

WHO Prequalification Scheme for ARVs

The Issue

The WHO Pre-qualification scheme for assessing the quality of ARVs was launched in March 2002. Opinion is divided regarding the robustness and appropriateness of the Scheme and whether or not the urgency of the global HIV crisis provides sufficient justification for its use as a formal regulatory process. GSK is regularly asked for its views on the Scheme and on the role of generic ARVs – in general – in helping to address the access crisis in developing countries. This paper seeks to address all these issues.

GSK's Position

- GSK supports the current health regulatory environment whereby all prescription drugs must meet the quality, safety, and efficacy requirements of the local health regulatory authority in order to achieve regulatory approval for use in each local country where the product will be used.
- Given the urgency of the HIV crisis, GSK accepts that the WHO Pre-qualification Scheme has a role to play in helping to inform local regulatory approval and scale up availability of WHO recommended ARVs. However, the Scheme should never be seen as a formal regulatory assessment process.
- The Scheme includes the explicit caveat that inclusion in the list does not constitute an endorsement, or warranty of the fitness, of any product for a particular purpose, including in regard of its safety and/or efficacy in the treatment of HIV/AIDS
- The WHO has confirmed that inclusion on its Pre-qualification List does not exempt the product from assessment under national regulatory procedures and that pharmaceutical suppliers are expected to register their products through the normal national drug registration process.
- The Global Fund recognises the WHO Pre-Qualification Scheme as a quality assurance scheme, but not a registration scheme.
- Quality and safety are important considerations when selecting a treatment. The ARVs produced by GSK meet the highest manufacturing and quality standards, including those set by U.S. and European regulatory agencies
- GSK has always maintained that generic medicines and generic companies have a role to play in improving access to medicines in the developing world. However, the offers made by the generic manufacturers must be sustainable and of good quality.

BACKGROUND

The WHO Prequalification Scheme

The WHO Pre-qualification Scheme for ARVs (<http://mednet3.who.int/prequal/>) was formally launched in March 2002 following a year long pilot project. Its stated aim is to assess the acceptability “in principle” of HIV/AIDS drugs for procurement by UN Agencies. The assessment procedure is aimed at identifying products and suppliers (both branded and generic) meeting WHO *quality* standards. These standards are universally recognized for their validity in comparing the quality of a generic with an existing innovator drug.

However, these same standards are applied by the WHO even when no equivalent innovator product (and/or published efficacy & safety data) exist, for example, to novel Fixed Dose Combinations (FDCs). Under established and internationally-recognised safety and efficacy rules, these FDCs should be considered to be “investigative new drugs” not generics, and assessed accordingly. Sole reliance by Regulatory Authorities on the WHO Scheme for novel FDCs could therefore mean that vital efficacy and safety data has not been assessed, resulting in the possible approval of sub-optimal products.

The WHO's Scheme includes the explicit caveat that inclusion in the list does not constitute an endorsement, or warranty of the fitness, of any product for a particular purpose, including in regard of its safety and/or efficacy in the treatment of HIV/AIDS

Products and manufacturing sites included in the list are re-assessed at “regular” intervals. Products and manufacturing sites will be removed from the list if, as a result of a reassessment, it is found that they no longer comply with the specified standards.

Further details on the scheme are attached at **Annex A**.

The Role of Generics

Generic medicines can have a role to play in improving access to medicines in the developing world, and in many countries they are perfectly legal because there are no patents. However, it would be wrong to think they alone can fix the crisis through the provision of more affordable prices than branded companies. GSK's not-for-profit prices are applicable to orders of any size and are not dependent on large order quantities. They also include insurance and freight costs and are generally comparable with the prices of generics when these additional elements are factored in.

The primary concern should be whether or not the offers made by generic manufacturers are *sustainable*. Clearly it is not in the interests of patients or those organising treatment programmes to embark on a treatment regimen or to set up all the support services required to run a treatment programme, and to then find that the manufacturer is unable to continue supply of quality products.

GLOBAL
PUBLIC POLICY ISSUES
GlaxoSmithKline's Position

The delistings and withdrawals from the WHO Prequalification Scheme for ARVs during the latter part of 2004 and confusion they caused for treatment programmes in developing countries, reinforces GSK's long held concerns in the area of generic manufacturing and our focus on selecting the most appropriate partners to whom to grant voluntary licenses for the manufacture of our ARVs. To date, GSK has signed 8 licensing agreements with generic companies across Sub-Saharan Africa.

October 2006

WHO Pre-qualification Scheme – A Summary

Interested suppliers are requested to submit *Expressions of Interest*, followed by product dossiers. These are then assessed against the *WHO Guiding Principles for Evaluation of Manufacturers for the Procurement and Sourcing of Pharmaceutical Products*. The two main components of the assessment process are dossier evaluation and manufacturing site inspections, although a number of other criteria are also considered, including bioequivalence data.

1) Dossier evaluation

Dossiers are evaluated for compliance with WHO recommendations and guidelines regarding the assessment of Multisource Products (*Marketing Authorization of Pharmaceutical Products with special Reference to Multisource (Generic) Products: A Manual for a Drug Regulatory Authority and bio-equivalence data*). Where appropriate, ICH guidelines, are also used to complement the aforesaid WHO recommendations and guidelines.

2) Manufacturing site inspections.

Inspections are performed at all manufacturing sites (excluding those sites that may have recently been inspected by regulatory authorities such as members from the Pharmaceutical Inspection Co-operation Scheme (PIC/S), or regulatory authorities with equivalent quality systems). The inspections include an "in-depth" evaluation to assess compliance with GMP. Detailed inspection reports, listing all the observations and non-compliances are drafted and communicated to manufacturers after each inspection.

Other criteria taken into account in the assessment process include:

- Valid regulatory approval to manufacture
- Regulatory or other approval of the product in accordance with national requirements
- Product manufactured in compliance with GMP as certified by the national regulatory authority and/or certified GMP inspectors
- Product certificate exists in accordance with the WHO certification scheme on the quality of pharmaceutical products moving in international commerce
- Product dossier of acceptable quality submitted and positive outcome of the assessment against the WHO recommended standards referred to below.
- Positive outcome of the inspection of the manufacturing site performed by inspectors appointed by WHO

WHO Disclaimer

Inclusion in the list does not constitute an endorsement, or warranty of the fitness, of any product for a particular purpose, including in regard of its safety and/or efficacy in the treatment of HIV/AIDS. WHO does not furthermore warrant or represent that:

- 1) *the list is complete or error free; and/or that*
- 2) *the products and manufacturing sites which have been found to meet the standards recommended by WHO, will continue to do so; and/or that*
- 3) *the products listed have obtained regulatory approval for use in the treatment of HIV/AIDS (or any other disease) in every country of the world, or that their use is otherwise in accordance with the national laws and regulations of any country, including but not limited to patent laws .*