WHO PREQUALIFICATION OF MEDICINES PROGRAMME (PQP)
FACTS AND FIGURES FOR 2009

The WHO Prequalification of Medicines Programme 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.

2009 was a good year for the WHO Prequalification of Medicines Programme: a record 44 medicines products were prequalified, of which 39 are generics. At the end of 2009, the WHO list of prequalified medicines totalled 237 products, manufactured in 16 countries. WHO prequalification "firsts" included 3 reproductive health products as well as generic lopinavir/ritonavir, generic oseltamivir, generic tenofovir, ciprofloxacin infusion, generic ceftriaxone and generic abacavir oral solution.

Three medicines quality control laboratories (QCLs) were also prequalified: 1 in Kenya and 2 in Singapore. At the end of 2009, a total of 11 QCLs had been prequalified and a further 29 were working towards becoming prequalified.

Invitations to manufacturers to submit an expression of interest (EOI) for product evaluation were issued for antimalarial medicines, antituberculosis medicines, HIV/AIDS-related care and treatment products, influenza-specific antiviral medicines and reproductive health products. The new invitations incorporate additional products and/or take into account revisions made to WHO treatment guidelines.

Assessment activities

The pace of dossier submissions and assessments of previous years was maintained. Eighty-four dossiers were submitted for evaluation and 53 dossiers were accepted for evaluation. Seven dossier assessment sessions were held in Copenhagen, during which 898 assessment reports were produced: 528 for HIV/AIDS-related products; 197 for antituberculosis medicines; 110 for antimalarial medicines; 28 for influenza-specific antiviral medicines and 35 for reproductive health products. An additional 100 "supporting reports" (for example, on APIs included in products, or on dossiers to be cancelled) were also produced.

The Copenhagen sessions include a training component for assessors from developing countries and are enabling a growing number of developing country assessors to acquire stringent regulatory expertise.

The Copenhagen sessions also incorporate technical consultations between assessors and applicants so that the latter 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. Applicants pay their own costs to attend consultations and must be committed to the prequalification process.

Problems continue to be seen regarding antituberculosis products: the number of related dossiers continues to be low and their quality is often poor. PQP therefore initiated a study to review dossier deficiencies for these products.
and to determine what deficiencies are most commonly observed at each evaluation stage. (The study results will be published and guidance on how to avoid these deficiencies may be developed.) Additionally, a member of the PQP team worked with the WHO China country office to secure funding from the Bill & Melinda Gates Foundation, for a project to provide technical support on quality issues to manufacturers of fixed-dose combination (FDC) antituberculosis products. It is hoped that this will lead to increased dossier submissions to PQP for FDC products.

Inspections

PQP inspectors carried out 52 inspections in 9 countries: 27 of finished pharmaceutical product manufacturing sites; 7 of API manufacturing sites; 10 of CROs; and 8 of pharmaceutical QCLs (including 2 pre-audit inspections). The majority of inspections were carried out in India, followed by China, South Africa, Singapore, Ukraine and Viet Nam.

A number of manufacturers were contacted in late 2009, and requested to submit inspection reports that they had received from stringent regulatory authorities (SRAs), together with a report of corrective actions they have implemented following the related SRA inspections. PQP is investigating the possibility of conducting a "desk review" of these documents, and of any relevant quality review reports prepared by the manufacturers. Such review would be in lieu of an on-site inspection by WHO, subject to specified conditions. The aim is to avoid duplication of site inspections and to optimize use of inspection resources. But only two cases were found in which the inspection reports and corrective actions were considered to meet the requirements set by the inspection team for allowing postponement of an on-site inspection by WHO. An amendment to the WHO procedure for prequalification of pharmaceutical products is now being considered, to make provision for this new process.

Advice and assistance

WHO assessors continued to provide scientific advice to manufacturers. This included review of bioequivalence protocols and responding on a daily basis to specific questions relating to quality and safety. New guidance was issued on Submission of Documentation for Prequalification of Multisource (generic) Finished Pharmaceutical Products approved by Stringent Regulatory Authorities, and an alternative procedure for accepting second-line TB product dossiers for assessment.

PQP organized 10 technical missions to pharmaceutical manufacturers and QCLs in 7 different countries. Missions focused principally on good manufacturing practice, but also on dossier preparation and on quality systems in QCLs. It also organized 12 training workshops and co-organized or supported a further 5 workshops, for nearly 800 participants. Workshops ranged from introductory workshops on the WHO Prequalification of Medicines Programme and how to meet its requirements, to assessment of multisource interchangeable medicines, to the planning, implementation and assessment of stability studies.

Testing of medicines quality

The pilot phase of an activity to sample and monitor the quality of paediatric and second-line antiretrovirals and co-trimoxazole, for treating HIV/AIDS, was completed. Nearly 400 medicines samples, produced by 24 manufacturers, were collected, mostly from treatment centres. Only 3 samples failed quality testing and none of the failures were life-threatening for patients. The results underscore that, provided procurement and distribution practices are sound, medicines prequalified by the Programme can be viewed with confidence, by health workers and patients alike.

The quality of antimalarial medicines was surveyed in 6 African countries, for artemisinin-based combination therapy and sulfadoxine-pyrimethamine oral dosage forms. Over 900 medicines samples were collected from all levels of the distribution chain and informal market and screened using "minilabs", in cooperation with the relevant national medicines regulatory authority. Thereafter, 306 samples were fully tested in the laboratory: 74 samples were non-compliant and demonstrated a range of quality problems, including absence of the API in 2 samples. A
A quality survey was also initiated in Armenia, Azerbaijan, Belarus, Kazakhstan, Ukraine and Uzbekistan. It focuses on antituberculosis medicines containing rifampicin, isoniazid, kanamycin and ofloxacin. Testing is ongoing for the 291 samples collected.

**Norms and standards underpinning or relevant to WHO prequalification activities**

The 44th meeting of the WHO Expert Committee on Specifications for Pharmaceutical Preparations adopted 7 monographs for HIV and related conditions, 5 monographs for antimalarial medicines, 6 monographs for antituberculosis medicines and 1 monograph for influenza-specific antiviral medicines. The Committee also adopted: an update of good practices for quality control laboratories; a guideline for the preparation of a CRO master file; a guideline on requalification of prequalification dossiers; various updates and revisions of good manufacturing practice texts; and an update of good distribution practices for pharmaceutical products. Each of these norms and standards is of direct relevance to PQP’s activities.

**Improving PQP services**

A business plan for PQP was completed in August. It analyses PQP’s current mandate and functions, maps PQP performance, estimates resources required for coming years, and makes recommendations on how PQP can improve organization and management. The recommendations are now being implemented. The plan projects an economic return on investment of 170:1 for the programme for the period 2009–2013. The projection is based on: projected availability of global funding for procuring medicines for treating HIV/AIDS, TB and malaria; projected prequalification of 105 additional medicines (around 90% of which will be generic medicines); and projected estimated impact on additional volume of medicines that can be purchased as a result of increased competition among generics.

**Survey of manufacturers**

In late 2009, work started on development of a first survey of manufacturers. The aim is to obtain feedback on the services provided by PQP, to analyse where and how improvements to those services might be made.

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](http://www.who.int/prequal)