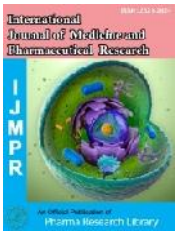
International Journal of Medicine and Pharmaceutical Research

Journal Home Page: www.pharmaresearchlibrary.com/ijmpr



Review Article **Open Access**

Evaluation and Comparison of Regulatory Strategy and Communications received from various Regulatory Authorities during Pre & Post Registration of "Piperacillin and Tazobactum for Injection"

Dr. Hareesh Dara*, D Siva Dinesh

St John College of Pharmcy, Hasanparthy, Hanamkonda, Telangana.

A B S T R A C T

Developing a new drug requires great amount of research work in chemistry, manufacturing, controls, preclinical science and clinical trials. Drug reviewers in regulatory agencies around the world bear the responsibility of evaluating whether the research data support the safety, effectiveness and quality control of a new drug product to serve the public health. Every country has its own regulatory authority, which is responsible to enforce the rules and regulations and issue the guidelines to regulate the marketing of the drugs. As the pharmaceutical industries throughout the world are moving ahead towards becoming more and more competitive, these are realizing that the real battle of survival lies in executing the work by understanding the guidelines related to various activities carried out to give an assurance that the process is under regulation. This article focuses on guidelines and regulatory requirements of different countries of different Regions like ASEAN, CIS, LATAM and African.

Keywords: Piperacillin and Tazobactum, Regulatory Strategy, Regulatory Authorities

A R T I C L E I N F O

CONTENTS

Article History: Received 18 July 2017, **Accepted** 15 August 2017, **Available Online** 10 October 2017

***Corresponding Author**
Dr. Hareesh Dara
St John College of Pharmcy,
Hasanparthy, Hanamkonda, Telangana.
Manuscript ID: IJMPR3311

PAPER-QR CODE

Citation: Hareesh Dara. Evaluation and Comparison of Regulatory Strategy and Communications received from various Regulatory Authorities during Pre & Post Registration of "Piperacillin and Tazobactum for Injection". *Int. J. Med. Pharm. Res.*, 2017, 5(5): 167-171.

1. Introduction

Importance of Regulatory Affairs: Regulatory Affairs in a Pharmaceutical industry, is a profession which acts as the interface between the pharmaceutical industry and Drug Regulatory authorities across the world. It is mainly

involved in the registration of the drug products in respective countries prior to their marketing. A drug Regulatory affair (DRA) is a process of interaction of the company with: Drug Regulatory Authorities, Internal Departments of the Organization throughout the lifecycle of a product that is from the synthesis of the active moiety to marketing to post approval activities. Drug Regulatory Affairs Department is the BACKBONE of Pharmaceutical Industry. It is revenue generator for Industry. Internally it cooperates with other department like drug development, manufacturing, marketing and clinical research. Externally, it is the key interface between the company and the regulatory authorities.

Regulatory Affairs involved in the development of new medicinal products, by applying regulatory principles and by preparing and submitting the relevant regulatory dossiers to health authorities. Regulatory professional obtains the marketing authorization for the product by presenting the registration document to regulatory agencies, and making the necessary subsequent negotiations. They contribute in the commercial and scientific success of the product development by giving strategic and technical advice, from the beginning of the product development. More than 15 years span is required to develop and launch a new pharmaceutical product in the market. During this scientific development many problems may arise.

This process can make fast by avoiding and solving the problem at appropriate steps only with the help of Regulatory Professional. They help the company for keeping proper records, appropriate scientific thinking, update with always changing regulatory guidelines/requirements and proper presentation of data. Some important Drug Regulatory Authorities (across the world) Each and every country has its own regulatory body. Some important authorities among them are mentioned below along with their country name.

- CDSCO-India
- USFDA- United States of America
- EMA- European Union
- MHRA- United Kingdom
- Health Canada – Canada
- TGA –Australia
- MCC- South Africa
- ANVISA- Brazil
- Medsafe- New Zealand

Functions of DRA department

- The different functions of RA personnel and DRA department in general
- Provide regulatory and technical inputs for product development.
- Prepare, review and submit different regulatory submissions.
- Act as interface between internal department of organization.
- Review and submit Annual drug reviews, adverse drug experience, recall coordination activities and different regulatory guidelines.
- Answer and negotiate with the Drug regulatory authorities on various issues on drug registration.
- Apply for the various certifications and arrange for the audit and also work on their renewal & many more.

Skills

- Regulatory affairs professional must take the initiative to keep current on all changes in regulations.
- They are also involved with coordinating and implementing the changes which calls for much sensitivity so that changes suggested are smoothly accepted by the company's management and the regulatory bodies.

2. Scope of Regulatory Affairs

- Proper development of the product.
- Assuring efficacy, safety and quality of the product.
- Review in-house documentation & updating other departments.
- Proper packaging and labeling
- Dossier filing/product submission and getting approval from health agency within specified time period.
- Making smooth roadways for placing quality product in the market.
- Helping pharmaco-vigilance of quality/safety issue post marketing.

General Description of Registration Process: The process of product registration ensures that pharmaceutical products are evaluated for its safety, efficacy and quality, whereas natural products are evaluated for its safety and quality, prior to being registered by the Authority and finally released into the market.

Figure 1: Phases of Product registration

Drug regulation generally covers the following areas:

- Pre-marketing assessment and evaluation of the quality, safety and efficacy of a medicine, including compliance of manufacturing sites and processes with Good Manufacturing Practice (GMP) standards
- Assessment and inspection of all components of the pharmaceutical supply chain
- Maintenance of a register of available products, and post-marketing surveillance activities, including random sampling of registered medicines for quality control and Pharmacovigilance.

- Promotion, advertising and provision of medicines information. Price control may or may not be part of drug regulatory activities.

3. Requirements for Product Registration

Administrative Requirements

Manufacturing License:

According to the CDCR 1984, any company who wishes to manufacture, import and/or wholesale any registered products needs to have Manufacturer's License, Import License and/or Wholesaler's License.

GMP Certificate:

- According to the CDCR 1984, compliance to Good Manufacturing Practice (GMP) is prerequisite to application of a manufacturing license, as well as product registration/ cosmetic notification. GMP is a standard which shall be followed by the manufacturers to ensure that the products manufactured are safe, efficacious and of quality.
- Upon complete application, a GMP certificate will be issued. If a manufacturer who wishes to build a new manufacturing premise, the manufacturer may submit a proposed premise layout plan to the Centre for Compliance and Licensing authority. GMP certificates should have, e.g. security seals, watermarks or holograms, to help prevent counter feiting, tampering and other fraudulent activities.

Certificate of Pharmaceutical Product:

A certificate issued in the format recommended by the World Health Organization (WHO), which establishes the status of the pharmaceutical product and of the applicant for this certificate in the exporting country. It is issued for a single product, because manufacturing arrangements and approved information for different pharmaceutical forms and strengths can vary. Issued to locally manufactured products that are to be exported. Upon receipt of complete application, the certificate shall be issued within fifteen working days.

Free sale certificate: A document required in certain countries or for certain commodities (such as pharmaceuticals), certifying that the specified imported goods are normally and freely sold in the exporting country's open markets and are approved for export.

General Requirements:

Full Evaluation: In accordance to ASEAN ACTD/ ACTR or ICH guidelines

Part I: Administrative data and product information

Part II: Data to support product quality (Quality Document);

Part III: Data to support product safety (Nonclinical Document)

Part IV - Data to support product safety and efficacy (Clinical Document) In accordance to CTD/ICH guidelines

Module 1: Administrative Information and Prescribing Information

Module 2: Common Technical Document Summaries

Module 3: Quality

Module 4: Nonclinical Study Reports

Module 5: Clinical Study Reports

Abridged Evaluation

Additional Information on Requirement

Bioavailability (BA) Study

Bioequivalent (BE) Study

Registration Procedure:

Pre- registration

Some countries need Pre-registration process like Nigeria, Iraq….etc. Pre-requisite and Pre- submission both comes under Pre-registration.

For example: in Nigeria

First Trade mark Registration is required

Step I: we should inform the proposed brand name to the NAFDAC for Brand name search (with Fee: 9,000 Naira).

Step 2: After that, NAFDAC enter the brand name in the published journal. If no object from anybody, then NAFDAC issue the Trade mark certificate. It will take 5 to 7 weeks.

The process of Pre-registration consists of two steps

Step I: Applicant shall purchase Registration Form per product for five hundred naira only.

First Original registration form (to be filled by electronic typing or by hand) along with required list of administrative documents (Legalized by Nigerian embassy attestation in the country of origin) should be submitted.

Step II: After NAFDAC finds the administrative documents in order, will issue a permit to import Samples. It will take 3 to 5 months.

Import permit license valid for 1 year.

Registration:

Then we need to submit Registration dossier (in country Specific format) along with samples. And also we should send a letter of invitation to inspect the factory facilities.

Query Response:

Failure to respond promptly (within 30 work days) to queries on enquiries raised on the application, will automatically lead to suspension of further processing of the application.

Pre-Approval steps:

Product Analysis Report likely to come out of the Laboratory is 6 – 8 weeks.

The time line for product registration from submission of samples up to issuance ofregistration number in hundred (100) work days. However, this depends on satisfactory Compliance by the applicant.

Post-registration:

- We should organize the samples with NAFDAC number for collection of Reg. Certificate.
- Product registration certificate takes a maximum of six (6) months after the date of approval to be ready.
- Registration is valid for 5 years.

Variation:

Variation refers to change of particulars of a registered product. Throughout the life cycle of a registered product, changes to improve the product's efficacy, quality and safety are likely to occur. Therefore, applicant shall inform the Authority pertaining to any changes or amendment made to particulars of a registered product via variation applications.

- For pharmaceutical products, there are three (3) types of variations, which are Major Variation (MaV), Minor Variation Prior Approval (MiV-PA) and Minor Variation Notification (MiV-N).
- For health supplement and natural product, there are two (2) types of variation, which are Variation Type I and Variation Type II.

Discussion: Product selection is done by product management team, if required business management team involved in selection of country.

- Regulatory has no role in the product Vs country matrix.
- Following are the few parameters which will be consider to identify the selecting the country for any particular molecule.
- Increase % growth in demand for the molecule year on year
- Number of companies are already lunched
- Price comparison with competitors
- Marketing strategy
- Based upon the above parameters we have selected a drug "Piperacillin and Tazobactam for Injection".

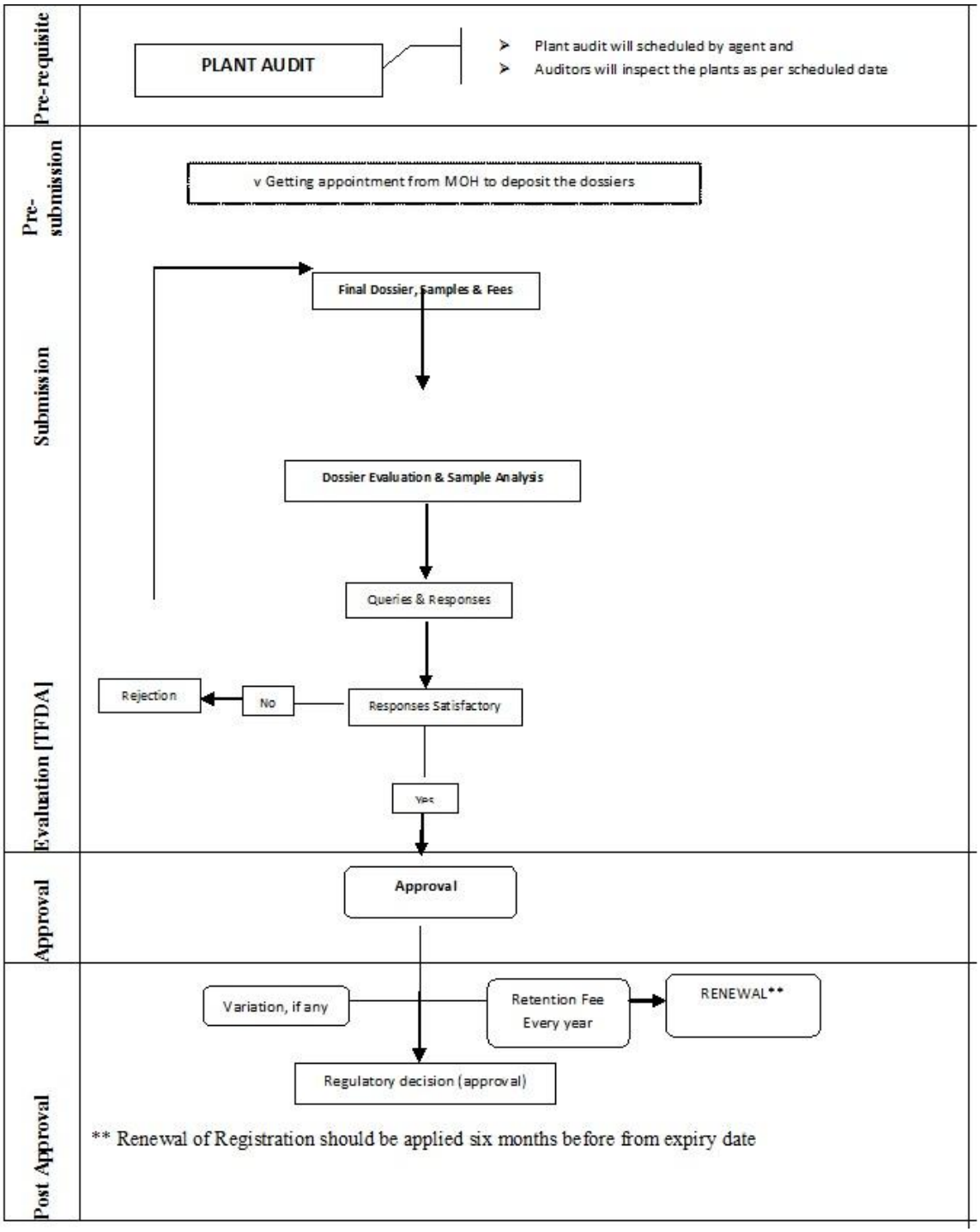


Figure 2: General Registration Process.

4. Conclusion

Based on the IMS data and market survey by project management team & business potential survey by business development team identified following countries to register "Piperacillin and Tazobactam for Injection". Malaysia, Phillipines, Vietnam, Kenya, Ivory cost, Kyrgyzstan, Uzbekistan, Venezuela, Colombia. After studying the regulatory requirements to register a pharmaceutical product for human use and after analyzing the communications received from respective regulatory authorities, the above countries are classified as regulated and semi-regulated countries.

Regulated countries	Semi-regulated countries
Malaysia	Philippines, Vietnam
	Kenya, Ivory coast
	Kyrgyzstan, Uzbekistan
	Venezuela, Colombia

Based on the experience gained from this product registration above said countries regulatory filing strategy has been developed to improve the quality of the submission file which helps to reduce the number of deficiencies received from each regulatory authority. It also helps to reduce the product registration lead time which allows commercial team to launch the product at the earliest.

5. References

[1] Brazil: http://www.anvisa.gov.br/eng/index.htm
[2] Ukraine:http://www.pharma-center.kiev.ua/view/en/index
[3] Philippines: www.fda.gov.ph/
[4] Thailand: www.fda.moph.go.th/eng/index.stm
[5] Malaysia: portal.bpfk.gov.my/index.cfm & menuid
[6] "Laporan Kiraan Permulaan 2010". Jabatan Perangkaan Malaysia.
[7] "Laporan Kiraan Permulaan 2010". Jabatan Perangkaan Malaysia. p. 27.
[8] "Federal Territories and State Governments". Malaysia.gov.my. Retrieved 21 September 2010.
[9] Wu, Min Aun & Hickling, R. H. (2003). Hickling's Malaysian Public Law, pp. 64–65
[10] "NRD: 'H' indicates holder is a Sabahan | Daily Express Newspaper Online, Sabah, Malaysia". Dailyexpress.com.my. 5 June 2010.
[11] Wu, Min Aun; Hickling, R H (2003). Hickling's Malaysian public law. Pearson Malaysia. pp. 65–66.
[12] Malaysia Districts". Statoids.com. Retrieved 3 November 2010.
[13] Shad Saleem Faruqi (8 September 2010). "From Malaya to Malaysia".
[14] http://www.fda.gov.ph/about-food-and-drug-administration
[15] http://www.fda.gov.ph/names-of-officials-position-designation-and-contact-information/fda-management-team
[16] http://www.pharmtech.com/pharmtech/News/Global-Market-Boom-for-Generic-
[17] Drugs/Article Standard/Article/detail/756488.