



PQP

QUALITY MEDICINES FOR EVERYONE

PREQUALIFICATION OF
MEDICINES PROGRAMME
A UNITED NATIONS PROGRAMME
MANAGED BY WHO



World Health
Organization

WHO PREQUALIFICATION OF MEDICINES PROGRAMME (PQP) FACTS AND FIGURES FOR 2010

The WHO Prequalification of Medicines Programme (PQP) was launched in 2001, in partnership with UNAIDS, UNICEF and the UN Population Fund, with support from the World Bank. Its focus was tackling the quality problems commonly associated with medicines for treating HIV/AIDS, malaria and tuberculosis (TB). In 2006, the Programme laid the groundwork for prequalifying medicines and commodities for reproductive health. This was in response to the fact that, in many developing countries, the need for family planning and reproductive health services remains urgent.

Evaluation of medicines by the Programme includes assessment of data and information on safety, efficacy and quality. In addition, inspections are performed to assess compliance with good manufacturing practices (GMP). Inspection activities expanded in 2003 to include manufacturers of selected active pharmaceutical ingredients (API), and in 2004, to include clinical sites. Clinical sites, including contract research organizations (CROs), are inspected to verify bio-equivalence with good laboratory practices and good clinical practices.

Thirty-six products were prequalified in 2010, of which 30 were generics. At the end of 2010, the WHO list of prequalified medicines totalled 252 products,¹ manufactured in 20 countries. WHO prequalification "firsts" included artesunate powder for injection (which was the first prequalified sterile product made in China); the first combination tenofovir disoproxil fumarate/lamivudine and the first generic emtricitabine.

Six medicines quality control laboratories (QCLs) were also prequalified: 1 in Bolivia, 1 in Canada, 1 in Peru, 2 in Ukraine and 1 in Uruguay. At the end of 2010, a total of 17 QCLs had been prequalified and a further 30 were working towards becoming prequalified.

Invitations to manufacturers to submit an expression of interest (EOI) for product evaluation were issued for anti-TB medicines, HIV/AIDS-related care and treatment products, and reproductive health products. The new invitations incorporate additional products and/or take into account revisions made to WHO treatment guidelines. Additionally, the 1st invitation to manufacturers of active pharmaceutical ingredients (APIs) was issued in October 2010, marking the launch of WHO prequalification of APIs. (A 2nd, expanded invitation to API manufacturers to submit an EOI was issued in March 2011.) It is expected that time taken to reach prequalification will be shorter for FPPs that are manufactured using WHO-prequalified APIs, than for FPPs that are manufactured using APIs that have not previously been evaluated by WHO PQP.



PQP

QUALITY MEDICINES FOR EVERYONE

PREQUALIFICATION OF
MEDICINES PROGRAMME
A UNITED NATIONS PROGRAMME
MANAGED BY WHO



World Health
Organization

Assessment activities

In 2010, 51 dossiers were submitted and 53 dossiers (some of which were received in late 2009) were accepted for evaluation. Nearly 1000 assessment reports were produced. PQP also assessed nearly 600 variations submitted by manufacturers of prequalified products.

The assessment sessions held in Copenhagen, Denmark, include a training component and are enabling a growing number of developing country assessors to acquire stringent regulatory expertise.

The Copenhagen sessions also incorporate technical consultations so that applicants can discuss technical issues relating to their dossiers with assessors. The consultations benefit from the presence of a range of assessors with considerable assessment experience.

A new collaborative procedure for facilitating registration of prequalified medicines in the East African Community (EAC) was piloted. The overall aim was to identify a framework, for WHO-EAC, for joint evaluation and approval of dossiers and inspections of medicine manufacturing sites, and to ensure that these assessments are integrated into national regulatory decision-making. Two assessors each from 3 EAC countries (Kenya, Tanzania and Uganda) and 6 WHO assessors jointly assessed 2 product dossiers submitted by a single manufacturer. The dossiers were submitted in parallel, and with identical content, to each participating EAC country and to PQP. The products were both prequalified: HA488 (abacavir, dispersible tablets 60 mg) in August 2010 and TB217 (amikacin, injection 500 mg/2 ml) in January 2011. For the manufacturer, the principal benefit of this joint assessment was that once the products had been jointly assessed and approved by WHO-EAC, they were granted immediate access to the markets of each of the countries that had participated in the joint assessment. For the regulators involved, such joint assessment contributes to harmonization of regulatory requirements at regional level. PQP is hoping to use the same model for assessing selected, technically complex, high-priority products. Several partners and stakeholders see joint assessment as an effective means of speeding up access to much needed products.

Inspections

PQP inspectors carried out 59 inspections in 18 countries: 38 of finished pharmaceutical product manufacturing sites; 5 of API manufacturing sites; 7 of CROs and 9 of pharmaceutical QCLs. (Inspections were carried out mostly in India and in China, but also in Algeria, Belgium, Bolivia, Egypt, France, Iran, Kenya, Morocco, the Netherlands, Peru, Russia, South Africa, Tanzania, Uganda, Uruguay, the United States and Zimbabwe.)

A new collaborative procedure for joint inspections was initiated at the beginning of 2010. A secure web site has been established for the sharing of inspection plans, arranging of joint inspections, and sharing of information and inspection reports, with recognition by participating EAC parties and PQP. This will be further explored and possibly expanded. Joint inspections are planned for 2011 in an attempt to prevent duplication of inspections. Inspection reports will be shared by the parties following the inspection. It is hoped that the outcome of the inspection will be accepted by all participating inspectorates. PQP continues to invite local NMRA staff or



PQP

QUALITY MEDICINES FOR EVERYONE

PREQUALIFICATION OF
MEDICINES PROGRAMME
A UNITED NATIONS PROGRAMME
MANAGED BY WHO



World Health
Organization

observers to participate in API, CRO, FPP and QCL inspections.

The risk assessment procedure for identifying which API manufacturing sites should be inspected has been completed for substances used to manufacture products for the treatment of malaria and TB. It is planned to expand this risk assessment to APIs used in products for the treatment of HIV/AIDS.

Advice and assistance

PQP continues to respond to manufacturers' request for assistance concerning issues relating to, for example, bioequivalence study protocols and choice of comparator products.

PQP continues to provide technical assistance to manufacturers and national QCLs that aims at resolving specific practical problems related to GMP, good practices for QCLs and/or meeting medicines regulatory requirements. Assistance is given in the form of an audit, advice on development of an improvement plan, and training in technical or regulatory areas. Follow-up missions are also organized to support implementation of improvement plans. In 2010, PQP organized 22 technical assistance missions to pharmaceutical manufacturers in 4 countries (Argentina, China, India and Indonesia) and 10 technical assistance missions to national QCLs (in Argentina, Brazil, Burkina Faso, China, Egypt, Jamaica, Panama, Peru and Yemen).

Training and hands-on practice remain crucial to capacity building. PQP organized, co-organized or supported 23 training courses. Training on general or specific technical issues was given to manufacturers, and to NMRA and QCL staff, as well as an introduction and/or update on PQP requirements and services. Training included group sessions as well as discussion sessions with members of assessment or inspection teams working with PQP. In 2010, these workshops involved more than 1200 participants representing regulatory authorities, pharmaceutical manufacturers and QCL staff.

Testing of medicines quality

When implementing sampling and testing projects PQP evaluates specifically the quality of WHO-prequalified products. In a study of the quality of antimalarials, concluded in 2010, the quality of WHO-prequalified products far exceeded that of non-WHO-prequalified products. (Less than 4% of WHO-prequalified artemether-lumefantrine and artesunate-amodiaquine samples failed to comply with international quality standards, whereas the failure rate reached 60% for non-WHO-prequalified samples of the same composition.) Similarly, a survey of the quality of anti-TB medicines conducted in 2009/2010 in Armenia, Azerbaijan, Belarus, Kazakhstan, Ukraine and Uzbekistan showed that all prequalified products sampled and containing isoniazid/rifampicin complied with international quality standards.

Norms and standards underpinning or relevant to WHO prequalification activities

The 45th meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations adopted 5 monographs for HIV and related conditions, 4 monographs for



PREQUALIFICATION OF
MEDICINES PROGRAMME
A UNITED NATIONS PROGRAMME
MANAGED BY WHO



World Health
Organization

antimalarial medicines, 6 monographs for antituberculosis medicines, 2 monographs for influenza-specific antiviral medicines and 1 for a reproductive health product. The Committee also adopted a number of new or revised guidelines and procedures of direct relevance to PQP's activities.

Improving PQP services

The results of a survey of manufacturers provided further information for developing greater "client" focus.² Based on the survey results, PQP staff worked on improvements to the Programme, some of which have already been implemented (for example, raising awareness of the opportunity for manufacturers to meet and consult with PQP assessors, clarifying procedure for resolving disagreements surrounding questions raised during the assessment of product dossiers) and some of which (e.g. reducing the time taken to review and reply to applicants during the dossier assessment process, providing the same assessors throughout the assessment process for a product dossier) depend upon completion of other activities (e.g. finalization of PQP's new information management system). Others (for example, the perceived greater stringency of WHO GMP requirements), will require further discussion with manufacturers.

Benefits to manufacturers

In 2010, PQP initiated a study to help it describe and quantify the potential benefits to manufacturers of having a product or products prequalified by WHO. PQP will use the results to develop a "business case for participation in WHO medicines prequalification" for presentation to manufacturers.

Further information on the WHO Prequalification of Medicines Programme, including the full list of medicines prequalified by WHO can be found at: <http://www.who.int/prequal>

¹ 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.

² At: http://www.who.int/medicines/publications/druginformation/issues/DrugInformation2010_Vol24-4/en/index.html ("WHO Prequalification of Medicines Programme: survey of service quality provided to manufacturers").