



Global Role of Pre-Qualification Programme of Essential Medicines

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ABSTRACT

Due to lack of enhanced and well-founded regulations and legislation for the registration of pharmaceutical products, poor distribution system, poverty and illiteracy developing countries i.e. having low-middle income struggle to fulfil the medicinal requirements of high burden diseases like HIV/AIDS, Malaria, Tuberculosis etc. to the population of the country. The medicines provided are of poor quality, in inadequate abundance, unsafe and absurdly costly. In order to provide safe, adequate, quality medicines at lower cost to the population of developing country the World Health Organization-WHO provided list of essential medicines. Far along in March, 2001 WHO launched Pre-qualification Programme for medicine in partnership with UNAIDS, UNICEF and UN Population Fund and it was supported by WORLD BANK. The medicines provided after the pre-qualification are of assured better quality, safe and comparatively cost-effective. Pre-qualified products are listed on WHO website. This article mainly focuses on the brief introduction of essential medicines, role of WHO in building essential medicine list, Overview of Pre-qualification programme-PQP, elements of PQP, procedure for pre-qualification of pharmaceuticals and on the impact of PQP at global level.

Keywords: Essential medicines, prequalification programme, world health organization

INTRODUCTION

A population is bursting hence affordable admittance to quality essential medicinal products and treatments depend on following factors:

1. Efficient regulation, provision as well as use of products
2. Sound policies for the selection, rating and supply
3. Qualified health personnel
4. Information system
5. Functioning health infrastructure
6. Good governance

Many poor countries i.e. low and middle income countries do not meet the above criteria because of limited resources and struggle to provide quality medical services to their countries.

The World Health Organization-WHO supports these countries to put up their ability, know-how, policies and information, to upraise availability of essential medical products at lower price and improve mechanisms to finance and for coverage of essential medicines and technologies in social protection schemes, for improvisation of quality and safety of products and reduction of sub-standard and counterfeit medicines, to improve selection, prescription, dispensing as well as use.

It also supports the implementation policies, transparency as well as good governance in the medical product segment.¹

Essential Medicines

Essential medicines are the medicines which fulfils the precedence health care requirements of the population. They are selected as per the stipulation of public health, their evident efficacy and safety as well as relative cost-effectiveness. They are expected to be available within the framework of health system at each time in ample amount, in applicable dosage forms, having assured quality with required information and at such cost that an individual can afford.²

Principles for the Selection of Essential Medicines

Essential medicines are selected as per disease incidence, substantiation on efficacy and safety, and reasonable cost-effectiveness. The perception of essential medicines itself is revolutionary. It integrates the need to frequently update medicines selections that reflects new therapeutic alternatives and changing therapeutic requirements; the need to safeguard quality of drug; the need for continual development of better medicines, medicines for nascent diseases, and medicines that meets changing resistance patterns.³

The evolution of medicine and the WHO Model list of essential medicines

1897	Introduction of the First Synthetic Pharmaceutical
1941	Introduction of the First Modern Anti-biotic
1943	Introduction of the First commercially formulated Anti-malarial
1944	Introduction of the First Anti-tubercular
1950	The first clinical use of oral contraceptives, of drugs for diabetes and of drugs for mental illness
1977	The first Model List of Essential Drugs-WHO

Figure 1: Evolution of Medicines³

In 1977 WHO issued the first Model List of Essential Drugs and acknowledged 208 discrete medicines which



collected could provide safe, effective treatment for the mainstream of transmissible and non-communicable diseases.³

Pre-qualification Programme [PQP]

Pre-qualification is a standardized quality assessment procedure of WHO to evaluate the suitability, in principle, of pharmaceutical products for purchase by agencies of United Nations. Agencies using information resulting from the prequalification procedure should perform additional steps of qualification prior to purchasing, such as confirming financial constancy and standing of the supplier, ability to supply the required measures, security of the supply chain, pre-shipment quality control and other related aspects.⁴

Pre-qualification Programme for vaccines was launched in 1987, PQP for Medicines was Launched in 2001 and PQP for diagnostic kits and Medicinal device became operational in 2010 by WHO in partnership with UNAIDS, UNICEF and UN Population Fund and it was supported by WORLD BANK.⁵

The programme is dealing with the quality problems which are commonly associated with medicines of following high burden diseases:

➤ Primary categories of medicines:

HIV/AIDS

Malaria

Tuberculosis

➤ Later added:

Reproductive health

Influenza

Acute diarrhoea

Neglected tropical diseases

This programme makes a firm, scientific assessment which is based on the WHO pre-qualification guidelines that are competent with internationally harmonized standards for the quality of generic as well as patented medicines. A pharmaceutical manufacturer submits an Expression of Interest-EOI along with a product dossier to WHO. The two appointed assessors examine the safety, quality and efficacy information provided in the product dossier and they both should approve the contents. If at all they disagree or in case the product is particularly complex additional assessors are consulted. When the dossier is about to get the approval inspection of the manufacturing sites of the active pharmaceutical ingredients and finished product is organized. Whether the result is positive or negative it is communicated to the manufacturers and Clinical Research Organizations-CROs. This technical feedback provided free of charge has proved to be having significant practical value because it helps manufacturers and CROs to enhance the quality of the product and the clinical studies.^{5,6}

Five elements of Prequalification Programme

Invitation

The WHO Prequalification of Medicines Programme (PQP), other UN agencies (UNAIDS and UNICEF) and UNITAID, issue a request to manufacturers to submit an expression of interest (EOI) for evaluation of product. Only products which are included in an EOI are entitled for prequalification.⁷

The enclosure of a medicine in an EOI is constructed on the following criteria:

- It should be listed on the WHO Model List of Essential Medicines;
- An application has been sent to the appropriate WHO Expert Committee for its addition in the Model List and it meets the criteria for inclusion (based on public health requirement, relative effectiveness, safety and cost-effectiveness);
- It should be recommended for use by an existing WHO treatment guideline.⁷

Dossier Submission

The manufacturer offers a complete set of data which depicts the quality, safety and efficacy of the product that is submitted for evaluation.

This includes:

- Data of the purity of all ingredients used in manufacture;
- Data of the finished pharmaceutical product (such as information about stability);
- Results of bioequivalence tests (clinical trials conducted in fit-healthy volunteers), unless waived.⁷

Assessment

All the data presented are assessed by a team of assessors which includes WHO staff and experts from national regulatory authorities around the globe.⁷

Inspection

A team of inspectors verifies that the manufacturing sites of active pharmaceutical ingredient(s) and finished pharmaceutical product meet the WHO good manufacturing practice. A team of inspectors also verifies that any contract research organization conducting any clinical studies regarding the submitted product complies with WHO good clinical practice and WHO good laboratory practice.⁷

Decision

If the submitted products are found to meet the If the product is found to meet the specified requirements, and the concomitant manufacturing site(s) and contract research organization(s) are acquiescent with WHO standards, the products are added to the WHO list of prequalified medicinal products.⁷



METHODOLOGY**Steps involved in the Process of Pre-qualification Programme for Pharmaceuticals:**

1. Invitation for Expressions of interest
2. Data and information to be submitted
3. Screening of dossiers submitted
4. Dossier assessment
5. Site Inspection
6. Reporting and communication of the results of the evaluation
7. Outcome of the pre-qualification procedure
8. Maintenance of pre-qualification status
9. Cost recovery
10. Confidentiality undertaking
11. Conflict of interest

4. Trade name of the product (if appropriate)
5. Applicant's name and official address
6. Name of manufacturer of finished pharmaceutical product (FPP)
7. Physical address of manufacturing sites and unit, if appropriate
8. Name of API manufacturer, physical address of manufacturing site(And unit, if applicable)
9. Product description
10. Pack size, primary and secondary packaging material
11. Storage conditions
12. Shelf-life (provisional, if applicable)
13. Summary of product characteristics
14. Package leaflet
15. Labelling

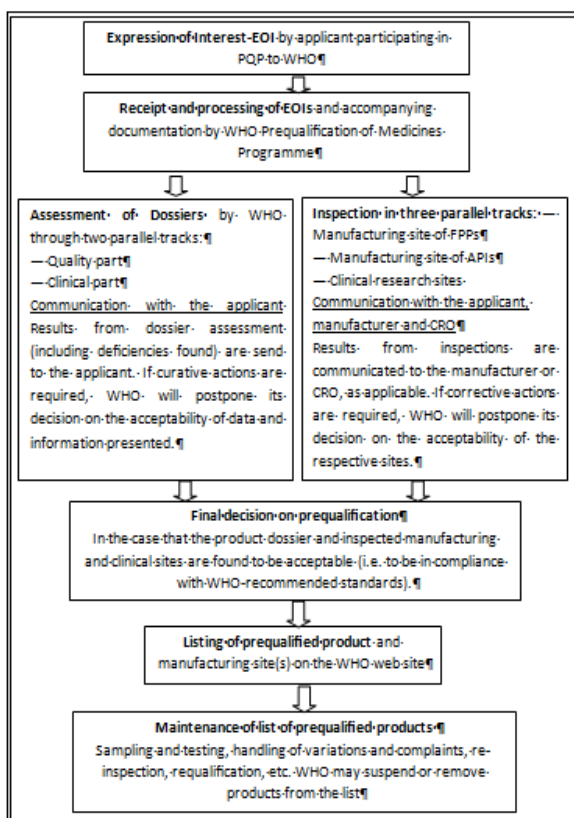


Figure 2: Pre-qualification Programme of Pharmaceuticals⁴

Characteristics of the pre-qualified pharmaceutical product which should be made available for public admittance on the WHO web site:

1. Reference number of WHO product
2. International Non-proprietary Name (INN) of active pharmaceutical ingredient
3. Dosage form and strength

Impact of Pre-Qualification Programme-PQP at Global level

Quality and Safety of pharmaceutical products have been the major concerns of public health issues which were neglected formerly. Pre-qualification Programme for Medicines launched by WHO has been boon like for the countries where there are weak regulations and legislations for medicines, where most of the medicines are unaffordable and where official supply takes longer to meet the need and demand of patients.

Initially it was difficult to provide medicines of high burden diseases i.e. HIV/AIDS, Malaria and TB at minimal cost with better quality, ease and in adequacy to developing countries. But after the launch of WHO-PQP it became possible to provide generic version of medicines essential for the treatment of high burden diseases. In November 2001, the Ministerial Conference adopted the Doha Declaration on TRIPS and Public Health. The Doha Declaration confirmed the independent right of governments to take measures to protect public health which included the use of compulsory licensing and parallel importation.⁸

Initially it focused on HIV/AIDS, Malarial and TB related drugs. Afterwards it included following categories,

- ⇒ Essential medicines for reproductive health, neglected tropical diseases (NTDs), and diarrhoea;
- ⇒ Quality control laboratories;
- ⇒ Active pharmaceutical ingredients (APIs);
- ⇒ Evaluation of clinical research used to prove equivalence of generic medicines with their comparators;
- ⇒ Aptitude of medicines regulators and pharmaceutical manufacturers in developing countries of Africa and Asia.

A competitive market for pre-qualified finished pharmaceutical products (FPPs) is now in place for most needed HIV-related and anti-malarial medicines and the prices of some products have reached minimum sustainable levels due to PQP for medicines. WHO has prequalified 397 FPPs since 2001.^{8,9}

An increasing choice of prequalified active pharmaceutical ingredients (APIs) has released new opportunities for production of inexpensive, good quality medicines, and has condensed the time of prequalification for the finished products that use them. In March-2010, WHO commenced prequalification of APIs – the essential building blocks of medicines. The WHO PQP has approved 23 APIs in 2013.^{8,9}

Prequalification of Quality Control Laboratory-QCLs throughout the world supports regulators, procurement agencies and specific public health programme implementers in testing whether pharmaceutical products meet the specifications defined for them.⁹

Prequalification helps to distinguish and safeguard patients from poor medicines quality, which can occur at any time and may be linked to problems in manufacture, storage or distribution.⁹

Engrossment in prequalification programme of medicine has fabricated regulators' trust in the Programme's standards and activities which has enabled successful introduction of collaborative procedures for joint inspections and for joint assessment. Prequalification has intensely changed the global markets of some significant medicines.

The prequalification programme can be used by regulatory authorities of all WHO Member States to evaluate other nationally important medicines i.e. life-saving antibiotics, to international standards.⁹

The Programme has elevated the bar for quality assurance. Its standards are recognized and endorsed by others that help to expand quality medicines production. From a public health standpoint, WHO PQP's greatest accomplishment is improved quality of key medicines used by millions of people in developing countries.

The price of the major fixed dose combinations-FDCs has reduced. The WHO PQP has become a global public good that has helped save lots of lives.⁹

Most of the international organizations and many governments that procure and supply medicines depend on the WHO PQP. Still very few choose to fund financially to its work which is the drawback of WHO-PQP.⁸

PQTM has promoted access to vital medicines by providing a quality-assurance service to international medicines procurers and countries. But its most noticeable contribution has been, and very much still is, to promote the application of international quality standards and more efficient regulatory systems.

The lasting impacts of that work are better treatments for patients and more equitable markets that respond to public health requirements.

This vital role could only be filled by a global, multi-stakeholder organization such as WHO which is driven by 194 Member States' policy consensus and offering a public good in an area otherwise beset by vested interests.¹⁰

As per Annual Report of 2013, WHO, the services provided to the countries and global health partners by Prequalification Team of Medicines include:¹⁰

- ⇒ Availability of medicines which are specifically designed to meet the requirements of low-income countries. Such as fixed-dose combinations and paediatric products for the treatment of HIV/AIDS, malaria and TB.
- ⇒ Encouraging the entry of generic medicines onto international markets and vitalizing fair price competition (based on unified standards), resulting in lower prices and enabling treatment to be offered to more people.
- ⇒ Endorsing and facilitating application of international pharmaceutical quality standards, to create a level playing field for medicines assessment.
- ⇒ Developing a mechanism for accelerated medicines registration that is based on prequalification decisions but that respects national autonomy and national legislation.
- ⇒ Conducting risk assessment of non-prequalified medicines (via the Expert Review Panel mechanism (ERP)) to guide procurement of urgently-needed products for the Global Fund to Fight HIV/AIDS, Tuberculosis and Malaria, UNFPA and UNICEF.
- ⇒ Increasing low-income countries' regulatory capacity through on-the-job training and by offering rotational fellowships at WHO headquarters.
- ⇒ Organizing training workshops for regulators and manufacturers that reach around 1300 participants annually.
- ⇒ Widely disseminating training modules on good manufacturing practice (GMP), quality control and prequalification assessment.

CONCLUSION

The article portrays that the Pre-qualification programme of medicines launched by WHO in partnership with UNAIDS, UNICEF and UN National Fund has upraised the quality standard of medicines provided to developing countries i.e. low as well as middle income countries with relative cost effectiveness.

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