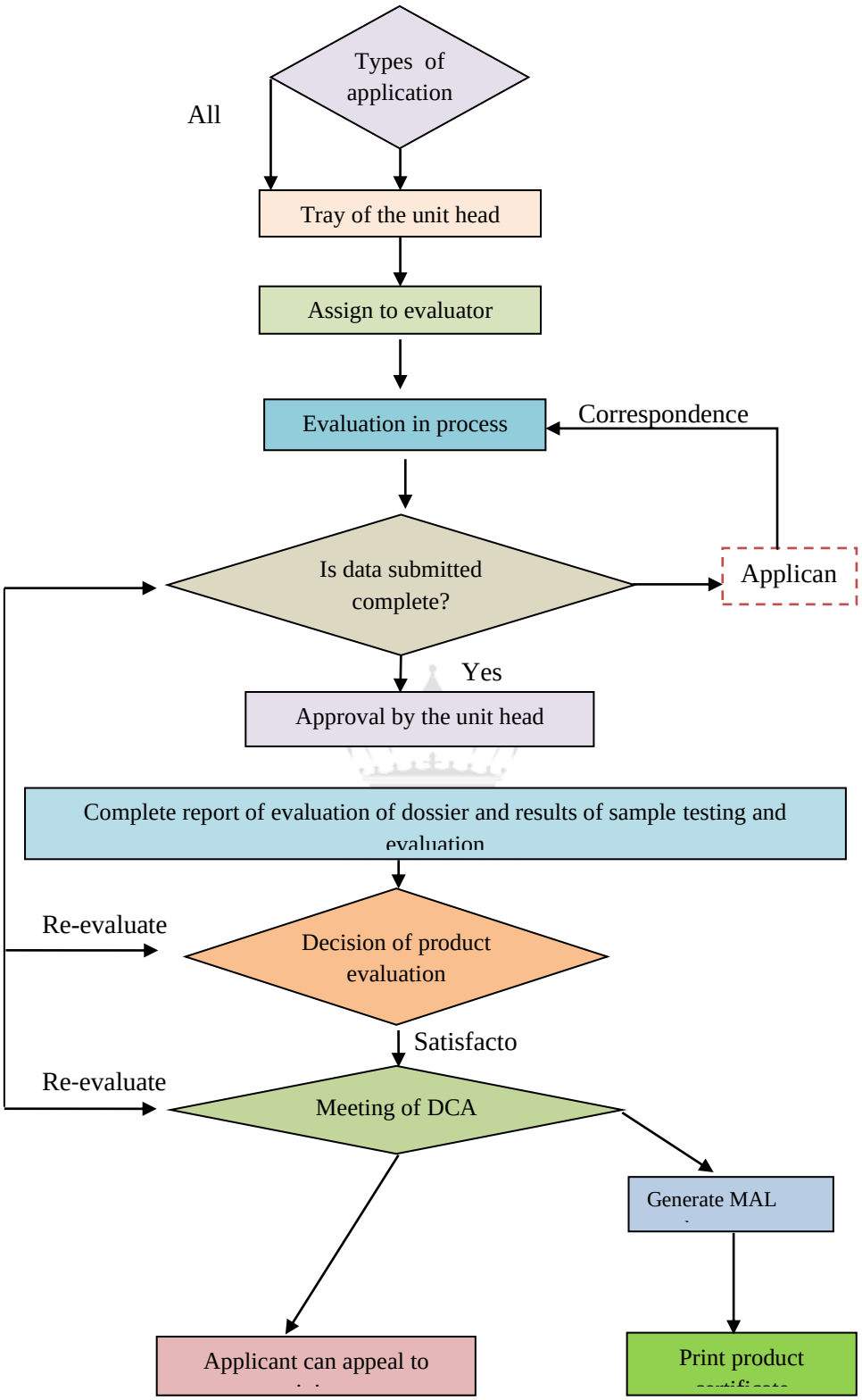

Figure 3: Review of the Application

The present work vehemently gives a picture of the lifestyle diseases scenario in the region and revolves around the submission methodology followed for the generic drugs that are used in the treatment of Lifestyle diseases disorders. Present day the more focus lies in tackling of the situation of lifestyle diseases and more emphasis is on the use of Generic drugs which are less expensive for the manufacturers and more affordable by the patients.

Maximum share of market is governed by the generic drug and more manufacturers are considering in investing in the generic sector rather than innovative sector. The choice of Southeast Asia as a platform for the business is considered as a golden bowl for the manufacturers as well as importers. The main to the point reason for considering Southeast Asia as a destination for the market is ever rising GDP and government initiatives by the nations respectively.

ASEAN region as it is famously known consists of 10 nations namely Indonesia, Malaysia, Thailand, Singapore, Philippines, Vietnam, Brunei, Laos, Myanmar and Cambodia. Of the above listed countries first five countries command a good share in generic sector, steadily growing economies, rest five countries lack certain resources and are hampered by certain constraints such as lack of support from the government, lack of industries manufacturing the medicines, and more reliability on traditional medicines which are of no match to the ones which are manufactured in the industry.

This region is ear marked to have high percentage of grey population with age over 65 and growing incidence of **lifestyle diseases** and ever increasing expenditures on the lifestyle disease treatment, thereof providing a chance for Pharmaceutical manufacturers to explore the market and gain much out of it.

Outcome

The present study helps in the following manner:

- **Assess** future market values with unique and regularly reviewed independent market forecasts.
- **Track** the latest developments with the news service that is included for every country.
- **Understand** the critical issues and drivers which are shaping the market.

- **Evaluate** the environment for branded and generic operators and stay in touch with the fast growing generic sector.
- **Shape** and support business plans and decisions with reliable regulatory data.
- **Benchmark** key market performance.

The markets in ASEAN region are purported to have the cumulative pharmaceutical value of **Billion 80$**.

The process of getting approval and the timelines associated with the approval play a crucial role in the process of establishing a product of a pharmaceutical company in a particular market region and segment. The selection of the particular region for the launch of a product will have a substantial impact on the sales and profit of the market as the product manufacturers are always faced with the time constraints and the timeline matters. Timelines in turn are a matter of concern to the company as more the time it takes for the approval of a drug more delayed it gets for the launch of the product and in turn leads to loss of the capital to the manufacturer. The availability of the medicines and the accessibility of them make the growth of the pharmaceutical manufacturing companies as well as establish a product in the mind of the consumers.

The market selection affects the sales to the larger extent as market is the main zone for the passage of the drugs from the manufacturer to the consumer. ***The understanding of the diseases in the particular region and launching a product to address an issue rising out of the region wise will help the drug manufacturer to accommodate a product in the market.***

Though getting the approval is a herculean task, the fruits borne out of the approval will be in form of the turnover generated and the sole contributor shall be the Market itself. South East Asian market is one of the most promising markets in the Asian region because of its wider population and good regulatory practices differing slightly in some parameters, as well as the pricing, making it one of the favourable destinations for the manufacturers and creating a best platform for the product development.

REFERENCES:

1. Ames G. Asia's Emerging Pharmaceutical Markets: A look at China Indonesia, Thailand, Philippines and Malaysia. Pacific Bridge Medical.

2. Generic Drugs. Drug Development, approval processhttp://www.fda.gov/downloads/Drugs/DevelopmentApprovalProcess/SmallBusinessAssistance/ucm127615.pdf .
3. The national agency of Drug and Food Control. http://www.pom.go.id/pom/profile/e_fungsi_badan_POM.php.
4. Decree of the head of national agency of drug and food control, republic of Indonesia- criteria for the registration of Drugs in Indonesia. [http://www.pom.go.id/public/hukum_perundangan/pdf/SK_KBPOM_HK.00.05.3.1950E.PDF.
5. The current status of clinical trials in Indonesia. Drug Information Journal. http://www.diahome.org/Tools/Content.aspx?type=eopdf&file=%2fproductfiles%2f8357%2fdiaj_12638%2Epdf.
6. Indonesian Drug Regulations. http://www.usdaindonesia.org/public/uploaded/Tata%20Laksana%20Pendaftaran%20Pangan%20Olahan%20(translation).pdf.
7. NA-DFC Registration procedure and technical Requirements for the drugs. http://www.pom.go.id/nonpublic/obat/e_default.asp.
8. WHO drug incentives: The case of ASEAN. WHO. http://www.who.int/intellectualproperty/studies/Drugregulationincentives.pdf.
9. Lin Hui Tham, Izatulshima Yahya. Malaysian Pharmaceutical outlook 2008. Frost and Sullivan. http://www.frost.com/prod/servlet/market-insight-top.pag?docid=126369590.
10. Lim GCC. Cancer in Malaysia- there is light at the end of the tunnel. Med J Malaysia 2003;58(5):632-5.
11. Gerard Chin Chye lim. Overview of cancer in Malaysia. Japaneese J Oncol. 2002;32(1):537-42.
12. National Pharmaceuticals Control Bureau: Regulatory Guidelineshttp://portal.bpfk.gov.my/index.cfm?&menuid=124&parentid=82
13. Terms of Reference. Drugs Control Authorityhttp://portal.bpfk.gov.my/aeimages//File/DCA/DCA_Term_Of_Ref_modified.pdf (Drugs Control Authority, Ministry of Health, Terms of Reference.)
14. Drug Registration Guidance Document. National Pharmaceuticals Control Bureau. http://members.wto.org/crnattachments/2010/tbt/MYS/10_3222_01_e.pdf.
15. Paul Russel, Neeranard Jinachai. Regulatory overview of Thailand Drug Registration procedure. Pacific Legal consulting group. http://www.pacificlegalgroup.com/249_255_Thailand.pdf.
16. A review of heart diseases in Thailand. Vejthani Hospitals. http://www.heartsurgery-asia.com/.
17. Prevalence of Non Communicable Diseases in Nepal. Nepal health research council