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A RETROSPECTIVE REVIEW OF PHARMACEUTICAL PREQUALIFIED APPROVED DRUGS FROM 2015 TO 2022

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ABSTRACT

Efficient regulation of pharmaceutical products is crucial in ensuring that the medicines within a specified territory meet the stipulated standards of quality, safety and efficacy. The process of drug registration requires submission of a dossier in Common Technical Dossier (CTD) format which essentially contains alladministrative, quality, clinical and non-clinical information about the product. This study is a retrospective review of Pharmaceutical prequalified approved dossiers from the period starting 2015 to 2022. The aim of this study was to carry out a retrospective review of pharmaceutical prequalified approved product dossiers from period starting 2015 to 2022. To compare the prequalified approved dossier with their dosage form, number of prequalified approved, applicant of the different countries and their therapeutic categories between 2015- 2022. The sample size of 373 files selected and studied, the prequalified approved dossiers in 2015, 2016, 2017, 2018, 2019, 2020, 2021, 2022 are 18, 35, 57, 54, 64, 51, 51, 41 numbers. According to the therapeutic use of the drugs in 2019, more number HIV/AIDS (31%) drugs are approved for prequalified compare to other years and in 2017 more number of tuberculosis (55%) drugs are approved for prequalified, in 2018 more number of malarial drugs 21% went for prequalified approval, in 2020 more number (16%) of reproductive health drugs are preapproved compare to other year. By comparing between the applicants and the number of prequalified drugs approved between 2015 to 2022, India submitted dossier has be approved by comparing with other country applicants. India dossiers approved more medicines (40 medicines) in 2019 compare to other years. Next to India, China is the next applicants for more number of prequalified drugs to be approved. According to the dosage form, the most frequently submitted dosage form was film coated tablets at 44.23%, followed by tablets at 33.51%. In this review of generic product dossiers submitted to the WHO Prequalification of medicines Programme during 2015 to 2022, there were considerably more quality-related deficiencies in TB, MA and RH dossiers compared to HIV dossiers, especially in the categories specification of APIs, development pharmaceutics, manufacturing method and FPP specifications. This may be related to the applicant's experience of interacting with SRAs, availability of information on comparator products, availability of pharmacopoeial monographs and the age of the product.

KEYWORDS: ICH, dossiers, CTD, prequalified.

INTRODUCTION

A "dossier" is a comprehensive and concise report containing all type of evidence (clinical and economic) and information about a medical product that is developed and communicated by the manufacturer to health care decision-makers (HCDMs) for the purpose of formulary, coverage, policy, and reimbursement decision-making.[1]

Brunei in 1984[2], Vietnam in 1995[3], Burma on 1997 and Combodia on 1999 joined as the member in Association of South East Asian Nation for the stabilization of its Government. ASEAN countries like Philipines, Malaysia, Singapore, Thailand, Indonesia, Brunei, Mynmas, Combodia and has follows Asian Common Technical Dossier (ACTD) format.[4]

Common Technical Dossier was a format introduced by Europe, United Nation and Japan for the drug safety, quality and efficacy. In 2000 CTD was officially signed off with ICH. CTD format was categorized by five modules. All these modules should be in a acceptable format to WHO and regulatory authorities.[5]

In this CTD triangle, module 1 was not considered as CTD and it will give only the information about regional or administrative information for getting the market authorization.

For Industries it works as a good Format because it has eliminated the need to reformat the information for submission to the different ICH regulatory authorities.[6]

Effort over the past 15- 20 years by ICH of technical requirements for "registration of pharmaceutical forhuman use" have resulted in a uni-field dossier for drug applications. CTD was officially signed off inNovember 2000, at 10th anniversary of ICH; San Diego, California.[7]

The CTD is organized into five modules. Module 1 is region-specific. Modules 2, 3, 4 and 5 are be common for all regions. Conformance with ICH guidelines should ensure that these four modules are provided in a format acceptable to WHO and regulatory authorities. An overview of module contents for a multisource product in greater details.

The module 1 is not part of CTD andit contains only the regional information and administration information of the dossier for getting the authorization. Module 2 is the overview and summary of module of 3 to 5, module 4 is for safety and module 6 is for efficacy (clinical studies).[8-12]

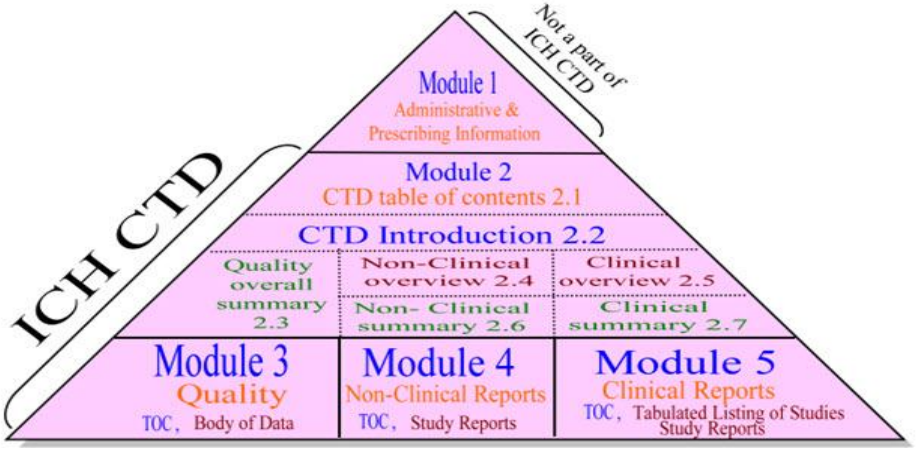


Fig 2: Modular Structure of ICH CTD.

MATERIALS AND METHODS

Study Design

A retrospective descriptive study of dossiers and the pharmaceutical prequalified finished medicine dossiers submitted at over a seven-years period (2015 to 2022) was conducted. Data was collected between August to November 2022 from the website https://extranet.who.int/pqweb/content/prequalified-lists/medicines. Information was collected on the therapeutic categories of the products submitted for registration, average time taken from the time of submission of the dossier to the time of registration and the adequacy of the compiled documents submitted by applicants for registration. Data was extracted from the selected dossiers using a predesigned data collection sheet. This retrospective study encompassed all generic product dossiers in the therapeutic areas of HIV, TB, MA and RH received by the WHO Prequalification of Medicines Programme between 2015 to 2022.

Study Area Description

The study was conducted in online WHO extranet website to meet the standards of quality, safety and efficacy.

Study Population

The pharmaceutical dossiers submissions for prequalified approved drug from 2015 to 2022. Medicinal products (as identified in the Invitations to Manufacturers to Submit for Expressions of Interest for Product Evaluation (EOI) issued by WHO) are added to the list after the data submitted for an invited product has been evaluated, and relevant sites have been inspected by WHO, and are considered (at the time of evaluation and inspection) to meet WHO prequalification requirements. WHO cannot guarantee that the listed products and manufacturing sites will continue to meet the aforesaid standards, and may suspend or remove products from the list, based on information that has subsequently become available to it.

Inclusion Criteria

The dossiers that were included in the study were those that fulfilled the following criteria: They were pharmaceutical product dossiers of FPP that is prequalified submitted between 2015 and 2022, products that were pharmaceutical in nature, and that the dossiers were complete with all the required modules.

Exclusion Criteria

The dossiers of FPP that were not included in the study were those that were submitted before 2015, products that were not pharmaceutical in nature that is food supplements, herbal or borderline products, and dossiers of FPP that had inadequate information and were incomplete.

Sample size determination

From the WHO online extranet website 2015 to 2022 a total of 373 pharmaceutical dossiers finished prequalified approved medicine were submitted by WHO. The data retrieved only contained the generic name of the product,

the respective CTD number and the date of approval. To ensure that the sample size obtained was a true representation of the total population, the 373 products were further classified into their respective therapeutic categories. This was done by quick search of the generic name of the product in the internet.

A comparative study survey has done for the therapeutic classification, dosage form, no of prequalified drugs, total number of prequalified medicine dossier submitted in each country between 2015 to 2022.

RESULTS AND DISCUSSION

Full Assessment Procedures

In order to be prequalified finished pharmaceutical product (FPP) must meet the requirements Finished Pharmaceutical Product (FPP) usually uses this process to prequalify. Generic products must meet all the requirements of active pharmaceutical ingredient(s) (APIs) use in the formulation, finished pharmaceutical product (FPP) requirement, and the GMP compliance requirement of site(s) at which the FPP is manufactured. This will include:

a) Bioequivalence study of the FPP.
b) Quality of the API(s).
c) Quality of the FPP.
d) WHO Good Manufacturing Practices compliance.
e) Inspection of that CRO with respect to the particular study performed and submitted in the dossier[39] (Figure 3).

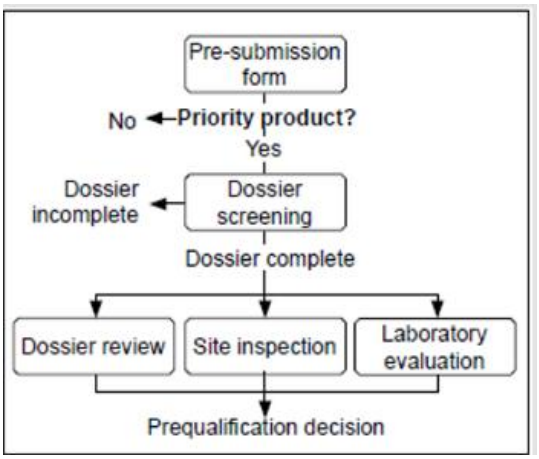
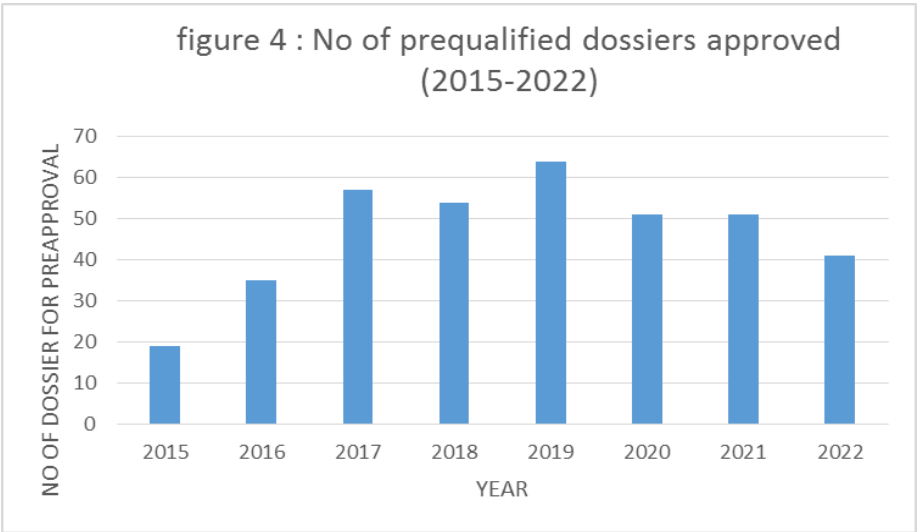


Figure: 3 Full Assessment Procedure.

Prequalified Approved Dossiers

The list of Prequalified medicine Dossiers where download from https://extranet.who.int/pqweb/content/prequalified-lists/medicines from the year 2015 to 2022 and the data was downloaded in the excel format for the further survey.

From the below mentioned data, the highest prequalified dossiers is approved in the year 2019 compared to the other year.

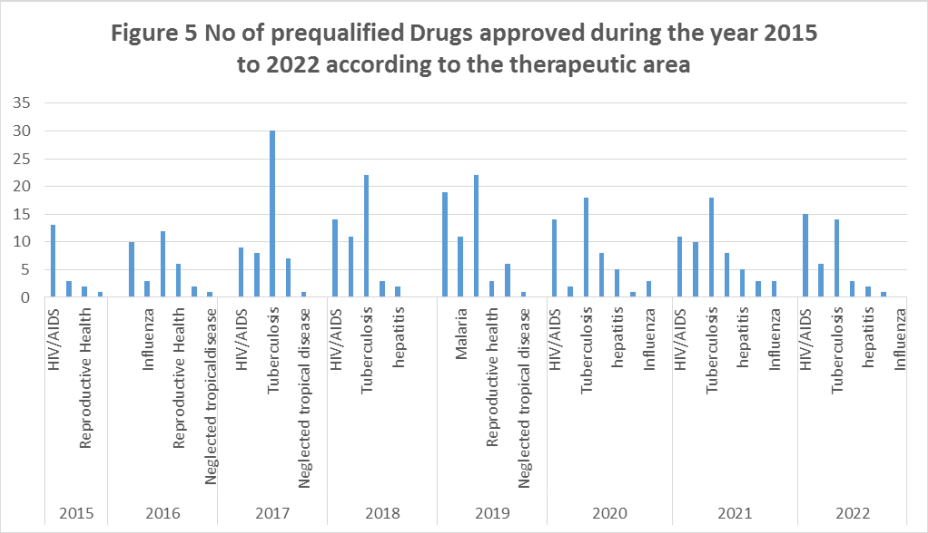


The prequalified approved dossiers in 2015, 2016, 2017, 2018, 2019, 2020, 2021, 2022 are 18, 35, 57, 54, 64, 51, 51, 41 numbers. The highest prequalified approval of dossiers are in 2019. In 2020 and 2021 same numbers 51 numbers of dossiers drugs are prequalified approved.

Therapeutic Area

In the given data, the therapeutic area were surveyed from the year 2015 to 2022 according to the classification of medicines.

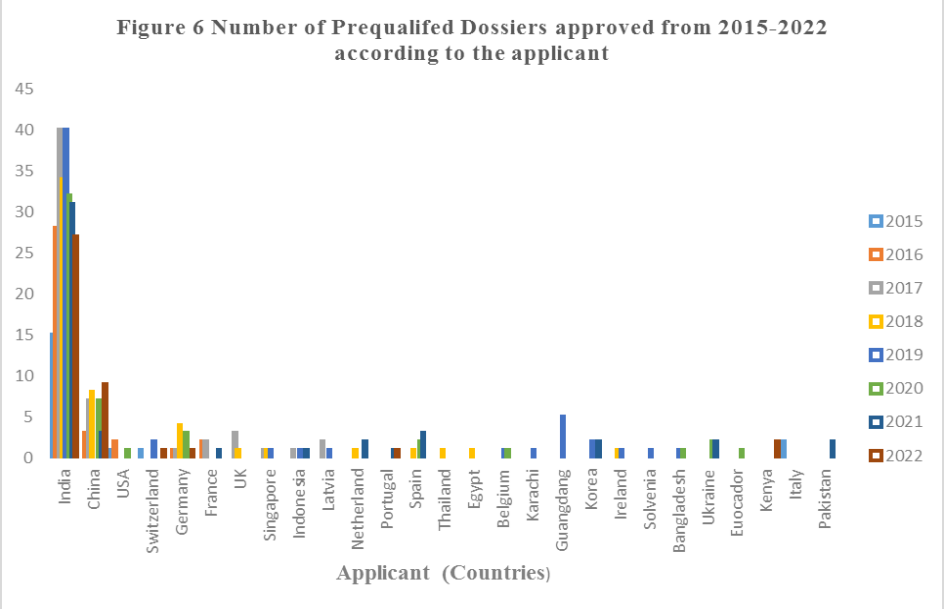
According to the therapeutic use of the drugs in 2019, more number HIV/AIDS (31%) drugs are approved for prequalified compare to other years and in 2017 more number of tuberculosis (55%) drugs are approved for prequalified, in 2018 more number of malarial drugs 21% went for prequalified approval, in 2020 more number (16%) of reproductive health drugs are preapproved compare to other year.



Origin of the Drug Product

Comparison between the Applicants and number of prequalified drugs approved between 2015-2022

By comparing between the applicants and the number of prequalified drugs approved between 2015 to 2022, India submitted dossier has be approved by comparing with other country applicants. India dossiers approved more medicines (40 medicines) in 2019 compare to other years. Next to India, China is the next applicants for more number of prequalified drugs to be approved.



Dosage Form Distribution

Drug substances are rarely administered to the patient as active ingredients, but instead are given as part of a formulation that includes one or more non-medicinal agents commonly known as excipients. These excipients serve varied and specialized pharmaceutical functions. The combination of the drug substance and the excipient produces various types of dosage forms, with each form

being unique in pharmaceutical and chemical characteristics.

Regardless of the dosage form, there needs to be compatibility between the drug substance and the excipients to ensure that the drug product produced is stable, safe, efficacious, attractive and easyto administer.

For this study, the products were divided into 11 dosage forms, which were tablets, injectable, capsules, suspensions, syrups, crèmes, ointments, and solutions for injection, solutions, eye/ear drop and other dosage forms. The different types of dosage forms are as shown in Table 7 below.

Table 2: Dosage form distribution.

Formulation	n	%
Tablets	125	33.51
Film Coated Tablets	165	44.23
Dispersible tablets	53	0.14
Capsules	26	0.07
Suspensions	03	0.008
Implants	01	0.002

The most frequently submitted dosage form was film coated tablets at 44.23%, followed by tablets at 33.51%.

CONCLUSION

Although there is a continuous process of harmonization taking place all around the world, still we see a huge challenge, which is yet to be overcome by the Pharmaceutical industry in case of generic drug development and filing. This is due to the heterogeneity in the regulatory landscape of the various countries. Therefore, to meet these challenges, a lot of strategic planning is required before the development of any generic drug product.

In this review of generic product dossiers submitted to the WHO Prequalification of medicines Programme during 2015 to 2022, there were considerably more quality-related deficiencies in TB, MA and RH dossiers compared to HIV dossiers, especially in the categories specification of APIs, development pharmaceutics, manufacturing method and FPP specifications. This may be related to the applicant's experience of interacting with SRAs, availability of information on comparator products, availability of pharmacopoeial monographs and the age of the product.

India is among the highest generic pharmaceutical product producers worldwide and contributes an estimated 20% of global generic product exports. Among the compelling reasons for the rise in India's pharmaceutical stature include inexpensive labor, lower production costs, strong government support and lower research and development costs. It is estimated that the production costs are 60% cheaper than the US and 50% cheaper than UK.

Future

Additional therapeutic areas may be included, Prequalification of API continued and Requalification continued.

Challenges

Declining number of submission, slow progress with respect to RH, TB, and malaria dossiers, increasing demand for technical assistance.

REFERENCES

1. U.S. Food & Drug Administration. Drug and device manufacturer communications with payors, formulary committees, and similar entities — questions and answers: guidance for industry and review staff. June 2018.
2. h*ttps://www.fda.gov/downloads/drugs/guidancecompliancere gulatoryinformation/guidances/ucm537347*.
3. *pdf.* Accessed October 19, 2019.
4. "Background Note: Brunei Darussalam/Profile:/ Foreign Relations" US State Department; 2007.
5. Vietnam in ASEAN: Toward Cooperation for Mutual Benefits". ASEAN Secretariat; 2011.
6. Carolyn L. Gates; Mya Than. ASEAN Enlargement:impacts and implications. Institute of Southeast Asian Studies. ISBN 981-230-081-3; 2001.
7. "Statement by the Secretary-General of ASEAN Welcoming the Kingdom of Cambodia as the Tenth Member State of ASEAN, ASEAN Secretariat; 1999.
8. ICH. The Common Technical Document [Internet]. ICH; 2019 [cited 2019 Mar 26]. Available from: https://www.ich.org/products/ctd.html
9. International Journal of Pharmaceutical Sciences Review and Research Homepagehttps://www.globalresearchonline.net/journalcontents/volume9issue2/Article-030.pdf. (accessed August2014).
10. ICH Homepage https://www.ich.org/products/ctd.html (accessed September 2014).
11. ICH Homepage https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4_R3_Organization/M4_R3__or

ganization.pdf. (accessed September 2014)
12. ICH Homepage
13. https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4_R1_ Quality/M4Q__R1_.pdf. (Accessed September 2014).
14. ICHHomepage https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4__R2__Safety/M4S_R2_.pdf. (accessed September 2014).
15. ICH Homepage
16. https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/CTD/M4__R1__Efficacy/M4E__R1_.pdf. (accessed September 2014).