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The WHO prequalification project

The Prequalification project, set up in 2001, is a service provided by the World Health Organization (WHO) to facilitate access to medicines that meet unified standards of quality, safety and efficacy for HIV/AIDS, malaria and tuberculosis.

From the outset, the project was supported by UNAIDS, UNICEF, UNFPA and the World Bank as a concrete contribution to the United Nations priority goal of addressing widespread diseases in countries with limited access to quality medicines.

Prequalification was originally intended to give United Nations procurement agencies, such as UNICEF the choice of a range of quality medicines. With time, the growing list of products (i.e. medicines) that have been found to meet the set requirements has come to be seen as a useful tool for anyone bulk purchasing medicines, including countries themselves and other organizations. For instance, the Global Fund to Fight AIDS, Tuberculosis and Malaria disburses money for medicines that have been prequalified by the WHO process.

How it works

Any manufacturer wishing their medicines to be included in the prequalified products list are invited to apply. Each manufacturer must present extensive information on the product (or products) submitted to allow qualified assessment teams to evaluate its quality, safety and efficacy. The manufacturer must also open its manufacturing sites to an inspection team which assesses working procedures for compliance with WHO Good Manufacturing Practices (GMP). Alternatively, the inspections carried out by stringent regulatory bodies are recognized and their work is not duplicated by WHO.

The standards against which the assessment teams evaluate both the quality specifications of medicines and the manufacturing sites are based on the principles and practices agreed by the world's leading regulatory agencies and adopted by the WHO Expert Committee on Specification for Pharmaceutical Preparations. In other words:

- The manufacturer provides a comprehensive set of data about the quality, safety and efficacy of its product, including details about the purity of all ingredients used in manufacture, data about finished products, such as information about

- stability, and the results of in vivo bioequivalence tests (clinical trials conducted in healthy volunteers).
- The team of assessors evaluates all the data presented and if satisfied with the evidence sends the product to professional control testing laboratories contracted by WHO in France, South Africa or Switzerland for analytical verification of quality.
 - If the product is found to meet the specified requirements, and the manufacturing site complies with GMP, both the product linked to this manufacturing site and company are added to a list hosted by WHO on a public web site.

All product and manufacturing site requirements, standards used in evaluating the product and the profile of the inspection teams are outlined on the WHO prequalification project web site. The site also includes the list of prequalified medicines and their manufacturers.

The assessment teams evaluating the products and manufacturers include experts from some of the national regulatory authorities of the European Union as well as Canada and Switzerland. These teams ensure that high quality, international standards are respected. The teams work with regulators from the developing countries where the medicines will be used to make sure that the process and results are at all times transparent and trusted by the end-users.

The prequalification process takes a minimum of three months if the product meets all the required standards. When products do not meet the appropriate standards the process can be longer and if the manufacturer fails to prove the quality, safety and efficacy of its medicine it will not be prequalified. Inclusion in the list does not mean that the prequalified status of a product lasts forever. All medicines are requalified after three years, or earlier, if needed. WHO also carries out random quality control testing of prequalified medicines that have been supplied to countries.

The list of medicines

Medicines which have been found to meet the required standards so far are from both brand name (42 medicines) and generic (61 medicines) manufacturers. These include 62 antiretrovirals and 33 medicines for HIV/AIDS-related diseases; two antimalarials and six drugs for the treatment of tuberculosis.

Medicines containing one active ingredient and those combining several active ingredients in one pill, usually called fixed-dose combination drugs, have been prequalified. For tuberculosis, there is one quadruple (four-in-one pill) and one double (two-in-one) fixed dose combination drug and for malaria one double fixed dose combination drug has been approved.

In the case of AIDS medicines, two different triple (three-in-one) fixed-dose combination drugs have recently been approved; one from an originator company and the other from two different generic companies.

The principles for assessing the quality of fixed-dose combination drugs are the same as those used by the European Agency for the Evaluation of Medicinal Products (EMA) and the USA Food and Drug Administration (FDA). In other words, the prequalification assessment team evaluates the required data, including in vivo bioequivalence tests carried out by the manufacturers. The fixed-dose combination drug is tested against the separate medicines taken together in the same dosage as is present in the fixed-dose combination pill.

In soliciting applications from companies, WHO does not question whether the products presented are patented or generic, since patent laws vary according to different national legal systems. It suffices that a company is duly authorized for pharmaceutical manufacture in its own country and that the final product meets stringent standards of quality, efficacy and safety.

An integrated process

The availability of quality, safety and efficacy of medicines is a major concern of WHO. To ensure that quality pharmaceuticals are available, WHO sets norms and standards, develops guidelines and advises Member States on issues related to quality assurance of medicines in national and international markets. WHO assists countries in building national regulatory capacity through networking, training and information sharing. These activities have been endorsed and supported by Member States through numerous World Health Assembly resolutions.

The Prequalification project is part of these activities and mandate. It does not intend to replace national regulatory authorities or national authorization systems for importation of medicines. Prequalification draws from the expertise of some of the best national regulatory authorities to provide a list of prequalified products that comply with unified international standards.

This is why, both in 2002 and in 2004, the International Conference of Drug Regulatory Authorities (ICDRA), made up of more than 100 national medicines regulatory authorities, made a formal recommendation that "WHO should continue the Pre-qualification Project of medicines for priority disease programmes, particularly for HIV/AIDS, malaria and tuberculosis".

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