The WHO Prequalification of Medicines Programme (PQP) was launched in 2001, in partnership with UNAIDS, UNICEF and UNFPA, with support from the World Bank. Its focus was evaluation of medicines for treating HIV/AIDS, malaria and tuberculosis (TB). Products in other therapeutic categories are now also evaluated.

The Programme reviews product dossiers, including data and information on safety, efficacy and quality, and inspects manufacturing sites, to assess compliance with good manufacturing practices (GMP). It also inspects clinical sites, including contract research organizations (CROs), to verify compliance with good clinical practice (GCP) and good laboratory practices (GLP), with respect to bioequivalence studies. It also prequalifies medicines quality control laboratories (QCLs).

For further information on medicines and QCL prequalification go to: http://www.who.int/prequal

Prequalification is needed more than ever

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 (Global Fund) took the unprecedented move of cancelling a round of funding grants. Against this background of reduced funding for priority diseases, the work of PQP continues to be highly relevant, unique and of great impact. It has created and maintains a level playing field for assessing the safety, quality and efficacy of medicines needed for treatment of priority diseases. It has saved procurement organizations considerable time and funds that would have otherwise been spent on verifying the quality, efficacy and safety of medicines to be procured. It stimulates price competition between suppliers, enabling more medicines to be purchased for more patients. And by contributing to the operation of a rapid quality risk assessment mechanism known as Expert Review Panel (ERP) process, it facilitates supply of products that are urgently needed, but that have not yet completed stringent assessment.

Key achievements in 2011

Thirty-five products (all generic, except one) were prequalified. They included the first amikacin injection formulation, the first generic product from ICH regions (prequalified via an abridged procedure), the first generic tenofovir/lamivudine/ Nevirapine combination and the first generic reproductive health medicine (ethinylestradiol + levonorgestrel). At the end of 2011, the WHO list of prequalified medicines totalled 269 products, manufactured in 25 countries. By the end of the year, PQP had also prequalified its first active pharmaceutical ingredients (APIs) (6 for antimalarials and 2 for anti-TB medicines) and 6 more medicines QCLs (1 each in Belgium, Brazil, India, the Netherlands, Portugal and Tanzania). At the end of 2011, a total of 23 QCLs had been prequalified, covering all WHO 6 regions, and a further 32 were working towards becoming prequalified.

Assessment activities

Sixty-eight dossiers were received and 46 dossiers were accepted for evaluation. Nearly 1000 assessment reports were produced and over 500 variations, submitted by manufacturers of prequalified products, were assessed.
The assessment sessions held in Copenhagen, Denmark, included a training component and enabled a growing number of developing country assessors to acquire stringent regulatory expertise. The sessions also incorporated technical consultations, allowing applicants to discuss technical issues relating to their dossiers with assessors. The consultations benefited from the presence of a range of assessors with considerable assessment experience in different technical areas.

An assessor from Botswana and an assessor from Ghana each completed a rotational fellowship with PQP during 2011, and continue to attend assessment sessions in Copenhagen. A third assessor – from Uganda – started a fellowship in late 2011. Assessors who have completed rotational fellowships with PQP generally participate in Copenhagen assessment sessions regularly thereafter, helping to maintain a strong and mutually beneficial relationship between PQP and national medicines regulatory authorities (NMRAs). Rotational assessors receive assessment training with PQP before starting their fellowship.

Inspections

PQP inspectors carried out 90 on-site inspections in 18 countries: 40 of finished pharmaceutical product manufacturing sites; 28 of API manufacturing sites; 15 of CROs and 7 of QCLs. (Inspections were carried out mostly in India and in China, but also in Belarus, Brazil, Chile, Egypt, France, Kenya, Republic of Korea, Morocco, Russia, South Africa, Viet Nam and Zimbabwe.) PQP also carried out 3 “desk review” inspections.

PQP inspections continued to benefit substantially from the participation of PIC/S inspectors. This participation helped to ensure that PQP inspections were objective, impartial and informed by the highest levels of regulatory expertise. And as in previous years, PQP invited local NMRA staff to participate in API, CRO, FPP and QCL inspections as observers, to help build inspection capacity.

Advice, assistance and training

PQP responded to many requests from manufacturers for advice concerning, for example, bioequivalence study protocols and choice of comparator products. It also continued to provide technical assistance to manufacturers and national QCLs that sought to resolve specific practical problems related to GMP, good practices for QCLs and/or meeting medicines regulatory requirements.

In 2011, PQP organized 17 technical assistance missions to 13 pharmaceutical manufacturers in 5 countries (Bangladesh, China, Kenya, Nigeria and Pakistan), for 5 CROs in China, and for 2 QCLs in China, and 1 QCL each in Benin, Cameroon, Madagascar and Thailand. Assistance took the form of an audit, followed by development of an improvement plan. Training in specific technical regulatory areas was also made available where needed. Follow-up missions were organized to support implementation of improvement plans. Additionally, staff in WHO’s Americas, Eastern Mediterranean and European Regional Offices provided technical support to manufacturers and QCLs in their respective regions.

PQP also organized, co-organized or supported 32 training courses, for nearly 1400 participants. Training on general or specific technical issues was given to manufacturers, and to NMRA and QCL staff. Courses generally also included an introduction or update on PQP requirements and services.
Norms and standards underpinning or relevant to WHO prequalification activities

The norms and standards developed and approved via the WHO Expert Committee on Specifications for Pharmaceutical Preparations underpin all of PQP’s activities. At its 46th meeting, the Committee adopted 1 monograph for HIV and related conditions, 2 monographs for antimalarial medicines, 3 monographs for anti-tuberculosis medicines, 2 monographs for reproductive health products and 1 international chemical reference substance for an antimalarial. It also adopted a wide range of new or revised guidelines and procedures of direct relevance to PQP’s activities, for example on development of multisource (generic) products, development of paediatric formulations and quality requirements of artemisinin as a starting material.

Ensuring supply

At the end of 2011 no products had been prequalified for many of the formulations included on current EOIs. Frequently, the reason for this is the fragmented nature of the market for the product concerned and/or the lack of commitment to procuring quality-assured products on the part of procurement agencies. WHO continues to highlight the health and economic impacts of poor-quality medicines. And together with the Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), it has created a mechanism to ensure that supply of products is not impeded in the short term. This mechanism — known as the Expert Review Panel (ERP) — provides risk-based advice to aid decisions about procurement of products that, as a rule, are in the PQP “pipeline”, but that have not yet been prequalified or approved by a stringent regulatory authority. It is important to mention that ERP is not a substitute for prequalification but rather an additional technical instrument to make ad hoc evidence-based procurement decisions.

Each ERP is a discrete operation: the procurement organization concerned issues an invitation to manufacturers to submit a product dossier for quality risk assessment, which is then conducted by ERP technical experts.

ERPs to date have ranged widely in the number of products assessed: from a few up to 80 product dossiers. By the end of 2011, nearly 350 product dossiers covering 230 different products had been reviewed by an ERP. Assessment is carried out by highly experienced regulators (assessors) and covers manufacturing process and specification, stability data, evidence of therapeutic equivalence, and quality and API source. An assessment report is issued for each product. Most importantly for procurers, each assessment report includes categorization of the level of risk associated with use of the product in question.

Today, the ERP mechanism is used not only by the Global Fund but also by the Global Drug Facility, UNITAID, UNFPA and several WHO departments. Assessment usually takes up to 4 weeks, but can be as short as several days when products and suppliers are few.

Accelerating registration

For procuring organizations, patients and manufacturers, the time to registration (and thus to access to or availability on national markets) is of vital importance. A procedure for accelerated approval of
prequalified products was developed and will be pilot-tested in 2012. Fifteen countries have been identified for participation in the pilot test, as have 2 candidate products.

External review

UNITAID is currently PQP’s major donor, providing about 90% of its funding. In 2011, it conducted a mid-term evaluation of PQP which concluded that, “WHO-PQP with its various and supplementary activities, including long-term objectives like capacity building in regulation and production, is a unique system that plays a role in the protection of public health... It is certainly worth the resources invested so far. It is beneficial to all stakeholders involved in the procurement of medicines to populations in need and its existence is essential.”

Articles and publications

PQP produced a number of articles and publications describing different aspects of its work:


Survey of the quality of anti-tuberculosis medicines circulating in selected newly independent states of the former Soviet Union. Available at: http://www.who.int/prequal/info_applicants/qclabs/quality_monitoring.htm

“Best medicines. Good-quality active pharmaceutical ingredients are vital to the product of good-quality medicines.” In: World Pharmaceutical Frontiers, September 2011. Available at: http://edition.pagesuite-professional.co.uk/launch.aspx?referral=other&pnum=77&refresh=5Wp1z0E20B4c&EID=daba9217-c7a4-4529-a687-a6fb6437e4c5&skip=&p=77

1 Outlook on Aid. Survey on Donors’ Forward Spending Plans 2012−2015. Available at: http://www.oecd.org/document/30/0,3746,en_2649_3236398_46010014_1_1_1_1,00.html
2 International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use.
3 The total number of products ever prequalified by PQP is higher since it includes products prequalified and removed from the WHO List of Prequalified Medicinal Products. Products may be removed for a number reasons, including ending of production by the manufacturer following a change in WHO-recommended treatment guidelines.
4 By reviewing site inspection reports from other stringent inspectorates, PQP concluded that inspections by PQP were not needed for the products concerned.
5 Pharmaceutical Inspection Convention and Pharmaceutical Inspection Co-operation Scheme (jointly referred to as PIC/S)
6 http://www.unitaid.eu/
7 The evaluation was carried out by AEDES. The term evaluation report is available at: http://www.unitaid.eu/medicinesqa