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PREREQUISITES FOR PHARMACEUTICAL VARIATION IN PRODUCTS FOR PHILIPPINES

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ABSTRACT

Human error have the tendency to generate mistakes which is called as pharmaceutical variation in pharmaceuticals. To minimise or correct this changes, variation filing is done by correspondence which is very consuming pathway. One can find out prerequisites very helpful to prepare in advance for variation filing. Prerequisites are set of documents prepared to overcome from the wait and watch policy. These prerequisites may be of any types according to the variation. General prerequisites are supposed to accelerate the filing process like variations for labeling, DMF, changes in manufacturing process, all the quantitative changes. Any kind of prerequisite can be developed as per variation encountered. If prerequisites are followed, the output will be speedy for overall marketing process. The present article describes some of the prerequisites for variation filing for Philippines.

INTRODUCTION

ASIA AN EMERGING PHARMACEUTICAL MARKET ^[1]

With a population of more than 600 million, this market represents another rapidly growing emerging market. The market has become more attractive in recent years as wages have risen and country governments have made healthcare sector growth a priority. Country governments are actively pushing investments in this sector, since opportunities for contract manufacturing has risen. Regional sales of pharmaceuticals in Asia have more than doubled from \$97 billion in 2001 to \$214.2 billion in 2010. It is predicted that sales will reach \$386 billion by 2016.

PHILIPPINES- PROMINENT PHARMACEUTICAL MARKET ^[2, 3]

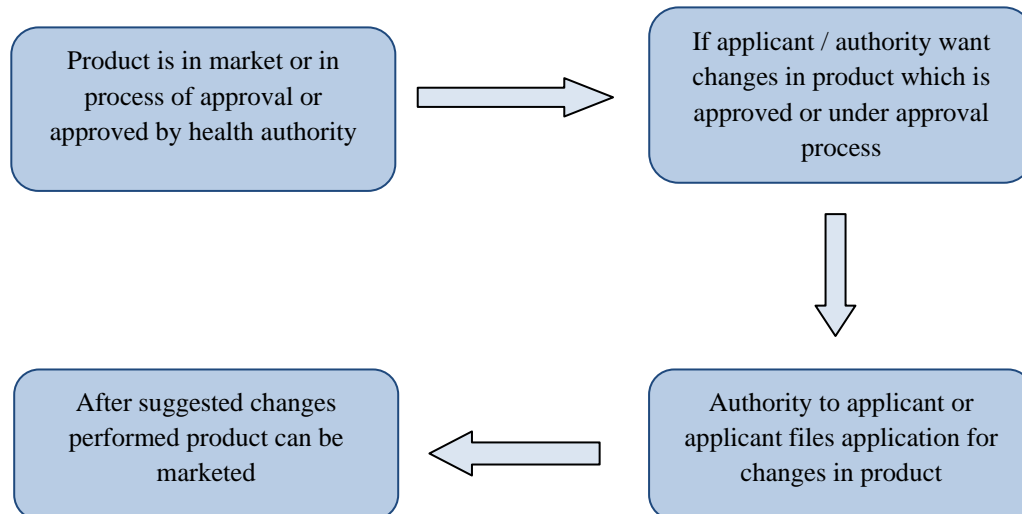
The market is expected to be especially volatile in the 2008-2010 periods. The Philippines pharmaceutical market is valued at \$1.4 billion in 2008, equal to nearly \$15 per capita. The overall market this is comparable to Pakistan and Thailand, and in per capita terms similar to China and Iran. It will be the ninth largest pharmaceutical market in the Asia Pacific region by 2016. The Philippines is having highest drug prices in the world having USD 3.25billion 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. Foreign pharmaceutical companies are the main players in the Philippines. In 2012, they captured three quarters of the Filipino drug market

REGULATORY AUTHORITY OF PHILIPPINES ^[4]

FOOD AND DRUG ADMINISTRATION PHILIPPINES

On June 22, 1963 Republic Act No. 3720 was passed & known as the “Food, Drug and Cosmetic Act”. FDA is headed by The Department of Health (DOH) is the health agency in the Philippines. It is responsible for 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.

PHARMACEUTICAL VARIATION ^[5, 6]



Generally different countries follow different guidelines but variations in products may be of these types:

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.

Variation is a change to a registered pharmaceutical finished product that may affect directly to the aspects of quality, safety and efficacy and it doesn't lie within 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. Main types of pharmaceutical variations considered by FDA Philippines are described below Change of content of product labeling, which may be in any matter.

- In case of exporters, addition of the manufacturing site of the drug product or replacement to other. This is frequently arising variation.
- Addition or change of indication & inclusion of clinical information extending the use of the product.
- Addition or Change of alternative manufacturer/site of drugs. Like loan-licence work.

- Addition or replacement of the alternative site for the primary packaging.
- Specification of the drug substance or product changes with process.
- Batch size of sterile drug product changes.
- Batch size of non-sterile drug product changes.
- Manufacturing process for the drug product have major changes.
- Change of excipients in the terms of quantitative or qualitative manner.
- Coating weight of tablets or weight a capsule shell for modified release oral dosage form.
- Primary packaging material for sterile product may be change, including 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.
- Inclusion or replacement of the solvent/diluent for the drug product.
- Extension of shelf-life of the drug product.
- Change of storage conditions of the 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.

Table 1: Types of variations and filing procedures in Philippines

Type of variation	Minor variation notification type	Minor variation prior approval type	Major variation
Procedure	Do & Tell -Policy. If the application fulfils the requirements, then only variation filing is approved by FDA Philippines	If the application for variation fulfils the requirements as per described by FDA Philippines, then only variation filing is approved.	If the application for variation fulfils the requirements as described by FDA Philippines, then only variation filing is approved.
Timeline for the Drug Regulatory Authority to evaluate the variation application	Within a duration which may be according to variation filled. Subject to FDA Philippines.	Within a short duration which may be according to variation filled. subject to FDA Philippines.	Within a duration which may be according to variation filled. subject to FDA Philippines.

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.

To bypass these complex filing procedure and its timeline, a person should follow some of the SOP and documentation as to finish the cycle. These kinds of documentation if completed as soon as possible after the variation filing, then it will be time saviour step for industries.

PREREQUISITES ^[6]

These are some of the important documentation or prerequisites which can accelerate the whole procedure of variation filing if completed earlier while dealing with a product in Philippines.

- A general format for changes containing clean and annotated version highlighting the changes made. Justifications for the changes proposed.
There should be a common format prepared for common changes made, after each change this documentation should be done in order to avoid time consuming process of filing then waiting for response.
- Drug master file and audit documents should be verified by the in charge person, to avoid need of clearing compliances, which is generally done by regulatory authority of reference country.
- Note down the changes in Product formula, and specification of drug substance, check for the Release and shelf life of the drug product at the regular interval.
- In case of change in manufacturing process a new format of description of the new manufacturing process and technical justification for the change. Which will give rapid back up if variation filed on the basis of new manufacturing process.
- A format for declaration on quantitative changes of the weight of the coating materials in products. Even if no any changes are made should be checked at regular interval. Which will give easy access to verify the data when variation filled.
- A clean version of labelling with its proper data should be noted on an official paper, if changes are made then it should be noted on a other format, at last all of them should compile for variation purpose.
- A proper format of test procedure should be noted including description of the analytical methodology. A summary of validation data, and analytical results. At regular interval this format should be amended. This will be mainly helpful in case of change in test procedure applied.
- In case of in process quality control test for manufacturing, proposed documentation should be made for in-process specifications together with justification and relevant process validation data. This document will play an important role when change in IPQC performed.
- For removal or addition of any substance, when performed as soon as possible justified reason should be prepared for removal or addition.

These are the main Prerequisites which can accelerate the whole process of variation filing, if completed.

CONCLUSION

By studying all the steps of market and variation filing procedure of Philippines, one can say that responses in this market are tremendous, equally for the growth of the industry as well as its business. Product registration and marketing approval is fast as compared to developed countries. But as the most of the companies exports their medicines in Philippines changes occurs and which leads to variation. Even after variation filled it takes time which is not particularly described by FDA Philippines so in order to escape as early as possible from this waiting longue, industries can develop prerequisites which will help to accelerate and make a beneficial move in this market. Described prerequisites are very helpful if owned by an industry.

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ABBREVIATIONS

DMF: Drug Master File

FDA: Food & Drug Administration

REFERENCES

1. Outlook of pharmaceuticals in South East Asia to 2013. The pharma letter. [Online]. [cited 2015 March 2]; Available from: URL: <http://www.thepharmaletter.com/article/outlook-of-pharmaceuticals-in-south-east-asia-to-2013>
2. Philippines pharmaceutical market outlook 2016. CEE/CIS Pharma Market Assessment and PMRA. [Online]. [cited 2015 March 5]; Available from: URL: <http://cispharma.blogspot.in/2013/01/philippines-pharmaceutical-market.html>
3. 2013 Philippines pharmaceutical market update. Pacific bridge medical. [Online]. [cited 2015 March 5]; Available from: URL: <http://www.pacificbridgemedical.com/publications/2013-philippines-pharmaceutical-market-update/>
4. Regulatory authority of Philippines. Food and drug administration Philippines. [Online]. [cited 2015 March 7]; Available from: URL: <http://www.fda.gov.ph/>
5. Who. General guidance on variations to multisource pharmaceutical products. [Online]. [cited 2015 March 2]; Available from: URL: http://www.who.int/medicines/areas/quality_safety/quality_assurance/VariationsMultisourcePharmaceuticalProducts_QAS14-575_24022014.pdf
6. ASEAN variation guideline for pharmaceutical product. Health science authority. [Online]. [cited 2015 March 25]; Available from: URL: http://www.hsa.gov.sg/content/dam/HSA/HPRG/Western_Medicine/Overview_Framework_Policies/Guidelines_on_Drug_Registration/ASEAN%20Variation%20Guideline%20for%20Pharmaceutical%20Products%207.2%20clean%20draft.pdf