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A STUDY ON VARIATIONS IN PHARMACEUTICAL PRODUCTS IN PHILIPPINES AND VARITAION POLICIES IN US, CANADA, AUSTRALIA

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ABSTRACT

The present study focuses on pharmaceutical product variations in Philippines including procedure and timeline and variation policies in US, Canada and Australia. Different countries follow different variation guidelines, Selection of regional guideline forms distinct working strategy which affects the country specific timeline for the variation filing. Philippines follows ASEAN variation guideline and having shorter timeline and procedure as compared to developed countries like US and Canada, conditions and documents based system is followed by Food and Drug Administration Philippines, only well justifiable application subjected to FDA Philippines get access through approval process. Amidst the developed countries like US, Canada& Australia, Australia is having less time consuming procedure and less types of application filing procedure. Whereas US and Canada have vast types of application filing procedure and the level of general consideration for risk and threats correspondence to safety and efficacy of pharmaceutical product is quite high as compared to least developed counties and other developed countries. This article gives a comprehensive review of types and procedure for variation filing in Philippines and policies followed for the same in US, Canada and Australia.

Key words: Variations in Pharmaceutical Products, Philippines, Variation Policies

INTRODUCTION

Philippines are a country associated with ASEAN, according to economy Philippines comes third among ASEAN countries. For Pharmaceutical industry ASEAN market is like oyster gives the pearl.

ASEAN – A PROMINENT PHARMACEUTICAL MARKET

Healthcare has been designated a priority sector for the ASEAN countries for several years. With a population of more than 600 million, this market represents another fastest growing market. In general, the market has become more attractive in recent years as the earning has increased and country governments have made health care sector growth a priority.

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Country governments are actively increasing investments in the sector, and opportunities for contract manufacturing have risen. Regional sales of pharmaceuticals in Asia have more than doubled from $97 billion in 2001 to $214.2billion in 2010. It is predicted that sales will reach $386 billion by 2016.

PHILIPPINES PHARMACEUTICAL MARKET

The Philippines has a large population (92 million according to its 2010 census) and they have similar trends in the rate of chronic disease as Indonesia. But due to the Universally Accessible Cheaper and Quality Medicines Act of 2008, the market for pharmaceuticals has noticeably changed. The Philippines pharmaceutical market is valued at $1.4 billion in 2008, equal to nearly$15 per capita. In terms of the overall market this is comparable to Pakistan and Thailand, and in per capita terms similar to China and Iran. It will be the ninth largest pharmaceutical market in the Asia Pacific region by 2016.The Philippines has some of the highest drug prices in the world having USD3.25billion in 2013, rising to USD 3.30billion in 2014.The Philippines' market for pharmaceutical products is growing at its fastest pace in years, at about 13 percent annually. By 2014, experts

shows the sign that it will have a value of $4 billion. This would make the drug market in the Philippines almost as large as those of Indonesia or Taiwan. This would make the drug market in the Philippines almost as large as those of Indonesia or Taiwan. Foreign pharmaceutical companies are the main players in the Philippines. In 2012, they captured three quarters of the Filipino drug market. [1-3]

PHARMACEUTICAL PRODUCT REGISTRATION IN PHILIPPINES

Industries involved in the manufacture, distribution, retailing, import, export and packaging of drugs in the Philippines must have a License to operate before they are eligible to register pharmaceutical products with the Filipino Food and Drug Administration (FDA). LTO applications take between one and two months to gain approval. This license to operate is exactly a local agent or company who is registered with Philippines regulatory authority and exporters do all activities on behalf of them. For pharmaceutical product registration in Philippines this submission is necessary. Products with new chemical entities cost $465 each to register and registration validity is for three years. Of the more than 525 drug traders, 690 drug importers and 5,100 drug distributors in the Philippines, three quarters of the top companies are foreign companies. [4]

FOOD AND DRUG ADMINISTRATION PHILIPPINES

On June 22, 1963 Republic Act No. 3720 was passed into law known as the "Food, Drug and Cosmetic Act". FDA is headed by The Department of Health (DOH) is the principal health agency in the Philippines. It is responsible for ensuring access to basic public health services to all Filipinos through the provision of quality health care and regulation of providers of health goods and services. Regulating several health programmes. [5] Products with new chemical entities cost $465 each to register and registration validity is for three years. Of the more than 525 drug traders, 690 drug importers and 5,100 drug distributors in the Philippines, three quarters of the top companies are foreign companies. [4]

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Changes in active drug substances, Change in formulation, Change in process and formulation, Change in test procedures, Changes in specifications, Changes in packaging material or labelling material, Change in manufacturing sites. [6]

PHARMACEUTICAL VARIATION IN PHILIPPINES

Throughout the life of a pharmaceutical product, the manufacturer or an industry is responsible for the product that is placed in the market and is also required to observe products' technical and scientific progress and data, and to make any revisions that may be required for safety and efficacy issues of pharmaceutical products and to coordinate with pharmaceutical regulatory authorities. Such amendments have to be approved by the Drug Regulatory Authority. In Philippines FDA is responsible for variation acceptance procedures. Mainly application would be made for implementation or change in pharmaceutical product. It may be post or prior.

Variation

Variation to a registered pharmaceutical finished product that may affect significantly and/or directly the aspects of quality, safety and efficacy and it does not fall within the definition of minor variation and new registration. Another type of variation is called as minor variation which may be applied before product is approved which is called as Prior Approval and if applicant has to just notify about changes then it is called as minor variation notification, Minor variation is variation which have minimal significant effect on aspect of quality, safety, efficacy of the product. Generally variation in Philippines is clarified as a possible threat in products which negatively affect on patients or public figure dealing with their safety. In case of efficacy it may be threat to own organisation as well as regulatory authority. For Philippines which is collaborated to ASEAN variations are likely to be these:

- Change of content of product labeling, which may be in any matter.
- Addition or replacement of the manufacturing site of the drug product. Especially in case of exporters.
- Change and/or additional indication/dosing population/inclusion of clinical information extending the use of the product.
- Change and/or addition of alternative manufacturer/site of drugs. Like loan-licence work.
- Addition or replacement ofthe alternative site for the primary packaging.
- Change of the specification drug substance and/or drug product.
- Change of batch size of sterile drug product.
- Change of batch size of non-sterile drug product.
- Major change in the manufacturing process for the drug product.
- Qualitative or quantitative change of excipients.

- Quantitative change in the coating weight of tablets or weight a capsule shell for modified release oral dosage form.
- Change in primary packaging material for sterile product, which may include type of container, inclusion of primary packaging material.
- Change or addition of pack size/fill volume and/or change of shape or dimension of container or closure for sterile solid and liquid drug product.

Procedure and timeline

Once the applicant files application for changes or variation to the regulatory authority, officer makes proposed assessment and if any revision needed again sent to applicant, and if passed then declaration letter undersigned by the head of regulatory officer is allotted.

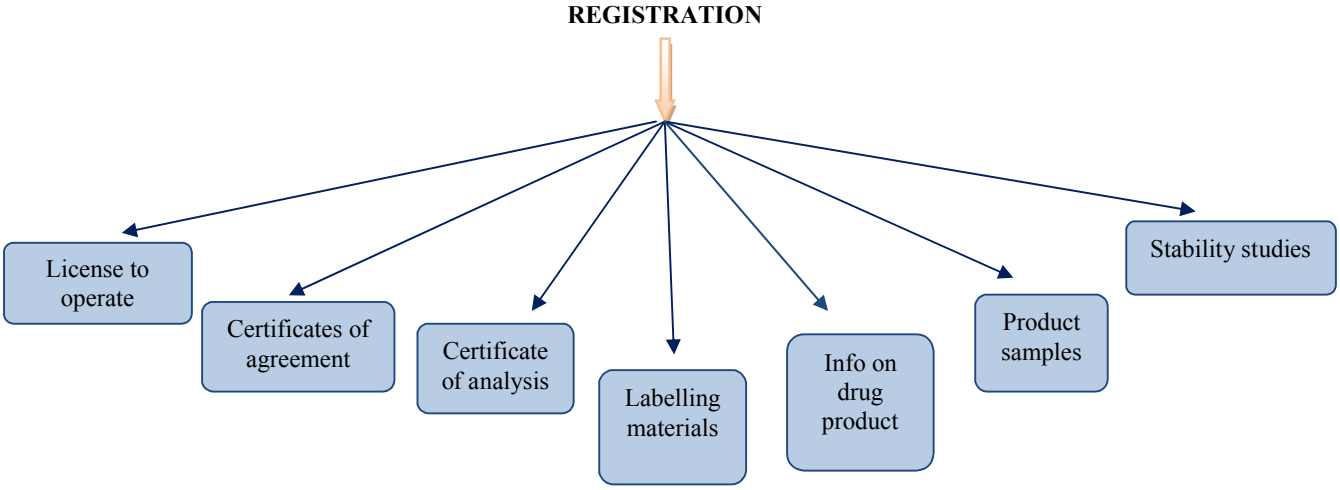

Figure 1: Product registration requirements

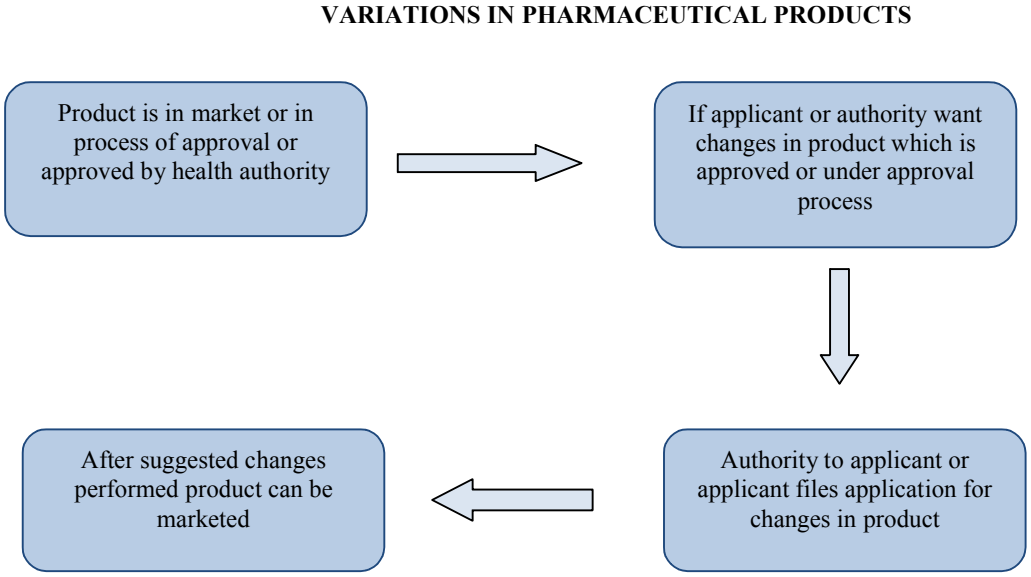

Figure 2: General process for variation filing

Table 1: Types of variations and filing procedures in Philippines

Type of variation	Minor variation notification	Minor variation prior approval	Major variation
Procedure	Notification, "Do & Tell" If the notification fulfils the requirements, then variation is approved.	If the application fulfils the requirements as per described by FDA Philippines, then only variation is approved.	If the application fulfils the requirements as per described by FDA Philippines, then only variation is approved.
Timeline for the Drug, Regulatory Authority to evaluate the variation application	Within duration subject to FDA Philippines, For a valid notification.	Within duration subject to FDA Philippines, For a valid application.	Within duration subject to FDA Philippines, For a valid application.

This table gives detail information about procedures and timelines for variations which are to be followed for approval of variation filing as per FDA Philippines. [7]

Table 2: Variation policies in US, Canada & Australia [8-10]

Country	USA	Canada	Australia
Types of application	IND, NDA, ANDA,OTC, BLA, DMF	New Drug Submission, Supplement to New Drug Submission, Supplement to New Drug Submission, Abbreviated New Drug Submission, Supplement to ANDS, Notifiable Change, Clinical Trial Applications & Amendments, Periodic Safety Update Report-Confirmatory	Category I: New dosage forms, new generic drugs Category II: when application has been previously approved in two acceptable countries which are Canada, Sweden, UK, Netherlands & USA. Category III: medicines already included on the Australian Register of Therapeutic Goods.
Procedures	Major changes: Tell, Wait & Do, Require approval by FDA prior to Distribution Of drug product made using the Change. Moderate changes: Tell & Do, Distribution can occur when FDA receives the supplement, Minor changes: Do and Tell, Shall be notified within 12 months from the date of implementation	Level I major quality changes: to have adverse effect. Level II Notifiable changes: which have moderate potential to have ADE on the quality, safety, purity of the drug. Level III Minor quality changes: Changes that have minimal potential to have ADE on the quality, safety, purity of the drug and Level IV Records of changes: Not expected to have adverse effect, Screening of application takes around 45 working days	Part I: Non-assessable changes, which do not affect on safety and efficacy Part II: self assemble changes, TGA considers to be minor but have effect on safety, quality, efficacy, and do not require prior approval. Part III: changes which can cause significant effect on quality, safety, efficacy of the drug, category III application is required.

CONCLUSION

On the basis of this study it can be manifested that in this decade Philippines has tremendous market for pharma sector attracting exporters with straight forward and distinct product registration process, indeed strict regulation is followed by FDA Philippines. Alike the product registration process, variation filing process is also concise and prominent. In case of variation filled in Philippines, FDA Philippines is supposed to criticise over the application within a short period of time. Due to shorter evaluation time period and simple application procedure, final timeline and procedure converts into a less time consuming process. This may be the advantage when dealing in pharma sector with ASEAN countries specially when filing a variation. In case of developed countries like US, Canada and Australia which already have a long application classification for fresh ones and further procedure for variation filing is much more complex as the proper assessment is made by authorities for consideration of risk associated with variation in products, and then application comes to the main stream of process for variation approval. This may be time consuming for the products which are already in market.

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