Improving quality for better treatment and greater access
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Quality in medicines is one of the cornerstones of health care and has a major impact on access and cost. Medicines of good quality improve the chances of successful treatment for individual patients and promote better outcomes for public health in general.

The Prequalification of Medicines Programme (PQP) is a unique initiative of the World Health Organization (WHO) that works to evaluate medicines quality to improve treatment results in developing countries and beyond. It was established in 2001 in response to the HIV/AIDS pandemic, to guide UN agencies purchasing large quantities of antiretroviral (ARV) medicines for developing countries. Since then, PQP has expanded to cover a range of services crucial to the manufacture, supply and regulation of quality medicines and the promotion of wider treatment access.

About the Programme

Life-saving quality medicines: PQP evaluates and assures the quality of medicines bought by international aid programmes and countries with weak pharmaceutical regulation. In so doing, it ensures that the medicines are safe and effective — in other words, better able to save lives and attain public health results.

Addressing the world’s health priorities: PQP was created to help advance quality treatment for the major pandemics: first for HIV/AIDS, and later for TB and malaria. Responding to the emerging priorities of today, it has expanded to cover reproductive health, some paediatric medicines, neglected tropical diseases and influenza.

Training and transfer of knowledge: Most low-income countries lack the capacity to produce, test and regulate quality medicines. PQP provides the additional service of boosting their in-country capacity through hands-on training of their regulators.

Unified world standard: PQP’s quality evaluation criteria are based on international pharmaceutical standards and a mix of the best practices applied by the world’s leading regulatory authorities. This promotes improved quality standards for medicines globally by providing a unified frame of reference and plays a critical role in harmonizing medicines quality within specific geographic and economic regions.

One-stop shop: The products certified by PQP are listed on a public web site (www.who.int/prequal) as a single-source reference for purchasers of medicines destined for developing countries, or for the countries themselves. The PQP list guides most of the product choices of the Global Fund to Fight AIDS, TB and Malaria, UNICEF, UNITAID and Médecins Sans Frontières.

"UNITAID would not be able to shape or create markets for urgently-needed, quality-assured products without WHO medicines prequalification. We also strongly support the work of WHO prequalification to build capacity and create mechanisms to sustain quality assurance activities in low- and middle-income countries."

Denis Braun, Executive Director, UNITAID

Malaria case study: WHO prequalification of medicines has been a critical element in the fight against malaria. It has led to a significant scale-up of quality-assured antimalarial medicines in Africa, contributing directly to the reduction in the disease burden. As an example, the availability of artemether-lumefantrine (AL), the most widely procured artemisinin-based combination therapy in the public sector, was expanded across Africa — with the number of quality-assured AL treatment courses increasing from 11 million in 2005 to 78 million in 2007, and reaching 131 million in 2010. In addition, the growing competition among prequalified manufacturers has led to significant decreases in the price of this life-saving medicine.

Dr Robert Newman, Director, Global Malaria Programme, WHO.

“Until 2000, the pattern was “poor quality medicines for the poor”. Today, thanks to prequalification, millions of people suffering from HIV/AIDS, tuberculosis (TB) or malaria in low-income countries have access to world standard treatment.”

Hanneke Pedersen, Deputy Director, UNICEF Supply Division

"Humanitarian Relief. WHO prequalification of medicines has been a critical element in the fight against malaria. It has led to a significant scale-up of quality-assured antimalarial medicines in Africa, contributing directly to the reduction in the disease burden. As an example, the availability of artemether-lumefantrine (AL), the most widely procured artemisinin-based combination therapy in the public sector, was expanded across Africa — with the number of quality-assured AL treatment courses increasing from 11 million in 2005 to 78 million in 2007, and reaching 131 million in 2010. In addition, the growing competition among prequalified manufacturers has led to significant decreases in the price of this life-saving medicine."
Paving the way for quality generic medicines and new treatments

Of the eight million people on HIV treatment today, 80% are taking PQP-certified ARVs, produced mostly by Indian manufacturers.

The pharmaceutical generic industry, particularly in India, has provided affordable, quality medicines to developing countries for over a decade. But it was not until 2002, when PQP prequalified the first Indian generic ARV for treating HIV/AIDS, that these products received international recognition and legitimacy. Today’s growing access to quality affordable medicines for HIV/AIDS and other conditions in developing countries is largely based on PQP’s work in assessing these medicines and transferring knowledge to manufacturers on the best practices to achieve international standards.

“The story of PQP is a compelling one: of how the world can come together in partnership and vision and address global problems such as HIV.”

Vincent Ahonkhai, Senior Regulatory Officer, Bill & Melinda Gates Foundation

WHO’s creation of PQP to assure the quality of the cheaper medicines gave aid agencies and countries the confidence to invest in quality products that were also affordable, thus ensuring the treatment of more patients. The impact of that early decision can be measured by the number of WHO prequalified generics on the market today, the dramatically lowered cost of treatment and the exponential growth in the number of patients treated. In 2012, the number of people receiving HIV/AIDS treatment reached 8 million, with about 80% of them taking PQP-certified ARVs, produced mostly by Indian manufacturers.

Price reductions for better products: Over the last decade PQP has validated numerous generic products’ legitimate entry into markets and procurement pools, including for HIV/AIDS, TB, malaria and reproductive health. The validation of generic products has provided an incentive for more generic manufacturers to raise their quality standards and increase the availability of affordable medicines. This, along with ramped-up generic production, has promoted competition and brought down prices even further. The price reduction of key ARVs, including of newer products — from US$ 12 000 per person annually to an average $ 200 today — has meant that many more people are getting treatment for the same outlay.

The price of a brand (innovator) ARV in 2002 was about US$ 12 000 for one year’s treatment for one person; 12 times the average annual income of a sub-Saharan African. An Indian generic manufacturer, Cipla, was offering an equivalent product for US$ 360–600 for developing countries.

“Without PQP, billions of dollars would have been spent on overpriced medicines; or money wasted on medicines that didn’t work.”

Ellen T’Hoen, Research Fellow, IS-Academy HIV/AIDS, School for Social Science Research, University of Amsterdam

Expanding markets for their products has also given generic manufacturers the incentive to innovate. For instance, generic companies are the only producers of some paediatric AIDS medicines, and the largest providers of fixed-dose combination (FDC) ARVs, pills combining several active pharmaceutical ingredients (APIs), recommended by WHO because they promote treatment adherence. PQP has facilitated the use of these products, better adapted to developing countries, by assuring their quality.

FDCs: In 2003 PQP prequalified the first-ever three-pills-in-one FDC ARV, produced by an Indian generic manufacturer. These combination medicines are easier to take and promote better compliance with treatment regimens, thereby improving therapeutic results for the patient and lowering the risk of drug resistance, which occurs when patients interrupt treatment or do not follow it with regularity. At the time, 3-in-1 pills were not manufactured by research-based industries, nor were they approved by regulators in the developed world.

Raising global quality standards: Beyond the service directly provided to medicines buyers, PQP has placed the issue of quality of medicines on the global health agenda and raised the standard for manufacturers and regulators. Since the first round of PQP-certified generic medicines, the generics industry has increased its efforts to improve the quality of its products. Today, many Indian manufacturers produce high-quality, affordable medicines for a number of conditions and export them to countries on both sides of the development divide.

“It’s easy to measure PQP’s impact. When we assess the products of manufacturers that are new to WHO prequalification we often find similar gaps in quality. When we assess manufacturers who have already been through the prequalification process for other products, we find that their standards are generally much higher. Experience with PQP benefits the manufacturers, who are consequently better positioned to approach international markets, and of course the raised standards benefit those receiving their medicines.”

Lynda Paleshnuk, Lead Quality Assessor for PQP
Just as importantly, and since the very beginning, the Programme has engaged national regulatory authorities to participate in the different steps of prequalification, thereby building capacity for regulators from developing countries, and internationalizing the skills of regulators from industrialized countries. Quality-assurance officers from all over the world — around 50 of whom are from developing regions — have joined forces with PQP to carry out site inspections and dossier assessments. The effect has been wider understanding of international quality standards and better communication between countries, resulting in harmonization of the benchmarks used to assess and assure the quality of an end product. PQP also organizes periodic workshops on medicines safely in developing countries. The long-term benefits are enhanced skills and, ultimately, greater country ownership.

“My personal experience with PQP has resulted in a tremendous improvement in my medicines regulatory expertise, especially dossier assessment, and given me the opportunity to learn from the best practices of international experts. PQP provides a great training ground and hands-on experience to developing country regulators.”

Gabriel Kaddu, Head, Drug Assessment and Registration, National Drug Authority, Uganda

Snapshot of key benefits of PQP

- Improved public health outcomes and aid effectiveness by ensuring that the millions of patients in developing countries now on treatment take quality-assured medicines designed for their specific needs, and by enabling medicines procurement agencies to purchase more for the funds available.

- More products available for priority diseases: to date, PQP has conducted 811 product assessments, including of APIs (the single chemical components that go into a medicine) and prequalified over 300 products. About 70% of WHO prequalified medicines are generic.

- Introduction of medicines designed specifically for developing country needs, for example: paediatric formulations for HIV, TB and malaria; combination therapies to prevent HIV transmission from mothers to their newborns; affordable antimalarials; and second-line medicines for drug-resistant HIV and TB.

- Trusted partner: PQP is universally accepted by developing countries. This ensures shorter lag times when national programmes purchase medicines because the PQP list provides them with a trusted and easy-to-use reference.

- Boosted pharmaceutical quality assurance in developing countries by supporting national regulators and manufacturers through numerous training and knowledge transfer activities.

- Support to manufacturers for improved quality: through the prequalification process, manufacturers learn to produce medicines according to international quality standards.

- Healthy competition between manufacturers and price reductions, including for brand (innovator) ARVs.

“We have had excellent support from the PQP assessment team in terms of technical guidance all through these years. This has enabled us to resolve many technical issues in a faster way.”

Vaishali Shridhankar, Regulatory Affairs, Cipla Ltd.

“PQP review is very well adapted to the needs of developing countries. PQP takes into account, for example, specific stability/temperature conditions and paediatric needs. These don’t apply in the same way in all countries. Some regulatory authorities therefore have less experience in evaluating medicines from these perspectives. No other evaluation system takes developing countries’ needs into account in the way that PQP does, PQP also monitors any variations (to content or manufacture) occurring after prequalification of a product — this is crucial if the continuous quality of the medicines distributed to users is to be guaranteed.”

Joelle Daviaud, Quality Assurance Specialist, The Global Fund to Fight AIDS, Tuberculosis and Malaria
How we work

The “prequalification” process is based on five fundamental steps:

1. **Invitation** to manufacturers to submit an expression of interest for evaluation of specific products.
2. **Submission** of dossiers by manufacturers providing a comprehensive set of data about the quality, safety and efficacy of the product(s) to be evaluated.
3. **Assessment** of all the data presented by a team of WHO staff and regulatory authority experts.
4. **Inspection** of the manufacturing sites for the finished pharmaceutical product and its API(s) and, if necessary, of the contract research organization (CRO) that conducted a clinical study for the product.
5. **Decision** to place the product on the WHO List of Prequalified Medicinal Products if it is found to meet the specified requirements and the associated manufacturing site(s) and CRO are compliant with WHO standards.

Invitations to manufacturers to submit an expression of interest for product evaluation are based uniquely on public health criteria which stipulate that the products concerned must be on the WHO Model List of Essential Medicines or are under consideration for inclusion in the List, and/or are recommended for use by a current WHO treatment guideline.

To ensure that prequalified products continue to meet WHO specifications, PQP regularly re-inspects manufacturing sites of prequalified products. It also evaluates any changes made to specifications, manufacturing processes and testing methods of prequalified products, and conducts random quality control tests on sampled prequalified products.

As well as prequalifying medicines, PQP also prequalifies pharmaceutical quality control laboratories, and conducts extensive advocacy in developing countries for medicines of guaranteed quality. Its long-term goal is to increase the availability of quality-assured medicines by assisting manufacturers to comply with WHO standards and supporting regulatory authorities to implement them.

An important recent addition to PQP’s work is the assessment of APIs for HIV/AIDS, malaria, TB and reproductive health products. Quality-assured APIs are the building blocks of good quality medicines. PQP is unique in providing this service, as stringent regulatory authorities generally do not assess APIs unless they are part of an application for a new medicine to be registered. An additional benefit of this service is that most medicines manufactured globally use APIs produced in Asia; therefore helping to ensure that imported APIs meet international standards of quality across the board.

**Our partners**

Many partners contribute to the work and outcomes of PQP. They include manufacturers, regulators, procurement agencies, WHO disease programmes and donors. The successes of PQP are dependent on the combined input of all of these partners.

**The future**

In spite of expanding treatment, developing countries still face enormous challenges in the areas of medicines quality, access and, more recently, funding.

New generation medicines for children and affordable second- and third-line ARVs for drug-resistant patients are urgently needed to ensure continuous progress in treating and preventing HIV/AIDS. The vast number of sub-standard antimalarials circulating in developing countries makes it extremely important to stimulate more competition between manufacturers to bring more quality-assured products into markets and close the door to sub-standard medicines. And the quality of numerous TB and reproductive health products must be improved.

Two crucial health areas for the near future are neglected tropical diseases and non-communicable diseases. Neglected tropical diseases occur only in developing countries and stand little chance of attracting the attention of research-based manufacturers to develop better medicines. While a number of private-public partnerships are mobilizing funds and some research for these, the quality of the resulting products will need careful oversight and assurance.

As non-communicable diseases, such as cardiovascular diseases, diabetes, asthma and cancer, take a bigger toll on developing countries, affordable access to user-friendly versions of existing generic medicines, and to low-cost versions of newly-developed medicines, for treating those diseases, will be needed. The quality of all these products will have to be assured.

In 2011 major donors’ aid to developing countries fell by nearly 2.5%, constituting a reversal of previous trends. In November 2011, the Global Fund to Fight AIDS, Tuberculosis and Malaria took the unprecedented move of cancelling a round of funding grants. Against this background of reduced funding for priority diseases, the responsibility for financing health programmes, and buying or producing medicines locally, will shift to countries.

PQP’s work in quality standard setting, assurance and capacity building continues to be of crucial importance in order to maintain and expand the catalytic achievements of the last decade.